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Amaç ve Kapsam

Haseki Tıp Bülteni, S.B.Ü. Haseki Eğitim ve Araştırma Hastanesi'nin süreli yayın organı olup, genel tıp içerikli, yayın dili Türkçe ve İngilizce olan, bağımsız ve önyargısız hakemlik ilkelerine dayanan uluslararası periyodik bir dergidir. Haseki Tıp Bülteni Mart, Haziran, Eylül, Aralık aylarında olmak üzere yılda dört sayı çıkmaktadır.

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Haseki Tıp Bülteni

The Medical Bulletin of Haseki

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The Medical Bulletin of Haseki is the official scientific journal of the University of Health Sciences Haseki Training and Research Hospital. It covers subjects on general medicine, published both in Turkish and English, and is independent, peer-reviewed, international periodical and is published quarterly (March, June, September and December).

The aim of The Medical Bulletin of Haseki is to publish original research papers of highest scientific and clinic value on general medicine. Additionally, educational material reviews on basic developments, editorial short notes and case reports are published.

The Medical Bulletin of Haseki is **indexed in Gale/Cengage Learning, Turkish Medline-National Citation Index, Excerpta Medica/EMBASE, SCOPUS, Reaxys, Engineering Village, Academic Keys, Emerging Sources Citation Index (ESCI), TUBITAK/ULAKBIM, CINAHL, DOAJ, J-Gate, and Turkiye Citation Index** databases.

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Haseki Tıp Bülteni

The Medical Bulletin of Haseki

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Yazılarda Türk Dil Kurumu'nun Türkçe Sözlüğü ve Yazım Kılavuzu temel alınmalıdır. İngilizce yazılan yazılar özellikle desteklenmektedir.

Editör veya yardımcıları tarafından, etik kurul onayı alınması zorunluluğu olan klinik araştırmalarda onay belgesi talep edilecektir. Yazıların içeriğinden ve kaynakların doğruluğundan yazarlar sorumludur.

Yazarlar, gönderdikleri çalışmanın başka bir dergide yayınlanmadığı ve/veya yayınlanmak üzere incelemede olmadığı konusunda garanti vermelidir. Daha önceki bilimsel toplantılarda 200 kelimeyi geçmeyen özet sunumlarının yayınları, durumu belirtilmek koşulu ile kabul edilebilir. Tüm otörler bilimsel katkı ve sorumluluklarını bildiren formu doldurarak yayına katılmalıdırlar.

Tüm yazılar, editör ve ilgili editör yardımcıları ile en az üç danışman hakem tarafından incelenir. Yazarlar, yayına kabul edilen yazılarda, metinde temel değişiklik yapmamak kaydı ile editör ve yardımcılarının düzeltme yapmalarını kabul etmiş olmalıdırlar.

Makalelerin formatı 'Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication' (http://www.icmje.org) kurallarına göre düzenlenmelidir.

Anahtar kelimelerin Türkiye Bilim Terimleri (http://www.bilimterimleri.com)'nden seçilmelidir.

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Başlık sayfası, kaynaklar, şekiller ve tablolar ile ilgili kurallar bu dergide basılan tüm yayın türleri için geçerlidir.

Hastalar mahremiyet hakkına sahiptirler. Belirleyici bilgiler, hasta isimleri ve fotoğraflar, bilimsel olarak gerekli olmayan durumlarda ve hasta (ebeveyn veya koruyucu) tarafından yayınlanmasına yazılı olarak bilgilendirilmiş bir onay verilmediği sürece yayınlanmamalıdır.

Bu amaçla, bilgilendirilmiş onay, hastanın yayınlanacak belirli bir taslağı görmesini gerektirir. Eğer gerekli değilse hastanın belirleyici detayları yayınlanmayabilir. Tam bir gizliliği yakalamak oldukça zordur ancak eğer bir şüphe varsa, bilgilendirilmiş onay alınmalıdır. Örneğin, hasta fotoğraflarında göz bölgesini maskelemek, yetersiz bir gizlilik sağlanmasıdır.

Haseki Tıp Bülteni'ne yayınlanmak amacıyla gönderilen ve etik kurul onayı alınması zorunluluğu olan deneysel, klinik ve ilaç araştırmaları için uluslararası anlaşmalara ve 2013'de gözden geçirilmiş Helsinki Bildirisi'ne uygun etik kurul onay raporu gereklidir (http://www.wma.net/en/30publications/10policies/b3/). Deneysel hayvan çalışmalarında ise "Guide for the care and use of laboratory animals (https://oacu.oir.nih.gov/regulations-standards) doğrultusunda hayvan haklarını koruduklarını belirtmeli ve kurumlarından etik kurul onay raporu almalıdırlar. Etik kurul onayı (onay numarası ile birlikte) ve "bilgilendirilmiş gönüllü olur formu" alındığı araştırmanın "Yöntemler" bölümünde belirtilmelidir. Yazarlar, makaleleriyle ilgili çıkar çatışması ve maddi destekleri bildirmelidirler.

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1) Başlık Sayfası (Sayfa 1): Yazı başlığının, yazar(lar)ın bilgilerinin, anahtar kelimelerin ve kısa başlıkların yer aldığı ilk sayfadır.

Türkçe yazılarda, yazının İngilizce başlığı da mutlaka yer almalıdır; yabancı dildeki yayınlarda ise yazının Türkçe başlığı da bulunmalıdır. Türkçe ve İngilizce anahtar sözcükler ve kısa başlık da başlık sayfasında yer almalıdır.

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Çalışma herhangi bir bilimsel toplantıda önceden bildirilen koşullarda tebliğ edilmiş ya da özeti yayınlanmış ise bu sayfada konu ile ilgili açıklama yapılmalıdır.

Yine bu sayfada, dergiye gönderilen yazı ile ilgili herhangi bir kuruluşun desteği sağlanmışsa belirtilmelidir.

2) Özet (Sayfa 2): İkinci sayfada yazının Türkçe ve İngilizce özetleri (her biri için en fazla 200 sözcük) ile anahtar sözcükler belirtilmelidir.

Özet Bölümü: Amaç, Yöntemler, Bulgular, Sonuç şeklinde alt başlıklarla düzenlenir. Derleme, olgu sunumu ve eğitim yazılarında özet bölümü alt başlıklara ayrılmaz. Bunlarda özet bölümü, 200 kelimeyi geçmeyecek şekilde amaçlar, bulgular ve sonuç cümlelerini içermelidir.

Özet bölümünde kaynaklar gösterilmemelidir. Özet bölümünde kısaltmalardan mümkün olduğunca kaçınılmalıdır. Yapılacak kısaltmalar metindekilerden bağımsız olarak ele alınmalıdır.

3) Metin (Özetin uzunluğuna göre Sayfa 3 veya 4'den başlayarak)

Genel Kurallar bölümüne uyunuz.

Metinde Ana Başlıklar Şunlardır: Giriş, Yöntemler, Bulgular, Tartışma, Çalışmanın Kısıtlılıkları ve Sonuç.

Giriş bölümü çalışmanın mantığı ve konunun geçmişi ile ilgili bilgiler içermelidir. Çalışmanın sonuçları giriş bölümünde tartışılmamalıdır.

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Bulgular bölümü de çalışmanın tekrar edilebilmesine yetecek ayrıntıları içermelidir.

Tartışma bölümünde, elde edilen bulguların doğru ve ayrıntılı bir yorumu verilmelidir. Bu bölümde kullanılacak literatürün, yazarların bulguları ile direkt ilişkili olmasına dikkat edilmelidir.

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Metinde fazla kısaltma kullanmaktan kaçınılmalıdır. Tüm kısaltılacak terimler metinde ilk geçtiği yerde parantez içinde belirtilmelidir. Özette ve metinde yapılan kısaltmalar birbirinden bağımsız olarak ele alınmalıdır. Özet bölümünde kısaltması yapılan kelimeler, metinde ilk geçtiği yerde tekrar uzun şekilleri ile yazılıp kısaltılmalıdırlar.

4) Kaynaklar: Kaynakların gerçekliğinden yazarlar sorumludur.

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Haseki Tıp Bülteni

The Medical Bulletin of Haseki

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Özgün Araştırma / *Original Article*

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Çocuklarda Enfeksiyonların Atopik Hastalıklar Üzerindeki Rolü

The Role of Infections in Atopic Diseases in Children

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***İstinye Üniversitesi, Medical Park Gaziosmanpaşa Hastanesi, Çocuk Nefrolojisi Kliniği, İstanbul, Türkiye*

Öz

Amaç: Özellikle gelişmiş ülkelerde olmak üzere son 40 yıldır atopik hastalıkların prevalansında artış görülmektedir. Bu durum iyileşen yaşam koşulları nedeni ile enfeksiyonlara maruziyetin azalması ile açıklanmaktadır. Çalışmamızda bazı enfeksiyonların atopik hastalıklar üzerindeki etkisi araştırılmıştır.

Yöntemler: Çalışmamıza atopik 50 hasta ile yaş ve cins olarak benzer 46 sağlam çocuk kontrol gurubu olarak alındı. Olguların deri testleri yapıldı ve serum immünoglobulin (Ig) E düzeyleri belirlendi. Hepatit A virüs (HAV), *Toxoplasma gondii*, Epstein-Barr virüs (EBV) ve sitomegalovirüs (SMV) seropozitivitelerini saptamak için serumda spesifik IgG belirlendi. *Helicobacter pylori* antijen pozitifliği gaitada arandı.

Bulgular: Atopik çocuklarda anti-HAV IgG seropozitivitesi (%30,0) ve *H. pylori* antijen pozitifliği (%22,0) kontrollerden (sırası ile, %52,1; %47,8) anlamlı olarak daha düşük bulundu. *T. gondii*, EBV viral kapsid antijeni ve SMV IgG seropozitifliği açısından her iki grupta anlamlı istatistiksel farklılık saptanmadı.

Sonuç: HAV ve *H. pylori* enfeksiyonları atopik hastalıklardan koruyucu enfeksiyonlar olabilir. Ancak genellenebilir sonuçlara ulaşmak için daha geniş ölçekli çalışmalara gereksinim vardır.

Anahtar Sözcükler: Atopi, alerji, enfeksiyon, hijyen, hepatit A virüs, *helicobakter pylori*

Abstract

Aim: Especially in the developed countries; there has been an increase in the prevalence of atopic diseases over the past 40 years. This is explained by the improved living conditions and reduced exposure to infections. In this study, effects of some infections on atopic diseases were investigated.

Methods: Fifty atopic patients and 46 age-and sex-matched healthy children were included in the study. Skin prick test was performed and serum immunoglobulin (Ig) E levels were determined in all subjects. Serum-specific IgG was investigated to detect seropositivity of hepatitis A virus (HAV), *Toxoplasma gondii*, Epstein-Barr virus (EBV) and cytomegalovirus (CMV). In addition, *Helicobacter pylori* feacal antigen test was done.

Results: Anti-HAV IgG seropositivity (30.0%) and *H. pylori* antigen positivity (22.0%) were significantly lower in atopic children than in controls (52.1%, 47.8%, respectively). There was no statistically significant difference between the two groups in seropositivities of *T. gondii*, EBV viral capsid antigen and CMV IgG.

Conclusion: HAV and *H. pylori* may be protective infections in atopic patients. However, there is a need for larger scale studies to achieve generalizable results.

Keywords: Atopy, allergy, infection, hygiene, hepatitis A virus, *helicobacter pylori*

Giriş

Astım, alerjik rinit ve atopik dermatit atopik hastalıklardandır (1). Epidemiyolojik veriler, bu hastalıkların prevalansının ve insidansının son yıllarda arttığını göstermektedir. Bu artış özellikle sosyo-ekonomik olarak gelişmiş batı toplumlarında dikkat çekmektedir (1-3).

Atopik hastalıklardaki artışın açıklamasına yönelik olarak sayısız risk faktörleri öne sürülmüştür. Bu faktörler

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arasında genetik yatkınlık, alerjenlerle sık temas, beslenme şekli, obezite, çevre kirliliği, sezaryen doğum, sigara maruziyeti, aşılanma, enfeksiyonlar, barsak mikrobiyotası ve anne sütüyle beslenme süresi bulunmaktadır (1,4,5). Ancak ilk olarak 1989 yılında Strachan'ın (6) ortaya attığı "hijyen hipotezi" atopik hastalıkların artışı ile ilgili halen en geçerli hipotez olarak yerini korumaktadır. Bu hipotez özetle değişen yaşam tarzları ile ailelerin küçülmesi ve enfeksiyonlara daha az maruz kalmanın atopiyi artırdığı yönündedir (6). Daha sonra yapılan çalışmalarda hijyen hipotezinin biyolojik temelleri desteklenmiş; çocukluk çağı enfeksiyonlarının T helper (Th) 1 yanıtı artırdığı ve atopi gelişiminde önemli olan Th2 yanıtı baskıladığı gösterilmiştir (7-11). Hipotezin ilk ortaya atıldığı andan itibaren virüs (9,10,12-16), bakteri (2,7,9,10,13,17) ya da parazit (3,8-11,13) olmak üzere çeşitli çocukluk çağı enfeksiyonları ile atopi arasındaki ilişki araştırılmış; lehte ve aleyhte birçok sonuçla tartışmaya günümüzde de devam edilmiştir (2,17-21).

Çalışmamızda, astım, alerjik rinit ve atopik dermatiti olan çocuklarda *Helicobacter pylori* pozitifliği, hepatit A virüs (HAV), *Toxoplasma gondii*, sitomegalovirüs (SMV), ve Epstein-Barr virüs (EBV) enfeksiyonlarının seropozitifliği araştırılmış ve sonuçlar atopik olmayan sağlıklı çocuklarla karşılaştırılmıştır.

Yöntemler

Çalışmamıza astım, alerjk rinit, atopik dermatit tanıları ile takipli, immünoglobulin (Ig) E düzeyleri yüksek ve deri prick testleri pozitif olan 50 atopik hasta alındı. Kontrol grubunu genel polikliniğimize diğer sebeplerle başvuran, alerjik hastalıklar yönünden herhangi bir tanısı ve yakınması olmayan, deri prick testleri negatif 46 sağlıklı çocuk oluşturdu. Kontrol grubu olgularının seçilmesinde uluslararası kabul gören Çocuklukta Uluslararası Astım ve Alerjiler Çalışması soru listesinden modifiye edilmiş bir anket formu kullanıldı. Daha önceden hepatit A aşısı olan çocuklar çalışmaya alınmadı. Çalışmaya başlamadan önce hastanemizin çalışmaya başlamadan önce Haseki Eğitim ve Araştırma Hastanesi Etik Kurulu'ndan onay alındı (protokol no: 27/10/08-09). Görüşme sırasında ebeveynlere çalışmanın amacı anlatıldı; yazılı onam formları alındı.

Hastaların isimleri, yaşları, cinsiyetleri, boy, kilo, vücut kitle indeksleri (VKİ), evde yaşayan birey sayısı, kardeş sayısı, evlerindeki oda sayısı, ailelerinin aylık geliri standart bir forma kaydedildi. Olgular kardeş sayısı, evdeki birey sayısı ve oda sayısına göre gruplandırıldı, ayrıca Devlet İstatistik Enstitüsü'nün verilerine göre yoksulluk sınırının altında geliri olanlar sosyo-ekonomik durumu düşük; yoksulluk sınırının üstünde geliri olanlar sosyo-ekonomik durumu orta düzey şeklinde iki gruba ayrıldı.

Deri prick testleri; allergopharma (Hamburg, Almanya) standart alerjenleri ve tek kullanımlık plastik lansetler kullanılarak yapıldı. Pozitif kontrol olarak histamin %0,1 (1 mg/mL) ve negatif kontrol olarak serum fizyolojik kullanıldı. Deri testinde 2+ ve üzeri reaksiyonlar veya negatif kontrole kıyasla 3 mm ve üzerinde sonuç elde edilen reaksiyonlar pozitif kabul edildi.

Serum total IgE ölçümleri otoanalizörde (ARCHITECT Cİ 1600, ABBOT; Barcelona-Spain) türbidimetrik yöntemle ölçüldü. Total IgE sonuçları her yaş grubu için ayrı ayrı değerlendirildi. Bir-beş yaş <60 IU/mL, altı-dokuz yaş <90 IU/mL, on-on altı yaş <200 IU/mL değerleri normal kabul edildi.

Enfeksiyonların serolojileri Triturus Grifols cihazında mikro ELISA yöntemi ile çalışıldı. Pozitif cut-off değerleri anti-HAV IgG için 0,650 ve üzeri; *T. gondii* IgG için 0,630 ve üzeri; EBV viral kapsid antijen (VCA) IgG için 0,550 ve üzeri; SMV IgG için 0,640 ve üzeri kabul edildi. Gaitada *H. pylori* antijenini tespit etmek için Coris BioConcept firmasının Pylori-strip testi kullanıldı. Tek yeşil çizgi negatif; bir yeşil, bir kırmızı çizgi pozitif; çizgi görülmezse geçersiz olarak değerlendirildi.

İstatistiksel Analiz

Karşılaştırmalar gruplar homojen dağılım gösterdiğinde bağımsız Student's t-testi ile; homojen dağılım göstermediğinde Mann-Whitney U testi ile yapıldı. Kategorik değişkenlerin karşılaştırılmasında ki-kare testi kullanıldı. Tüm istatistiksel analizler "SPSS (Statistical Package for Social Sciences Inc; Chicago, IL, USA) for Windows version 16.0" paket program ile yapıldı. Test sonuçlarına göre $p<0,05$ değeri anlamlı kabul edildi.

Bulgular

Atopik hastalık grubundaki hastaların 27'sinde (%54) yalnız astım, dokuzunda (%18) yalnız alerjik rinit, birinde (%2) yalnız atopik dermatit, 12'sinde (%24) astım ve alerjik rinit birlikte, birinde (%2) astım, alerjik rinit ve atopik dermatit tanıları birlikte mevcuttu.

Atopik hastalık grubundakilerin yaş ortalaması 11,03±3,18 (4-16) yıl iken, kontrol grubundakilerin 10,28±3,89 (4-16) yıl olarak bulundu. Atopik hastalık grubunda 24 kız (%48), 26 erkek (%52); kontrol grubunda 19 kız (%41,3), 27 erkek (%58,7) olgu bulunuyordu (Tablo 1). Her iki grup arasında yaş ve cinsiyet açısından istatistiksel anlamlı fark bulunmadı.

Atopik hastalık grubunun boy ortalaması 139,94±19,15 cm, ağırlık ortalaması 39,88±10,8 kg, VKİ ortalaması 19,96±1,48 kg/m^2; kontrol grubunun ise sırası ile 133,91±21,88 cm, 38,65±13,68 kg, 21,11±2,63 kg/m^2 olarak bulundu (Tablo 1). Gruplar arasında boy, ağırlık ve VKİ açısından istatistiksel olarak anlamlı fark saptanmadı.

Atopik hastalık grubundan 34 (%68), kontrol grubundan 34 (%74) çocuğun evinde birey sayısı beş

ve altında; atopik hastalık grubundan 16 (%32), kontrol grubundan 12 (%26) çocuğun ise beşin üzerindeydi. Atopik hastalık grubunda evdeki birey sayısı ortalaması 5,7 kişi, kontrol grubunda ise 5,1 kişi olarak saptandı. Atopik hastalık grubundan 43 (%86), kontrol grubundan 41 (%89) çocuğun üç ve daha az kardeşi varken; atopik hastalık grubundan yedi (%14), kontrol grubundan beş (%11) çocuğun üçün üzerinde kardeşi vardı. Atopik 41 (%82) çocuğun evinde oda sayısı üç ve altında iken kontrol grubundan 37 (%80) çocuğun evindeki oda sayısı üç ve altındaydı (Tablo 1). İki grup arasında evde yaşayan birey, kardeş ve oda sayıları açısından istatistiksel anlamlı farklılıklar saptanmadı.

Atopik hastalık grubundan 28 (%56), kontrol grubundan 25 (%54) çocuğun ailesi düşük gelir grubunda iken; atopik gruptan 22 (%44), kontrollerden 21 (%46) çocuğun ailesi orta gelir grubunda idi (Tablo 1). Gelir düzeyleri açısından istatistiksel olarak anlamlı fark bulunmadı. Atopik hastalık grubundan 28 (%56), kontrol grubundan 25 (%54) çocuğun evinde en az bir kişi sigara içiyor iken; atopik gruptan 22, kontrol grubundan 21 çocuğun evinde sigara içen yoktu (Tablo 1). Gruplar arasındaki fark istatistiksel olarak anlamlı bulunmadı.

Tablo 1. Sosyo-demografik özelliklerin ve antropometrik ölçümlerin gruplara göre karşılaştırılması

		Atopik hastalık grubu (n=50)	Kontrol grubu (n=46)	p
Yaş (yıl), Ort ± SS		11,03±3,18	10,28±3,89	0,278
Kız/erkek, n (%)		24 (48,0)/26 (52,0)	19 (41,3)/27 (58,6)	0,325
Boy (cm), Ort ± SS		139,94±19,15	133,91±21,88	0,176
Tartı (kg), Ort ± SS		39,88±10,82	38,65±13,68	0,284
VKİ (kg/m^2), Ort ± SS		19,96±1,48	21,11±2,63	0,190
Evdeki birey sayısı, n (%)	≤5	34 (68,0)	34 (73,9)	0,341
	>5	16 (32,0)	12 (26,0)	
Kardeş sayısı, n (%)	≤3	43 (86,0)	41 (89,1)	0,440
	>3	7 (14,0)	5 (10,8)	
Oda sayısı, n (%)	≤3	41 (82,0)	37 (80,4)	0,525
	>3	9 (18,0)	9 (19,5)	
Gelir düzeyi, n (%)	Düşük	28 (56,0)	25 (54,3)	0,517
	Orta	22 (44,0)	21 (45,6)	
Evde sigara içen, n (%)	(+)	28 (56,0)	25 (54,3)	0,218
	(-)	22 (44,0)	21 (45,6)	

Ort: Ortalama, SS: Standart sapma, VKİ: Vücut kitle indeksi

Atopik hastalık grubundaki çocukların 39'unda (%78) SMV IgG, 15'inde (%30) anti-HAV IgG seropozitifliği, 11'inde (%22) *H. pylori* antijen pozitifliği, yedisinde (%14) *T. gondii* IgG ve üçünde (%6) EBV VCA IgG pozitifliği gözlendi (Tablo 2). Kontrol grubunda ise 42'sinde (%91) SMV IgG, 24'ünde (%52) anti-HAV IgG, 22'sinde (%48) *H. pylori* antijen pozitifliği ve 12'sinde (%26) *T. gondii* IgG pozitifliği vardı. Kontrol grubunda EBV VCA IgG pozitif olgu saptanmadı (Tablo 2). Atopik hastalık grubunda anti-HAV IgG seropozitifliği ve gaitada *H. pylori* antijen pozitifliği non-atopik kontrol grubundan istatistiksel olarak anlamlı düşük saptandı (sırasıyla, p=0,022; p=0,007). Gruplar arasında *T. gondii*, EBV VCA IgG ve SMV IgG seropozitifliği açısından istatistiksel olarak anlamlı fark bulunmadı (Tablo 2).

Tartışma

Atopik hastalıklarda son yıllardaki önemli boyuttaki artış; nedenlerinin anlaşılabilmesi amacı ile birçok bilimsel çalışmaya konu olmuştur (1-5). Doğal immünite ile bir çevresel alerjenin etkileşmesi T hücresi tarafından Th2 tip yanıtı oluşturan interlökin (IL)-4, IL-5 ve IL-13 gibi sitokinlerin üretilmesine neden olur (22). Bu sitokinler de IgE üretimini, mast hücre ve eozinofillerin sayısını artırarak enflamasyonun oluşumunu sağlarlar (22). Düzelen hijyen ve sosyo-ekonomik koşulların enfeksiyonların azalmasını sağlaması sonucunda Th1 yanıtının uyarılamaması ve Th2 yanıtının baskılanamamasının alerjik hastalıkların prevalansında artışa yol açtığı düşünülmektedir (7,10,16,17). Son yıllarda alerjik hastalıkların patogenezinde önemli rol oynadığı düşünülen T regülatuvar (Treg) hücreler ile ilgili gelişmeler atopik hastalarda hijyen hipotezinin ve enfeksiyonların

Tablo 2. Enfeksiyon pozitifliklerine göre grupların karşılaştırılması

		Atopik hastalık grubu n (%)	Kontrol grubu n (%)	p
EBV VCA IgG	Negatif	46	46	0,133
	Pozitif	3	0	
SMV IgG	Negatif	11 (22,0)	4 (8,6)	0,640
	Pozitif	39 (78,0)	42 (91,3)	
Toksoplazma IgG	Negatif	43 (86,0)	34 (73,9)	0,110
	Pozitif	7 (14,0)	12 (26,0)	
Anti-HAV IgG	Negatif	35 (70,0)	22 (47,8)	0,022
	Pozitif	15 (30,0)	24 (52,1)	
H. pylori	Negatif	39 (78,0)	24 (52,1)	0,007
	Pozitif	11 (22,0)	22 (47,8)	

EBV: Epstein-Barr virüs, VCA: Viral kapsid antijen, Ig: İmmünoglobulin, SMV: Sitomegalovirüs, HAV: Hepatit A virüs

rolünü tekrar gündeme getirmiştir (2,10,11). Treg hücrelerin alerjik hastalıkların kliniğinde iyileşme sağlayan IL-10 ve dönüştürücü büyüme faktörü-beta'yı ürettikleri anlaşılmıştır (2,10).

Çalışmamızda atopik hastalık gelişiminde etkili olabilecek faktörler (yaş, cins, VKİ, sosyo-demografik parametreler ve sigaraya maruziyet) açısından benzer iki grupta (atopik ve non-atopik kontrol); üç orofekal enfeksiyonun (HAV, *H. pylori*, *T. gondii*) ve onların yanı sıra insandan insana direkt temasla bulaşan iki enfeksiyonun (SMV ve EBV) pozitiflik oranlarını karşılaştırdık.

Çalışmada orofekal yolla bulaşan hastalıklardan HAV ve *H. pylori* seropozitivitesi atopik hastalıklar grubunda non-atopik kontrol grubundan istatistiksel olarak anlamlı daha düşük saptandı. Bazı çalışmalarda orofekal mikroorganizmalar için iyi bir örnek olan HAV seropozitifliğinin atopi ile negatif korelasyonu gösterilmiştir (12,13,20). Ancak Brezilya'da (23), İsveç'te (15) ve İspanya'da (24) yapılan çalışmalarda ise HAV ile atopik hastalıklar arasında ilişki saptanmamıştır. Bu çelişkili sonuçlar bölgesel nedenlerden ve/veya konağın genetik farklılıklardan kaynaklanabilir. McIntire ve ark. (25) HAV reseptörü olan TIM-1'deki genetik polimorfizmin önemli olduğunu ve hepatit A ile enfekte kişilerde bu genetik polimorfizmin Th2 fenotipini değiştirerek atopik hastalıklara karşı koruyucu olabileceğini ileri sürmüşlerdir. Ülkemizde yapılan bir çalışmada sonuçlarımıza benzer olarak atopik hastalıklarda HAV seropozitivitesi kontrol grubuna göre anlamlı derecede düşük saptanmıştır (26).

H. pylori zayıf ev halkı hijyeninin biyolojik göstergesi olarak kabul edilir (2). Uzun yıllardır *H. pylori* ile enfekte insanların gastrik mukozasında gamma interferonun artmış, IL-4 salgısının ise azalmış olduğu bilinmektedir (27). İlave olarak *H. pylori* ile enfekte insan gastrik mukozasında Treg hücrelerinin de artmış olduğu gösterildi (28). Farelerde yapılan bir çalışmada ise *H. pylori'*nin iki antijeninin (γ-glutamyl transpeptidase ve VacA) Treg hücreleri uyardığı gösterildi (29). Çok yeni yayınlanan bir çalışmada *H. pylori* seropozitivitesi astımlı çocuklarda atopik olmayan sağlam çocuklardan anlamlı olarak düşük bulunmuş ve astımın ağırlığı ile de negatif korelasyon göstermiştir (21). Yine ülkemizden bir yeni çalışmada da non-atopik çocuklarda *H. pylori* seropozitivitesi ve IL-10 düzeyleri yüksek bulunmuştur (17). Ancak *H. pylori* enfeksiyonlarının gastrik peptik ülser ve kanserlerin primer nedeni olarak uzun yıllardır bilindiğini de unutmamak gerekir (30).

Çalışmamızda her iki grup arasında toksoplazma IgG seropozitifliği yönünden istatistiksel olarak anlamlı fark saptanmadı. Alcantara-Neves ve ark'nın (9) Brezilya'da yaptıkları bir çalışmada *T. gondi* seronegatif çocuklarda seropozitif olanlardan anlamlı olarak daha yüksek serum IgE düzeyleri saptanmıştır. Fernandes ve ark. (8) atopik erişkin hastalarda daha düşük *T. gondii* seropozitivitesi göstermişlerdir. Bu çalışmaların aksine, sonuçlarımıza benzer olarak, Fernández-Fígares ve ark'nın (3) çalışmasında *T. gondii* seropozitivitesi atopi ile ilişkili bulunmamıştır. Jeong ve ark'nın (31) farelerde yaptığı çalışmada *T. gondii* enfeksiyonunun Th2 yanıtı baskıladığı, Th1 yanıtı ve IL-10 salgısını artırdığı sonuç olarak da atopi ile negatif ilişki gösterdiğine dikkat çekilmiştir. Ayrıca *T. gondii* enfeksiyonlarının, Th1 yanıtın baskın olduğu otoimmün olayları da IL-10 salgısını artırarak azalttığına dikkat çekilmiştir (31). Bu birbiri ile çelişkili görünen sonuçlar IL-10'un hem Th1 hem de Th2 yanıtı baskılamasına bağlanmıştır (31). Bu veriler *T. gondii* atopi ilişkisinde henüz bilmediğimiz mekanizmalar olduğunu göstermektedir.

Matricardi ve ark. (12) *T. gondii*, *H. pylori* ve hepatit A gibi oral fekal yol ile bulaşan enfeksiyonların atopi riskini %60'dan fazla azalttığını bildirmişlerdir. Aynı çalışmada diğer yollar ile geçen 6 virüs (kızamık, kabakulak, rubella, varicella, SMV ve herpes simplex virüs tip 1) ile atopi arasında ilişki gösterilememiş ve orofekal mikroorganizmaların barsakta lenfoid dokuyu uyararak atopiyi önledikleri yorumu yapılmıştır (13). Fakat daha sonraki çalışmalarda orofekal yol dışında geçişi olan mikroorganizmalar ile de atopi arasında ilişki gösterilmesi bu varsayımı geçersiz kılmıştır (14-16,20). Çalışmamızda da üç orofekal enfeksiyondan ikisi (HAV ve *H. pylori*) atopi ile negatif ilişkili bulunurken biri (*T. gondii*) ile ilişki saptanmamıştır.

SMV (15,16) ve EBV (14,16) enfeksiyonlarının atopiden koruyucu olabileceğine dair çalışmalar vardır. Yeni ve önemli bir çalışmada ise SMV ve EBV enfeksiyonlarının barsak mikrobiyotası üzerine etkileri araştırılmış; EBV ile bir ilişki gösterilmezken yaşamın erken yıllarında geçirilen SMV enfeksiyonlarının barsaklarda *Staphylococcus aureus* kolonizasyonunu azaltarak alerjiyi artırabileceği ileri sürülmüştür (32). Sonuçlarımızda SMV ve EBV seropozitivitesi ile atopi arasında ilişki gösterilemedi. Ancak SMV seropozitivitesi hem atopik (%78) hem de non-atopik kontrol grubumuzda (%91,3) çok yüksek oranlarda olmakla birlikte non-atopik grupta daha yüksek saptandı. Çalışmamızda EBV seropozitivitesi yalnız üç olguda pozitif bulundu.

Bir çalışmada sekiz patojen (*T. gondii*, *H. pylori*, EBV, HAV, herpes simpleks virüs, herpes zoster virüs, A lumbricoides ve T trichiura) ile alerji arasında tek tek ilişki gösterilememiş ancak üç ve daha az enfeksiyonu olan grupta; dört ve daha fazla enfeksiyonu olanlardan daha yüksek serum IgE düzeyleri ve deri prik test pozitifliği saptanmıştır (9). Bu çalışma enfeksiyonların atopiden koruyucu etkisinin enfeksiyonun türüne değil de sayısına bağlı olabileceğini ileri sürmesi açısından ilginçtir.

Çalışmanın Kısıtlılıkları

Çalışmamızda enfeksiyon sayısına göre gruplar oluşturulmadığı için bu yönde bir karşılaştırma yapamadık.

Sonuç

Çalışmamızda HAV IgG ve *H. pylori* pozitifliğinin atopiden koruyucu olabileceği gösterildi. Ancak *T. gondii* ile atopi arasında ilişki saptamadığımız için orofekal enfeksiyonların koruyucu olabileceğine dair bir genelleme yapmamız mümkün değildir. Yeni immünolojik gelişmeler ışığında geniş kapsamlı çalışmalar çelişkili sonuçlara açıklık getirecektir.

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The Use of Negative Pressure Therapy for the Treatment of the Defects on Extremities due to High-Energy Trauma

Yüksek Enerjili Travma Nedeni ile Oluşmuş Ekstremite Defektlerinin Tedavisinde Negatif Basınçlı Terapi Kullanılması

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Abstract

Aim: Defects of the extremities due to high-energy trauma are common and it is necessary to repair these defects. Reconstruction is possible with simple surgeries using skin grafts and negative pressure therapy (NPT). In this study, we present our results of the reconstruction of extremity defects caused by high-energy trauma with a simple surgical procedure using NPT.

Methods: Patients with soft tissue defects of the upper and lower extremities caused by high energy trauma, who were treated with NPT between November 2009 and June 2015, were included in the study.

Results: NPT was performed in 63 patients. The average defect size was 60 cm^2. The patients underwent an average of nine sessions. The average length of hospital stay was 26 days. The defects were reconstructed using skin grafts and local flaps in 58 and two patients, respectively. None of the patients required free flaps.

Conclusion: Extremity defects occurring due to high energy trauma can be closed by simple surgical techniques using NPT, patients can be protected from the complications of free tissue transfer, and also treatment is possible at much lower costs.

Keywords: Wounds, negative pressure therapy, extremity, trauma

Öz

Amaç: Ekstremitelerde yüksek enerjili travmalar sonucu defekt oluşması sık görülmektedir ve bu defektlerin onarılması zorunludur. Negatif basınçlı terapi (NBT) kullanılarak bu defektlerin deri greftleri gibi daha basit cerrahi işlemler ile rekonstrüksiyonu mümkün olabilmektedir. Bu çalışmada yüksek enerjili travma sonrası ekstremitelerinde oluşmuş defektlerin NBT kullanılarak basit cerrahi işlemlerle kapatılması konusundaki sonuçlarımızı sunmaktayız.

Yöntemler: Kasım 2009-Haziran 2015 yılları arasında üst ve alt ekstremitelerinde yüksek enerjili travma sonucu yumuşak doku defekti oluşan ve tedavisinde NBT kullanılan hastalar çalışmaya alındı.

Bulgular: Altmış üç hastada NBT uygulandı. Hastalardaki yara alanı ortalaması 60 cm^2 olarak hesaplandı. Hastalara ortalama dokuz seans NBT uygulandı ve ortalama 26 gün yatarak tedavi edildiler. Elli sekiz hastanın yarası deri grefti ile iki hastanın yarası lokal flepler ile onarıldı. Hiçbir hastada serbest flebe gerek olmadı.

Sonuç: NBT ile yüksek enerjili travma sonucu ekstremitelerde oluşan yaralar basit cerrahi teknikler ile kapatılabilmekte, hastalar serbest doku transferinin komplikasyonlarından korunabilmekte, hem de çok daha az maliyetle tedavi sağlanabilmektedir.

Anahtar Sözcükler: Yaralar, negatif basınçlı terapi, ekstremite, travma

Introduction

High-energy trauma to the extremities that lead to open fractures with major soft tissue losses is frequent, especially in young adults. In extremity injuries caused by high energy trauma, it is necessary to remove the dead tissue from the site and properly close the soft tissue in order to protect the affected extremity from amputation. Soft tissue defects in the extremities are caused by the effects of trauma and posttraumatic debridements (1,2). The surgical method which will be used in closing the defect is decided according to the size of the wound, whether there are tissues such as bone or tendon at the

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base of the wound, and exposure of the implants used in stabilizing the bone. Skin grafts, local myocutaneous and fasciocutaneous flaps, distant flaps, and free flaps can be used in closing defects, which cannot be closed primarily. Although reconstruction with skin grafts is the easiest surgical method, it requires a well-vascularized recipient bed and cannot be performed if there is exposed bone, cartilage, tendon or surgical implants. It is mandatory to use flaps in these cases (1). Free tissue transfer is necessary if the soft tissue loss is too large to be closed with local flap and sometimes more than one flap may be required in wide defects. As the size and depth of the wound increases, the need for more extensive surgeries arises; and as a result of these major surgeries, donor-site morbidity, frequency of complications, and length of hospital stay increases (1,3).

Negative pressure terapy (NPT) systems have been used frequently as a non-surgical method in wound treatment for the last 20 years. NPT, which has been developed for closing large, chronic, and infected wounds, has also started to be used in traumatic wounds. Thanks to these systems, it is possible to close the wounds, if not at least wound closure with simpler surgical techniques can be provided (4,5).

In this study, we present patients whose extremity defects caused by high energy trauma were treated with NPT.

Methods

This research was conducted in compliance with all ethical standards given in the Helsinki Declaration of 1975 as revised in 2008 and was approved by Clinical Research Ethics Committee of Ankara Numune Training and Research Hospital (2009/21). Written informed consent was obtained from all individual participants included in the study. Patients, who had developed soft tissue defects with exposed bone and tendon in the upper and lower extremities due to high-energy trauma and were treated with NPT between November 2009 and June 2015, were included in the study. No exclusion criteria were used in the study. The patients with bone and joint injuries were treated by the department of orthopaedic surgery using appropriate methods. Surgical debridement was performed under anesthesia in the operating room environment and necrotic tissues were removed from the wound site in all patients. Debridements were repeated every two days in patients in whom adequate debridement was not achieved in the first time. NPT was initiated after the dead tissue was removed from the wound site. NPT was implemented using a vacuum-assisted closure system (Kinetic Concepts, Inc, San Antonio, Texas, USA) in all patients. Polyurethane foam was cut according to the wound size and placed on the surface of the wound, so it would close the entire surface yet would not overflow it. The sponge was then dressed by an adhesive cover to form an airtight environment. A tube was placed in a small hole opened in the foam and the other end of the tube was connected to the device's collection container.

The patients underwent three sessions of NPT weekly during their stay, and it was adjusted so the foam was changed on mondays, wednesdays, and fridays. All patients underwent negative pressure of 125 mmHg. NPT was implemented continuously for the first three practices, and intermittently as active five minutes followed by passive two minutes in the continuing practices.

When NPT would be implemented on the exposed bones, holes were drilled in the bone cortex at 1 cm intervals during surgical debridement in order to ensure the formation of granulation tissue from the bone medulla as well.

Statistical Analysis

Data analysis was performed by using IBM SPSS Statistics version 17.0 (IBM Corporation, Armonk, NY, USA). The Kolmogorov-Smirnov test was used to assess whether the continuous variables were distributed normally or not. Levene's test was used for the evaluation of homogeneity of variances. Descriptive statistics for continuous variables were expressed as mean ± standard deviation or median (minimum-maximum), where applicable. Numbers and percentages were used for categorical data. While the mean differences among groups were analyzed by One-Way ANOVA, otherwise, the Kruskal-Wallis test was applied for the comparisons of not normally distributed data. A p-value of less than 0.05 was considered statistically significant and when a p value was statistically significant, post-hoc Tukey HSD or Conover's multiple comparison test were used to know which group differ from which others. Categorical data were evaluated by Pearson's chi-square test. Degrees of association between continuous variables were evaluated by Spearman's rank correlation analyses.

Results

The treatment was performed in a total of 63 patients (56 male, 7 female) with a mean age of 36.8 (3-73) years. 7.9% of the defects were on the forearm and elbow, 15.9% on the hand and wrist, 38.1% on the thigh and leg, 22.2% on the dorsum of the foot and ankle, and 15.9% on the sole of the foot. Thirty nine of the wounds were caused by traffic accidents, three were due to burn injury, 15 were because of work accidents, and six were related to a fall. The bone, tendon, or plaque/screw used in bone stabilization was exposed in defects in all patients. For all defects, the average of the defect areas was estimated at 60 cm^2 (4-800); an average of nine sessions (3-24) of NBT was performed and the average length of hospital stay was 26 (10-65) days (Table 1). Wound care dressing was done at the bedside in all patients and no pain was endured. No problem occurred in any of the patients including four pediatric patients aged three-nine years.

The average size of the defect area was estimated at 45 cm² (4-90) on the forearm and elbow, 30 cm² (12-60) on the hand and wrist, 110 cm² (24-800) on the thigh and leg, 55 cm² (24-100) on the dorsum of the foot and ankle, and 45 cm² (24-80) on the sole of the foot. The defect area on the thigh and leg was statistically significantly larger than on other sites (p<0.001) (Table 2) (Figure 1).

An average of eight sessions (4-15) of NPT was performed for the hand and wrist defects, five sessions (3-7) for the forearm and elbow defects, 9.5 sessions (5-24) for the thigh and leg defects, eight sessions (4-11) for the defects of dorsum of the foot and ankle, and 11 sessions (4-13) were performed for the defects of the sole of the foot. The average number of NBT session for the forearm and elbow was statistically significantly lower than for the other sites (p<0.001) (Table 2) (Figure 2).

The mean length of hospital stay was 23.5 days (14-42) in patients who had hand and wrist defects, 15 days (10-20) in those with forearm and elbow defects, 29 days (17-65) - thigh and leg defects. 20.5 days (13-38) - foot and ankle defects, and 32 days (16-36) in those with defects on the sole of the foot. The mean length of hospital stay in patients with forearm and elbow defects was statistically significantly lower than in those with defects in the other sites (p<0.001) (Table 2) (Figure 3).

After NPT, one thigh defect and two dorsum of foot defects closed secondarily, one hand and wrist defect and one thigh and leg defect were reconstructed with local flaps and the remaining 58 defects were reconstructed with partial thickness skin grafts.

Table 1. Demographical and clinical characteristics of cases	
Number of cases, n	**63**
Age (years), mean ± SD	36.8±17.1
Range of age (years)	3-73
Gender, n (%)	
Male	56 (88.9)
Female	7 (11.1)
Defect level	
Hand and wrist, n (%)	10 (15.9)
Forearm and elbow, n (%)	5 (7.9)
Thigh and leg, n (%)	24 (38.1)
Dorsum of the foot and ankle, n (%)	14 (22.2)
Sole of the foot, n (%)	10 (15.9)
Defect size, cm² (range)	60 (4-800)
Number of NPT session, n (range)	9 (3-24)
Hospitalization (days), n (range)	26 (10-65)
Type of reconstruction, n (%)	
Flap	2 (3.2)
Secondary healing	3 (4.8)
Skin graft	58 (92.1)
SD: Standart deviation, NPT: Negative pressure therapy	

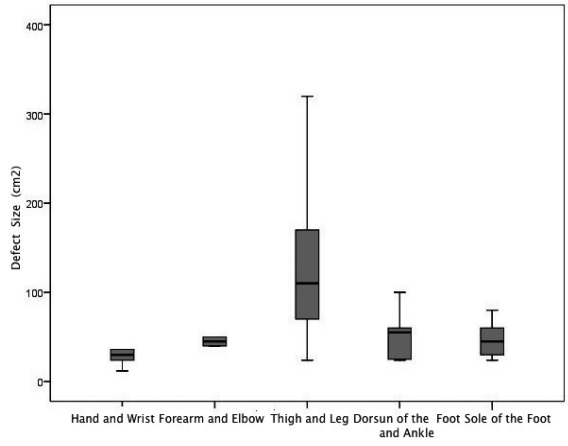

Figure 1. Distributions of defects levels according to defects size

Table 2. Demographical and clinical characteristics of cases						
	Hand and wrist	**Forearm and elbow**	**Thigh and leg**	**Dorsum of the foot and ankle**	**Sole of the foot**	**p-value**
Age (years), mean ± SD	33.9±18.3[A]	30.4±4.5[A]	36.7±14.0[A]	25.5±15.4[A]	58.8±7.5[B]	<0.00†
Gender, n (%)	-	-	-	-	-	0.080‡
Male	9 (90.0)	5(100.0)	18 (75.0)	14 (100.0)	10 (100.0)	
Female	1 (10.0)	0 (0.0)	6 (25.0)	0 (0.0)	0 (0.0)	
Defect size, cm² (range)	30 (12-60)[A]	45 (4-90)[A]	110 (24-800)[B]	55 (24-100)[A]	45 (24-80)[A]	<0.001¶
Number of NPT session, n (%)	8 (4-15)[A]	5 (3-7)[B]	9.5 (5-24)[A]	8 (4-11)[A]	11 (4-13)[A]	0.025¶
Hospitalization, days (range)	23.5 (14-42)[A]	15 (10-20)[B]	29 (17-65)[A]	20.5 (13-38)[A]	32 (16-36)[A]	0.010¶
Type of reconstruction						
Flap, n (%)	1 (10.0)	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	0.637‡
Secondary healing, n (%)	0 (0.0)	0 (0.0)	1 (4.2)	2 (14.3)	0 (0.0)	0.397‡
Skin graft, n (%)	9 (90.0)	5 (100.0)	22 (91.6)	12 (85.7)	10 (100.0)	0.712‡
SD: Standart deviation, NPT: Negative pressure threrapy, The different upper-case letters in each row indicate that statistically significant difference between groups (A vs B) (p<0.05)						

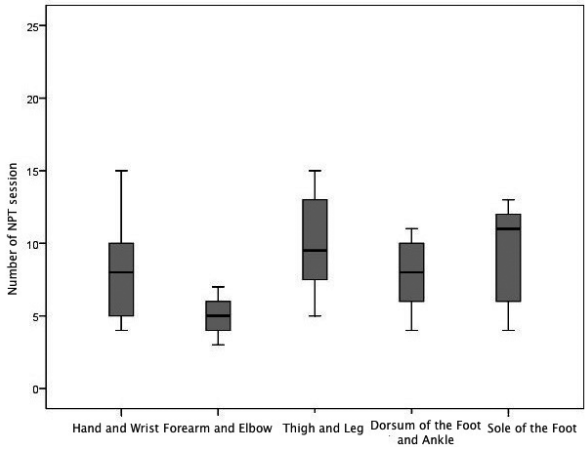

Figure 2. Distributions of defects levels according to number of negative pressure therapy sessions
NPT: Negative pressure therapy

Table 3. The results of correlation analyses between defect size and number of negative pressure therapy session

	n	Coefficient of correlation	P
Hand and wrist	10	0.928	<0.001
Forearm and elbow	5	0.100	0.873
Thigh and leg	24	0.422	0.040
Dorsum of the foot and ankle	14	0.285	0.324
Sole of the foot	10	0.794	0.006
Overall	63	0.519	<0.001

None of the patients required free tissue flaps. There was a graft loss of 30% in a 73-year-old diabetic patient whose defect was located on the dorsum of the hand and was reconstructed using a graft and this defect recovered secondarily. No complications occurred in other than this case.

After making correlation analyses between defect size and number of NPT session in all cases, there was a statistically significant correlation between increasing defect size and number of NBT session (r=0.519, p<0.001), but when only defects on the forearm and elbow and defects on the dorsum of the foot and ankle were considered, there was no statistically significant correlation between defect size and number of NBT session (r=0.100, p=0.873 and r=0.285, p=0.324, respectively) (Table 3).

Discussion

NBT was developed for treating large, chronic wounds and was mainly developed to turn the wound beds of chronic, wide, and infected wounds into ones suitable for reconstruction (4,6). NPT, which is administered after appropriate surgical debridement of such chronic wounds, increases granulation tissue formation and thus, makes it possible to close the wound with less aggressive surgical procedures (4,6,7). It is also an alternative treatment option in patients not suitable for surgical procedures and those with small defects (6).

The positive effect of NPT on wound healing is due to multiple factors. With NPT, excess wound exudate, which contains factors that inhibit fibroblasts, endothelial cells, and keratinocytes are removed from the site (4,6). Also, the edema surrounding the wound decreases with NPT and with this decrease, the blood vessels around the wound dilate and the blood flow to the wound increases. Herscovici et al. (1) determined that over 500 cc of fluid is taken from the tissues in the first 24 hours in NPT applications after high-energy trauma. The increase

Figure 3. (a) Three years old boy, the wound located on the dorsum of the left foot and ankle as a result of a traffic accident. View of a 10x5 cm defect with exposed tendon on the base of the wound. (b) View of the defect after debridement and bone stabilization. (c) The surface of the tendons were completely covered by granulation tissue. (d) The defect was reconstructed with skin grafts. (e) View of the defect in the second year postoperative. There were no complications

in blood flow to the wound site helps the granulation tissue form more rapidly. In a randomized prospective study, NPT and wet dressing were compared in terms of granulation tissue formation and it was shown that granulation tissue formed much faster with NPT (2). Also, NPT prevent colonization of anaerobic bacteria and decrease bacterial load of the wound. It has been shown that with NPT, the bacterial load reduced from 107 to 103 in four-five days (1,4,5). Another factor is that NPT transmits an equal amount of mechanical force against the tissue surrounding the wound. It was shown for the first time in 1911 that mechanical force stimulates tissue angiogenesis and growth. Clinically used techniques, such as tissue expanders and the Ilizarov techniques, both apply mechanical force. With NPT, the mechanical force applied on the tissues surrounding the wound ensures the surrounding tissue to migrate towards the center of the defect, and as a result, the wound decrease in size (1,8,9).

Different surgical techniques have been identified for closure of large soft tissue defects in extremities, especially due to high-energy trauma, such as skin grafts, local fasciocutaneous-musculocutaneous flaps, and free flaps (10). Skin grafting is a simple surgical procedure and the fact that grafts can be obtained in large amounts allows them to be used when repairing large defects and therefore makes them the most preferred method, however, the success depends on the vascularity of the recipient bed. Skin grafts cannot be applied on bone, cartilage, tendon or surgical implants (11). Local flaps are needed in such cases. As for defects which are too large to be repaired locally, free flaps are needed. Although successful results can be achieved with the use of free flaps, these surgeries cause problems such as sacrificing major arteries, prolonged operative time, and donor site morbidity. They also require special equipment and surgical skills (1,11). There is a 5% failure rate after free flap surgery and this rate increases especially in defects located at the tibial region. There is a 7% risk for amputation of the lower extremity after free flap surgery (12).

Various studies have been conducted regarding the use NPT for reconstruction of extremity defects due to high energy trauma, without the need for free flaps. In a prospective study conducted by Mullner et al. (13) in 1997, it was reported that lower extremity defects due to high energy trauma in 12 patients, in which the bone and plates were exposed, recovered within an average of 16 days of NPT treatment following rigid bone stabilization. In their series including 75 patients, DeFranzo et al. (8) reported that lower extremity wounds with exposed bone and tendons were the result of trauma in 49 patients without osteomyelitis of the lower extremity; the patients were treated with NPT after debridement and a success rate of 95% was achieved. The wounds were closed primarily in 12 patients, skin grafts were used in 58, and local flaps were used in five patients. None of the patients required free flap surgery. There were no complications in the patients who were followed up for a period of six months-six years. As for a series including 96 patients, NPT treatment was administered in 96 patients who had defects on the foot or ankle due to trauma with exposed tendon, bone, or implants. In 92 patients, the wounds could be closed with an average of six weeks of topical negative pressure (TNP) treatment after the injury, without the need for free flaps (14). As for our study, NPT treatment was administered in 63 patients who had an average of 60 cm^2 defects with exposed bone, tendon, and implants in different locations of the upper and lower extremities. The defects were reconstructed with grafts in 58 of the 63 patients after an average of 26 days hospital stay and nine sessions of TNP treatment and none of the patients required free flaps.

In our study, the relationship between defect size and NBT session required was directly proportional in all regions except forearm and elbow and dorsum of the foot and ankle. For defects on those levels, fewer NBT sessions and shorter hospital stay were needed according to defects size.

TNP is generally accepted as a reliable method of treatment. The most important complication of the treatment is the pain endured while changing the sponges (15). The pain is intermittent and is particularly due to the negative pressure itself, and the pain can mostly be eliminated by lowering the pressure. There were no complications, particularly pain, encountered during the sponge changes or treatment process in our study. Theoretically, NPT can cause arterial injury and major bleeding, thus, application of the sponge directly on the vessels is contraindicated. In their study including 75 patients, DeFronzo et al. (8) reported that none of the patients who were treated with NPT had bleeding. However, White et al. (16), reported a case of anterior tibial artery injury associated with NPT 22 days after treatment. Excessive granulation tissue formation may also cause bleeding especially in children and young adults (4,5,17). In our study, none of the patients, including the pediatric patients, had bleeding.

Cases of bacterial infections and toxic shock syndrome associated with NPT treatment have been reported in the literature (14). The anaerobic environment caused by NPT is particularly favorable for the growth of anaerobic bacteria (18,19). In contrast to these publications, many clinical trials have shown that NPT reduced bacterial load (20,21).

Four of the patients treated with NPT in our study were pediatric patients aged three-nine years and there was no problem during the treatment period. Similarly, Mooney et al. (7) used TNP treatment for soft tissue defects in 27 children, 20 of whom had defects on the extremities, and stated that the children tolerated the treatment very well.

In a study by Herscovici et al. (1), NPT was compared with wet dressings and free tissue transfers in terms

of cost. When the total costs of dressing materials and nursing were included, the daily cost of wet dressing was estimated to be 100 dollars, the daily cost of NPT was 103 dollars; whereas for free tissue transfer, only the cost of surgery was estimated to be 6000 dollars. According to this calculation, NPT is not more expensive than wet dressing and it also has advantages other than its positive effect on wound healing such as allowing ambulation of patients during the treatment and requiring only a few dressing changes. Sixty days of NPT treatment is required for the cost of NPT to equal the cost for free tissue transfer, and according to our study, the average length of hospital stay was 26 days.

Study Limitations

The fact that NBT and early conventional flap coverage were not compared and a relatively small number of cases for such an in homogenous group were the limitations of this study.

Conclusion

With the use of NPT using simpler methods, particularly skin grafts, in the treatment of acute extremity wounds due to high-energy trauma, it has been possible to close defects without the need for free flaps. Thus, the patients are protected from the complications of free tissue transfer, and also treatment is possible at much lower cost.

Authorship Contributions

Surgical and Medical Practices: E.O., B.E. Concept: E.O., B.E. Design: E.O., B.E. Data Collection or Processing: E.O. Analysis or Interpretation: E.O. Literature Search: E.O. Writing: E.O.

Conflict of Interest: No conflict of interest was declared by the authors.

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Medical Results and Psychosocial Factors in Obesity Surgery

Obezite Cerrahisinde Medikal Sonuçlar ve Psikososyal Faktörler

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Abstract

Aim: Obesity is one of the most important health problems of our age. It causes serious psycho-social problems as well as medical problems. We aimed to investigate the preoperative and postoperative medical and psycho-social changes in patients undergoing obesity surgery.

Methods: One hundred four patients, who underwent surgery between January 2016 and August 2016 and accepted to participate in the survey, were included in the study. Six questions were asked about the factors predicting the need for surgery as well as the medical and psychosocial changes after surgery.

Results: When the results of the surgical procedures were examined, there was a statistically significant difference in only the fifth question between sleeve gastrectomy group and gastric bypass group ($p<0.05$). No statistically significant difference was found in other questions. All patients in the gastric bypass group discontinued medication after surgery. The result was statistically significant.

Conclusions: Besides the positive medical results, we think that in the treatment of obesity, the role of surgery is increasing because of positive psycho-social outcomes in patients.

Keywords: Obesity, psychosocial factors, social media, surgery

Öz

Amaç: Obezite ciddi psikososyal sorunlara ve tıbbi sorunlara neden olabilir. Bu çalışmada obezite cerrahisi geçiren hastalarda preoperatif ve postoperatif medikal ve psikososyal değişiklikleri araştırmak amaçlanmıştır.

Yöntemler: Morbid obezite nedeniyle Ocak 2016-Ağustos 2016 tarihleri arasında ameliyat edilen hastalardan, çalışmaya katılmayı kabul eden 104 hastaya anket çalışması uygulandı. Hastalara kendilerini ameliyat olmaya yönlendiren faktörler, cerrahi sonrası medikal ve psikososyal değişiklikler hakkında altı soru yöneltildi. Hastalar gastrik bypass ve sleeve gastrektomi operasyonu geçirenler olarak iki gruba ayrıldı. İki grup arasındaki sonuçlar analiz edildi.

Bulgular: Cerrahi işlemlerin sonuçları incelendiğinde, gastrik bypass grubu ile sleeve gastrektomi grubu arasında sadece "sistemik hastalık nedeniyle ameliyat öncesi kullanılan ilaçlara devam ediyor musunuz?" şeklindeki soruda sonuçlar istatistiksel olarak anlamlıydı ($p<0,05$). Gastrik bypass grubundaki tüm hastalar cerrahi sonrası ilaç tedavisini bıraktığını bildirdi. Diğer sorularda istatistiksel olarak anlamlı bir fark bulunmadı.

Sonuç: Başarılı tıbbi sonuçların yanı sıra, olumlu psikososyal geri dönüşler nedeniyle obezite tedavisinde cerrahinin rolünün giderek arttığını düşünüyoruz.

Anahtar Sözcükler: Obezite, psikososyal faktörler, sosyal medya, cerrahi

Introduction

Obesity is one of the most important health problems of our age. It has serious morbidity rates. Obesity is among the leading causes of preventable death in developed countries. It causes serious psychosocial problems as well as medical problems. The role of surgery in the treatment of obesity is increasing. In this study, we aimed to investigate the preoperative and postoperative medical and psycho-social changes in patients undergoing obesity surgery (1-3).

Methods

Patients who underwent surgery at Elazığ Medical Park Hospital, General Surgery Clinic between January 2016 and August 2016 were informed about the survey.

One hundred four patients who accepted to participate in the survey were included in the study. Six questions were asked about the factors predicting the need for surgery as well as the medical and psycho-social changes after the surgery. The participants were asked to

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respond the questions which are the most important for themselves and explain the reasons if they wanted to. In the light of the answers, it was researched whether the surgical procedure could meet the expectations of the patients. Informed consent statement does not apply to this retrospective study. For this retrospective study ethical approval statement formal consent is not required.

Statistical Analysis

The results of the survey were evaluated by the SPSS data analysis program. The groups were divided according to gender and surgical procedure and compared with the non-parametric Mann-Whitney U test. A p-value of less than 0.05 was considered statistically significant.

Results

The average age of the participants was 38.7 (17-63), 59.6% were female (n=62) and 40.4% were male (n=42). Ninety patients had laparoscopic sleeve gastrectomy and 14 patients underwent laparoscopic Roux-en-Y gastric bypass surgery. The shortest follow-up period was 12 months and the longest follow-up period was 18 months.

The first question asked was "What was the most important problem for you before surgery?". 63.5% of patients (n=66) reported physical appearance and 36.5% (n=38) systemic disease (Table 1).

The second question was "What was the most important factor for taking the decision of surgery?". 61.5% of the patients (n=64) stated social media and environmental influences and 24% (n=25) physical appearance. Only 14.4% (n=15) reported health problems (Table 2).

The third question was "Would you take the same decision of surgery if you had a second chance". 95.2% of the participants responded "Yes" (n=99). Only five patients reported that they would not want to have surgery because of the pain after surgical procedure (Table 3).

The fourth question was "Did the surgical procedure satisfy your expectations?". 87.5% (n=91) responded "Yes" and 12.5% (n=13) "Partially". There was no participant responding "No" (Table 4).

The fifth question was "Do you continue the medications you used for your systemic disease you had before the surgery?". 89.4% (n=93) of participants, who used drugs for a systemic disease before surgery, did not use any medicine after surgical procedure and 6.7% (n=7) reported that the amount of medication they regularly used was decreasing. 3.8% (n=4) of patients continued to use drug after surgery (Table 5).

The last question was "What was the most important change in your life after surgery?". For this question, 43.3%

Table 1. First questions results

Operation			Gender, n (%)		Total, n (%)
			Male	Female	
Sleeve gastrectomy	What was the most important problem before surgery for you?	Physical appearance	26 (68.4)	34 (65.4)	60 (66.7)
		Systemic diseases	12 (31.6)	18 (34.6)	30 (33.3)
			38 (100)	52 (100)	90 (100)
Gastric bypass	What was the most important problem before surgery for you?	Physical appearance	1 (25)	5 (50)	6 (42.9)
		Systemic diseases	3 (75)	5 (50)	8 (57.1)
			4 (100)	10 (100)	14 (100)

Table 2. Second questions results

Operation			Gender, n (%)		Total, n (%)
			Male	Female	
Sleeve gastrectomy	What was the most important factor in making an operation decision?	Social media, environmental influences	24 (63.2)	33 (63.5)	57 (63.3)
		Physical appearance	7 (18.4)	7 (13.5)	14 (15.6)
		Health problems	7 (18.4)	12 (23.1)	19 (21.1)
			38 (100)	52 (100)	90 (100)
Gastric bypass	What was the most important factor in making an operation decision?	Social media, environmental influences	3 (75)	4 (40)	7 (50)
		Physical appearance	0 (0)	1 (10)	1 (7.1)
		Health problems	1 (25)	5 (50)	6 (42.9)
			4 (100)	10 (100)	14 (100)

of participants (n=45) reported increased self-confidence and resolved psychological problems and 41.2% (n=43) reported improved quality of life. Only 15.4% (n=16) regarded improvement of health problems as the most important change in their life (Table 6).

There was no statistically significant difference in the responses between genders (p>0.05). The difference in the answers to the 5th question was statistically significant between the two groups. No statistically significant difference was found in other questions. All patients in

Table 3. Third questions results

Operation			Gender, n (%)		Total, n (%)
			Male	Female	
Sleeve gastrectomy	If you went to your old self, would you decide again on surgery?	Yes	37 (97.4)	48 (92.3)	85 (94.4)
		No	1 (2.6)	4 (7.7)	5 (5.6)
			38 (100)	52 (100)	90 (100)
Gastric bypass	If you went to your old self, would you decide again on surgery?	Yes	4 (100)	10 (100)	14 (100)
			4 (100)	10 (100)	14 (100)

Table 4. Fourth questions results

Operation			Gender, n (%)		Total, n (%)
			Male	Female	
Sleeve gastrectomy	Did the surgical procedure respond to your expectations before the surgery?	Yes	36 (94.7)	41 (78.8)	77 (85.6)
		Partially	2 (5.3)	11 (21.2)	13 (14.4)
			38 (100)	52 (100)	90 (100)
Gastric bypass	Did the surgical procedure respond to your expectations before the surgery?	Yes	4 (100)	10 (100)	14 (100)
			4 (100)	10 (100)	14 (100)

Table 5. Fifth questions results

Operation			Gender, n (%)		Total (n) (%)
			Male	Female	
Sleeve gastrectomy	Do you continue to use the medications you used due to systemic diseases after surgery?	No	36 (94.7)	49 (94.2)	85 (94.4)
		Decreased	2 (5.3)	3 (5.8)	5 (5.6)
			38(100)	52 (100)	90 (100)
Gastric bypass	Do you continue to use the medications you used due to systemic diseases after surgery?	No	2 (50)	6 (60)	8 (57.1)
		Decreased	0 (0)	2 (20)	2 (14.3)
		Yes	2 (50)	2 (20)	4 (28.6)
			4 (100)	10 (100)	14 (100)

Table 6. Sixth questions results

Operation			Gender, n (%)		Total, n (%)
			Male	Female	
Sleeve gastrectomy	What was the most important change in your life after surgery?	Increased self-confidence, resolved psychological problems	14 (36.8)	24 (46.2)	38 (42.2)
		Increased in living standards	17 (44.7)	22 (42.3)	39 (43.3)
		Resolved health problems	7 (18.4)	6 (11.5)	13 (14.4)
			38 (100)	52 (100)	90 (100)
Gastric bypass	What was the most important change in your life after surgery?	Increased self-confidence, resolved psychological problems	2 (50)	5 (50)	7 (50)
		Increased in living standards	2 (50)	2 (20)	4 (28.6)
		Resolved health problems	0 (0)	3 (30)	3 (21.4)
			4 (100)	10 (100)	14 (100)

the gastric bypass group discontinued medication after surgery. The result was statistically significant.

Discussion

Obesity is a multifactorial disease caused by genetic, environmental and psychological factors. For this reason, it is one of the most difficult diseases to treat (4,5).

Psychiatric disorders are common in obese patients. The most common diagnoses are anxiety disorders, mood disorders, binge eating disorder and personality disorders, respectively. Psychosocial problems, such as dissatisfaction with physical appearance, unhappiness in marriage, and difficulty in sexual life, are more common in obese individuals than in healthy individuals (6-8).

The expectation of the patients who undergo obesity surgery is also very important. Patients, who have many problems in many areas of their life, may assume that all their problems will end up after surgery. This can lead to long-term psychiatric treatments after surgery (9). Bariatric surgery has been shown to improve quality of life as well as to improve comorbidities and maintain weight loss (10,11). There are also studies reporting that many psychiatric problems existing prior to surgery decreased after surgery (12).

Obesity surgery provides significant psychosocial improvements as well as medical outcomes. In this study, it was observed that, social media and environmental influences were more effective than health problems in patient's decision making on surgey. Again, in the majority of patients, who decided to undergo surgery, their physical appearance played a more dominant role in deciding on surgery when compared to systemic diseases or difficulties caused by obesity. According to the results of this study, technological improvements and information accessibility have significant effects on patients' decision on obesity surgery.

Conclusion

In conclusion, besides the positive medical results, we think that obesity surgery will continue to increase its role in the treatment of obesity because of positive psychosocial outcomes.

Author Contributions

Surgical and Medical Practices: F.D. Concept: M.D., F.D. Design: M.D., F.D. Data Collection or Processing: M.D., F.D. Analysis or Interpretation: M.D., F.D. Literature Search: M.D., F.D. Writing: M.D., F.D.

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Original Article / *Özgün Araştırma*

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Are Mean Platelet Volume and Neutrophil-to-Lymphocyte Ratio Valuable in The Early Detection of System Involvements in Henoch-Schönlein Purpura?

Ortalama Trombosit Hacmi ve Nötrofil-Lenfosit Oranı Henoch-Schönlein Purpurası'nda Sistem Tutulumlarının Erken Saptanmasında Değerli mi?

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Abstract

Aim: Henoch-Schönlein purpura (HSP) is the most common type of vasculitis in childhood, and severe complications due to intestinal and renal involvement can be observed. In this study, it was planned to investigate the value of mean platelet volume (MPV) and neutrophil-to-lymphocyte ratio (NLR) in early detection of system involvement in HSP.

Methods: A total of 119 patients diagnosed with HSP and 75 healthy controls were included in the study. Data on age, gender and physical examination as well as complete blood count, complete urine examination and faecal occult blood test were obtained from the files of the patients.

Results: Gastrointestinal system (GIS) involvement was detected in 41 patients (34.45%), renal involvement in 35 patients (29.41%) and arthritis was detected in 21 patients (17.65%). It was determined that the mean hemoglobin (p=0.02) and MPV values (p=0.0001) o were significantly lower and the mean leukocyte (p=0.0001), platelet (p=0.0001), neutrophil (p=0.0001) count and NLR value (p=0.0001) were significantly higher in patients than in controls. No statistically significant difference was observed in the MPV and NLR values between patients with and without GIS involvement, renal involvement and arthritis.

Conclusion: It is thought that MPV and NLR cannot be used as laboratory parameters in the early detection of system involvement in HSP.

Keywords: Henoch-Schönlein purpura, mean platelet volume, neutrophil-to-lymphocyte ratio

Öz

Amaç: Henoch-Schönlein purpurası (HSP) çocukluk çağının en sık görülen vasküliti olup intestinal ve renal tutuluma bağlı ağır komplikasyonlar görülebilir. Çalışmamızda HSP'nin sistem tutulumlarını erken saptamada ortalama trombosit hacminin (OTH) ve nötrofil lenfosit oranının (NLO) değerlendirilmesi amaçlanmıştır.

Yöntemler: HSP tanısı alan 119 hasta ve 75 sağlıklı kontrol çalışmaya alındı. Hastaların yaşı, cinsiyeti, fizik muayene bulguları, tam kan sayımı, tam idrar incelemesi, dışkıda gizli kan tetkiki dosyalarından kaydedildi.

Bulgular: Hastaların 41'inde gastrointestinal sistem (GİS) tutulumu (%34,45), 35'inde renal tutulum (%29,41), 21'inde artrit (%17,65) tespit edildi. Hastaların hemoglobin (p=0,02) ve OTH (p=0,0001) değeri ortalaması anlamlı derecede düşük, lökosit (p=0,0001), trombosit (p=0,0001), nötrofil (p=0,0001) sayısı ve NLR değeri (p=0,0001) ortalaması anlamlı derecede yüksek bulunmuştur. GİS tutulumu, renal tutulumu ve artriti olan ve olmayan hastaların ortalama OTH ve NLO değeri arasında istatistiksel olarak anlamlı farklılık gözlenmemiştir.

Sonuç: HSP'de sistem tutulumlarını erken saptanmada OTH ve NLO'nun laboratuvar parametresi olarak kullanılamayacağını düşünmekteyiz.

Anahtar Sözcükler: Henoch-Schönlein purpura, ortalama trombosit hacmi, nötrofil lenfosit oranı

Introduction

Henoch-Schönlein purpura (HSP), which is the most common childhood vasculitis, usually improves without treatment; complications rarely occur in the course of the disease, and long-term renal outcomes depends on the initial clinical presentation (1). HSP is a systemic

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vasculitis characterized by palpable purpura without thrombocytopenia, colic-like abdominal pain, joint involvement in the form of arthritis and/or arthralgia, and renal involvement varying from microscopic haematuria to acute glomerulonephritis. It is most frequently observed between the ages of three and 15 years and 1.5 times more commonly among males than in females (2).

The emergence of the disease exhibits seasonal differences, and it is observed more frequently during the autumn and winter months, and after an upper respiratory tract infection. It is known that infectious agents, especially beta-haemolytic streptococci, trigger the disease. Apart from this, *Mycoplasma pneumoniae*, *Bartonella henselae* and vaccines are other most frequently blamed predisposing factors (3,4).

Immune complexes in the systemic circulation formed by various antigenic stimuli accumulate in the capillary wall and activate the complement system, chemotaxis occurs, polymorphonuclear leukocyte migration takes place, polymorphonuclear leukocytes disintegrate as a result of degranulation, and this leads to the deconstruction of and around the blood vessel wall (5). The frequent immunoglobulin (Ig) A accumulation in blood vessels gives rise to the thought that the immune system response in relation to IgA may play a role in the pathogenesis of the disease. Nevertheless, the exact pathogenesis of the disease is not known (4).

The diagnosis of HSP is based on clinical findings. While thrombocytosis, leucocytosis, moderate anaemia, C-reactive protein (CRP), elevated sedimentation are the laboratory findings of HSP, they are not specific to HSP (6,7). Furthermore, there is no unique laboratory that estimates multisystem involvement in HSP. Hemogram parameters have started to be frequently used in recent years in the diagnosis of HSP and other inflammatory diseases, and in the assessment of the severity of clinical findings since assessment of neutrophil-to-lymphocyte ratio (NLR) and mean platelet volume (MPV) is cheap and easily-accessible (8-12).

In this study, we investigated the value of MPV and NLR in the early detection of system involvement in patients with HSP.

Methods

Medical records of 119 patients diagnosed with HSP between January 2013 and December 2016 in the Pediatrics Clinic at University of Health Sciences, Bağcılar Training and Research Hospital and 75 healthy children of the same age and gender were investigated in this retrospective study.

HSP diagnosis was made according to the "EULAR/PRINTO/PRES" criteria (13). There was at least one another system [joint, gastrointestinal system (GIS) or renal] involvement that accompanied typical palpable purpura in all the patients. The epidemiological, clinical and laboratory findings and treatment information in children with HSP were obtained by examining their records. Patients who used drugs due to a chronic disease that would affect platelet functions and those who received oral steroid treatment before admission were excluded from the study.

Patients' age, gender and physical examinations in terms of system involvement on the day of admission, complete blood count, complete urine examination and faecal occult blood (FOB) test were recorded.

Arthritis was defined as limited movement in the joint or painful periarticular, soft tissue oedema. Gastrointestinal involvement was defined as the presence of abdominal pain and/or GIS bleeding. GIS bleeding was defined as a positive FOB test and presence of haematochezia or melena. Nephritis was defined as "macroscopic" or microscopic haematuria (microscopically >5 erythrocytes in every area of centrifuged urine), with proteinuria The present study was approved by the Ethics Committee of Bağcılar Training and Research Hospital (approval number: 2016/497). Study participants and/or their parents provided written informed consent.

Statistical Analysis

Statistical analyses were performed using the Number Cruncher Statistical System (NCSS) 2007 Statistical Software (Utah, USA). In the data evaluation, in addition to descriptive statistical methods (mean, standard deviation), the independent t-test was used in the comparison of the paired groups of variables exhibiting a normal distribution, the Mann-Whitney U test was used in the comparison of the paired groups of variables that did not exhibit a normal distribution, and the chi-square test was used in the comparison of qualitative data. The results were evaluated at a significance level of $p<0.05$.

Results

Seventy-five of 119 patients diagnosed with HSP were male and 44 were female. The mean age of the patients was 7.82±3.01 years. The control group consisted of 75 children with an mean age of 8.55±3.09 years, 37 of whom were female and 38 were male. No statistically significant difference was observed in mean age and gender distribution between the control and HSP groups ($p>0.05$) (Table 1).

Upon examining the hemograms in the patient and control groups, the mean hemoglobin value in the patients was found to be significantly lower ($p=0.02$), the mean leukocyte count was found to be significantly higher ($p=0.0001$), the mean platelet count was found to be significantly higher ($p=0.0001$), the mean MPV value

was found to be significantly lower (p=0.0001), the mean neutrophil value was found to be significantly higher (p=0.0001) and the mean NLR value was found to be significantly higher than in controls (p=0.0001) (Table 1).

GIS involvement was determined in 41 (34.45%) patients, renal involvement in 35 (29.41%), and arthritis was determined in 21 patients (17.65%). While all the patients with GIS involvement had abdominal pain, FOB was determined in 36 (30.25%), proteinuria in 10 (8.4%), and haematuria was determined in 32 patients (26.89%) (Table 2).

Upon examining the hemogram parameters in patients diagnosed with HSP with and without GIS involvement, the MPV in patients with and without GIS involvement was found to be 428.11±163.86 (x1000/μL) and 341.98±104.71 (x1000/μL), respectively. The MPV in patients with GIS involvement was found to be statistically significantly higher than in patients without GIS involvement (p=0.0001).

The mean MPV value in patients with and without GIS involvement was 6.58±1.05 and 6.88±1.17, respectively. No statistically significant difference was observed in MPV values between patients with and without GIS involvement (p=0.170).

The mean NLR value in patients with and without GIS involvement was found to be 2.86±1.89 and 2.17±1.27, respectively and no statistically significant difference was observed in the mean NLR value between patients with and without GIS involvement (p=0.060) (Table 3).

The mean MPV value in patients with and without renal involvement was 6.66±1.08 and 6.83±1.16, respectively. No statistically significant difference was observed in MPV values between patients with and without renal involvement (p=0.461).

The mean NLR value in patients with and without renal involvement was 2.55±1.46 and 2.34±1.58, respectively and no statistically significant difference was observed in the mean NLR value between patients with and without renal involvement (p=0.503) (Table 4).

The mean MPV value in patients with and without arthritis was 6.83±1.1 and 6.77±1.15, respectively.

Table 1. Demographic characteristics and hemogram parameters of the patient and control groups

		Control group n=75	HSP group n=119	p
Age* (Years)		8.55±3.09	7.82±3.01	0.104
Gender, n (%)	Male	38 (50.67)	75 (63.03)	0.089
	Female	37 (49.33)	44 (3.97)	
Hemoglobin* (g/dL)		13.08±0.9	12.71±1.15	0.02
Leukocyte* (10^3/μL)		8.47±2.02	12.34±4.64	0.0001
Platelet* (10^3/μL)		281.41±65.42	367.62±133.96	0.0001
MPV* (fL)		7.77±1.64	6.78±1.14	0.0001
Neutrophil* (10^3/μL)		4.19±1.51	7.62±4.1	0.0001
Lymphocyte* (10^3/μL)		3.28±1.02	3.75±2.28	0.318
NLR* (10^3/μL)		1.38±0.57	2.41±1.54	0.0001

MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, HSP: Henoch-Schönlein purpura
*Mean ± standard deviation

Table 2. Clinical features of the patients

		n	%
GIS involvement	Negative	78	65.55
	Positive	41	34.45
Renal involvement	Negative	84	70.59
	Positive	35	29.41
Arthritis	Negative	98	82.35
	Positive	21	17.65
FOB	Negative	83	69.75
	Positive	36	30.25
Proteinuria	Negative	109	91.60
	Positive	10	8.40
Haematuria	Negative	87	73.11
	Positive	32	26.89

GIS: Gastrointestinal system, FOB: Faecal occult blood

Table 3. Comparison of the hemogram parameters in Henoch-Schönlein purpura patients with and without gastrointestinal system involvement

	GIS (-) n=78	GIS (+) n=41	p
Platelet* (10^3/μL)	341.98±104.71	428.11±163.86	0.0001
MPV* (fL)	6.88±1.17	6.58±1.05	0.170
Neutrophil* (10^3/μL)	7.11±3.74	8.57±4.61	0.092
Lymphocyte* (10^3/μL)	3.78±2.16	3.7±2.5	0.504
NLR* (103/μL)	2.17±1.27	2.86±1.89	0.060

MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, GIS: Gastrointestinal system *Mean ± standard deviation

Table 4. Comparison of the hemogram parameters in Henoch-Schönlein purpura patients with and without renal involvement

	Renal involvement (-) n=84	Renal involvement (+) n=35	p
Platelet* (10^3/μL)	363.61±147.30	390.98±172.76	0.229
MPV* (fL)	6.83±1.16	6.66±1.08	0.461
Neutrophil* (10^3/μL)	7.56±3.86	7.76±4.68	0.811
Lymphocyte* (10^3/μL)	3.96±2.57	3.24±1.2	0.116
NLR* (103/μL)	2.34±1.58	2.55±1.46	0.503

MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, HSP: Henoch-Schönlein purpura *Mean ± standard deviation

Table 5. Comparison of the hemogram parameters in Henoch-Schönlein purpura patients with and without arthritis

	Arthritis (-) n=98	Arthritis (+) n=21	p
Platelet* (10^3/μL)	363.12±127.26	411.49±159.11	0.104
MPV* (fL)	6.77±1.15	6.83±1.1	0.833
Neutrophil* (10^3/μL)	7.36±3.9	8.82±4.84	0.711
Lymphocyte* (10^3/μL)	3.83±2.42	3.39±1.44	0.163
NLR* (103/μL)	2.27±1.39	3.06±2.04	0.351

MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio,
* Mean ± standard deviation

No statistically significant difference was observed in MPV values between patients with and without arthritis (p=0.833). The mean NLR value in patients with and without arthritis was 3.06±2.04 and 2.27±1.39, respectively and no statistically significant difference was observed in the mean NLR value between patients with and without arthritis (p=0.351) (Table 5).

Discussion

HSP is a leukocytoclastic systemic vasculitis involving small vessels, affecting the GIS, kidneys, joints, and less rarely, other organs and systems, and especially the skin, and of which the aetiology is not exactly known. The disease is especially observed between the ages of five and 15 years (1,2). The mean age of the patients in this study was 7.82±3.01 years. It has been reported that HSP was more common among boys, and the male-to-female ratio was 1.5-2/1 (14). In this study, 75 of patients were male, 44 were female, and the male-to-female ratio was found to be 1.7/1, compatible with the literature.

HSP is characterized by purpuric rashes that are concentrated in the lower extremities and vary from small petechiae to wide ecchymosis. As in this study, it has been reported in various publications in the literature that nonthrombocytopenic palpable purpura was the only finding observed in all cases (14,15). Arthritis is the second most prevalent clinical picture in HSP. The joint involvement rates vary between 62 and 82% (15-17). Arthritis was detected in 17.65% of patients in this study, and this does not comply with other studies.

GIS involvement is found in 45-75% of HSP cases. It is the most prevalent finding after rash and joint pain (10,18). There was GIS involvement in 41 of our patients (34.45%). The most important finding suggesting GIS involvement in HSP is accepted to be abdominal pain that can be accompanied by nausea, vomiting and bleeding (19,20). In approximately 40% of patients, pain has been reported to be severe (21). All our patients with GIS involvement had abdominal pain.

The frequency of renal involvement in HSP has been reported to be between 15% and 62%, and the prognosis is generally good (22). The involvement may vary from isolated microscopic haematuria to rapidly progressive glomerulonephritis. It is believed that the long-term prognosis of the disease is related to this involvement (15,23). In our cases, renal involvement was defined according to the presence of haematuria and proteinuria, and renal involvement did not have a progressive course in any of our cases.

HSP is accompanied by thrombocytosis, leukocytosis, moderate anaemia, and elevated CRP and erythrocyte sedimentation rate (6,7). As it was also expected in this study, it was observed that leukocyte and platelet counts were significantly higher in the patient group with HSP when compared to the control group. However, the hemoglobin level was significantly lower in patients than in controls.

The hemogram parameters NLR and MPV have started to be widely used in the diagnosis of HSP and other inflammatory diseases and assessment of the severity of clinical findings in recent years since their measurement is cheap and easily accessible (8-12). Studies on the use of MPV as an indicator in pediatric patients with HSP are quite limited in the literature (11,12). While platelets play a significant role in haemostasis and endothelial repair, they are also important in the formation of atherothrombosis (24). Platelet volume is an indicator that determines platelet functions and activation (25). It has been reported that platelet count increased while MPV decreased in inflammatory diseases (26,27). In this study, it was observed that platelet count increased and MPV decreased in patients with HSP when compared controls, in line with other studies. It has been reported that MPV decreased in the active periods of ulcerative colitis and Crohn's disease, which are other inflammatory diseases affecting the GIS (26,28). It was also reported that MPV was lower in patients with ankylosing spondylitis and rheumatoid arthritis when compared to that in healthy controls (29).

It is believed that certain cytokines that increase throughout the inflammatory process in HSP affect platelet count and volume. Interleukin (IL)-6 is the most important proinflammatory cytokine that causes an increase in platelets and affects the platelet volume (30,31). It has been reported that administration of IL-6 increased platelet count and MPV in cancer patients (31,32). It is believed that IL-6 is responsible for changes in platelets in HSP. Lin et al. (33) reported that serum IL-6 levels were higher in patients with HSP when compared to the controls. Nevertheless, it was observed that the

level of IL-6 was significantly lower in patients with GIS and renal involvement in HSP when compared to those without organ involvement. This was explained in the literature by the fact that IL-6 is consumed in the early phase of the disease (in the early period of inflammation), and it was protective against internal organ involvement and other complications (12). In line with the present study, in a study by Benzer et al. (34), the level of MPV in patients with HSP was found to be lower when compared to healthy controls. In a study by Makay et al. (12), it was reported that the MPV was significantly lower in patients with GIS involvement in HSP when compared to those without GIS involvement. Again, in the study of Benzer et al. (34), it was observed that MPV was significantly lower in patients with GIS involvement. Differently from these two studies, it was observed in the present study that there was no significant difference in MPV between HSP patients with and without GIS involvement. However, the MPV value was significantly lower in patients with HSP when compared to controls, in line with the literature. This can be explained by the fact that IL-6 is protective against internal organ involvement and other complications by being consumed in the early phase of the disease (in the early period of inflammation), as it is explained above.

No study evaluating the relationship between other system involvements apart from GIS involvement and MPV in HSP was encountered in the literature. However, no significant difference in terms of MPV was observed in HSP patients with and without arthritis and in HSP patients with and without renal involvement.

NLR is used as a beneficial indicator that shows the clinical course in inflammatory diseases (35-37). NLR is used in cardiovascular diseases, malignancies, cystic fibrosis and familial Mediterranean fever (35-38). In the study of Makay et al. (11), NLR was found to be significantly higher in HSP children with GIS bleeding when compared to those without GIS involvement. In their study, Gayret et al. (10) found that NLR was significantly higher in patients with HSP when compared to controls, however, no significant difference was observed between HSP children with and without GIS involvement. Similarly, in the present study, NLR was found to be higher in children with HSP than in healthy controls group, and no significant difference was observed between those with and without GIS involvement. NLR is calculated by dividing neutrophil count by lymphocyte count. Increased neutrophil and decreased lymphocyte count can be observed in various infectious diseases or certain inflammatory conditions and stressful situations (39,40). Decreased lymphocyte count is observed in sepsis and lymphocyte apoptosis in inflammatory diseases (40). In the present study, it was observed that neutrophils were significantly higher in the patient group with HSP, but the lymphocytes were not very low. Nevertheless, no significant increase was observed in NLR in patients with GIS involvement, although NLR is high in HSP patients.

Steroid treatment is used in HSP with GIS involvement. Early steroid treatment reduces HSP-related GIS complications (41). It has been reported that patients with GIS bleeding had higher NLR values when compared to patients without GIS bleeding but with abdominal pain (11). It was found out that the detection of high NLR may result in fewer complications by ensuring that the use of steroids is started early with the early detection of the possibility of GIS bleeding in HSP. In the present study, it was observed that there was no difference in NLR between HSP patients with GIS and other system involvements and those without organ involvement.

Study Limitations

The retrospective design and small sample size were the limitations of this study.

Conclusion

When compared to other studies, it is observed that MPV and NLR were significant bioindicators in patients with HSP. HSP is an inflammatory condition, and it was observed that MPV was low and NLR was high, indicating inflammation. However, it was observed that MPV and NLR were not very significant in patients diagnosed with HSP with and without GIS or other organ involvement. Low MPV and high NLR values are expected in patients with GIS involvement, however, in the present study, it was observed that there was no difference in these parameters between patients with and without GIS involvement. Therefore, prospective studies are required. Again, in the literature, we found no study investigating the relationship between MPV and NLR in patients with renal involvement and arthritis. In the present study, it was observed that there was no difference in MPV and NLR values between patients with renal involvement and arthritis and those without involvement.

Authorship Contributions

Surgical and Medical Practices: A.Ö., Ö.B.G. Concept: A.Ö., Ö.B.G. Design: A.Ö., Ö.B.G. Data Collection or Processing: A.Ö., Ö.B.G. Analysis or Interpretation: Ö.B.G., M.E., Ö.Y., F.M. Literature Search: Ö.B.G., M.E., Ö.Y., F.M. Writing: Ö.B.G., M.E., Ö.Y., F.M.

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Long-Term Outcomes of Chest Wall Resection in Non-Small Cell Lung Cancer in Geriatric Patients

Geriatrik Hastalarda Küçük Hücreli Olmayan Akciğer Kanserinde Göğüs Duvarı Rezeksiyonunun Uzun Dönem Sonuçları

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Abstract

Aim: Lung cancer has become a global health problem today. Both patients and physicians prefer oncologic treatment approaches rather than surgery in T3 and T4 lung cancers in the geriatric age group. The objective of this study was to assess the long-term survival outcomes of patients aged 70 years and older, who underwent chest wall resection due to non-small cell lung cancer, and the prognostic factors affecting morbidity.

Methods: Eighteen patients, who underwent chest wall resection due to non-small cell lung cancer, were assessed retrospectively.

Results: A total of 18 patients (16 male and 2 female) with a mean age of 74.28±3.81 years were included in the study. The most common surgery was right upper lobectomy (55.6%, n=10). Complications were detected in nine patients (50%). The most common complication was arrhythmia. Mortality was detected in four patients (22%). The mean two-year and five-year survival rates were 77.9% and 41.4%, respectively. Lymph node status, adjuvant treatment and tumor stage were prognostic factors affecting survival (p=0.001).

Conclusion: Age should not be the only criterion for surgery. Appropriately selected patients should be offered anatomical resection. Long-term survival can be achieved in these patients.

Keywords: Thoracic wall resection, geriatric thoracic surgery, non-small cell lung cancer, advanced stage tumors

Öz

Amaç: Akciğer kanseri günümüzde global bir sorun haline gelmiştir. Geriatrik yaş grubundaki T3 ve T4 akciğer kanserlerinde hastalar ve doktorlar cerrahiden ziyade onkolojik tedavi yaklaşımlarını tercih etmektedirler. Bizim bu çalışmadaki amacımız 70 yaş ve üzerinde küçük hücreli dışı akciğer kanseri nedeniyle toraks duvar rezeksiyonu yapılan hastaların uzun dönem sağkalım sonuçlarını ve morbiditeye etki eden prognostik faktörleri değerlendirmektir.

Yöntemler: Küçük hücreli dışı akciğer kanseri nedeniyle toraks duvar rezeksiyonu operasyonu yapılan 18 hasta retrospektif olarak değerlendirildi.

Bulgular: On altı erkek, iki kadın hastanın yer aldığı çalışmada hastaların ortalama yaşı 74,28±3,81 yıl idi. En sık yapılan operasyon sağ üst lobektomi idi (%55,6, n=10). Dokuz hastada (%50) komplikasyon saptandı. En sık saptanan komplikasyon aritmi şikayetiydi. Dört hastada (%22) mortalite saptandı. Ortalama iki yıllık sağkalım oranı %77,9; beş yıllık sağkalım oranı %41,4 idi. Lenf nodu durumu, adjuvan tedavi alması ve tümörün evresi sağkalımı etkileyen prognostik faktörlerdir (p=0,001).

Sonuç: Yaş tek başına operasyon için kriter olmamalıdır. Özellikle seçilmiş hastalarda tedavi amacıyla anatomik rezeksiyon önerilmelidir. Bu hastalarda uzun dönem sağkalım izlenebilmektedir.

Anahtar Sözcükler: Torasik duvar rezeksiyonu, geriatrik torasik cerrahi, küçük hücreli dışı akciğer kanseri, ileri evre tümörler

Introduction

The number of people aged 70 years and over is constantly growing in the western countries. The elderly population of Turkey constituted 7.7% of the nation's total in 2013. This ratio is expected to increase up to 12.2% in 2020 (1). With aging, the incidence of cancer increases. Lung cancer has become a global health problem.

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Worldwide, approximately 1.2 million people are newly diagnosed with lung cancer annually. Accordingly, more than 1 million die of the disease every year. In their study, made between 1993 and 1996, the Southwest Oncology Group found that 25% of the population was in the geriatric age group and 39% of the geriatric population had lung cancer (2). Both patients and doctors prefer oncologic treatment approaches rather than surgery in T3 and T4 lung cancers in the geriatric age group. The most important reason for this is that comorbid diseases and post-surgery complications are seen more often in this population.

In this study, we assessed the long-term survival outcomes in patients 70 years of age and older who underwent thoracic wall resection due to non-small cell lung cancer (NSCLC) and the prognostic factors affecting morbidity.

Methods

Ethics committee approval was obtained for the study from the University of Health Sciences, Keçiören Training and Research Hospital (version number: 497). The consent of the patients included in the study was taken by the authors.

Data of patients, who underwent wall resection due to NSCLC in the department of thoracic surgery in Gazi University Faculty of Medicine between January 2007 and December 2014, were reviewed retrospectively from the data-set prepared prospectively. A thousand and forty-eight patients were operated on for NSCLC in the above-mentioned period. From these patients, 19 patients in the geriatric age group, who underwent an R0 chest wall resection, were assessed. One patient, whose data could not be obtained, was excluded from the study. The remaining 18 patients were retrospectively evaluated.

Detailed anamneses, physical examinations, electrocardiography, respiratory function tests and standard laboratory tests of the patients were reviewed. All patients had been assessed with lung X-ray, computed tomography (CT) and fiberoptic bronchoscopy before surgery. Magnetic resonance imaging (MRI) had been required for patients who were suspected of having paravertebral sulcus or vertebral or vascular invasion. Positron emission tomography (PET)/CT and cranial MRI had been performed in all patients for clinical staging and screening for distant metastasis.

PET/CT, endobronchial ultrasonography and mediastinoscopy had been used to assess the lymph node status. All patients were evaluated with mediastinoscopy before resection.

Three patients had been administered neoadjuvant therapy. All patients had undergone lobectomy and pneumonectomy together with en bloc chest wall resection. Postoperative pathological staging was done according to the 8th edition of the tumor node metastasis classification for lung cancer (3). Patients whose tumor diameter was 7 cm and above were accepted as having T3 according to the International Association for the Study of Lung Cancer (IASLC) 7th lung cancer staging. In our study, we accepted this group as T4, according to the IASLC 8th Edition (3).

The postoperative comorbid diseases were divided into three groups: endocrine disorders (diabetes and goiter), cardiac problems (hypertension, heart failure and coronary artery disease), and pulmonary problems (asthma and chronic obstructive pulmonary disease).

Major complications were assessed in the study. The complications occurring from postoperative day one to day 30 were included in the study. The complications were postoperative arrhythmia, renal failure, atelectasis, pneumonia, empyema, and bronchopleural fistula.

The patients were followed up through physical examination and thoracic CT quarterly for two years, semiannually after two years, and annually after five years.

Statistical Analysis

Statistical analysis was done using the SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). For descriptive statistics, a chi-square test was used to calculate frequency values, Student's t-test was used in independent groups to compare means, and the Mann-Whitney U test was used to compare medians. Patient survey analyses were calculated using the Kaplan-Meier method. Since the number of patients aged 80 and over was too small among the age groups for achieving statistical significance, these patients were included in the group of patients aged 75 and over. A p value of 0.05 was considered statistically significant.

Results

The mean age of the patients was 74.28±3.81 (minimum: 70, maximum: 84) years; 88.9% of them were male (n=16) and 11.2% were female (n=2). The mean number of cigarettes smoked per year was 35.9±19.1 (minimum: 0, maximum: 70) packs. The rate at which the patients quit smoking before the operation was 88.9% (n=16). The preoperative diagnosis rate was 66.7% (n=6). The distribution of demographic characteristics by the groups is shown in Table 1.

Mostly, right chest wall resections were done in the geriatric age group (61.1%, n=11). The most frequent resection type was upper right lobectomy with 55.6% (n=10) (Table 2). Of the patients who underwent chest wall resection, 27.8% (n=5) were operated due to Pancoast tumor. Four of the Pancoast tumors were right-sided, and one was left-sided.

Table 1. Distribution of demographic characteristics	
Age (year), mean ± SD	74.28±3.81
Gender, n (%)	
Male	16 (88.9)
Female	2 (11.1)
Smoking habit (packet/year), mean ± SD	35.9±19.1
Preoperative comorbidities, n (%)	
Cardiac	14 (77.8)
Pulmonary	8 (44.4)
Endocrinologic	6 (33.3)
ASA, n (%)	
2	9 (50)
3	6 (33.3)
4	3 (16.7)
ASA: American Society of Anesthesiologists, SD: Standard deviation	

Table 2. Operations involved in thoracic wall resections	
Resection types, n (%)	
Upper right lobectomy	10 (55.6)
Lower right lobectomy	1 (5.6)
Upper left lobectomy	3 (16.7)
Lower left lobectomy	1 (5.6)
Left pneumonectomy	3 (16.7)

Table 3. Clinical and pathological data of patients	
Histopathology, n (%)	
Adenocarcinoma	6 (33.3)
Squamous cell carcinoma	10 (55.6)
Other lung carcinomas	2 (11.1)
Hospitalization time (days), mean ± SD	10.56±8.02
Drainage time (days), mean ± SD	6.06±4.09
SD: Standard deviation	

A review of postoperative pathologies showed that squamous cell carcinoma was the most common with 55.6% (n=0). The mean length of hospital stay was 10.56±8.02 (minimum: 4 - maximum: 30) days, and the mean drainage time was 6.06±4.09 (minimum: 2, maximum: 18) days (Table 3). The mean tumor diameter was 5.27±2.25 (minimum: 2 - maximum: 11.5) cm. When their pathological stages were assessed in line with the IASLC 8th Edition of Staging, stage 3A was the most common in both groups. Histopathological features of the patients are shown in Table 4. Major complications were found in 50% (n=9) of patients. The most common complication was arrhythmia in 50% of cases. The features of complications are shown in Table 5.

Table 4. Histopathological characteristics	
Tumor diameter (cm), mean ± SD	5.27±2.25
N status, n (%)	
N0	9 (50)
N1	8 (44.4)
N2	1 (5.6)
8th edition of staging, n (%)	
2b	8 (44.4)
3a	9 (50)
3b	1 (5.6)
Number of removed lymph nodes, mean ± SD	23.06±11.17
SD: Standard deviation	

Table 5. Postoperative major complications	
Variables, n (%)	
Atelectasia	5 (27.8)
Arrhythmia	9 (50)
Bronchopleural fistula	2 (11.1)
Acute kidney failure	4 (22.2)
Pneumonia	5 (27.8)
Emphysema	2 (11.1)

Mortality occurred in four patients (22%) in the first 30 days. All the patients who died were those who underwent lobectomy. There was no mortality in patients who underwent pneumonectomy. The rate of mortality was significantly higher in patients with higher American Society of Anesthesiologists scores (p=0.01). While preoperative cardiac and pulmonary comorbidities were not found to be correlated with mortality, endocrinologic comorbidities were associated with a higher mortality rate (p=0.04).

The mean survival rate was 47.5±7.5 months in patients who underwent chest wall resection; the two-year survival rate was 77.9% and the five-year survival rate was 41.4% (Figure). A comparison of the factors affecting survival is shown in Table 6.

Discussion

The geriatric patient population is rapidly growing today due to advanced treatment methods and improved living conditions. The prevalence of lung cancer has increased up to 14%, particularly in those aged 80 years and over (4). In addition, lung cancers are more common in male gender in geriatric patients (4). In our study, 88.9% of patients who underwent chest wall resection were male.

Cardiopulmonary complications are among the major causes of mortality and morbidity in the geriatric age group. Pulmonary complications are seen in 20-50%

Table 6. Comparison of factors affecting survival					
	Mean survival (Months), mean ± SD	95% Confidence interval	Two-year survival (%)	Five-year survival (%)	p
Age group					
Age 70-74 (n=10)	48.8±8.4	32.1-65.4	78.8	39.4	0.90
Age >75 (n=4)	35.2±10.0	15.4-55.0	50	0	
Resection type					
Lobectomy (n=11)	48.1±8.4	31.6-64.6	81.8	43.6	0.59
Pneumonectomy (n=3)	25.5±0.3	24.8-26.1	50	NS	
Neoadjuvant treatment (n=3)	16±7.6	1.0-30.9	33.3	0	0.03
Adjuvant treatment (n=11)	56.6±7.5	7.5-41.8	90	27	
Histopathology					
Adenocarcinoma (n=5)	37.5±5.5	27.3-47.6	100	25	0.22
Squamous cell carcinoma (n=7)	60±10.5	39.9-80.1	85	64.3	
N status					
N0 (n=6)	43.6±10.9	22.1-65.1	66.7	33.3	0.001
N1 (n=7)	48±5.0	38.1-57.8	100	60	
N2 (n=1)	6	6-6	0	0	
Stage					
2B (n=5)	50.2±10.8	29.0-71.3	100	40	0.001
3A (n=8)	43.3±6.1	31.2-55.4	87.5	52.5	
3B (n=1)	6	6-6	0	0	
NS: Non significiant, SD: Standard deviation, N: Nodal					

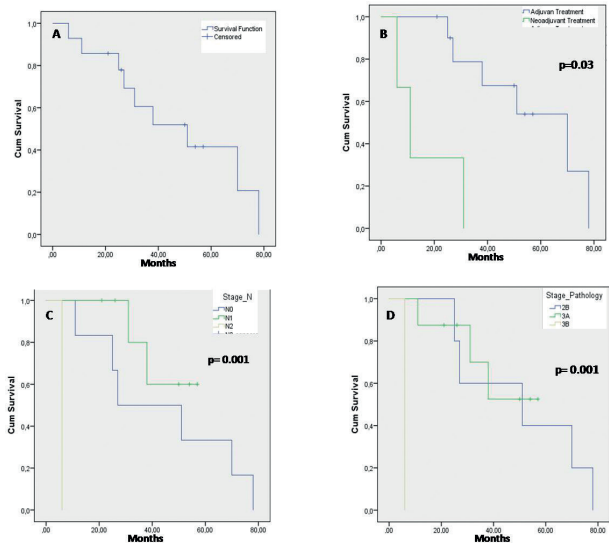

Figure. Kaplan-Meier graph of survivals
A. Median survival, B. Adjuvant and neoadjuvant treatment survival, C. N stage survival, D. 8th lung cancer pathological stage

of patients. These complications occur mostly due to preoperative pulmonary function disorders or long-term smoking. Postoperative respiratory failure or complications associated with secretion retentions are seen in patients with a restricted respiratory function reserve in the preoperative period. Lee et al. (5) have reported that the rate of major morbidity was 13% in geriatric patients. They have stressed that from these major morbidities, pneumonia, in particular, had a negative impact on the postoperative clinics of patients. Pneumonia occurred in five patients (27.8%) in our study. After pneumonia, four patients needed a mechanical ventilator and their prognosis was extremely poor. Arrhythmia was seen more frequently in patients aged 75 years and over, and this was statistically significant (p=0.01).

While lung cancer is seen more in the form of adenocarcinoma in younger people, squamous cell carcinoma is more common in patients older than 70 years. In their study of 212,709 geriatric patients with lung cancer, Owonikoko et al. (4) found that squamous cell carcinoma was the leading cancer type, involving 23% of the patients. In our study, we found that squamous cell carcinoma was the most common type with 55.6% of patients aged 70 years and over.

Japanese literature on mortality revealed no postoperative mortality in the two series conducted with those aged 80 and over (6,7). However, since the number of patients was 35, and 18 in these publications, it is difficult to make comparison between them and other papers (8). In the series where mortality was high, the incidence of stage 3 was found to be higher. Mizushima et al. (9) found in their study made in 1997 that the mortality rate was 22% after pneumonectomy in patients aged 70 and over. In our study, there was no mortality after pneumonectomy. We think that this was due to the small number of patients.

The data in the literature regarding the treatment of locally advanced NSCLC are quite inadequate. In superior sulcus tumors, the mortality rate was found to be 0-6.4% in patients under 70 years of age (10-15). The mortality rate of lung resections in the geriatric age group is 0-20% (11). In the study of Sağıroğlu et al. (16), there was no statistically significant difference in 30-day mortality between patients below and over 70 years of age (p=0.97). The mortality rate in our study was 22% (n=4). Our mortality rate in the geriatric age group was found to be higher than in the literature. The reason is that our patients had a lot of comorbidities and our sample size was small. Differing results are ranging from 24% to 66% in the literature on five-year survival rates in geriatric patients (11,17-20). In their series with 367 cases of stage 1 NSCLC, Okami et al. (17) found a five-year survival rate of 56.1%. Brock et al.

(21) found in their 20-year follow-up outcomes of stage one patients that they had a five-year survival rate of 34%. The highest five-year survival rate in the studies made with geriatric patients was found in a study by Mun and Kohno (19). In 2008, they found a survival rate of 65.9%. Some authors argued about the high rates of Kohno's survey, stating that the patients included in the study were quite selective, and smaller surgeries besides pneumonectomy were administered to the patients in the study (11). The major reasons for obtaining differing survival rates are the small number of patients and uncompleted follow-up periods. The five-year survival rate we found in our study was 41.4% in patients with T3-T4 lung cancers.

In our study, N2-positive group was found to be fewer than. other reviews. We think that the most important reason is that we performed mediastinoscopy in all patients before resection.

van Meerbeeck et al. (22) found a five-year survival rate of 33% after pneumonectomy. In our study, the two-year survival rate in patients who underwent a pneumonectomy was 50%.

Study Limitations

We found fewer risk factors and higher mortality rates compared to that in the literature because the number of patients was small in our study. The retrospective design of the study may also have affected the results because today's advanced postoperative care and surgical techniques have changed the morbidity rates. Apart from these, five-year survival rates could not be established for some patients, as their follow-up periods were not long enough. The reason for high mortality rates in the study is that our patients had lots of comorbidities.

Conclusion

We can conclude that the postoperative outcomes of patients in the geriatric age group who undergo an operation are quite favorable in experienced centers. Our findings suggest that complication rates increase as patient age advances, however, we think that these patients should be offered anatomical surgical resection because long-term morbidity and mortality outcomes are favorable in experienced centers. Appropriately selected geriatric patients should be offered anatomic surgical resection for cure. These patients can anticipate long-term survival and should not be denied surgery on the basis of age alone.

Authorship Contributions

Surgical and Medical Practices: C.B.S., A.İ.T., S.D., S.A.A. Concept: C.B.S., A.A. Design: C.B.S., A.A., A.İ.T. Data Collection or Processing: C.B.S. Analysis or Interpretation: C.B.S., S.D. Literature Search: C.B.S., A.İ.T. Writing: C.B.S., S.D.

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Hiperemezis Gravidarumda Serum İskemi Modifiye Albümin ve İskemi Modifiye Albümin/Albümin Oranının Değerlendirilmesi

Serum Ischemia-Modified Albumin Concentration and Ischemia-Modified Albumin/Albumin Ratio in Hyperemesis Gravidarum

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Öz

Amaç: Hiperemezis gravidarum (HEG) erken gebelikte gözlenen, ağır bulantı ve kusma, kilo kaybı ve nütrisyonel eksikliklerle karakterize tıbbi bir durumdur. Her ne kadar bu durumun nedeni tam olarak bilinmemekte ise de HEG patogenezinde oksidatif stresin katkısı birçok çalışmada gösterilmiştir. Bu çalışmanın amacı iskemi modifiye albüminin (İMA) ve İMA/albümin oranının (İMAO) HEG'deki tanısal rolünü araştırmaktır.

Yöntemler: Çalışma için bir hasta grup ve iki kontrol grubu oluşturuldu. Gebe kadınlar HEG (n=31) yaş, gestasyonel yaş ve vücut kitle indeksi (VKİ) uyumlu kontrol grubu (n=30) olarak ayrıldı. İkinci kontrol grubu (n=30) ise gebe olmayan yaş ve VKİ uyumlu kadınlardan oluşturuldu. Gruplardaki serum İMA, İMAO, hemoglobin, lökosit, platelet, açlık kan şekeri, albümin, üre, kreatinin, alanin aminotransferaz, aspartat aminotransferaz ve tiroid stimule edici hormon değerleri ölçüldü.

Bulgular: HEG hastalarında serum medyan İMA düzeyleri [0,55 (0,43-0,68)] gebe kontrol grubu [0,52 (0,34-0,61)] ve sağlıklı kontrol [0,48 (0,27-0,57)] grubu ile kıyaslandığında istatistiksel olarak yüksek idi (p=<0,001). İMAO düzeyleri de benzer şekilde HEG hastalarında istatistiksel olarak yüksek saptandı. İMA ve İMAO seviyeleri ile C-reaktif protein düzeyleri arasında korelasyon belirlendi.

Sonuç: HEG'de artmış olarak saptanan serum İMA ve İMAO düzeyleri artmış oksidatif stresin periferik yansıması olarak değerlendirilebilir.

Anahtar Sözcükler: Hiperemezis gravidarum, iskemi modifiye albümin, iskemi modifiye albümin/albümin oranı, oksidatif stres

Abstract

Aim: Hyperemesis gravidarum (HEG) is characterized by severe nausea and vomiting, weight loss and nutritional deficiency. Although exact cause of this condition is still a matter of debate, contribution of oxidative stress to pathogenesis of HEG was demonstrated in some studies. The aim of this study was to investigate the diagnostic value of ischemia-modified albumin (IMA) concentration and IMA/albumin ratio (IMAR) in HEG patients.

Methods: One patient group and two control groups were constituted. Pregnant subjects with HEG were included in HEG group (n=31) and age-, gestational age-, and body mass index (BMI)-matched healthy pregnant women in control group (n=30). The second control group was constituted from age- and BMI-matched non-pregnant women (n=30). Serum IMA, IMAR blood glucose, albumin, urea, creatinine, alanine aminotransferase and aspartate aminotransferase levels were measured in all subjects.

Results: Serum median IMA levels [0.55 (0.43-0.68)] was found to be elevated in HEG patients compared with pregnant [0.52 (0.34-0.61)] and non-pregnant controls [0.48 (0.27-0.57)] (p=<0.001). IMAR levels were also found to be significantly elevated in HEG patients compared to both control groups. According to correlation analysis, IMA and IMAR levels were only correlated with C-reactive protein levels.

Conclusion: Elevated levels of IMA and IMAR in HEG patients might be due to ischemic intrauterine environment.

Keywords: Hyperemesis gravidarum, ischemia-modified albumin, ischemia-modified albumin/albumin ratio, oxidative stress

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Giriş

Hiperemezis gravidarum (HEG) gebelik boyunca gerçekleşen tüm hospitalizasyonların 1/3'ünden sorumlu olan ve sıklıkla sıvı-elektrolit bozukluğu ve asit-baz dengesizliğine sebep olan klinik bir durumdur (1). Her ne kadar tüm gebeliklerin %70 ile %80'i arasında görülebilen gebeliğe bağlı bulantı ve kusmalar klinik olarak HEG ile benzer özellikler göstermekte ise de, HEG'de klinik tabloya sıklıkla kilo kaybı, idrarda keton pozitifliği ve dehidratasyon gibi tablolar da eşlik etmektedir (2). HEG'nin nedenini tam olarak açıklayabilecek net bir bilgi halen mevcut olmamakla birlikte, etiyoloji çoğunlukla multifaktöryel olarak değerlendirilmektedir. Günümüzde hastalık etiyopatogenezinden sıklıkla endokrin (insan koryonik gonadotropini, östradiol ve progesteron), immünolojik ve kişisel faktörler (artmış vücut ağırlığı vb.) sorumlu tutulmaktadır (3). Bunlara ek olarak lipid bozuklukları, sempatik sinir sistem aktivasyonu, hipertiroidizm, oksidatif stres yolaklarındaki aktivasyon ve *Helicobacter pylori* gibi diğer bazı patolojik faktörler hastalığın patofizyolojisinde günümüzde üzerinde sıklıkla durulan diğer faktörlerdir (4-6). Ancak tüm bu bilgilere rağmen HEG'nin klinik çeşitliliğindeki farklılıkları açıklayabilecek ve çeşitli patogenetik faktörleri tek bir çatı altında birleştirebilecek bir teori halen ortaya konmamıştır.

Gebelik döneminde gözlenen komplikasyonlarla oksidatif stres arasındaki ilişkiyi gösteren çok sayıda çalışma mevcuttur (6,7). Fait ve ark. (8) 2002 yılında yayınladıkları bir çalışmada bir antioksidan olan glutatyonun HEG'li hastalarda gebe olan ve olmayan kontrol grubu ile kıyaslandığında belirgin olarak düşük olduğunu göstermişlerdir. Düşük glutatyon seviyesi HEG'deki oksidatif stresin bir kanıtı olarak değerlendirilmiştir. Buna benzer şekilde HEG'de artmış oksidatif stres kanıtları gün geçtikçe artarak devam etmiş, ancak bunun aksini gösteren çalışmalar da literatürde kendine yer bulabilmiştir (1,7,9). Tüm bu bulgular birlikte değerlendirildiğinde HEG patogenezinde oksidatif stresin rolünü net bir şekilde söylemek halen mümkün değildir.

İskemi modifiye albümin (İMA) esas olarak akut koroner hadiselerin erken tanısı için öne sürülmüş biyokimyasal bir belirteçtir (10,11). Ancak ilerleyen dönemlerde İMA'nın inme, mezenterik iskemi, değişik kanser tipleri gibi diğer iskemik durumlarda da düzeylerinin etkilendiği saptanmıştır (12-14). Çünkü asidoz, serbest radikal hasarı ve hipoksi gibi akut iskemik bir duruma sebep olabilecek hadiselerde, albüminin N terminal ucu modifiye olmakta ve kobalt, nikel, ve bakır gibi geçişli metalleri bağlama kapasitesi azalmaktadır. Albüminin bu modifiye şekli İMA olarak adlandırılmakta ve spektrofotometrik olarak albümin kobalt bağlama testi ile ölçülmektedir (15). İMA/albümin oranı (İMAO) ise ölçülen İMA'nın serum albümin düzeyine oranlanması ile elde edilen bir değerdir. Kronik karaciğer hastalarında, karaciğerin sentez kapasitesinde azalma olacağından dolayı albümin düzeyinin düşmesine bağlı olarak İMA ölçümü yanında, daha değerli bir veri olabileceği düşünülerek bazı çalışmalarda İMAO da hesaplanmıştır (16,17). Gebelik döneminde ve HEG'de serum albümin düzeylerinin etkilenebileceği göz önüne alındığında İMAO'nun bu grup hastalarda faydalı olabileceği düşünülebilir. Biz bu çalışmamızda bir oksidatif stres durumu olan HEG'de serum İMA ve İMAO düzeylerinde herhangi bir değişiklik olup olmadığını saptamayı amaçladık.

Yöntemler

Hastalar

Bu çalışma için Çanakkale Onsekiz Mart Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan onay alınmış (onay no: 2017-20) ve çalışma katılımcılardan onam formu alındıktan sonra Helsinki deklarasyonuna uygun bir şekilde yapılmıştır. Çalışmaya dahil edilen hastalar; kadın hastalıkları ve doğum kliniğine 6-13 haftalık gebe iken başvurarak HEG tanısı alan hastalar arasından seçilmiştir. Kontrol grubu olarak hasta grup ile yaş ve vücut kitle indeksi (VKİ) açısından uyumlu iki grup belirlenmiştir. Birinci kontrol grubu hasta grup ile VKİ, yaş ve gestasyonel yaş açısından uyumlu gebelerden seçilmiş, ikinci kontrol grubu ise hasta grup ile yaş ve VKİ açısından uyumlu gebe olmayan sağlıklı bireylerden seçilmiştir.

HEG tanısı koymak için kullanılan kriterler şu şekilde belirlenmiştir; gebelik dönemi boyunca devam eden şiddetli bulantı ve kusma, %5'den fazla kilo kaybı ve idrar tetkikinde ketonüri saptanmasıdır. Çalışmadan dışlanma kriterleri ise ovülasyon indüksiyonu, molar gebelik, iskemik kalp hastalığı hikayesi, diabetes mellitus, çoğul gebelik, yeme bozuklukları, sigara kullanımı, tiroid hastalıkları ve kronik hastalık hikayesidir. Çalışmaya dahil edilen hastaların yaş, gestasyonel yaş, gravida, parite, VKİ gibi demografik verileri bu çalışma için dizayn edilen veri formlarına kaydedildi. Gestasyonel yaş son menstrüel kanamanın ilk günü belirlenerek saptandı ve ultrasonografi ile konfirme edildi. VKİ değerleri çalışmaya dahil edilen her hasta için kilo/boyun karesi şeklinde hesaplandı. Kan örnekleri antekübital venden antikoagülan kullanılmadan ve bir gece açlık sonrası alındı. Hemogram, eritrosit sedimentasyon hızı (ESH), C-reaktif protein (CRP) düzeyleri ve temel biyokimyasal testler hastane hematoloji ve biyokimya laboratuvarında gerçekleştirilerek kayıt altına alındı.

Serum İskemi Modifiye Albümin Ölçümü

İMA düzeyi ölçümü Bar-Or ve ark.'nın (18) tanımladığı kolorimetrik metod kullanılarak yapıldı. Ölçüm için 200 µl hasta serumu cam tüplere kondu ve 50 µl %0,1 $CoCl_2.6H_2O$ (Sigma-Aldrich, Missouri, USA) tüplere eklendi. Bu karışım yeterli kobalt albümin bağlanmasını sağlamak

için 10 dakika boyunca inkübe edildi. Sonrasında 50 µl 1,5 mg/m dithiothreitol (DTT) renklendirmek için bu karışıma eklenerek spektrofotometrede 470 nm'de ölçüm yapıldı. Numuneler, DTT içermeyen kontrol tüpleri ile mukayese edildi ve sonuçlar absorbans ünitesi (ABSU) olarak belirtildi.

İskemi Modifiye Albümin/Albümin Oranı Ölçümü

İMA düzeyleri serum albümin düzeylerine bölünerek İMAO düzeyleri hesaplandı. İMAO düzeyleri ABSU/g (absolü ünite/gram) şeklinde belirtildi.

İstatistiksel Analiz

Veri istatistiği SPSS (Sosyal Bilimler için İstatistiksel Paket) 18.0 paket programı kullanılarak yapıldı. Değişkenlerin normal dağılıma uyup uymadıkları analitik metotlar kullanılarak araştırıldı. Normal dağılıma uyan değişkenler ortalama ± standart sapma, normal dağılıma uymayan değişkinler ise medyan (minimum-maksimum) şeklinde verildi. Üç grubun analiz edildiği durumlarda normal dağılıma uyan değişkenler One-Way ANOVA metodu kullanılarak, normal dağılıma uymayan veriler ise Kruskal-Wallis testi kullanılarak analiz edildi. P<0,05 istatistiksel olarak anlamlı kabul edildi.

Bulgular

Bu çalışmaya HEG tanısı almış 31 gebe kadın, benzer gebelik haftasında herhangi bir şikayeti olmayan 30 gebe kadın ve 30 gebe olmayan, sağlıklı kadın dahil edilmiştir. HEG hastalarının, gebe ve gebe olmayan kadınların medyan yaşları sırasıyla 27 (19-36), 27 (19-40) ve 28 (17-35) olarak saptanmıştır (Tablo 1). Çalışmaya dahil edilen hastalar arasında yaş, gestasyonel yaş ve VKİ açısından istatistiksel olarak anlamlı fark saptanmamıştır.

Çalışmaya alınan hastalar kan sayımı ve biyokimyasal parametreler açısından değerlendirildiklerinde beyaz küre değerleri dışında aralarında anlamlı bir fark saptanmamıştır (Tablo 1). HEG hastalarında lökosit değerleri anlamlı bir şekilde yüksek saptanmıştır (p=<0,001). HEG hastalarında serum medyan İMA düzeyleri 0,55 (0,43-0,68) olarak saptanmış, gebe kontrol grubu ve sağlıklı kontrol grubunda bu değerler sırasıyla 0,52 (0,34-0,61) ve 0,48 (0,27-0,57) olarak bulunmuştur (Tablo 2). Serum İMA düzeyleri kontrol grupları ile kıyaslandığında HEG hastalarında belirgin bir şekilde yüksek saptanmıştır (p<0,001) (Şekil 1). Benzer şekilde HEG hastalarında İMAO düzeyleri her iki kontrol grubu ile kıyaslandığında anlamlı olarak yüksek saptanmıştır (p<0,001) (Şekil 2). Çalışma gruplarındaki CRP ve sedimentasyon değerlerinin ortalamaları Tablo 2'de verilmiştir.

HEG hastalarında İMA ve İMAO düzeylerinin diğer belirteçlerle korelasyonunun incelenmesi sonucunda sadece CRP ile korelasyon saptanmış (İMA ile r=0,249, p=0,020; İMAO ile r=0,353, p=0,001), diğer belirteçlerle İMA ve İMAO arasında herhangi bir korelasyon saptanmamıştır (Tablo 3).

Tartışma

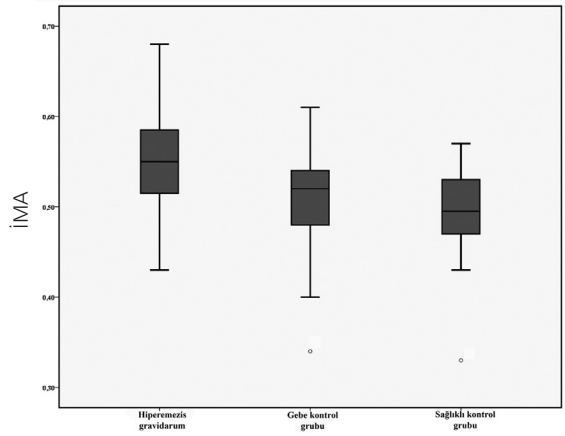
Bu çalışmada, HEG nedeniyle takip edilen hastalarda serum İMA ve İMAO düzeyleri kontrol grubu ile kıyaslandığında istatistiksel olarak yüksek olduğu saptandı. Bununla birlikte İMA ve İMAO düzeylerinin enflamatuvar belirteçlerle arasındaki korelasyon incelendiğinde sadece CRP ile korelasyon olduğu belirlendi. Her ne kadar sadece İMA ve İMAO düzeyleri bakılarak HEG'deki oksidatif stres durumu hakkında net bir yorum yapılması doğru olmasa da, bulgularımız HEG'de gözlendiği belirtilen oksidatif stres durumunun İMA düzeyleri ile ilişkili olabileceği tezini desteklemektedir.

İskemi, asidoz, artmış serbest radikaller ve hipoksi gibi durumlarda arttığı saptanan İMA'nın değişik hastalıklardaki rolünü aydınlatmaya yönelik çok sayıda çalışma mevcuttur. Bu çalışmaların temelinde de İMA'nın akut koroner hadiselerde troponin ve elektrokardiyografi ile birlikte %95'lik bir tanısal değerinin olduğunu gösteren literatür verileri yatmaktadır (19,20). Akut koroner hadiselerde tanısal değeri tartışmasız olarak saptanan İMA'nın kadın doğum pratiğindeki kullanımı ile alakalı kanıtlar son 10 yılda giderek artmaktadır. Prefumo ve ark. (21) 2007 yılında erken gebelikte maternal serum İMA düzeylerinin arttığını saptamışlar ve bunun normal trofoblast gelişiminin hipoksik intrauterin ortam ile ilişkili olduğunun bir kanıtı olduğunu belirtmişlerdir. Benzer şekilde Ustün ve ark. (22) serum İMA düzeylerinin preeklampsi şiddeti ile ilişkili olduğunu, cut-off değeri olarak 0,31 kullanıldığında %80 sensitivite ve %77,8 spesifisite ile preeklamptik gebeliklerin saptanabileceğini belirtmişlerdir. Bu bulgulara zıt olarak Iacovidou ve ark. (23) normal ve intrauterin gelişim geriliği gösteren gebeliklerde kord kanındaki İMA düzeylerinin farklı olmadığını yayınladıkları bir çalışma ile göstermişlerdir. Perinatoloji pratiğinde İMA'nın rolü ise yakın zamanlı yayınlanan bir derlemede ayrıntılı bir şekilde incelenmiştir (24). Yarcı Gürsoy ve ark. (24) preeklampsi, diabetes mellitus ve intrauterin büyüme geriliği gibi komplikasyonlarla seyreden gebeliklerde, İMA seviyelerinin yükseldiğine dair yeterli kanıtın mevcut olduğunu belirtmişler, ancak inceledikleri çalışmalardaki metodolojik bazı sorunlar nedeniyle bu çalışmaların sonuçlarına dikkatli yaklaşılması gerektiğini belirtmişlerdir.

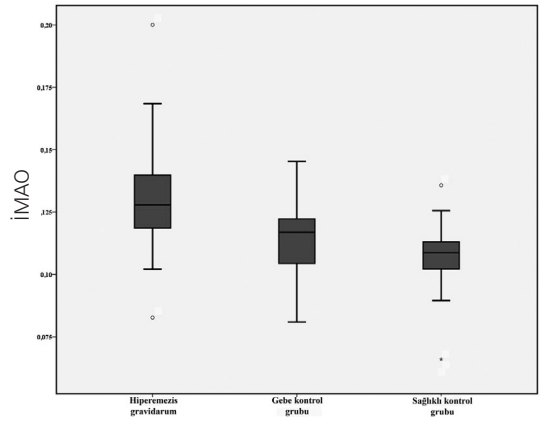
Komplike gebeliklerde İMA'nın rolünü araştıran çok sayıda çalışmanın mevcudiyetine rağmen, literatürde HEG hastalarında İMA düzeyini inceleyen tek bir çalışma mevcuttur (7). Bu çalışmaya 45 HEG hastası ve bu hastalarla yaş ve VKİ açısından uyumlu 45 sağlıklı gebe kontrol hastası dahil edilmiştir. HEG hastalarında serum İMA düzeyi kontrol grubu ile kıyaslandığında anlamlı

şekilde yüksek saptanmıştır. Erken gebelik döneminde uterus içinde gelişen hipoksik ortamın bu yükselmenin temel nedeni olduğu belirtilmiştir. Bununla birlikte yazarlar uterus içindeki hipoksik ortam sonucu ortaya çıkan oksidatif stresin, fizyolojik trofoblast gelişimi için önemli olduğunu da belirtmişlerdir. Benzer şekilde çalışmamızda, serum İMA düzeyleri kontrol grupları ile kıyaslandığında belirgin derecede yüksek saptandı. Buna ek olarak İMAO düzeylerinin de HEG hastalarında yüksek olduğunu belirledik. HEG gibi malnütrisyona neden olabilecek ve buna sekonder hipoalbüminemi gelişebilecek hastalarda İMAO düzeylerinin İMA düzeylerinden daha önemli olabileceği göz önüne alındığında çalışmamızın önemi daha da artmaktadır.

Karaciğer hastalıkları ve şiddetli HEG gibi klinik durumlarda serum albümin düzeyleri değişkenlik gösterebilir (25-27). Bu nedenle HEG hastalarında İMA düzeylerinin dışında İMAO düzeylerinin de değerlendirilmesi klinik olarak büyük önem arz etmektedir. İMAO, ölçülen İMA'nın serum albümin düzeyine oranlanması ile elde edilen sayısal bir değerdir. Teorik olarak serum albümin konsantrasyonunun düşük olduğu durumlarda albümin



Şekil 1. Çalışma ve kontrol grubu hastalarındaki İMA düzeylerinin box-plot olarak prezentasyonu
İMA: İskemi modifiye albümin



Şekil 2. Çalışma ve kontrol grubu hastalarındaki İMAO düzeylerinin box-plot olarak prezentasyonu
İMAO: İskemi modifiye albümin/albümin oranı

Tablo 1. Çalışmaya dahil edilen hasta ve kontrol gruplarının demografik özellikleri

	Hiperemezis gravidarum (n=31)	Gebe kontrol grubu (n=30)	Sağlıklı kontrol grubu (n=30)	p
Yaş (yıl)*	27 (19-36)	27 (19-40)	28 (17-35)	0,683
VKİ (kg/m²), ort ± SS	22,11±3,04	23,19±3,92	21,41±4,02	0,419
Gestasyonel yaş (hafta), ort ± SS	9,16±1,09	10,12±1,56	-	0,765
Gravida (medyan, min-maks), ort ± SS	1,42±0,27	1,62±0,32	-	0,622
Hemoglobin* (g/dL)	12,5 (9,7-14,4)	12,7 (10,8-13,9)	12,8 (10,2-15,1)	0,192
Lökosit* (/mm³×10³)	8,4 (6,7-13,2)	8,1 (6,3-12,9)	6,6 (4,1-10,5)	<0,001
Platelet* (/mm³×10³)	252 (115-409)	258 (168-321)	248 (163-455)	0,809
Glukoz (mg/dL)*	90 (73-121)	97 (70-120)	96 (81-134)	0,706
Albümin (g/dL)*	4,3 (3,4-5,4)	4,4 (3,9-4,9)	4,5 (4,2-5,0)	0,501
ALT (U/L)*	11 (7-1140)	12 (7-174)	13 (7-76)	0,231
AST* (U/L)	15 (11-52)	17 (10-56)	17 (12-42)	0,159
TSH (µIU/mL)	1,37 (0,1-7,3)	1,01 (0,2-4,7)	1,62 (0,18-5,9)	0,161
Üre (mg/dL)*	18 (9-33)	17 (13-26)	20 (12-34)	0,069
Kreatinin (mg/dL)*	0,7 (0,6-0,9)	0,7 (0,6-0,9)	0,7 (0,6-1,0)	0,765

VKİ: Vücut kitle indeksi, ALT: Alanin aminotransferaz, AST: Aspartat aminotransferaz, TSH: Troid stimule edici hormon, ort: Ortalama, SS: Standart sapma
*Ortanca (minimum-maksimum) olarak belirtilmiştir

Tablo 2. Çalışmaya dahil edilen hastaların oksidan ve enflamatuvar belirteç düzeyleri				
	Hiperemezis gravidarum (n=31)	Gebe kontrol grubu (n=30)	Sağlıklı kontrol grubu (n=30)	p
İMA	0,55 (0,43-0,68)	0,52 (0,34-0,61)	0,48 (0,27-0,57)	<0,001
İMAO	0,13 (0,08-0,20)	0,12 (0,08-0,015)	0,11 (0,06-0,14)	<0,001
CRP (mg/L)	4,1 (0,3-42)	3,5 (0,5-14)	1,00 (0,2-14,6)	0,005
ESH (mm/h)	14 (2-47)	14 (2-44)	12,0 (2-57)	0,302

İMA: İskemi modifiye albümin, İMAO: İskemi modifiye albümin/albümin oranı, CRP: C-reaktif protein, ESH: Eritrosit sedimentasyon hızı
*Tüm değerler ortanca (minimum-maksimum) olarak belirtilmiştir

Tablo 3. Hiperemezis gravidarum hastalarında iskemi modifiye albümin ve iskemi modifiye allbümin/albümin oranı; düzeylerinin diğer belirteçlerle korelasyonunun incelenmesi			
	CRP	ESH	WBC
İMA			
r	0,249	0,122	0,199
p	0,020	0,259	0,064
İMAO			
r	0,353	0,211	0,209
p	0,001	0,063	0,052

İMA: İskemi modifiye albümin, İMAO: İskemi modifiye allbümin/albümin oranı, CRP: C-reaktif protein, ESH: Eritrosit sedimentasyon hızı, WBC: Beyaz kan hücresi

molekülüne daha az kobalt bağlanmakta ve kobalt iyonları ile DTT arasında daha yoğun bir tepki oluşmaktadır. Sonuç olarak da daha düşük albümin konsantrasyonları, aynı hastalarda oransal olarak daha yüksek İMA düzeylerine sebep olabilmektedir. Bu nedenle biz bu çalışmamızda İMAO düzeylerinin de kullanılmasının uygun olacağına karar verdik. Bu çalışmanın sonuçlarına benzer şekilde oksidatif stres durumlarında İMAO düzeylerinin yükseldiğini gösteren birçok kanıt mevcuttur (28-30). D'souza ve ark.'nın (28) preeklamptik gebeler üzerinde yaptıkları yakın zamanlı bir çalışma bu açıdan son derece önemlidir. Preeklamptik gebelerin serum ve tükrüklerinde saptanan artmış İMAO düzeyleri preeklampsi patogenezinde oksidatif stresin rolünü bir kez daha ortaya koymuştur. Bununla birlikte bu çalışmada serum İMAO düzeyi ile fetal doğum ağırlığı arasındaki negatif korelasyon dikkati çekmiştir. Yazarlar plasental kan akımındaki bozulmanın sebep olduğu oksidatif stres yolaklarının preeklamptik gebelerdeki fetal büyüme geriliğinin nedenlerinden bir tanesi olduğunu ve bu çalışmanın sonucuna dayanarak İMAO'nun komplike gebeliklerde tanısal bir belirteç olabileceğini belirtmişlerdir.

HEG patogenezinde suçlanan bir diğer faktör de enflamasyondur (31,32). Yoneyama ve ark. (33) HEG hastalarında enflamasyonu değerlendirmek için bu hastaların plazmalarında adenozin, norepinefrin ve tümör nekroz faktörü (TNF)-alfa düzeylerini incelemişlerdir. HEG hastalarındaki TNF-alfa düzeylerindeki artışlar enflamasyon açısından anlamlı kabul edilmiştir. Benzer şekilde Kaplan ve ark. (34) da sitokin seviyelerinin HEG hastalarında yükseldiğini belirtmişlerdir. Enflamasyon belirteci olarak CRP düzeylerinin kullanıldığı çalışmalarda, CRP düzeylerinin HEG hastalarında yükseldiği net bir şekilde ortaya konmuştur (31,35). Engin-Ustun ve ark. (35) tarafından yapılan bu çalışmalardan birinde HEG hastalarında serum vaspin seviyelerinin CRP'ye benzer bir şekilde yükseldiği gösterilmiş, bunun vaspinin fetal üretimine bağlı olabileceği belirtilmiştir. Biz de bu çalışmamızda HEG hastalarında kontrol grubu ile kıyaslandığında CRP düzeylerinde anlamlı bir yükseklik saptadık. Bunun HEG hastalarında süregelen subklinik enflamasyonun bir göstergesi olduğu ve hastalık şiddeti ile alakalı olabileceğini düşünmekteyiz.

Bu çalışma literatürde İMA ve İMAO'nun HEG hastalarında birlikte değerlendirildiği ilk çalışmadır. Her ne kadar Sari ve ark. (7) yakın zamanlı yayınlanan bir çalışmalarında HEG hastalarında İMA seviyelerini değerlendirilmiş olsalar da, yazarlar çalışma gruplarında serum albümin düzeylerini belirtmemişler ve aynı zamanda konvansiyonel enflamasyon belirteçleri ile İMA arasındaki korelasyonu incelememişlerdir.

Çalışmanın Kısıtlılıkları

Tüm bunlara rağmen bizim çalışmamızın da bazı kısıtlamalarının olduğu mutlaka belirtilmelidir. Bu kısıtlamalardan en önemlisi çalışmamızın istatistiksel olarak değerlendirilmesine engel olmayan relatif hasta sayısı azlığıdır. Buna ek olarak çalışma metodumuz kesitsel olduğundan gebelik devamındaki İMA değişiklikleri incelenmemiştir. Bununla birlikte çalışmamızda oksidatif stres belirteci olarak sadece İMA ve İMAO, enflamasyon belirteci olarak ise sadece CRP ve ESH değerleri kullanılmıştır. Oksidatif ve enflamatuvar yolakların değerlendirilmesine daha fazla katkı sağlayacak belirteçlerin kullanılmasının çalışmanın kalitesini belirgin şekilde artıracağı gerçeği gözardı edilmemelidir. Son olarak ise gruplar arasında hemoglobin düzeyleri, karaciğer ve böbrek fonksiyon testleri gibi biyokimyasal parametreler açısından anlamlı bir fark saptanmamış olması tanıda zorluk çıkaran bir faktör olarak değerlendirilebilirse de, bu biyokimyasal parametrelerin tanı kriterleri arasında yer almadığı akılda tutulmalıdır.

Sonuç

Sonuç olarak bu çalışmada HEG patogenezindeki en önemli faktörlerden biri olan oksidatif stresin değerlendirilmesinde İMA ve İMAO seviyelerinin yararı gösterilmiştir. Ancak çalışmamızın sonuçları değerlendirilirken sözü edilen kısıtlılıklar da göz önüne alınmalı ve HEG patogenezinde İMA ve İMAO'nun rolünü araştıran ileri çalışmalar daha geniş hasta popülasyonları kullanılarak yapılmalıdır.

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Bone Protrusion That We Should be Aware of: Foraminal Osteophytes; Classification and Surgical Results

Farkında Olmamız Gereken Kemik Çıkıntı: Foraminal Osteofitler; Sınıflama ve Cerrahi Sonuçlar

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Abstract

Aim: The aim is to report our surgical results and techniques and to establish a common classification system for lumbar foraminal osteophytes.

Methods: Thirty-six patients who underwent surgery at our institution were included. Because of the presence of radicular pain in these patients, after magnetic resonance imaging, computed tomography (CT) of the lumbar spine was performed to confirm foraminal stenosis. Osteophytes were classified using CT images in patients with findings of foraminal stenosis related to osteophyte formation. Preoperative and postoperative visual analouge scale scores for leg pain were compared.

Results: Statistical analysis revealed significant improvements after surgical treatment. Osteophytes in the lumbar foramina were examined and classified as grades 1 to 4. A treatment algorithm for osteophyte-related radiculopathy was established.

Conclusion: Foraminal osteophytes induce radiculopathy in degenerative spine disease and have a high incidence. If there are radicular findings in degenerative lumbar diseases and problems at the foraminal level, then the size of the foramen and grade of osteophytes should be evaluated with lumbar CT. Surgical treatment can achieve significant results.

Keywords: Foraminal osteophytes, foraminal stenosis, osteophytes classification, radiculopathy

Öz

Amaç: Amaç lomber foraminal osteofitlerde cerrahi sonuçları ve tekniği paylaşıp, ortak bir sınıflama oluşturmak ve tedavi algoritması belirlemektir.

Yöntemler: Opere ettiğimiz 36 hasta çalışmaya dahil edildi. Radiküler ağrıları olan ve lomber manyetik rezonans görüntülemede foraminal stenozu olan hastalara lomber bilgisayarlı tomografi (BT) çekimi yapıldı. Osteofit formasyonuna bağlı foraminal stenozu olan ve tarafımızca buna bağlı olarak ameliyat edilen hastalarda BT görüntüleri kullanılarak belirli kriterlere göre osteofitler sınıflandırıldı. Preoperatif ve postoperatif bacak visual analog skala değerleri karşılaştırıldı.

Bulgular: İstatistiksel analizde cerrahi sonrasında anlamlı iyileşme gözlendi. Ameliyat ettiğimiz hastalarda lomber foramendeki osteofitler belirli kriterlere göre sınıflandırıldı. Sınıflama grade 1'den grade 4'e kadar düzenlendi. Radikülopati nedeni olan osteofitler için bir tedavi algoritması düzenlendi.

Sonuç: Foraminal osteofitler dejeneratif omurgada radikülopati nedenidir ve önemli oranda görülürler. Dejeneratif lomber omurgada eğer radiküler bulgular var ise ve foramen seviyesinde problem görülüyor ise lomber forameni değerlendirmek ve osteofit derecesini görmek için lomber BT gerekecektir. Cerrahi tedaviler önemli sonuçlara ulaşabilmektedir.

Anahtar Sözcükler: Foraminal osteofitler, foraminal darlık, osteofit sınıflaması, radikülopati

Introduction

Osteophytes develop because of degeneration in the bone surfaces, and osteophytes in the spine are regarded as both a result of degeneration and a defensive mechanism. The occurrence of osteophytes during degeneration due to aging is increasing. Osteophytes in the lumbar region are occasionally encountered by clinicians, but most related studies focus on the anterior

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osteophytes and their effects. Posterolateral osteophytes and their clinical effects at the foraminal level, which can cause neural compression, have not been examined in any study to date. In this study, we evaluated patients treated for osteophytes at the foraminal level and developed a grading system for osteophytes based on our findings. We also described our surgical technique for foraminal osteophytes, which are a cause of radicular symptoms.

Methods

The study was retrospective. Ethical approval from relevant institution and informed consents from patients were obtained. We included patients with radiculopathy who were evaluated using both magnetic resonance imaging (MRI) and computed tomography (CT) of the lumbar spine and underwent surgery for foraminal osteophytes on one level. Patients who did not benefit from conservative treatment and had to undergo surgical treatment were also included.

We employed the following criteria for patient selection:

1. No soft tissue-disc appearance to explain radicular findings,
2. No significant angulation in the coronal plane,
3. No additional bone pathology (such as rheumatoid arthritis, osteoporosis, and ankylosing spondylitis),
4. No listhesis to narrow foramen,
5. Surgical treatment for single level foraminal osteophytes.

We included 36 patients in the study and assessed 360 lumbar foramina on sagittal CT images in the classification phase.

The following parameters were used for classification:

1. Bone spur size,
2. Corpus and end plate sclerosis,
3. Loss of height at the intervertebral disc on CT images.

The age range for patients was between 32 and 87 years (average 56.4 years). Further, 26 patients were female and 10 were male. The mean preoperative and postoperative visual analouge scale (VAS) values for leg pain were compared. The mean length of hospital stay was 1.8 days, and the mean postoperative follow-up period was 25.2 (18-54 months) months.

Statistical Analysis

For statistical analysis of this study, Statistical Package for Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA) was used. Data were calculated with the help of computer, analysis was performed using the paired Samples t-test. A p value of less than 0.0001 was considered statistically significant.

Results

The mean preoperative and postoperative VAS values for leg pain were 7.864±1.322 and 2.205±1.212 ($p<0.0001$) (Table 1). Surgical treatment was highly effective in relieving radicular complaints. Foraminal distributions for patients were as follows: twenty nine L5, five L4, one L2, and 1 L3.

After surgical treatment, one patient experienced temporary causalgia due to root dermatome decompression in the foramen and spontaneously recovered within a few days.

The lumbar foramina were examined for all patients, and osteophytes were graded. Measurements using sagittal CT revealed that the foramen narrowed due to an osteophytic spur on the sagittal plane. A collapsed intervertebral disc was also the second leading cause of foraminal narrowing. Osteophytes were classified as follows:

Grade 1: Osteophytes appeared to disrupt the integrity of the bone surface. No narrowing of the foramen was observed at the sagittal plane. Foraminal height was unaffected, and intervertebral disc distance was generally preserved (Figure 1).

Grade 2: Osteophytes protruded from the bone surface. Sclerotic surfaces were sometimes visible. The integrity of the foramen had begun to deteriorate in the sagittal plane, but the foramen was not significantly narrow (Figure 2).

Grade 3: Narrowed foramen due to osteophytes was apparent. The transverse diameter of the foramen at the sagittal plane was smaller by ≥50%.

The bone spur was conspicuously protuberant. Sclerosis could be seen, and the intervertebral disc had nearly collapsed (Figure 3).

Grade 4: Osteophyte duplicated the foramen. The integrity of the foramen had completely deteriorated in the sagittal plane. There was definite collapse at the intervertebral disc space. Foraminal stenosis was evident due to a collapse of the disc distance, and "foraminal duplication" could be seen (Figure 4).

We also recorded the surgical techniques used. For 12 patients, the foraminal osteophyte was extended in the lateral direction according to the facet joint, and stabilization was performed because of shaving/excision of the facet joints.

Table 1. Comparison of visual analouge scale values for leg pain between preoperative and postoperative periods

	Mean ± standard deviation	p
Preoperative VAS for leg pain	7.864±1.322	<0.0001
Postoperative VAS for leg pain	2.205±1.212	

VAS: Visual analouge scale

Figure 1. Grade 1 osteophyte

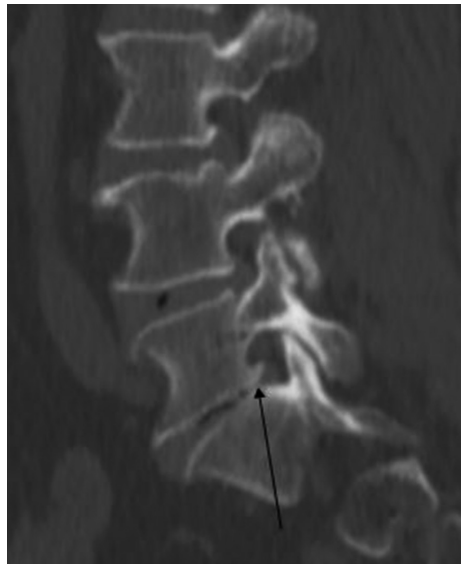


Figure 3. Grade 3 osteophyte

Figure 2. Grade 2 osteophyte

Figure 4. Grade 4 osteophyte

Decompression (foraminotomy+osteofitectomy) was sufficient for 24 patients (Table 2), and radicular symptoms decreased in all patients after treatment.

Case 1

A 44-year-old female patient presented with severe pain in her left leg (VAS 9) and foot drop after a long trip with prolonged sitting. Lumbar MRI of the patient, who previously underwent surgery for left L5-S1 disc herniation, showed compression at the left foraminal level of the L5 root. Soft disc herniation was not considered due to the collapse of the intervertebral disc, and lumbar CT was performed. A grade 3 osteophyte originating from the upper end plate (lower border of L5 corpus) was observed on lumbar CT. She was injected with a local anesthetic (2 cc 0.25% bupivacaine) in the left L5 foramen. Once the pain temporarily improved, she underwent surgical treatment for severe motor deficits. After osteophyte resection, she experienced significant improvements in motor deficits and pain (Figure 5). Postoperative leg pain score was 1 at the first month.

Case 2

This 48-year-old male patient was receiving medical treatment (gabapentin, for 12 years) for long-term low back and left leg pain. He underwent lumbar MRI due to

complaints of increased pain (VAS for left leg pain, 10). Foraminal stenosis was observed in the left L5 foramen. Due to reduction in the intervertebral disc distance, the problem was considered to be related to osteophytes, and the patient underwent lumbar CT. A grade 3 osteophyte in the left L5 foramen was observed on lumbar CT (Figure 6). Transforaminal injection (2 mL 0.25% bupivacaine+40 mg methylprednisolone acetate) was administered firstly because of the absence of neurodeficits. Surgical treatment was planned for the patient when pain control could not be achieved. Because he suffered from chronic low back pain and lateralization of the osteophyte according to the facet joint, facetectomy and osteophyte resection were performed along with stabilization. Postoperative VAS score for leg pain was 2 at the first month. He discontinued the long-term medical treatment (gabapentin) on postoperative day three.

Surgical Technique

The patient was placed in the prone position under general anesthesia. Paravertebral muscles were laterally stripped on the side of the surgery. The root was found after laminotomy or hemilaminectomy at the operation side. The lamina at the same location as the root (e.g., L5 laminotomy for L5 root decompression) was excised upwards. After the root was found, it was laterally followed. The foramen narrowed due to the collapse of the intervertebral space and osteophyte. The bone protrusion—osteophyte—was fractured and excised using an appropriately sized osteotome. The osteotome was tilted from the medial to the lateral direction in an attempt to break the bone protrusion (Figure 7). Few important points should be noted at this stage:

1. If the osteophyte is more laterally located than the anterior articulation point of the facet joint, then resection may be inadequate and excising the facet joints may be necessary. Adding stabilization at this stage will prevent possible instability during the postoperative period.

2. Removal of the bony protrusion in one piece while breaking the osteotome will help ensure complete decompression. It is difficult to remove lateralized portions piece by piece, but removing the spur with osteotome in one piece may enable unblock extraction and complete decompression without excision of the facet joint.

3. The placement of the facet joint according to the sagittal plane is also important for preserving the facet joint. Preservation of sagittal orientated facet joints is more difficult because of the angulation of facet articulation faces.

Generally, the contused root rapidly recovers after decompression. If no further intervention is needed, then the surgery is terminated.

Discussion

Vertebral osteophytes depend on degeneration of the nucleus pulposus in the intervertebral discs. Over time, degeneration of the nucleus pulposus leads to a loss of

Table 2. Distribution of patients according to foraminal levels and osteophyte grades

	Grade 2	Grade 3	Grade 4	Total
Number of cases	2	29	5	36
Stabilization	1*	8**	3	12
L2 foramen	1	–	–	1
L3 foramen	1	–	–	1
L4 foramen	–	5	–	5
L5 foramen	–	24	5	29

*This patient had osteophytes in the L2 foramen. **Four patients in this group had osteophytes in the L5 foramen, and other four patients had osteophytes in the L4 foramen

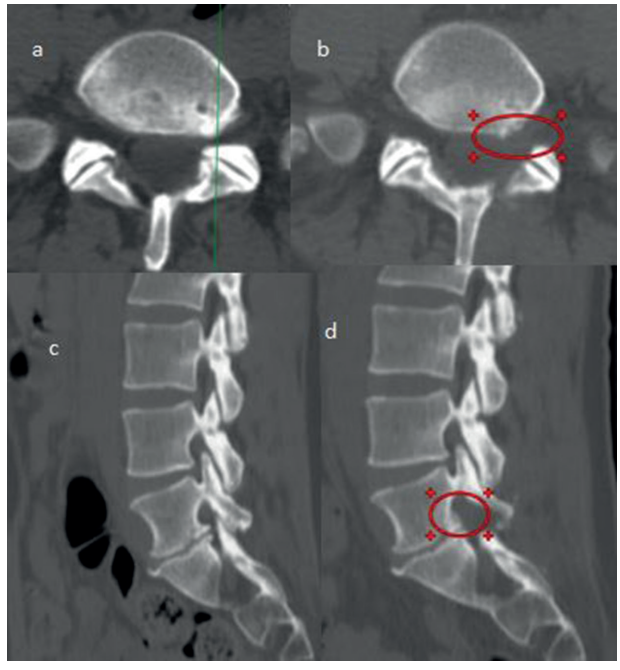


Figure 5. a) Osteophyte formation can be observed in the L5 left foramen. b) Postoperative axial image shows decompression, indicating that the foramen was expanded. Decompression was performed with hemilaminectomy and osteophytectomy. Osteophytic spur can be seen at the medial side of the vertical red line (a) which cross from the anterior point of articulation faces of facet joint. Therefore, the facet joint could be protected. Preoperative (c) and postoperative (d) sagittal computed tomography images also showed differences after surgical treatment. The patient's complaint of left leg pain dramatically decreased after surgery

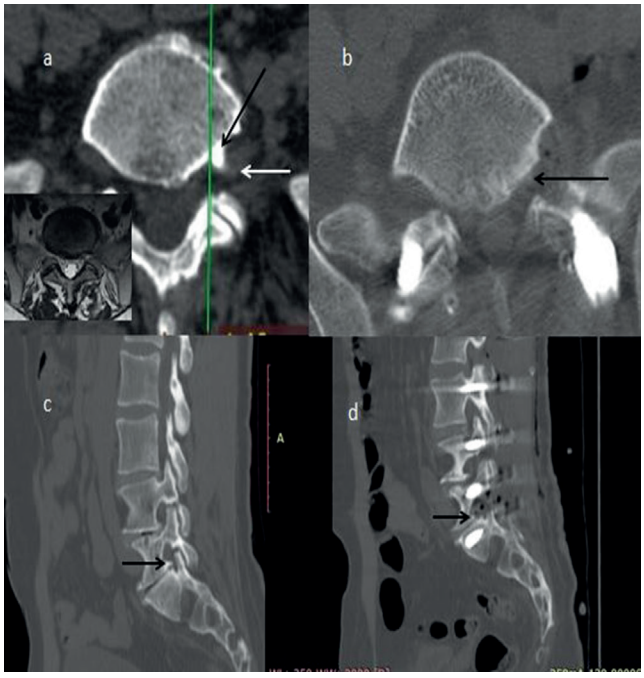


Figure 6. a) Axial magnetic resonance and computed tomography (CT) images show how the root (white arrow) was compressed by a grade 3 osteophyte (black arrow). CT image shows that this is purely osseous pathology. b) Black arrow in postoperative axial CT section shows decompression. An osteophytic spur can be seen on the lateral side of the vertical red line, (a) which crosses from the anterior point of the articulation faces of the facet joint. Facetectomy and osteophytectomy were performed for L5 root decompression. In addition to facetectomy, the patient was stabilized because of chronic low back pain. Black arrows in preoperative (c) and postoperative (d) sagittal CT sections show differences after surgical treatment. Left radicular pain completely regressed

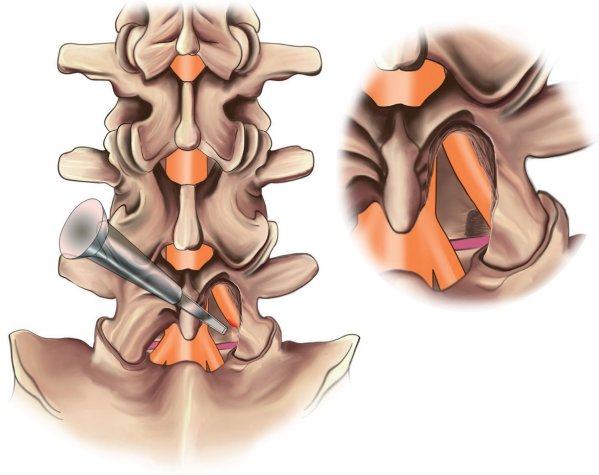


Figure 7. Surgical opening, osteophyte resection, nerve roots, and post-decompression view

intervertebral disc height and diminished load-sharing capacity. Osteophytes occur due to an attempt to increase the weight distribution surface.

Reduced disc height is also associated with intervertebral disc calcification (1,2).

Numerous reports have been published discussing osteoarthritis in extremities that concern orthopedists. Some of these involve narrowing of the joint space, bone sclerosis, and hypertrophy (3,4). We conducted our study based on similar changes in the vertebrae. Pye et al. (5) have shown that increased osteophyte formation is associated with decreased disc space, but the level of collapse of the intervertebral disc is not always correlated with the degree of osteophyte formation (1,6).

Osteophytes can form at all levels of the lumbar vertebrae. Previous studies have shown that the probability of osteophyte formation above a certain age is very high and that osteophytes can be found at all levels. Osteophytes form at inappropriate locations on the body and, therefore, compress adjacent tissues.

Anteriorly located osteophytes have always been of interest. Patients with associated vascular compression symptoms have been reported (7-9). Posteriorly located osteophytes cause neural compression.

No studies to date have reported on posterolateral osteophytes that can develop in the foramen. This report describes the first classification system for foraminal osteophytes and outcomes of surgical treatments.

Osteophytes are found 100% in the elderly, this indicates a necessity for better understanding of the associated effects.

Neurosurgeons are often interested in neural decompression and foraminotomy. In addition to soft tissue excision (i.e., disc, flavum), it is necessary to recognize that osteophytes can cause serious foraminal compression at the posterolateral side of the corpus. Therefore, the development of a common classification system is necessary.

Various classification systems for vertebral osteophytes have been reported. However, none of these systems have considered the foraminal pressure (except Lee's study, but it is not directly related to osteophytes), and they are mostly related to the shape and extent of osteophytes. Nearly all of these classification systems were applied to anteriorly located osteophytes. We developed a classification system by examining osteophytes in the foramen and consequences of these osteophytes.

The first comprehensive study on vertebral osteophytes was conducted by Nathan (10) and involved anterior claw osteophytes. Later studies progressed as extensions of this study. Vertebral osteophytes were later classified as traction, claw, or mixed type by McNAb in 1971 (11).

He suggested that osteophytes protrude 2 mm from the vertebral corpus. Thereafter, different studies were conducted to investigate the severity and orientation of the protrusion of osteophytes from the surface (12-14).

Yuichi Kasai's study also classified anterior vertebral osteophytes according to their orientation. This classification, which is based on the association of spurs from the lower and upper end platelets, does not provide new data on neural compression related to osteophytes (12).

The appearance of osteophytes indicates a deterioration of stability and is thought to be an attempt to provide stability. Even, it has even been shown that anterior osteophytes are regressed in instrumented patients (15). However, some surgeons have observed that posterior or posterolateral osteophytes, which we studied here, do not regress (16,17). Osteophytes limit movement and cause pain, and their excision leads to an increase in lumbar movement. In addition, foraminal osteophytes may cause neural compression, and if they do not benefit from conventional treatments, then excision of osteophytes will induce recovery from radicular complaints. This procedure is known as cheilectomy in the orthopedic community and should be called foraminal osteophytectomy for the lumbar vertebra. There was a positive correlation between the size of lumbar vertebral osteophytes and age of patients. Some studies have indicated that osteophytes are caused by aging changes. Some reports even estimate age according to the osteophyte rating (18-20). According to Stewart (14), there is a 75% probability of osteophyte formation in patients aged >20 years and 100% probability of vertebral osteophyte formation in patients aged >40 years. According to Chanapa et al. (21), patients aged >35 years definitely have vertebral osteophytes. Our study included patients who underwent surgical treatment at nearly 30 years of age. We observed an increase in osteophyte ratios as the age increased. The study by Chanapa et al. (21) is the largest study on lumbar osteophytes. In the study, lumbar osteophytes were separated according to the locations of the vertebrae for the first time and posterolateral appearance rates were reported. Osteophytes on the upper and lower surfaces of the corpus were also recorded for each level. According to the authors, the least visible places are the left and right posterolaterals, i.e., the foraminal levels. There is an increase in the rate and severity of osteophyte appearance from the upper to the lower levels of the lumbar foramina (21).

In our study, the majority of patients underwent surgery for osteophytes in the lower lumbar levels. Particularly, higher grades of osteophytes in the L4 and L5 foramina were observed and these were more common. For our classification system, we evaluated osteophytes that developed from the lower end plates of the upper corpus. This was because osteophytes more frequently develop in the lower end plates of the upper corpus and induce radicular complaints because of the closer relation to the root when exiting the foramen (the uppermost part of the foramen).

Lee published a classification of foraminal stenosis not directly related to osteophytes. This classification system uses perineural fat obliteration, disc space narrowing, thickened ligamentum flavum, facet arthropathy, and disc osteophytic protrusion. However, the system does not provide an idea on foraminal osteophytes and surgical options for the pathology because the study was radiological and was conducted using MRI (22).

In a subsequent study, the clinical correlation with foraminal stenosis was studied using MRI. Clinical correlation has been determined based on neurological examination, but neurological assessment does not always indicate the correct nerve root. In the study, several causes of foraminal stenosis were evaluated together, but surgical options were not explored (23).

Patients with slowly developing pathology may sometimes present with acute symptoms. When the treatment of patients is evaluated, surgical treatment should be considered if pain control cannot be achieved with medical treatment and transforaminal steroid injections (24,25).

A point worth mentioning is how much the osteophyte laterally and superiorly extends. In patients with osteophytes extending in the superior direction in the foramen, root pressure may be observed at earlier grades because of the root's course in the foramen. In our study, surgery was most frequently performed for L5 foraminal osteophytes.

Above L5, it becomes more difficult to protect the joint because the facet joints are more medialized and stabilization rates are greater (Table 2). The majority of patients in this study had grade 3 osteophytes because patients are more likely to experience clinical symptoms during this period (grade 3) and, therefore, more likely to be treated at this time. It is rather difficult to the proportion of osteophytes that affect the clinical condition because symptoms develop in some patients before the osteophyte grade has progressed. However, patients with grade 3 osteophytes dominated the group overall. Therefore, we can conclude that patients in or close to this category are likely to experience radicular complaints.

There is no need for additional intervention if osteofitectomy using an osteotome or a high-speed drill provides neural decompression after hemilaminectomy and foraminotomy (Figure 5) (Table 2). We usually use

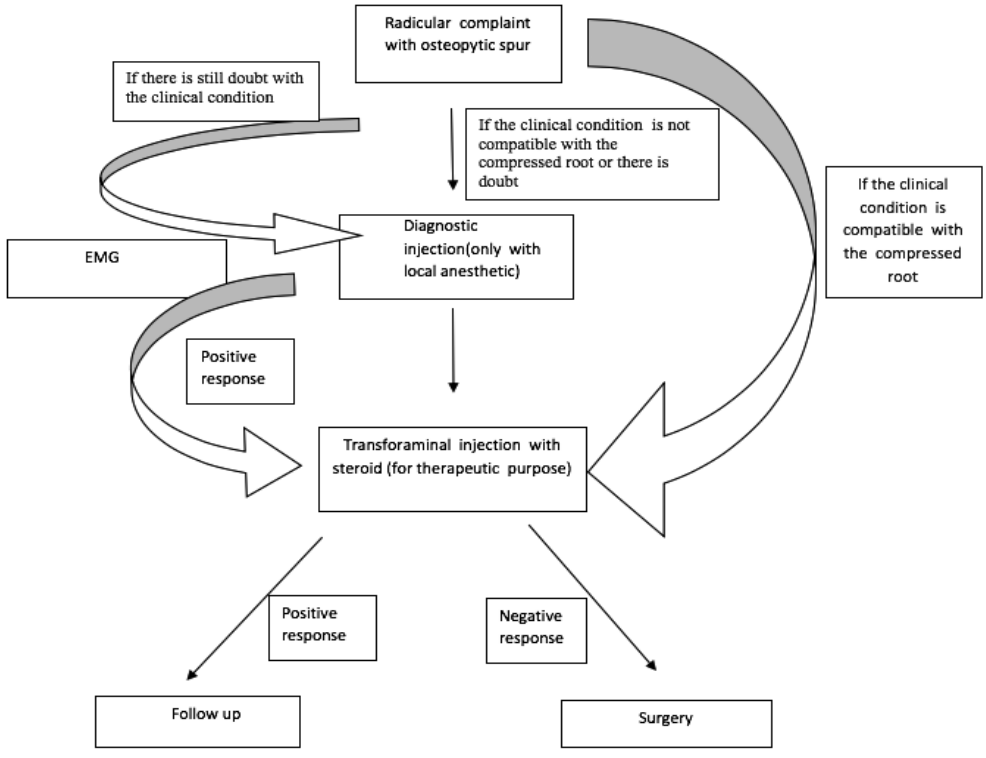
an osteotome because it is easier to excise osteophytes in one piece by digging underneath the protrusion and more difficult to remove the parts extending laterally after carving into the bony protrusion with a drill. This process was sufficient for 24 patients. However, if the root pressure persists beyond the foramen and passes through the extraforaminal section, then it is usually necessary to perform facetectomy and stabilization. An extraforaminal approach can be employed, but it is difficult to remove osteophytes with proper decompression using this approach. We performed stabilization after applying facetectomy for osteophyte resection and root decompression in 12 patients (Figure 6) (Table 2).

The presence of osteophytes at any level does not predict the existence of radiculopathy, and multiple foraminal osteophytes may be the source of radicular pain. The same surgical procedures can be performed for multiple levels, and diagnostic transforaminal injections or electromyography (EMG) can be helpful for the localization of radiculopathy. We also applied medical treatment first if the neurological deficit was not severe, followed by transforaminal injection if complaints persisted. If the patient did not benefit from these conservative methods, then we progressed to surgical treatment (Graphic). Osteophytes can be found in a majority of the foramina. To determine the affected neural root and the root responsible for radiculopathy, clinical and radiological evaluation must be performed first. If the evaluation is insufficient or if there are doubts as to which root is responsible for the clinical condition, then we apply diagnostic injections to the foramina only with a local anesthetic. Nevertheless, we requested EMG examinations for some patients for whom we were forced to identify the responsible foramen (Graphic). These tests and injections were beneficial to diagnose some patients.

An increase in the diagnosis of posterior and posterolateral osteophytes has been reported. Our study was aimed at establishing a common discourse, classification for this situation, investigating the cause of osteophyte-related radicular symptoms, and evaluating the state of surgical treatments.

Conclusion

Studies on foraminal osteophytes are lacking, and a comprehensive classification system has not been developed to date. Surgeons should evaluate patients using CT if foraminal stenosis or osteoarthritic pathology is suspected. After clinical evaluation, it may be necessary to identify the osteophyte responsible for radicular symptoms



Graphic. Treatment and diagnosis methods for radiculopathy associated with foraminal osteophytes
EMG: Electromyography

using EMG and diagnostic foraminal injections. Facet joint excision may be warranted depending on localization of the osteophyte or condition of the facet when surgical treatment is required.

Significant results can be obtained using surgical treatment for radiculopathies originating from foraminal osteophytes. We aimed to create a common discourse regarding the classification of foraminal osteophytes and to share our surgical results.

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Alterations in Biomechanical Properties of the Cornea After Selective Laser Trabeculoplasty

Selektif Laser Trabeküloplasti Tedavisi Sonrasında Korneanın Biyomekanik Özelliklerindeki Değişiklikler

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Abstract

Aim: To investigate changes in corneal biomechanical properties after selective laser trabeculoplasty (SLT).

Methods: Patients who have received SLT and underwent evaluation of corneal biomechanical properties by ocular response analyzer (ORA) in the preoperative period, one week, and one month after SLT were analyzed. Statistical analyzes were performed by examining pre- and post-SLT examination findings and ORA measurement values from the patients' files.

Results: The mean corneal compensated intraocular pressure (IOP) values were found to be significantly reduced one week and one month after the SLT than the values before the treatment (17.14±4.06 mmHg, and 16.91±3.55 mmHg, 19.96±5.00 mmHg; respectively; p=0.004). The mean corneal hysteresis (CH) measurements one week and one month after the SLT were not different from the preoperative measurements (9.89±2.17, 10.12±1.90, and 9.81±2.46, respectively) (p=0.662). The mean corneal resistance factor (CRF) measured prior to the SLT was higher than that in the first week and first month after SLT (11.09±2.08, 10.16±2.04 and 10.39±2.13, respectively) (p=0.002).

Conclusion: CH was found to be unchanged, while CRF was found to be decreased. The development of IOP reduction without statistically unaffected changes in CH and decreased CRF suggests that SLT does not have a significant side effect on the structural integrity of the cornea.

Keywords: Laser trabeculoplasty, cornea, corneal biomechanical properties, corneal hysteresis, corneal resistance factor

Öz

Amaç: Selektif laser trabeküloplasti (SLT) tedavisi sonrasında korneanın biyomekanik özelliklerinde meydana gelen değişiklikleri araştırmak.

Yöntemler: SLT tedavisi uygulanmış ve işlem öncesi, operasyon sonrası birinci hafta ve birinci ayda oküler cevap analizörü (OCA) ölçümleri yapılmış hastaların dosyaları tespit edildi. Hastaların dosyalarından SLT öncesi ve sonrasındaki muayene bulguları ve OCA ölçüm değerleri tespit edilerek istatistik analizleri yapıldı.

Bulgular: Korneal etkilerin düzeltildiği göz içi basınç (GİB) değerleri işlem sonrası birinci hafta ve birinci ayda işlem öncesi değerlere göre istatistiksel olarak anlamlı düzeyde azalmış bulundu (sırasıyla 17,14±4,06 mmHg, 16,91±3,55 mmHg, 19,96±5,00 mmHg; p=0,004). Ortalama korneal histerezis (KH) değerleri işlem öncesinde 9,81±2,46 bulundu. SLT sonrası ortalama KH değerleri birinci hafta ve birinci ayda istatistiksel olarak SLT öncesi ortalama değerlerden farklı değillerdi (sırasıyla 9,89±2,17; 10,12±1,90 ve 9,81±2,46; p=0,662). SLT öncesi ölçülen ortalama korneal rezistans faktör (KRF) değerleri ise işlem sonrasında birinci hafta ve birinci ayda ölçülen değerlerden istatistiksel olarak yüksek bulundu (sırasıyla 11,09±2,08; 10,16±2,04 ve 10,39±2,13; p=0,002).

Sonuç: Göz içi basınç (GİB) değerleri işlem öncesi değerlere göre birinci hafta ve birinci ayda KH değişmemişken KRF azalmıştı. GİB'deki düşüş ile KH'de istatistiksel olarak anlamlı etkilenme olmaması ve KRF'de azalma gelişmesi SLT'nin korneanın yapısal bütünlüğünde ciddi bir yan etki göstermediğini düşündürmektedir.

Anahtar Sözcükler: Laser trabeküloplasti, kornea, korneal biyomekanik özellikler, korneal histerezis, korneal rezistans faktör

Introduction

Glaucoma is a chronic disease in which the rate of progression can be slowed down by reducing intraocular pressure (IOP) with appropriate treatments, and the visual function and quality of life must be maintained at a reasonable cost (1). It is a difficult art to measure IOP

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and decrease IOP with different treatment methods (2,3). Goldmann applanation tonometry (GAT) remains the gold standard for IOP measurement, but new methods such as those using ocular response analyzer (ORA) are being developed for more accurate IOP measurements (4-6). In addition to anti-glaucoma eye drops used to reduce IOP, treatment methods such as selective laser trabeculoplasty have been used in recent years (3,7).

ORA evaluates the biomechanical properties of the cornea and attempts to reduce erroneous measurements due to cornea-related factors during IOP measurement. ORA evaluates corneal biomechanics by calculating corneal hysteresis (CH) and corneal resistance factor (CRF) accordingly. Basically, every substance having elasticity holds hysteresis, and Young's modulus is used for calculating its hysteresis (8,9). Hysteresis is found by calculating the amount of alterations in elasticity and viscosity of the cornea which is the cornea's ability to dampen and dissipate applied energy (10). When the air is applied to the cornea 400 times a second by the ORA device, a depression occurs and then the cornea returns to its original state. Two sets of IOP values are measured in the form of the depression and the transition to the old state. At this time, the energy that is emitted and absorbed in the cornea is analyzed as CH. CRF is mathematically calculated with the help of a constant coefficient.

Since the definition of selective laser trabeculoplasty (SLT) by Latina and Park (7), it has taken its place as an important method for the treatment of glaucoma disease all over the world. SLT is a preferred method because of minor side effects, easy feasibility, and temporary effectiveness in reducing IOP (11,12). There have been recent studies showing that SLT usually makes temporary and clinically negligible changes on corneal topography and corneal specular microscopy findings (13-16). In addition, anterior segment interventions are known to affect the cornea (17). However, as far as we can reach, there is not enough literature on the effects of SLT treatment on corneal biomechanics. In this retrospective study, we investigated the effects of SLT therapy on ORA findings in patients undergoing SLT therapy for primary open angle glaucoma (POAG) and ocular hypertension (OHT).

Methods

In this retrospective study, the files of patients who were followed in a tertiary training and research hospital glaucoma unit were scanned. The files of POAG and OHT patients, who were previously treated with SLT, were collected. These files were further inspected for revealing ORA measurements before and after the SLT treatment. This study protocol was approved by the Bağcılar Training and Research Hospital Ethics Committee (date: 24.11.2017, approval no: 2017.11.1.06.004.r1.014). All the authors worked according to the Helsinki declaration. Informed consent forms were provided.

Patient Selection

The files of 2458 patients followed in the glaucoma unit were reviewed. Since the ORA device was provided to our clinic in 2015, the records of patients who underwent SLT treatment between January 2015 and March 2016 were provided. Among these dates, 133 patients who received SLT treatment were identified.

Clinical characteristics and demographic data of patients and anamnesis of systemic disease, were recorded. Preoperative and postoperative examinations notes including best corrected visual acuity results, biomicroscopy and retinoscopy examination findings, and IOP measurement with GAT were checked (IOP_{gat}). Patients with a spherical equivalent above +5.00 diopter and below -5.00 diopter were not included in the study.

Selective Laser Trabeculoplasty Technique

An Ellex™ solo (Adelaide, Australia) device was used for SLT application. The treatment method that we routinely apply in our patients is as follows: one drop of sterile topical anesthetic eye drop (Alcaine™, proparacaine hydrochloride, 0.5%) is instilled into both eyes of the patients. Before the procedure, iridocorneal angles are examined again with gonioscopy and SLT therapy is applied between 90 and 100 shots until 360 degree of the trabecular meshwork is treated. The initial energy level is selected to be 0.8 mJ as described by Latina and Park (7) and is gradually increased to 1.3 mJ until the bubble formation at the angle is observed after laser application. After treatment, a non-steroidal anti-inflammatory drop is prescribed (Nevenac™, Nepafenac 1%, four drops per day). All patients continue to use antiglaucomatous drops initiated before SLT.

Ocular Response Analyzer Technique

Biomechanical properties of the cornea were evaluated with an ORA (Reichert Ophthalmic Instruments, Buffalo, New York, USA). Analysis of corneal biomechanical properties with ORA device has been described in detail in the literature (10,18). However, briefly, ORA sends a short stream of air to create a depression in the cornea. In this applanation process, as the shape of the cornea changes, an electro-optic sensor processes and examines two independent IOP values called P1 and P2. The value of CH is obtained by subtracting P2 from P1. CRF is detected with the help of another software registered in the main memory of the device. This software uses the following formula for CRF detection:

CRF=P1-*kP2*

In the formula, k is a constant coefficient and is obtained after analysis of the relationship of P1 and P2 with central corneal thickness. As another important data, the ORA device outputs two different IOP measurement results. The first of these is IOP_g which is correlated with the IOP measured by GAT. The second result is called IOP_{cc}. It is the corrected IOP value of the corneal effects which is obtained as a result of the calculation of the linear combination of P1 and P2 (19). In addition, the device has software that analyzes the measurement quality and extracts it as data called wave score. Measurements with ORA device are performed at least three times in our clinic. For statistical reasons, the study included only eyes with the best wave scores at pre-SLT measurements. In addition, only patients with a wave score over six were included, taking into account the guideline of the ORA device. In our clinic, all ORA measurements are made before instilling any drops. The measurements were made between 10:00 and 16:00 with diurnal variation in mind.

Statistical Analysis

Analysis of the data was done with Statistical Package for the Social Sciences 21.0. The Kolmogorov-Smirnov test was used to analyze whether the data fit the normal distribution. The Bonferroni correction for the analysis of pre-SLT, first-week post-SLT, and first-month measurements was performed using the ANOVA test for repeated measures. Statistical significance level was taken as p=0.05.

Results

Only 22 of 133 patients had suitable pre-SLT, first-week and first-month post-SLT ORA measurements, and met all of the inclusion criteria, therefore, the information of these 22 patients was analyzed. Sixteen of the patients were female (72.7%) and six were male (27.3%). Nineteen of the patients were treated for POAG and three for OHT (86.4% and 13.6%, respectively). Normal distribution of IOP_{gat}, CH, CRF, IOP_{cc}, and IOP_g was analyzed by the Kolmogorov-Smirnov test and yielded p values over 0.05. The basic descriptive data for the studied patients are shown in Table 1.

Mean CH values did not show a statistically significant difference at pre-SLT, first week, and first month (p=0.662). The mean CRF values were significantly decreased in the first week and the first month after SLT treatment (p=0.002). IOP_{gat}, CH, CRF, IOP_{cc}, IOP_g and values of the patients before and after SLT are shown in Table 2.

Correlation analysis was performed between IOP_{gat}, CH and CRF (Table 3). There was a statistically significant positive correlation between mean IOP_{gat} and CRF. However, there was a statistically insignificant correlation between IOP_{gat} and CH.

Discussion

SLT is an important and effective treatment in patients with PAAG and OHT to reduce IOP (20). Previous investigations examining the efficacy of SLT therapy reported positive results with regard to this treatment method, although temporary and mild side effects, such as eye pain, conjunctivitis, corneal edema and blurred vision were observed (11,12,21). This study examined the early effects of SLT therapy on corneal biomechanics and found that CRF decreased statistically significantly in the early period (p=0.002).

Table 1. Basic descriptive data of patients

	n	Minimum	Maximum	Mean	Standard deviation
Age	22	27	74	53.32	12.144
C/D[a]	22	0.1	0.9	0.4545	0.21762
RNFL[b]	22	58	112	93.55	14.272
MD[c]	22	-18.1	0.7	-6.588	5.6017

C/D[a] : Cup/disk ratio, RNFL[b] : Retinal nerve fiber layer, [c]: Computerized visual field mean deviation value, MD: Mean deviation

Table 2. Corneal biomechanical parameters and intraocular pressure$_{gat}$ values before and after selective laser trabeculoplasty treatment

	n	Pre-SLT		Post-SLT 1st week		Post-SLT 1st month		p*
		Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	
IOP_{gat} (mmHg)	22	12-28	19.64±4.293	10-22	16.18±3.157	10-29	16.91±3.951	0.000
CH	22	4.5-14.4	9.81±2.46	4.8-14.3	9.89±2.17	4.8-13.0	10.12±1.90	0.662
CRF	22	7.2-15.8	11.09±2.08	4.9-15.0	10.16±2.04	4.9-14.7	10.39±2.13	0.002
IOP_{cc} (mmHg)	22	13.9-33.4	19.96±5.00	12.6-30.6	17.14±4.06	11.8-25.4	16.91±3.55	0.004
IOP_g (mmHg)	22	13.8-28.4	19.39±4.11	11-26	16.20±3.54	11.6-25.4	16.24±3.78	0.000

SLT: Selective laser trabeculoplasty, IOP: Intraocular pressure, CH: Corneal hysteresis, CRF: Corneal resistance factor, GAT: Goldmann applanation tonometry SD: Standard deviation, *p: Significance level for repeated measures ANOVA test after Bonferroni correction

Table 3. Analysis of correlation between intraocular pressure$_{gat}$, corneal hysteresis and corneal resistance factor

		Pre SLT IOP_{gat}	IOP_{gat} 1st week	IOP_{gat} 1st month	Pre SLT CH	CH 1st week	CH 1st month	Pre SLT CRF	CRF 1st week	CRF 1st month
Pre SLT IOP_{gat}	r*	1	0.638	0.778	0.052	0.257	0.134	0.491	0.476	0.441
	p*		0.001	0.000	0.817	0.248	0.552	0.020	0.025	0.040
IOP_{gat} 1st week	r*	0.638	1	0.700	0.240	0.154	0.163	0.578	0.498	0.322
	p*	0.001		0.000	0.283	0.494	0.469	0.005	0.018	0.144
IOP_{gat} 1st month	r*	0.778	0.700	1	0.311	0.447	0.415	0.636	0.717	0.660
	p*	0.000	0.000		0.158	0.037	0.055	0.001	0.000	0.001
Pre SLT CH	r*	0.052	0.240	0.311	1	0.732	0.697	0.825	0.637	0.711
	p*	0.817	0.283	0.158		0.000	0.000	0.000	0.001	0.000
CH 1st week	r*	0.257	0.154	0.447	0.732	1	0.787	0.679	0.858	0.839
	p*	0.248	0.494	0.037	0.000		0.000	0.001	0.000	0.000
CH 1st month	r*	0.134	0.163	0.415	0.697	0.787	1	0.644	0.753	0.852
	p*	0.552	0.469	0.055	0.000	0.000		0.001	0.000	0.000
Pre SLT CRF	r*	0.491	0.578	0.636	0.825	0.679	0.644	1	0.805	0.831
	p*	0.020	0.005	0.001	0.000	0.001	0.001		0.000	0.000
CRF 1st week	r*	0.476	0.498	0.717	0.637	0.858	0.753	0.805	1	0.899
	p*	0.025	0.018	0.000	0.001	0.000	0.000	0.000		0.000
CRF 1st month	r*	0.441	0.322	0.660	0.711	0.839	0.852	0.831	0.899	1
	p*	0.040	0.144	0.001	0.000	0.000	0.000	0.000	0.000	

*r: Represents the Pearson's correlation coefficient, p: Represents the statistical significance level, Statistically significant values are shown in bold, SLT: Selective laser trabeculoplasty, IOP: Intraocular pressure, CH: Corneal hysteresis, CRF: Corneal resistance factor, GAT: Goldmann applanation tonometry

The effects of SLT on the cornea have been investigated by various investigators using different methods because of the cornea forming the upper wall of the iridocorneal angle, and conflicting results have been obtained (13-16,22).

The effects of SLT on the corneal endothelium have been investigated by some researchers using specular microscopy (13,14). In a study conducted by Ong et al. (13) and colleagues in 147 eyes of 94 patients, it has been reported that the number of endothelium decreased in the first month after SLT, although not statistically significantly (p=0.1), and the corneal dark spots were reversibly increased. These authors advised to be careful with SLT applications in patients with recurrent SLT and endothelium pigment accumulations. Another study by Lee et al. (14) and colleagues found that 111 eyes had a statistically significant decrease in endothelial counts at the first week after SLT but did not show a statistically significant decrease when compared to pretreatment values at the end of the first month. It has been noted by Lee et al. (14) that increased dark areas observed in the first week may be associated with decreased endothelial numbers. Both Ong et al. (13) and Lee et al. (14) have reported that inflammatory triggering effects of SLT may help explain the change in specular microscopy findings. This inflammatory effect has been associated with corneal edema and refractive changes in the literature (23). Although the above studies have indicated that there was a change in endothelial measurements after SLT, the effect of these changes on the corneal biomechanics may be limited due to the fact that in our retrospective study the CH did not change.

Scheimpflug corneal topography is an important method used to examine the cornea and anterior segment (24). In a study conducted by Guven Yilmaz et al. (16) and his colleagues, the central corneal thickness increased in the first month after SLT and the anterior chamber depth decreased, but in the third month, normalization was detected in both parameters. In addition, a study by Atalay et al. (15) and colleagues found a statistically significant but clinically insignificant decrease in central corneal thickness in the third month post-SLT. Both authors have proposed extensive investigations to investigate the effects of SLT on corneal topography. Corneal thickness is a factor that can affect CH and CRF (10,25). In normal and naive eyes, the viscous damping capacity of the cornea increases as the corneal thickness increases. This increase is eventually recorded as a high CH and CRF. However, transient increases in corneal thickness and changes in corneal biomechanical properties with reduced

CH and CRF values were observed after surgery, such as transparent corneal cataract surgery, which had effects on the number of endothelium and anterior chamber inflammation (26,27).

In a study of determining the effect of corneal biomechanics on the outcome of SLT therapy in medically uncontrolled glaucoma, CH and CRF together with pretreatment IOP values predicted a good modeling of the outcome of treatment (22). The data obtained by Hirneiß et al. (22) were obtained by using linear regression analysis of OCA measurements performed one year after SLT treatment in medically uncontrolled patients, as the authors have indicated. In a study conducted by Pillunat et al. (28) and colleagues on high pressure glaucoma and normal pressure glaucoma patients, the IOP_g and IOP_{cc} adjusted measurements of CH and CRF mean values were not statistically different before and after SLT. They also included patients with an uncomplicated cataract surgery, wave scores above 3.5, and reviewed measurements at least four weeks later (13.6±7.0 weeks). In our study, we planned to investigate the early effects of SLT therapy on ORA data and found that CH did not change in the early period, but CRF changed statistically significantly (p=0.662 and p=0.002, respectively). Our study differs from the study of Pillunat et al. (28) and colleagues in that there was a significant difference in CRF value probably due to early inflammation and IOP spikes after SLT. An insignificant correlation between mean IOP_{gat} and CH values after SLT may be due to the formula CH = P1-P2 used in the calculation of CH, although CH values were affected by corneal thickness. In addition, the use of corneal thickness in the calculation of CRF may have led to a decrease in CRF, which correlates positively with IOP_{gat} reduction, because of temporary changes in corneal thickness and structure early in the course of SLT therapy. The lack of significant correlation between decreased IOP_{gat} and CH, and the significant positive correlation of CRF with IOP_{gat} may have been obtained as a result of transient changes in the early post-SLT period, which was noted in previous studies examining the corneal endothelium and corneal structure.

Our study has important limitations to be emphasized. First, our study was not randomized and prospective. CH and CRF are known to have some changes with age (29). Although the average age of our patients was 53.3, the fact that PAAG has an increasing frequency with age restricts the results of our study to adaptation to different age groups.

Conclusion

SLT therapy maintains its important place in the treatment of PAAG and OHT. We believe that comprehensive, prospective, randomized trials investigating early and long-term effects of this treatment method on corneal biomechanics will be an important contribution to the treatment and follow-up plans in PAAG and OHT patients.

Authorship Contributions

Surgical and Medical Practices: K.A. Concept: K.A. Design: K.A. Data Collection or Processing: K.A., A.K. Analysis or Interpretation: K.A., A.K. Literature Search: K.A., A.K. Writing: K.A.

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Multifokal Tiroid Papiller Kanserlerinde Boyun Metastatik Hastalığı

Metastatic Neck Disease in Multifocal Thyroid Papillary Cancer

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Öz

Amaç: Multifokal papiller tiroid kanseri (MPTK) agresif ve kötü prognoza sahiptir, bu çalışmada MPTK'li hastalarda boyun lenf nodu metastaz özellikleri değerlendirilmesi amaçlanmıştır.

Yöntemler: Ocak 2010 - Aralık 2017 tarihleri arasında papiller tiroid kanseri tanısı ile total tiroidektomi yapılmış 2530 hastanın dosyası retrospektif olarak incelendi ve multifokal tiroid papiller kanseri saptanan 515 olgunun yaş, cinsiyet, tümör boyutu, tiroid kapsül invazyonu, boyun metastatik hastalığı değerlendirildi.

Bulgular: Olgular multifokal/unifokal olarak iki gruba ayrıldı ve iki grup tiroid kapsül invazyonu (%29,9/%10,86), tümör ortalama çapı (15,9 mm/16,1 mm), santral lenf nod metastazı (%56,5/%18,3), lateral boyun lenf metastazı (%23,1/%6,3) bakımından karşılaştırıldı. Kapsül invazyonunun, multifokalite riskinde artış ile bağlantısı olduğu görüldü. Multifokal hastalarda kapsül invazyonu, santral ve lateral boyun metastazları unifokal hastalarla karşılaştırıldığında istatistiksel olarak anlamlı fark saptandı (p<0,001).

Sonuç: Multifokal tiroid kanseri hastalarında primer cerrahi tedavisi olarak bilateral total tiroidektomi ile beraber bilateral santral boyun diseksiyonu yapılması tavsiye etmekteyiz.

Anahtar Sözcükler: Papiller kanser, multifokal tümör, boyun metastazı

Abstract

Aim: Multifocal papillary thyroid cancer (MPTC) has aggressive and poor prognosis. The main aim of this study was to evaluate the lymph node metastasis pattern in MPTC patients.

Methods: We retrospectively investigated the records of 2530 patients who underwent thyroidectomy for papillary thyroid cancer between January 2010 and December 2017. The age, gender, tumor size, thyroid capsule invasion and neck metastatic disease were evaluated in 515 of these patients having MPTC.

Results: We compared multifocal and unifocal papillary thyroid cancer patients considering papillary thyroid capsule invasion (29.9%/10.86%), mean tumor diameter (15.9 mm/16.1 mm), central lymph node metastasis (56.5%/18.3%) and lateral neck lymph node metastasis (23.1%/6.3%). Capsule invasion was associated with an increased risk of multifocal disease. The incidence of capsular invasion and central and lateral neck metastases in MPTC patients was statistically significantly higher than in patients with unifocal thyroid papillary cancer (p<0.001).

Conclusion: We recommend bilateral total thyroidectomy and bilateral central neck dissection as primary surgical treatment in multifocal thyroid cancer patients.

Keywords: Papillary cancer, multifocal tumor, neck metastasis

Giriş

Son dekatlarda tiroid kanseri insidansı hızla artış göstermektedir (1). Bunun nedeni özellikle yüksek rezolüsyonlu ultrasonografi ve ince iğne aspirasyon biyopsisi gibi tanısal araçlarda gelişmeler ve bunların sık olarak kullanılmasıdır (2,3). Tiroid kanserleri arasında en sık görülen histopatolojik tip olan papiller kanser, tüm hastaların %85'inden fazlasını oluşturmaktadır ve tiroid kanserlerinde artış oranında sorumlu olan tiptir (4). Her ne kadar bu tümörler; yavaş ve iyi seyirli olarak bilinse de bazı

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klinikopatolojik özellikli tümörler kötü prognozu olan agresif davranış sergileyebilir (5,6). Papiller tiroid kanserinde (PTK) unilateral veya bilateral olarak multifokal tümör görülmesi nadir değildir. Klinik olarak tiroid bezi içerisinde anatomik olarak birbirinden ayrı iki veya daha fazla odağın olması multifokal tiroid papiller kanseri olarak adlandırılır. Daha sık olarak multipl mikrokarsinomlar olarak görülür iken bazen de multipl makroskopik lezyonlar olarak saptanabilir (7). Diferansiye tiroid kanserlerinde servikal lenf nodu (LN) metastazlarının önemi konusunda tartışmalar halen devam etmektedir. Diferansiye tiroid kanserli hastalarda bölgesel servikal LN metastazları, erken ve sık olarak görülür (8). Güncel evreleme sistemlerinde nodal metastazların özellikle yaşlı hastalarda daha kötü prognozlu olduğu bilinmektedir. Artan sayıda yayında metastatik LN'nin sayısı ve boyutu gibi özelliklerin de prognoz üzerine etkili olabileceği vurgulanmaktadır.

Multifokal tümörler; tek bir malign kaynaktan çıkıp intratiroid yayılımla olabilmekte veya çok sayıda birbirinden bağımsız odaktan köken alabilmektedir (7). Multifokal tiroid papiller kanser sıklığı değişik çalışmalarda %18-87 arasında bildirilmiştir (5,6,7,9). Tiroid kanserlerinde multifokalite ile boyun LN'lerine, özellikle de santral bölge LN'lerine metastazlar arasında sıkı bir ilişki olduğu bildirilmektedir (10). Papiller multifokal tiroid kanserli hastalarda santral kompartman LN metastatik hastalığın olguların %30-90 oranında saptandığını bildiren çalışmalar mevcuttur (11). Ancak multifokal PTK hastalarında servikal LN tutulumları sıklığını etkileyen faktörler ve klinik özelliklerine ilişkin yeterince sonuç bildirilmemiştir.

Bu çalışmada amacımız multifokal PTK hastalarda retrospektif olarak dosya incelemesi ile boyun metastatik hastalığı risk faktörlerinin ortaya konması ve klinikte tedavi kararı vermeye ve hastayı bilgilendirmeye ışık tutmaktır.

Bu çalışmada santral LN metastazları olan multifokal TPK'ye odaklanılmıştır.

Yöntemler

Bu çalışma Maslak Acıbadem Hastanesi Tiroid Cerrahisi Kliniğinde Ocak 2010 - Aralık 2017 tarihleri arasında PTK tanısı ile total tiroidektomi yapılmış 2530 hastanın dosyaları retrospektif olarak incelenmiş ve olgular multifokal (n=515) ve unifokal (2015) tiroid papiller kanseri tanısı almış olmalarına göre iki grupta değerlendirilmiştir. Her iki grup tümör özellikleri ve boyun metastatik hastalıkları yönünden karşılaştırılmıştır. Preoperatif ince iğne aspirasyon biyopsileri ve cerrahi sonrası patoloji parçaları aynı patoloji ekibince incelenmiştir. Tüm cerrahiler aynı ekip tarafından gerçekleştirilmiştir. Patolojik sonuçlarında tümör tanısı ve odak sayısı ayrıntılı olarak değerlendirilmiştir. Multifokal tümör saptanan 515 hastanın tamamında bilateral santral boyun diseksiyonu ile beraber bilateral total tiroidektomi uygulanmış idi. Hastaların yaşları 18 ile 84 arasında değişmekteydi. Soliter tiroid papiller kanserli 2015 hasta ise diğer grubu oluşturmakta idi.

Total tiroidektomi dışı cerrahiler yapılan, bilateral santral boyun diseksiyon yapılmayan hastalar, ailede PTK hikayesi olan, radyasyon maruziyet hikayesi olan veya kayıtlarında eksiklik görülen hastalar çalışma dışında tutuldu. Bu çalışmada tümörlerden en büyük olanın boyutu multifokal tümörde en büyük tümör olarak değerlendirildi.

Hasta klinik özellikleri (yaş, cinsiyet), tümör histolojik özellikleri (en büyük tümör boyutu, tek veya multifokal olması, kapsüler invazyon, ekstratiroid yayılım) değerlendirildi.

Hastalardan cerrahi öncesi tıbbi onamları alınmıştır ve çalışmamızın etik kurul onayı Acıbadem Mehmet Ali Aydınlar Üniversitesi Etik Kurulu 2018-12/6 karar numarası ile verilmiştir.

Histolojik tanılar Dünya Sağlık Örgütü sistemine göre sınıflandırıldı. Univaryant ve multivaryant analizlerde multifokal PTK santral boyun kompartmanları tutulumu riskleri üzerine yoğunlaşıldı.

İstatistiksel Analiz

Çalışmamızın istatistiki analizlerinde SPSS programı kullanıldı. Kategorik değişkenler numaralar ile temsil edildi ve Student's sample t-test ve chi-square test veya Fisher-exact chi-square test kullanıldı.

Bulgular

PTK soliter tümörlü olanlar ile multifokal tümörlü olan hastalarda; yaş cinsiyet, kapsüler invazyon, ekstratiroid yayılım, en büyük tümör boyutu gibi klinik ve patolojik faktörler karşılaştırıldı.

İki bin beş yüz otuz PTK hastanın yaş ortalaması 39,32 (18-84 yaş arası) idi. Hastaların 236'sı erkek (%9,32), 2294'ü kadın (%90,68) idi. Erkek hastalarda yaş ortalaması 42,16±12,8, kadınlarda ise 38,99±14,6 idi (Tablo 1).

Multifokal hastalığı olan 515 hastada hastalık 176'sında bilateral, 339'unda tek lobda idi (156 sağ lob, 183 sol lob'da).

Multifokal hastalığı olan 515 hastanın 432'i kadın, 83'ü erkekti. Yaş ortalaması 38,11±8,1 (18-81 yaş arası) idi.

Multifokal 515 hastanın patolojik incelemesinde tiroid kapsül invazyonu 154 (%29,9) olguda vardı, tümör çapı ortalama 15,9 mm (3-75 mm), santral LN metastazı 291 olguda (%56,5), perinodal invazyon 82 olguda (%28,1) ve metastatik LN sayısı ortalama 3,81 adet (1-15 arası) idi.

Lateral boyun diseksiyonu toplamda 236 (%9,32) olguda uygulandı. Bunların 119'u (%23,1) multifokal, 127'si (%6,3) ise unifokal hastalığa sahip hastalardı. Lateral boyun diseksiyonu hastaların 109'unda bilateral boyuna, 55'inde sağ boyuna, 72'sinde sol boyuna uygulandı. Böylece 236 olguda 345 boyun diseke edildi (Tablo 2).

Tablo 1. Multifokal ve unifokal hastalıkta demografik bilgiler ve tümör özelliklerinin karşılaştırılması

	Multifokal	Unifokal
Hasta sayısı, n (%)	515 (20,3)	2015 (79,7)
Yaş, ort ± SS (min-maks)	38,11±8,1 (17-81)	40,04±7,2 (18-84)
Cinsiyet (E/K), n	83/432	153/1862
Tümör çapı, ort ± SS (min-maks)	15,9±9 mm (3-75 mm)	16.1±11 mm (4-55 mm)
Tiroid kapsül invazyonu, %	%29,9	%10,86
Santral lenf nodu metastaz, %	%56,5	%18.3
Santral perinodal invazyon, %	%28,1	%17,07
Lateral boyun metastaz, %	%23,1	%6,3
Lateral boyun perinodal invazyon, %	%36,97	%15,74

E: Erkek, K: Kadın, ort: Ortalama, SS: Standart sapma, min: Minimum, maks: maksimum

Tablo 2. Lateral boyun diseksiyonu boyun lenf düğümü metastazlarının bölgelere göre dağılımı

	Multifokal		Unifokal	
Boyun metastaz bölgeleri	**Sağ**	**Sol**	**Sağ**	**Sol**
2. bölge	13	12	12	14
3. bölge	30	23	17	11
4. bölge	34	48	21	32
5. bölge	19	21	14	19

Sol boyun diseksiyonu uygulanan multifokal PTK'li hastalarda metastazların bölgelere göre dağılımı incelendiğinde; 2. bölgede 12, 3. bölgede 23, 4. bölgede 48 ve 5. bölgede 21 hastada metastaz saptandı. Perinodal invazyon 18 hastada mevcuttu.

Sağ boyun diseksiyonu uygulanan multifokal PTK'li hastalarda metastazların bölgelere göre dağılımı incelendiğinde; 2. bölgede 13, 3. bölgede 30, 4. bölgede 34 ve 5. bölgede 19 hastada metastaz saptandı. Perinodal invazyon 26 hastada mevcuttu.

Unifokal hastalığı olan 2015 hastada hastalık 1261'inde sağ lob, 754'ünde sol lobda idi. Unifokal hastaların 1862'si kadın, 153'ü erkekti. Yaş ortalaması 40,04±7,2 (17-84 yaş arası) idi.

Unifokal 2015 hastanın patolojik incelemelerinde tiroid kapsül invazyonu 219 (%10,86) olguda mevcuttu, tümör çapı ortalama 16,1 mm (4-55 mm) idi, santral LN metastazı 369 olguda (%18,3), perinodal invazyon 63 olguda (%17,07) mevcuttu ve metastatik LN sayısı ortalama 2,1 adet (1-16 arası) idi.

Sol boyun diseksiyonu uygulanan unifokal PTK'li hastalarda metastazların bölgelere göre dağılımı incelendiğinde; 2. bölgede 14, 3. bölgede 11, 4. bölgede 32 ve 5. bölgede 19 hastada metastaz saptandı. Perinodal invazyon dokuz hastada mevcuttu.

Sağ boyun diseksiyonu uygulanan unifokal PTK'li hastalarda metastazların bölgelere göre dağılımı incelendiğinde; 2. bölgede 12, 3. bölgede 17, 4. bölgede 21 ve 5. bölgede 14 hastada metastaz saptandı. Perinodal invazyon 11 hastada mevcuttu.

Multifokal/unifokal olgular incelendiğinde tiroid kapsül invazyonu (%29,9/%10,86), tümör ortalama çapı (15,9 mm/16,1 mm), santral LN metastazı (%56,5 /%18,3), lateral boyun lenf metastazı (%23,1/%6,3) olarak saptandı.

Çalışmamızda multifokal tümörlerin unifokal tümörler ile karşılaştırıldığında daha agresif, daha fazla santral ve lateral boyun metastazı yaptığı ve iki grup arasındaki farkın istatistiği olarak anlamlı olduğu görüldü (p<0,001).

Tartışma

PTK en sık görülen tiroid kanseri histopatolojik tipi olup, LN metastazları özellikle santral bölgeye (6. bölgeye) metastaz yapmaya meyillidir (10). Bu konuda multifokal TPK'de LN metastazları ile ilgili çok fazla çalışma İngilizce literatürde yer almamaktadır. Genellikle PTK'lerinin mükemmel prognoza sahip ve düşük mortalite oranlarının olduğu bilinmektedir. PTK'lerin 30 yıllık sağkalım oranları total ve near total tiroidektomilerde birbirine benzer ve radyoaktif iyot (RAİ) ablasyonu ile beraber veya onsuz %90'ların üzerinde son derece iyi sonuçlar bildirilmektedir (12). Fakat halen oldukça agresif seyirli olgular da literatürde bildirilmektedir (13).

Bu çalışmada daha evvel yapılan çalışmalarda bildirilen sonuçlara benzer olarak multifokal hastalık unifokal hastalık ile karşılaştırıldığında multifokal hastalığın daha agresif olduğu görülmektedir (5,14). Multifokal TPK sıklığı değişik serilerde %18-87 arasında bildirilmektedir, bizim serimizdeki oran ise %20,3 idi (9).

Soliter PTK'lerin hastalarda santral LN tutulumu %50 olarak bildirilmektedir. Bizim çalışmamızda soliter tirod tümörlü hastalarda santral LN metastazı sıklığı %18,3 iken multifokal tümörlü hastalarda ise santral lenf nodu metastazı sıklığı %56,5 saptanmıştır. Bu iki grup arasındaki farkın istatistiksel olarak anlamlı olduğu görülmüştür.

PTK'lerde LN metastazlarının kötü prognostik faktör olup olmadığı konusunda tartışmalar devam etmektedir. Birkaç çalışmada (15-18) LN metastazlarını kötü prognostik faktör olarak bildirmişken, diğer bazı çalışmalarda (19,20) ise LN pozitifliğinin hasta prognozları üzerine uzun süreli etkisi olmadığı bildirilmektedir. Fakat LN metastazı olan olgularda rekürens ile sıkı bağlantısı olduğu oldukça kabul gören bir bağlantılı faktördür (21).

Çalışmamızda multifokal tiroid kanserli hastalarda tiroid kapsül invazyonu ve boyun LN'lerine metastazı ile arasında istatistiki olarak anlamlı bir ilişki olduğu saptanmıştır.

Tek ve çok değişkenli analizlerde özellikle 6. bölge LN'lerine metastaz üzerine multifokal tümörlerin bağımsız bir risk faktörü olduğu görülmüştür.

Multifokalite; PTK'lerde özellikle santral kompartman LN'lerine metastaz riskini arttırmaktadır.

Amerikan Tiroid Derneği'nde klinik LN metastazı olan olgularda tedavi edici santral boyun diseksiyonu tavsiye edilmektedir (22). Buna karşılık proflaktik boyun santral bölge diseksiyonunun rolü halen tartışmalı bir konu olarak devam etmektedir (23). PTK'li hastalarda yaklaşık %30-90 arasında klinik veya okült LN metastazı olduğunu bildiren çalışmalar mevcuttur (11). Proflaktik santral boyun diseksiyonundan postoperatif ciddi komplikasyon sıklığı artışı nedeniyle (rekürren larengeal sinir paralizisi ve hipoparatiroidizm riskleri) çoğu cerrah tarafınca uygulamaktan kaçınılmaktadır (24). Bu nedenle birkaç çalışmada proflaktik boyun diseksiyonunun sadece yüksek riskli hasta grubunda (erkek, çok genç yaşta, büyük tümör hacmi olan hastalarda ve ekstratiroid uzanım olan hastalarda) düşünülmesi gerektiği bildirilmiştir (25,26).

Bununla beraber santral bölge LN'lerinin diseke edilmesi, tümorün tam ve doğru evrelemesini sağlayarak postop RAİ tedavisi gerekliliğini daha doğru olarak değerlendirecek bir parametre oluşturur. Ayrı bir önemi de tümör rekürrensi durumunda santral kompartman bölgesinde özellikle ikinci cerrahi gereksiniminde bu bölgede komplikasyon riskinin çok daha fazla artışıdır (27).

Önemli bir konu da tecrübeli cerrahların elinde yapılan santral kompartman diseksiyonu göreceli olarak güvenli bir cerrahi olararak yapılabilmektedir. Bu lokal rekürenslerden koruyacak ve santral kompartmanda mikroskopik metastazların çıkarılmasını sağlayarak sağkalım üzerine pozitif katkısı olacaktır (28).

Bizim çalışmamız retrospektif olmasına rağmen, tüm operasyonların aynı cerrahi ekip tarafından gerçekleştirilen ve aynı patolog ekibince yorumlanan geniş bir seri olması nedeniyle değer taşımaktadr. Wang ve ark. (29) insular histotip ve tall cell varyant hastalarında daha kötü prognoz olduğunu, klasik PTK hastalara göre daha agresif olduğunu ve multifokalitie, ekstratiroid yayılım, LN metastazı, uzak metastaz ve rekürrensin daha sık görüldüğünü bildirmişlerdir.

Sonuç

Çalışmamızda saptadığımız sonuçlar göz önüne alındığında multifokal tümör daha agresif ve kötü prognoza sahiptir. Multifokal TPK'li hastaların primer cerrahi tedavisinde bilateral total tiroidektomi ve bilateral santral LN diseksiyonu yapılmasını tavsiye etmekteyiz.

Yazarlık Katkıları

Cerrahi ve Medikal Uygulama: M.D., B.E. Konsept: M.D., B.E. Dizayn: M.D., B.E. Veri Toplama veya İşleme: H.K., A.Ö. Analiz veya Yorumlama: B.E., M.D., S.G. Literatür Arama: H.K., S.G., F.T. Yazan: B.E.

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Pulmoner Kapak Yokluğu Sendromu ile Beraber Olan Fallot Teralojisi'nde Nadir Görülen Kardiyak Anomali

A Rare Cardiac Anomaly in Absent Pulmonary Valve Syndrome with Tetralogy of Fallot

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Öz

Fallot tetralojisi (FT) ve pulmoner kapak yokluğu sendromu olan hastalarda (PKYS) FT hastalarından farklı olarak kalp yetersizliği ve kardiyomegali saptanır. Bu hastalarda ek kardiyak anomaliler sık olmamakla birlikte görülebilir. Bu olgumuzda sağ ve sol pulmoner arterin birbiri ile bağlantısız olduğunu (ana pulmoner arterin sağ pulmoner arter ile devam ettiği ve sol pulmoner arterin patent duktus arteriozusdan kanlandığını) saptadık. Bu yazı ile PKYS ile beraber olan diğer kardiyak anomalileri hatırlatmak istedik.

Anahtar Sözcükler: Pulmoner kapak yokluğu, Fallot tetralojisi, patent ductus arteriosus, kesintili pulmoner arterler

Abstract

Heart failure and cardiomegaly are observed in patients with absent pulmonary valve syndrome with tetralogy of Fallot (TOF), unlike in those with TOF alone. Additional cardiac anomalies can also be seen in these patients, although not frequently. In our case, we found that the right and left pulmonary arteries were disconnected (the main pulmonary artery continued only with the right pulmonary artery and the left pulmonary artery originating from patent ductus arteriosus). In this paper, we wanted to remember other cardiac anomalies associated with absent pulmonary valve syndrome with tetralogy of Fallot.

Keywords: Absent pulmonary valve, tetralogi of Fallot, patent ductus arteriosus, non-confluent pulmonary arteries

Giriş

Pulmoner kapak yokluğu sendromu (PKYS), Fallot tetralojisine (FT) benzer fakat farklı bir klinik tablodur. Anatomik özellik olarak rudimente pulmoner kapak (hem darlık hem yetersizlik olan), masif dilate pulmoner arterler ve sıklıkla geniş ventriküler septal defekti (VSD) içerir. Hemen daima patent duktus arteriosus (PDA) yokluğu ile beraberdir. Çocukluk formu iyi seyretmesine rağmen infant formu ciddi solunum problemleri ile beraber olup erken cerrahi (ilk üç-altı ay) gerektirir (1).

Olgu

Doğduktan sonraki muayenesinde üfürüm duyulması üzerine ekokardiyografi yapılan ve FT-PKYS tanısı konulan hasta, solunum şikayetleri hafif olduğundan yenidoğan döneminde değil, tarafımıza 10 aylıkken operasyon açısından değerlendirilmek üzere yönlendirildi.

Hastanın ateşi, siyanozu ve çomak parmağı yoktu; solunum sayısı 50/dk, kalp hızı 130/dk, arteriyel tansiyonu 90/45 mmHg saptandı. Kardiyovasküler muayenesinde ikinci kalp sesi tekti ve "to and fro" üfürümü vardı. Solunum sistemi muayenesinde hafif ekspiryum uzunluğu vardı. Karaciğer kot altında bir parmak ele geliyordu. Diğer sistem muayeneleri normaldi. Telekardiyografisinde kardiyomegali vardı (Resim 1). On iki kanal elektrokardiyografisi sinüs ritminde ve sağ aks sapması vardı. Ekokardiyografisinde geniş malalignment outlet VSD, aortanın %50 dekstropozisyonu, pulmoner kapağın displastik olduğu, sağ pulmoner arterin belirgin dilatasyonu görüldü ve sol pulmoner arterin PDA ile

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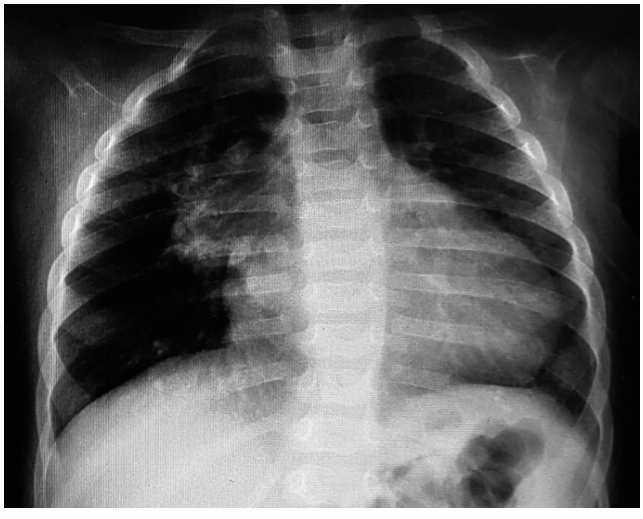
devamlı olduğu düşünüldü. Hasta kateter anjiyografi ile değerlendirildi. Kateter anjiyografide sağ ventrikül basıncı: 85 mmHg, sağ pulmoner arter ortalama basıncı: 25 mmHg saptandı. Arkus aortaya yapılan enjeksiyonda PDA'dan sol pulmoner arter çıktığı ve ortalama basıncın 15 mmHg olduğu ve PDA ile olan bağlantının kopmak üzere olduğu gözlendi. Tanı doğrulanarak hasta cerrahiye verildi (Resim 2). Cerrahide sol pulmoner arter, PDA'dan ayrılarak sağ pulmoner arter ile birleştirildi. Pulmoner arter pilikasyonu yapıldı. Sağ ventrikül çıkış yolu genişletilerek, ana pulmoner arter konduit ile sağ ventriküle bağlandı ve VSD kapatıldı. Operasyondan sonraki 2. gün mekanik ventilatör desteğinden ayrılan hasta 3. gün servise çıktı ve sorunsuz bir şekilde 5. gün taburcu edildi. Hasta 18 yaşından küçük olduğundan hastanın anne ve babasından onam alınmıştır.

Tartışma

PKYS, FT'ye benzer fakat farklı bir klinik tablodur. İlk kez Chever (1) tarafından 1847'de tanımlanmıştır. Anatomik özellik olarak rudimente pulmoner kapak (hem darlık hem yetersizlik olan), masif dilate pulmoner arterler ve sıklıkla geniş malalignment outlet VSD içerir. Hemen daima PDA yokluğu ile beraberdir. Pulmoner arter displazisinin patogenezinde PDA yokluğunun olduğu düşünülmektedir. İntrauterin dönemde duktus arteriozusun yokluğu desendan aortaya pulmoner arterden kan geçişini önler. Bu durum pulmoner arter basıncını arttırır ve sonuçta pulmoner arterlerde dilatasyon ve ciddi pulmoner yetersizlik olur. FT tanısı konulan hastaların sadece %2,5'ini oluşturur ve bu hastaların %75'de 22q11 delesyonu saptanır (1). Bu hastalarda masif dilate pulmoner arterlerin trakeobronşiyal ağaca basısı ve buna bağlı olarak önemli solunumsal sıkıntılar vardır. İntakt ventriküler septum varsa genellikle normal pulmoner arterler ve normal duktus arteriozus vardır (2).



Resim 1. Hastanın telekardiyografi görüntüsü

Klinik olarak infant ve çocukluk tipi vardır. İnfant formunda, genellikle düşük oksijen düzeyi, çok dilate ana pulmoner arterler ve yüksek diyastolik pulmoner arter basıncı vardır ve bu formda solunum problemleri çok ciddi olur. Çocukluk formunda ise solunum problemleri daha hafiftir.

Bazı otörler tarafından anatomik özelliklere göre de PKYS farklı iki gruba ayrılmıştır. FT/PKYS ve FT'nin eşlik etmediği intakt ventriküler septum veya küçük VSD'nin eşlik ettiği tip PKYS/IVS (3).

FT'den ayrımında kullanılan ekokardiyografik özellikler:

1. Pulmoner kapağın yok veya displazik olması,
2. Pulmoner anuluste yetersizlik ve darlık olması,
3. Pulmoner arterlerde anevrizmatik dilatasyon,
4. Pulmoner arter basıncında düşüklükten ziyade artış olmasıdır.

a) Yatay ok: Sağ ventrikül çıkış yolu (infundibulum)
(Dikey ok: İleri derecede genişlemiş ana pulmoner arter)

b) Ok: Arkus aortadan çıkan patent duktus arteriosus

c) Ok: Patent duktus arteriosus ile dolan sol pulmoner arter

Resim 2. a) Sağ ventrikül enjeksiyonunda infundibuler darlık, sağ pulmoner arterin belirgin dilatasyonu ve ventriküler septal defekti yoluyla aortanın dolduğu gözlenmekte. b) Arkus aortadan patent duktus arteriosusun çıkışı. c) Sol pulmoner arter görülmekte

Çeşitli çalışmalar yapılmış ve PKYS'ye eşlik edebilecek anomaliler yayınlanmıştır: Sol pulmoner arter yokluğu, sol pulmoner arterin PDA'dan çıkması, sağ pulmoner arterin asendan aortadan çıkması ve sağ arkus aorta, triküspit atrezisi, sol pulmoner arterin asendan aortadan çıkması, sol ana koroner arter atrezisi, aort koarktasyonu, Ebstein anomalisi, dekstrokardi, atriyoventriküler septal defekt, büyük arterlerin transpozisyonu, trikuspit atrezisi veya ağır triküspit stenozu, intakt ventrikular septum, kesintili aortik ark tip B, aortopulmoner kollateraller, double aortik ark ile birliktelik bildirilmiştir (4-18).

Cerrahi öncesi PKYS+FT'de sağ pulmoner arterin superior vena kavaya basısı da bildirilmiştir (19). Cerrahi düzeltme sırasında solunumsal basıyı ortadan kaldırmak için "lecompte" manevrası yapılır ve buna bağlı komplikasyonlar görülebilir (sağ pulmoner arterde darlık ve supravalvüler aort bölgesinde darlık) (20). Postoperatif ventilasyon süresini ve mortaliteyi preoperatif solunum durumu belirler (21).

Bu olgu ışığında PKYS tanısı koyduğumuz hastalarda ek kardiyak anomalilerin de eşlik edebileceğini hatırlatmak istedik.

Yazarlık Katkıları

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Case Report / *Olgu Sunumu*

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Traumatic Middle Cerebral Artery Occlusion: A Case Report

Travmatik Orta Serebral Arterin Tıkanması: Olgu Sunumu

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Abstract

Traumatic occlusion of the middle cerebral artery (MCA) is a rare cause of cerebral infarction. Malignant infarction of the MCA is associated with a mortality rate of 80%. Arterial dissection, cerebral vasospasm, and thrombosis may be the pathogenesis of this condition. Poor admission Glasgow coma scale score, low systolic blood pressure, and brain herniation are significantly associated with development of posttraumatic cerebral infarction. There is no effective medical treatment for malignant MCA infarction. Decompressive craniotomy is the last solution to prevent severe damage or death. We report a 51-year-old female having craniofacial injury, multiple chest trauma, hemothorax, pneumothorax, and cerebral infarction after a traffic accident. Despite decompression surgery, she died two days after the injury.

Keywords: Middle cerebral artery, trauma, decompressive craniectomy, posttraumatic cerebral infarction

Öz

Orta serebral arterin (OSA) travmatik kapanması serebral damar tıkanıklığının nadir sebebidir. Malign OSA damar tıkanıklıkları %80 mortalite oranı ile ilişkilidir. Arter duvarının yırtılması, serebral damar spazmı ve trombozis bu durumun patogenezinde rol oynuyor olablir. Glasgow koma skorunun düşük olması, düşük sistolik kan basıncı ve beyin herniasyonunun travma sonrası serebral damar tıkanıklığı gelişmesi ile manidar ilişkisi vardır. Malign OSA damar tıkanıklığının etkili bir medikal tedavisi yoktur. Dekompresif kraniyotomi devam eden hasar veya ölümden korunmada son çözüm yoludur. Biz, trafik kazası sonrası yüz ve kafa travması, çoklu gögüs travması, hemotoraks, pnömotoraks ve serebral damar tıkanıklığı olan 51 yaşında bayan hastayı sunduk. Dekompresif cerrahiye rağmen hastamız travma sonrası iki gün sonra kaybedilmiştir.

Anahtar Sözcükler: Orta serebral arter, travma, dekompresif kraniektomi, travma sonrası serebral damar tıkanıklığı

Introduction

Posttraumatic cerebral infarction (PTCI) is a well-known complication of traumatic brain injury, with a frequency ranging from 1.9% to 10.4 %. After head trauma, PTCI may be seen as a complication (range: 1.9%- 10.4%) (1-4). Despite appropriate medical and surgical interventions, PTCI has poor clinical outcome with a high mortality rate. The prognosis of malignant middle cerebral artery (MCA) infarctions is poor, with case fatality rates in intensive-care-based series of nearly 80% (5).

PTCI risk factors are lower Glasgow coma scale (GCS) score, hypotension and higher intracranial pressure (ICP). Early identification of patients who are at a particular risk for PTCI would be extremely helpful in surgery. Early decompressive surgery (DC) confers a survival benefit (2,4,6).

Cerebral vasopasm, vascular injury, and hypoperfusion may cause PTCI. (1,3,4). Traumatic brain injury pathophysiology includes brain swelling, increased ICP, reduction in blood and oxygen supply, energy failure, and cell death (4). Thrombus formation is unclear. Acceleration,

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deceleration, or rotational motions between the brain, skull, and neck may cause vascular injury (7).

First of all, the patients should be checked out about cardiac, vascular and blood diseases (8).

After severe traumatic brain injury, in order to control brain swelling, either medical or surgical therapies should be used. ICP should be lower than 20-25 mmHg. Simple therapeutic maneuvers, including sedation, ventilation, and head-up position, should be done as the first step. After these, more advanced medical treatment, including application of inotropes, hypertonic saline, mannitol, and hypothermia can be performed. External ventricular drainage of the cerebrospinal fluid can be useful. If these modalities fail to control ICP, we need more advanced therapy, especially barbiturate coma therapy or DC (5,9-11).

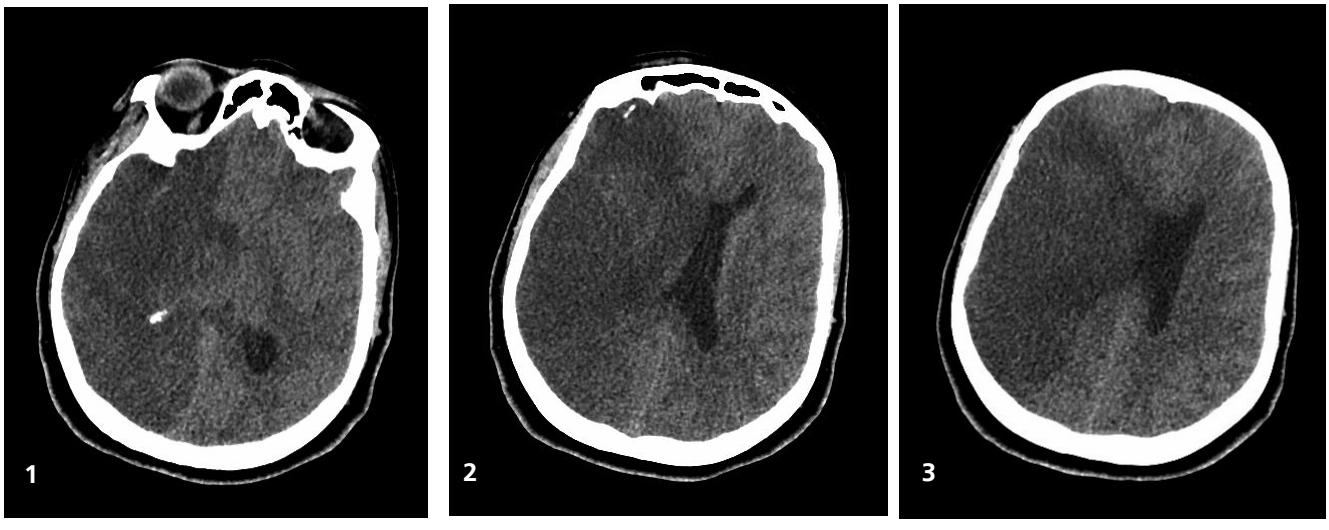
DC (removal of a part of the skull and duraplasty) is a good way to accommodate shifts of brain tissue and normalize ICP. DC is a radical and fast way of solution for the management of brain tissue shift and ICP. Surgical decompression reduces death rate and improves the functional outcome of patients. DC is mostly used as the last solution to prevent severe damage or death. In MCA infarction, DC reduces mortality by nearly 52.8%, but there is no consensus on if and when to proceed to surgery. DC may save one's life at the expense of creating a vegetative state and severe disability (10,12).

Computed tomography (CT) is useful in the detection of various cerebral pathologies, including infarction. Magnetic resonance imaging (MRI), MR angiography, CT angiography, and CT perfusion can be used for the diagnosis of cerebral infarction (2,13).

Case

A 51-year-old female was admitted to our emergency department with multiple trauma after a traffic accident. On presentation to the emergency department, she became confused, disoriented, and combative. She was noted to have left-sided hemiparesis and facial paralysis and was not obeying commands. Her systolic blood pressure was low (80 mmHg). After admitting emergency department, maintain the hemodynamic balance, preventing hypotension, hypoxia, elevation of the head by 20° to 30°, hyperosmolar therapy with mannitol or hypertonic saline treatments were started. On CT images, maxillofacial fractures, multiple rib fractures, hemothorax, and pneumothorax were seen. A chest tube was inserted urgently. After admission, the patient was taken to the intensive care unit. After three hours, the patient's GCS score was 6, and she had anisocoria but did not lose pupillary reaction to light. She had irregular breathing and pulse and underwent mechanical ventilation with controlled hyperventilation and sedation (using propofol and fentanyl). CT scans revealed right-sided hypodensity, MCA infarction and midline shift (Figures 1-3). Despite the conservative medical therapy, the ICP was over 25 mmHg. We could not take cerebral angiography or MRI, be cause of her poor general condition.

Except for the international normalized ratio (INR), other blood tests were normal, and she did not require an anticoagulant therapy, but her INR was 6. Fresh frozen plasma was given to the patient in order to reduce the INR. High-dose steroid treatment was given on the day of admission, and after 12 hours, the INR was normalized. After obtaining written informed consent from her family, operation was performed.



Figures 1-3. Preoperative computed tomography scans show the hypodense infarction area and midline shift effect

Surgery

DC consisted of a duraplasty and the creation of a large bone flap. Removal of head bone and enlargement of dura with duraplasty is DC's mainstays. In summary, a large skin incision in the shape of a question mark based at the ear is made. Frontotemporal question mark skin incision was made. A frontotemporoparietal bone flap was removed. The dura was opened, and a fascia lata graft was used for duraplasty. Dural tenting sutures were used in order to stop epidural hemorrhage. The temporal muscle and skin flap were then reapproximated and sutured.

After surgery, the patient was transferred to the intensive care unit. We did not use sedation or muscle relaxants. Her GCS score was 3 after the day of injury. A control CT scan revealed right-sided malignant MCA infarction and decreased midline shift (Figures 4-6). She died on the third day of her admission to the hospital.

Discussion

Due to high mortality and mortality rate, PTCI is destructive complication of trauma (1,2,14). Overall mortality rate is 75%. A GCS score between 3 to 5 is a high risk factor for mortality. Traumatic herniation of the brain may cause malignant high ICP which causes brain death. Despite modern medicine, CT scans, drugs, intensive care and monitoring, PTCI's mortality and morbidity rate is still high (2).

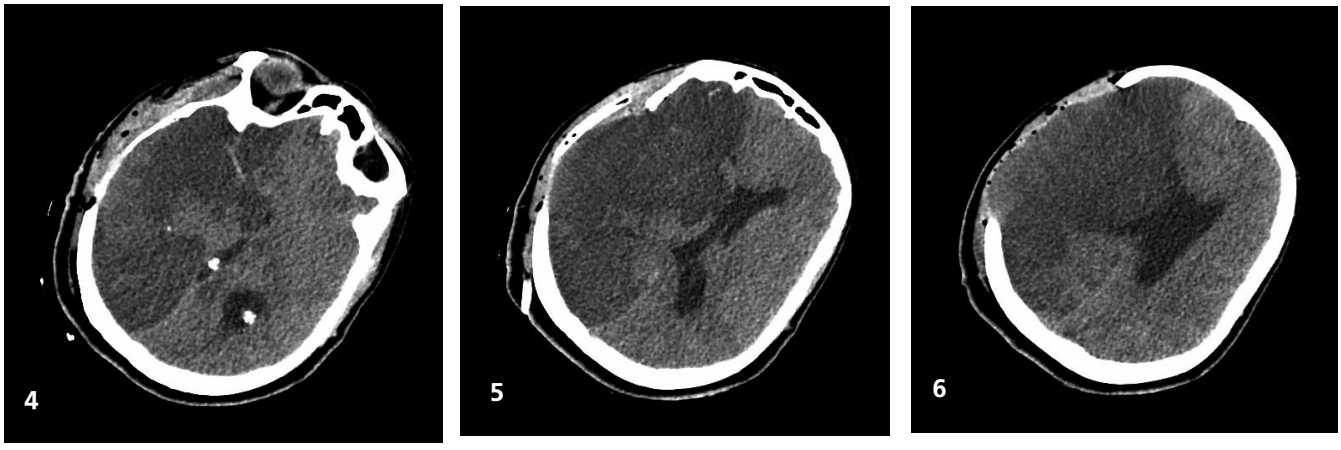
Low GCS (3-8), hypotension, and head trauma with vascular damage are main risk factors for brain shift and herniation with occurrence of fatal brain edema (2,4). The radiological factors for midline shift and postsurgical affected-to-contralateral side ratio are important clues of predicting clinical outcomes (15-18).

Regarding neurological status, the GCS score at admission and prior to surgery was 8 and 6, respectively. In addition, there was hypotension (60 mmHg-30 mmHg). On CT, it was observed that the midline shift was 10 mm. The time interval between injury and surgery was 12 hours. Hypotension is lustily associated with cerebral infarctions. Primarily, head trauma is complicated with craniofacial and limb fracture, chest trauma, and hemothorax.

Hypotension and hypoxia are significant predictors of mortality (4). If arterial perfusion is limitted with direct effect over cerebral cortex, infarction may occur. Intracranial vasospasm is also likely to occur in patients with severe injury (8). Rotational forces following trauma are secondary to the arterial wall intimal dissection, with primary thrombosis and vasospasm as less likely causes (1). Spasm may be due to direct vascular trauma or the effect of adjacent contusion and hemorrhage or may be mediated by release of a vasoactive humoral factor (6). The reported incidence of intracranial arterial spasm following moderate to severe head injury is in the range of 5% to 10% (1,19).

Massive hemispheric infarctions cause poor clinical outcome. If not treated surgically, case fatality is 80% (5). In several studies, there was a dramatic effect of surgery, with a highly significant absolute reduction of 52.8% in the death rate in the surgery group compared with the no-surgery group (9,10,15,20).

Anticoagulation using orally-administered low-molecular-weight heparin and thrombolysis using a recombinant tissue plasminogen activator have been found to be effective in adult patients when given within three hours of the thrombotic event. We could not use heparin and acetylsalicylic acid therapy because of high INR. Head trauma may cause coagulation abnormalities with poor clinical outcome. Elevated admission INR, elevated INR at 24 hours, and overall trend in INR strongly predict mortality in the trauma population (22,23). After giving the patient frozen plasma and vitamin K and, decreasing the level of INR, DC operation was started.



Figures 4-6. Postoperative computed tomography scans show the infarction area and still the midline shift

Unless medical treatments are succesful, DC is an established modality. Fastest way in order to reduce ICP, early DC and duraplasty are needed (2,12,14,21). In patients with a GCS less than 5, the risk of mortality increases. At this point, irreversible ischemic damage has no chance of recovery (2,15).

In the presence of bilaterally fixed or dilated pupils, a GSC of 3 or haemorrhagic transformation of the infarct, known coagulopathy or systemic bleeding disorder, contraindication for anesthesia, pregnancy, or contralateral ischemia, surgery should be avoided (5).

Death from brain herniation is not the only outcome. After a cerebral infarction, prolonged intensive care is needed, and worse outcomes, such as pneumonia, venous thromboembolic complications, seizures, depression, urinary tract infection, cerebral abscess, tracheostomy, gastric ulcer, etc., may occur (10).

Early diagnosis and successful management of traumatic cerebral infarction require a high degree of clinical suspicion. Close monitoring of the patient's neurologic condition is necessary for early diagnosis and succesful management of PTCI The decision about whether to perform DC or not is based on the patient's age, medical history, laboratory findings, neurological condition (GCS, clinical examination), imaging (CT or MRI) findings, in case of failure of conservative treatment and clinical deterioration. According to the literature, in the first 12 to 48 hours, early DC confers a survival benefit.

If PTCI occurs earlier with poor clinical status, this may cause high mortality and morbidity. Delayed surgery may cause irreversible ischemic infarcts. Even though we used medical and surgical treatment, the patient died. Malignant MCA infarction treatment is so difficult. In our patient, the presence of multiple trauma, including chest trauma, hemothorax, pneumothorax, craniofacial, and limb fractures, coagulation problems, and hypotension made it more difficult.

Decompressive craniectomy is widely accepted and applied as a rescue therapy in patients with refractory elevated ICP. DC provides the fastest relief by immediate reduction in raised ICP and resolution of midline shift.

Authorship Contributions

Design: A.A., U.E. Data Collection or Processing: A.A., U.E. Analysis or Interpretation: A.A., E.K., U.E., B.M.K. Literature Search: A.A., E.K. Writing: A.A., E.K., B.M.K.

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Subtotal Gastrektomi Geçirmiş Bir Hastada Perkütan Endoskopik Gastrostomi Uygulaması: Olgu Sunumu

Percutaneous Endoscopic Gastrostomy in a Patient with a History of Subtotal Gastrectomy: A Case Report

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Öz

Perkütan endoskopik gastrostomi (PEG) oral alımı yeterli olmayan hastalarda uzun yıllardır güvenli bir şekilde uygulanmasına rağmen daha önce geçirilmiş mide cerrahisi olan hastalarda pek tercih edilen bir işlem olmamaktadır. Ancak subtotal gastrektomi PEG uygulaması için kesin bir kontrendikasyon değildir. Bu olguda, peptik ülser nedeniyle daha önce subtotal gastrektomi yapılmış 83 yaşındaki bir hastada serebrovasküler olay sonrasında beslenmenin enteral yolla devamı için uygulanan PEG girişimini sunmayı amaçladık.

Anahtar Sözcükler: Enteral beslenme, gastrektomi, perkütan endoskopik gastrostomi

Abstract

While percutaneous endoscopic gastrostomy (PEG) has been used successfully for many years in patients for whom oral intake is not possible, it has been thought not to be a feasible procedure for patients who have had previous gastric surgery. However, history of a previous partial gastrectomy is no longer considered a contraindication for PEG-placement. In this case, we aimed to report an 83-year-old patient with a history of subtotal gastrectomy who required a PEG for enteral feeding because of cerebrovascular event.

Keywords: Enteral nutrition, gastrectomy, percutaneous endoscopic gastrostomy

Giriş

Perkütan endoskopik gastrostomi (PEG), oral alımı yeterli olmayan hastalarda enteral beslenmenin sağlanması için kullanılan güvenilir bir yöntemdir (1). Beslenmenin bu şekilde sürdürülmesi ile hem mukozal bütünlük korunmakta, hem de intestinal immün yanıtın devamlılığı sağlanmaktadır (2). Ayrıca, uzun vadede parenteral beslenmeye göre daha ucuz ve daha kolaydır (3,4). Koagülasyon bozuklukları, hemodinamik instabilite, sepsis, ciddi asit, peritonit, peritoneal karsinomatozis, mide çıkım obstrüksiyonu ve ciddi gastroparezi kesin kontrendikasyonlar arasında sayılmakta iken; orolaringeal veya özofageal maligniteler, hepatomegali, splenomegali, periton diyalizi ve parsiyel gastrektomi öyküsü rölatif kontrendikasyonlar olarak düşünülmektedir (2). PEG, subtotal gastrektomi öyküsü olan hastalarda kalan midenin yüksek yerleşimli olması ve yeterli gerginliğin sağlanamaması nedeniyle teknik olarak zor olduğu düşünülerek rölatif kontrendikasyonlar arasında sayılsa da deneyimli endoskopistler tarafından güvenle uygulanabilecek bir girişimdir (1,5-7). Bu çalışmada, peptik ülser nedeniyle daha önce subtotal gastrektomi yapılmış 83 yaşındaki bir hastada serebrovasküler olay (SVO) sonrasında beslenmenin enteral yolla sağlanması için uyguladığımız PEG olgusunu sunmayı amaçladık.

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Olgu

Seksen üç yaşında erkek hasta, yaklaşık iki ay önce geçirdiği SVO nedeni ile geriatri kliniğinde yatmakta iken yutma fonksiyonlarının zayıflaması üzerine önce nazogastrik tüp ile bir süre beslendikten sonra PEG açılmak üzere kliniğimize konsülte edildi. Hemiplejik olan hastanın özgeçmişinde apendektomi ve subtotal gastrektomi öyküsü vardı. Muayenede göbek üstü medyan kesi, orta hat transvers kesi ve sağ alt kadranda apendektomi kesi skarları mevcuttu. Preoperatif laboratuvar incelemesinde koagülasyon parametreleri normal sınırlarda olan hastaya, gerekli ön hazırlıkları takiben sedasyon altında, endoskopik olarak gastroenterostomi hattı görüldükten sonra "pull through (çekme) yöntemi" ile anastomoz hattının 1 cm proksimaline PEG kateteri yerleştirildi (Resim). İşlem sırasında komplikasyon görülmeyen hastanın beslenmesine 24 saat sonra PEG yoluyla başlandı ve takiplerde ek problem izlenmedi. Hasta verilerinin bilimsel amaçlı kullanımı için kendisinden ve yakınlarından onam alınmıştır.

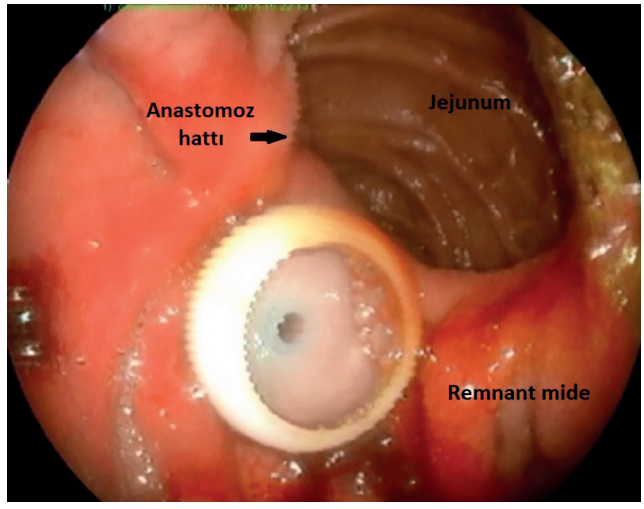
Tartışma

Endoskopi kılavuzluğunda yerleştirilen bir tüp sistemiyle uygulanan PEG, verimli, yüksek derecede etkili ve kullanılması kolay bir tekniktir (1,2). İlk defa 1980 yılında Gauderer ve ark. (8) tarafından tanımlandığından beri, yutma fonksiyonu bozuk olan ve yeterince beslenemeyen hastalarda en sık kullanılan enteral beslenme yöntemidir (9). Düşük maliyeti, gastrointestinal sistemin fonksiyon olarak devamlılığını sağlaması, bakteriyel translokasyonu azaltması ve intravenöz beslenmenin riskleri nedeniyle enteral beslenme, parenteral beslenmeye göre daha avantajlıdır (2,3).

PEG, yetersiz oral alım nedeniyle metabolik gereksinimi tam olarak karşılanamayan tüm hastalarda endikedir. Ancak en sık endikasyonları motor nöron hasarı, SVO, multipl skleroz ve demans gibi nörolojik hastalıklar ile baş-boyun maligniteleri, uzamış koma, kısa barsak sendromu ve gastrik dekompresyon olarak sayılabilir (2,10). Koagülasyon bozuklukları, sedasyona izin vermeyecek bir hemodinamik instabilite, sepsis, ciddi asit, peritonit, mide çıkım obstrüksiyonu veya ciddi gastroparezi kesin kontrendikasyonlar olarak gösterilirken; orolaringeal veya özofageal maligniteler, periton diyalizi, geçirilmiş karın cerrahisi ve parsiyel gastrektomi rölatif kontrendikasyonlar olarak düşünülmektedir (2).

PEG'nin endikasyon ve kontrendikasyonlarının doğru bilinmesi dışında; doğru olarak uygulanması, eksternal fiksasyonunun doğru yapılması ve uygun tüp bakımı komplikasyonları azaltmak için çok önemlidir (2). Ancak tüm bu uygulamalara rağmen komplikasyonlar kaçınılmazdır. Majör komplikasyonları sepsis, dislokasyon ve peritonit olup nadir olarak rastlanmaktadır. Yara enfeksiyonu, ağrı veya lokal kanama gibi minör komplikasyonlar ise daha sıktır (11). Uygun hasta seçimi, perioperatif antibiyotik kullanımı ve işlem sonrası problemlerin erken tanınması postoperatif komplikasyonları azaltırken; komorbid hastalıkların eşlik ettiği yaşlı hastalarda komplikasyon riski daha fazladır (12). Bazı çalışmalara göre teknik başarısı %95-98 gibi yüksek oranlarda olan bu işlemin; %3-12 oranında morbidite ve %0-2 oranında mortalitesi mevcuttur (4,10,13).

Löser ve ark. (3) tarafından 2005 yılında yayınlanan bir kılavuzda geçirilmiş gastrointestinal cerrahinin (Billroth I, Billroth II veya total gastrektomi) PEG/jejunostomi (PEG/PEJ) uygulaması için kesin bir kontrendikasyon olmadığı ancak bu hastalarda başarı oranının daha düşük olduğu bildirilmiştir. Sellers ve Brock (7) tarafından yayınlanan bir makalede, bu kılavuzu destekleyecek şekilde, daha önce Roux-En-Y bypass yapılmış 23 hastaya tek balonlu enteroskopi eşliğinde uygulanan PEG işleminin başarı oranının yaklaşık %70 olduğu bulunmuştur. Singh ve ark. (1) tarafından yayınlanan başka bir retrospektif çalışmada ise subtotal gastrektomi öyküsü olan hastalarda PEG/PEJ'in güvenle uygulanabileceği vurgulanmış; ancak mide cerrahisi geçirmiş hastaların geçirmemiş olanlara göre daha yüksek oranda beslenme intoleransı yaşadığı ve aspirasyon pnömonisi riskinin daha yüksek olduğu bildirilmiştir. Ayrıca bu çalışmada, ilginç bir şekilde, aspirasyon pnömonisine PEJ işlemi yapılan hastalarda PEG'e göre daha sık rastlandığının vurgusu yapılmıştır. Geçirilmiş mide cerrahisi olan hastalara uygulanan PEG işlemi, önceki cerrahiye bağlı yapışıklıklar ve değişen mide ve barsak anatomisi nedeni ile çeşitli riskler de içermektedir. Kolon veya karaciğer yaralanması direkt olarak ortaya çıkabilen komplikasyonlar olduğu gibi küçülen mide hacmi nedeni ile ortaya çıkan gastroözofageal reflü ve buna bağlı olarak aspirasyon pnömonisi riski de artmaktadır (1,7). Bir grup



Resim. Anastomoz hattının proksimaline yerleştirilmiş perkütan endoskopik gastrostomi tüpü

yazar ise özellikle riskli hastalarda gerçekleştirilecek PEG/PEJ işleminin bilgisayarlı tomografi eşliğinde yapılmasını önermişler, ancak bu sayede komplikasyon riskinin azalacağını belirtmişlerdir (14).

PEG, bazı hastalarda enteral beslenmenin devamı için gerekli bir işlemdir. Literatürde az sayıda olguya uygulanmış olsa da geçirilmiş mide cerrahisi, PEG uygulaması için kesin bir kontrendikasyon değildir. Parsiyel gastrektomi geçirmiş bir hastaya uygulanacak PEG işlemi, yüksek deneyimli endoskopistler tarafından, gerekirse ek görüntüleme yöntemlerinin yardımıyla yapıldığında teknik olarak uygun ve güvenilir bir prosedürdür.

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Mesaneye Rahim İçi Araç Migrasyonu: Total ve Parsiyel Migrasyonlu İki Olgunun Sunumu

Intravesical Migration of Intrauterine Device: A Report of Cases of Total and Partial Migration

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Öz

Rahim içi araç (RİA); uzun süreli, etkili ve tekrar kullanım için uygun, yaygın bir doğum kontrol yöntemidir. Uterusun perforasyonu ve RİA'nın mesane içerisinde yer değiştirmesi nadir olarak rastlanılan bir komplikasyondur. Çalışmamızda, mesaneye RİA migrasyonunun farklı aşamalarını saptadığımız iki olguyu sunmayı amaçladık. Olguların ilkinde RİA tamamen mesaneye migre olmuş ve tamamen taşlaşmış olarak saptandı. Diğerinde ise RİA mesane duvarında asılı idi ve sadece uçları taşlaşmıştı.

Anahtar Sözcükler: Rahim içi araç, mesane, migrasyon, uterus perforasyonu, yabancı cisim

Abstract

Intrauterine devices (IUD) are the commonly used long-acting, reversible and effective method of contraception. Migration of IUD into the bladder via uterine perforation is a very rare complication. In this paper, we aimed to present two different cases with different migration steps. In the first case, IUD was petrified and completely migrated into the bladder wall; in the second case, IUD was hanged on to the bladder wall.

Keywords: Intrauterine device, bladder, migration, uterine perforation, foreign body

Giriş

Rahim içi araçlar (RİA), geri dönüşün mümkün olmasının yanı sıra, düşük komplikasyon ve maliyet oranları nedeniyle doğum kontrolü amacıyla kullanılan yöntemlerin başında gelmektedirler (1). Bununla birlikte nadir olsa da pelvik bölge enfeksiyon ve apsesi ile uterus yaralanması ve perforasyonu gibi komplikasyonlara sebep olabilirler. Uterusun perforasyonu sonrası RİA'nın mesane içerisine migrasyonu ender de olsa meydana gelebilir (2,3). İntravezikal yabancı cisimler sıklıkla alt üriner sistem semptomlarına ve tekrarlayan üriner sistem enfeksiyonlarına neden olmaktadırlar (4). Biz bu çalışmamızda migrasyonun farklı aşamalarını göstermesi açısından, birisi mesaneye tamamen migre olmuş ve taşlaşmış, diğeri mesane içerisine migre olma aşamasında ve mesane duvarında asılı olarak saptanan iki olguyu sunmayı amaçladık.

Olgular

Olgu 1

Kırk bir yaşında, yedi yıl önce RİA takılan ve son iki yıldır idrar yaparken yanma, sık idrar yapma, ağrılı idrar yakınmaları olan hasta polikliniğimize başvurdu. Fizik muayenede anormallik saptanmadı. Yapılan idrar tahlilinde bol lökosit ve eritrosit saptandı. İdrar kültüründe üreme yoktu. Kan biyokimyası ve hemogram değerleri normaldi. Direkt üriner sistem grafisinde (DÜSG) kemik pelvis içerisinde RİA ile uyumlu ve etrafı taşlaşmış görüntü mevcuttu (Resim 1a). Ultrasonografide (USG) mesanede 18 ve 23 mm çaplı iki adet taş tespit edildi (Resim 1b).

Hasta bu bulgularla kliniğimize yatırıldı. Spinal anestezi altında yapılan sistoskopide mesane içerisinde 40x25 mm boyutunda, hareketli bir adet taş saptandı. Pnömotik litotriptörün çalışmaması üzerine, göbek altı 5 cm transvers insizyon ile hastaya açık cerrahi uygulanarak taş dışarı

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alındı (Resim 1c). Operasyon sonrası 7. gün sondası çekilen hasta şifa ile taburcu oldu. Takiplerinde sıkıntı olmadı.

Olgu 2

Otuz üç yaşında, altı yıl önce RİA takılan ve son bir yıldır idrar yaparken yanma, kanlı idrar, sık idrar yapma, pelvik ağrı yakınmaları olan hasta polikliniğimize başvurdu. Fizik muayenede anormallik saptanmadı. Yapılan idrar tahlilinde bol lökosit ve eritrosit saptandı. İdrar kültüründe üreme yoktu. Kan biyokimyası ve hemogram değerleri normaldi. DÜSG'de kemik pelvis içerisinde RİA ile uyumlu görünüm dikkati çekti (Resim 2a). USG'de mesanede 23 mm çaplı bir adet taş rapor edildi (Resim 2b). Hasta bu bulgularla kliniğimize yatırıldı. Spinal anestezi altında yapılan sistoskopide mesane içerisinde sol anterior duvarda asılı, uçları taşlaşmış RİA gözlendi (Resim 2c, 2d). Taşlı kısım pnömotik litotriptör ile kırıldı. RİA yabancı cisim forsepsi ile tutularak çıkarıldı (Resim 2e). Operasyon sonrası 7. günde çekilen sistografisinde mesane dışına kaçak saptanmayan hasta şifa ile taburcu edildi. Takiplerinde sıkıntı olmadı.

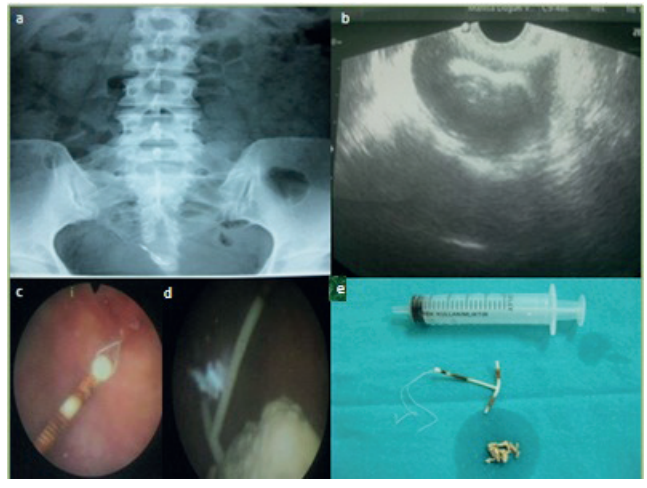
Tartışma

Mesane içerisinde JJ stent parçaları, gazlı bezler, sonda parçaları, sütür materyelleri, rezektoskop seramik uçları, perkütan sistostomi parçaları, iğne, saç tokası, kalem, tel, çivi, mermi gibi yabancı cisimler raporlanmıştır. Bu yabancı cisimler, tıbbi girişimlerin komplikasyonu, ateşli silah yaralanması ya da kişinin kendisine yaptığı uygulamalar sonucu, üretral veya transmural yolla mesaneye yerleşebilirler (5-7). Çok çeşitli yabancı cisim mesane içerisinde raporlanmış olmasına rağmen bunların sadece %8 gibi bir oranı RİA'dır (7). RİA'nın komşu ya da batın içi organlara migrasyonu nadir görülen bir komplikasyondur (1,2). RİA migrasyonu nedeniyle oluşan uterus perforasyonu insidansı 1000 olguda 0,87-3,6 oranında saptanmıştır (3). RİA'nın göç ettiği organ ve dokulara bağlı olarak da değişik klinik tablolar karşımıza çıkabilmektedir (8,9). Kassab ve Audra (10) 165 kayıp RİA olgusu üzerine yaptığı çalışmada; omentum, rektosigmoid, periton, mesane, appendiks, barsaklar, adneksiyal alan ve iliak ven gibi çok farklı alanlara migrasyonu gerçekleşmiş RİA bildirilmiştir.

RİA migrasyonu olan hastaların büyük çoğunluğunda, RİA'nın doğumdan hemen sonra, serviks ağzının tam olarak kapanmadığı dönemde takıldığı saptanmıştır. Bu durumda RİA uterin kavite dışına atılabilmekte ve perforasyon olabilmektedir (11). Ayrıca daha önce sezaryen ile doğum yapmış kadınlarda uterusta oluşan skar dokusundan dolayı perforasyon riski artabilmektedir (12). İmmobil uterus, miyometriyum defektinin varlığı ve retrovert yerleşimli uterus varlığı gibi anatomik sebeplerle de perforasyon riski ilişkili bulunmuştur (13,14). Uterus perforasyonlarının genellikle RİA'nın uygulanması esnasında meydana geldiği tahmin edilmektedir. Bundan dolayı, işlem öncesi detaylı jinekolojik muayene ile işlem sonrası USG ile kontrol yapılması önemlidir. (11). Sunulan iki olgu da sezeryan anamnezine sahip değildi; vajinal yolla iki doğum yapmıştı ve RİA uygulamaları da doğumdan hemen sonra gerçekleştirilmişti. Hastalarımızda uterus küçülmesi gerçekleşmeden ve serviks kapanması tamamlanmadan RİA uygulanmış olma olasılığı, mesaneye RİA migrasyonlarının sebebi olabilir.

RİA mesane migrasyonu total veya parsiyel olabilir. Bu durum uterusta oluşan defektin anatomik yerine, enfeksiyonun eşlik edip etmemesine ve geçen süreye göre değişiklik göstermektedir (15). Bizim olgularımızdan ilkinde mesaneye total migrasyon ve taşlaşma saptanırken, RİA yedi yıl önce yerleştirilmiş ve üriner sistem yakınmaları iki yıl önce başlamıştı. Diğer olguda parsiyel migrasyon ve taşlaşma saptanırken, RİA altı yıl önce yerleştirilmişti ve üriner sistem yakınmaları bir yıl önce başlamıştı. Süreler

Resim 1. Mesaneye tam migrate olmuş rahim içi araç olgusu



Resim 2. Mesaneye parsiyel migrate olmuş rahim içi araç olgusu

ve tanı anındaki RİA mesane ilişkisinin doğru orantılı olması, belki de parsiyel ve total migrasyonun aynı sonuca giden sürecin farklı aşamalarının yansımaları olabileceğini düşündürmektedir.

Mesane içerisine göç etmiş RİA'larda taş formasyonu mesane içi idrardaki partiküllerin RİA üzerinde birikiminden kaynaklanmaktadır. Literatürde taş oluşum derecesinin değişken olabileceği ve RİA'nın mesanede bulunma süresinden bağımsız olabileceği belirtilmektedir. Cihazın tümü ya da bir kısmı taşlaşabilir (12,16,17). Bizim olgularımızda da farklı aşamalarda taş oluşumları izlenmiştir. Her iki olgumuzda da yakınmalar RİA uygulamasından 5 yıl sonra ortaya çıkmış olsa da; iki yıldır yakınmaları olan hastada RİA tamamıyla taşlaşmış iken, bir yıldır yakınmaları olan hastada ise taşlaşmanın kısmi olduğu görülmüştür. Bu nedenle idrar ile RİA'nın temas süresinin taş oluşumu ile direkt ilişkili olduğunu düşünmekteyiz.

Mesane içi RİA, asemptomatik olabileceği gibi dizüri, hematüri, tekrarlayan idrar yolu enfeksiyonu, vajinal kanama ve pelvik bölgede ağrıya neden olabilir (6,7). Kadın hastaların üroloji polikliniklerine sık başvuru nedenlerinden olan bu şikayetlerin nedeninin nadir de olsa RİA migrasyonu olabileceği unutulmamalıdır.

Kayıp RİA olgularında lokalizasyon tanısı için USG, histeroskopi, X-ray, gerekirse bilgisayarlı tomografi (BT) ve cerrahi prosedür (laparoskopi veya laparatomi) işlemleri yapılmalıdır (18). Mesane içi RİA saptanmasında da, USG (abdominal yada vajinal), DÜSG, pelvik grafi veya BT kullanılabilmektedir (19). Sunulan her iki olguda da tanı için DÜSG ve USG kullanılmıştır. USG ve DÜSG ile yeri saptanamayan RİA olgularında ya da migrasyonun tamamlanıp tamamlanmadığı, RİA'nın uterus ile ilişkisinin net ortaya konulamadığı durumlarda BT çekilmesi gerekmektedir.

Mesaneye migrate olmuş RİA açık ya da endoskopik yöntemler ile tedavi edilmektedir. Açık cerrahi, endoskopik taş kırıcı araçlar kısıtlı ise ya da RİA'da büyük boyutlu taşlaşma mevcut ise uygulanabilir (20-22). Sunulan olgulardan 1. olguda taş büyük olduğu için açık cerrahi tercih ettik.

Tedaviye dirençli üriner enfeksiyon, dizüri gibi alt üriner sistem semptomları ve vajinal kanama, disparoni, kronik pelvik ağrı varlığında mesaneye migrate olmuş RİA ayırıcı tanıda düşünülmelidir.

Yazarlık Katkıları

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Closed Fracture of the Medial Malleolus Accompanied by A Rupture of the Tibialis Anterior Tendon: An Unusual Case Report

Medial Malleol Kapalı Kırığına Eşlik Eden Tibialis Anterior Tendon Rüptürü: Nadir Görülen Bir Olgu Sunumu

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Abstract

Isolated medial malleolus fractures comprise two-thirds of all ankle fractures and are rarely accompanied by a posterior tibial tendon rupture and dislocation. However, a medial malleolus fracture accompanied by an anterior tibial tendon rupture is unusual, and has not yet been reported. In this paper, a case of medial malleolus fracture accompanied by a tibialis anterior tendon rupture is presented and discussed.

Keywords: Medial malleolus, fracture, anterior tibial tendon, rupture

Öz

İzole medial malleol kırıkları tüm ayak bileği kırıklarının üçte ikisini kapsar. Nadiren posterior tibial tendon rüptürü ve dislokasyonu eşlik eder. Bununla birlikte, anterior tibial tendon rüptürüne eşlik eden medial malleol kırığı nadirdir ve henüz rapor edilmemiştir. Bu nedenle; bu olgu çalışmasında, tibialis anterior tendon rüptürü eşliğinde medial malleol kırığı sunulmuş ve tartışılmıştır.

Anahtar Sözcükler: Medial malleol, kırık, Anterior tibial tendon, rüptür

Introduction

Ankle fractures are among the most frequently seen fractures, and age, bone quality, increased body weight, previous ankle fracture, and the mechanism of the injury are the most important risk factors (1,2). The incidence is approximately 187 fractures per 100.000 people each year (3). Isolated medial malleolus fractures comprise two-thirds of all ankle fractures (4) and are rarely accompanied by tendon ruptures. Medial malleolus fractures accompanied by a posterior tibial tendon rupture and dislocation have been reported (5,6), however, a medial malleolus fracture accompanied by an anterior tibial tendon rupture is unusual, and has not yet been reported. In this paper, a medial malleolus fracture accompanied by a tibialis anterior tendon rupture is presented and discussed.

Case

A 54-year-old man was admitted to the hospital with a crush injury of the ankle caused by a log. Physical examination revealed medial left ankle and medial midfoot swelling and tenderness. Limited ankle movement was thought to be due to severe pain. There was no additional injury, and neurovascular examination was normal. On the anteroposterior and lateral radiographs of the ankle, an isolated medial malleolus fracture was seen (Figure 1). After the application of a temporary short-leg splint, the patient was taken into surgery. During the operation, it was noticed that the tibialis anterior tendon had ruptured. After fixation of the medial malleolus by two 4.5 mm cannulated screws, the incision was extended towards the medial cuneiform. It was then detected that the tendon

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had split from its insertion site. The distal tip of the tendon was slightly shortened and refreshed because of the degeneration. Due the shortening, it was attached to the navicular bone using two 3.5 mm anchors (Figure 2). After fluoroscopic control, the operation was completed, and a short-leg splint in mild dorsiflexion was applied (Figure 3).

The next day, the patient was mobilized on the healthy limb using two Canadian walkers, and was discharged on the second day. The short-leg splint was removed six weeks later, and a rehabilitation program that included passive and active ankle exercises was initiated. Full weight-bearing was allowed in the eighth week after surgery. At the three-month follow up, the patient had a full range of motion (Figure 4), and the American Orthopedic Foot and Ankle Society (AOFAS) score was 90 according to mild pain after a long walk. At the six, 12, and 18 month follow ups, the patient had no complaints, and the AOFAS scores were 100.

Figure 1. The anteroposterior and lateral radiographs of the ankle and the foot before surgery

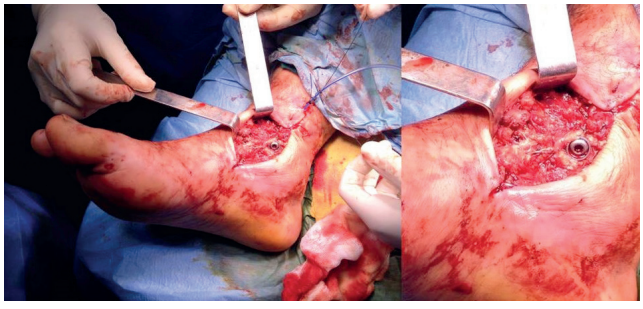

Figure 2. The fixation of the medial malleolus using two cannulated screws and the tibialis anterior tendon using two anchor sutures

Figure 3. The anteroposterior and lateral radiographs of the ankle and the foot after surgery

Discussion

The tibialis anterior muscle is the most important muscle of the foot for dorsiflexion and is responsible for approximately 80% of the power required for this movement. It occupies the anterior compartment of the leg, and originates from the lateral condyle and upper two-thirds of the lateral surface of the tibia, the interosseous membrane, and the deep surface of the fascia and the intermuscular septum. Its insertion site is on the plantar surface of the first metatarsal and the medial plantar surface of the first cuneiform. It also helps with the inversion of the foot at the subtalar and midtarsal joints, and assists with holding up the medial arch of the foot (7).

Acute rupture of the tibialis anterior tendon is quite rare and traumatic (8-11), and spontaneous ruptures due to gout, systemic lupus erythematosus, rheumatoid arthritis, diabetes mellitus, and psoriasis have been reported (12-15).

The loss of the tendon contour over the ankle and weakness of dorsiflexion of the foot are highly suggestive

Figure 4. The patient had full movement of the ankle three months after surgery

of a tibialis anterior rupture, but the diagnosis of a ruptured tendon accompanied by a medial malleolus fracture may be overlooked during the physical examination because of pain, swelling, and the limited movement due to the fracture. Direct roentgenograms may demonstrate avulsion fractures at the insertion site. The diagnosis can be confirmed by ultrasound and magnetic resonance imaging (MRI) (9,16). Early diagnosis of the tendon rupture is very important because early repair of the tendon results in a better outcome, whereas delayed surgery often requires grafting and has a lower success rate (17). In this rare injury, surgeons may be suspicious on tendon tension during surgery, and physical examination findings such as edema, swelling and ecchymosis in tendon insertion could be doubted.

Screw fixation and tension band wiring techniques are the most popular fixation methods for medial malleolus fractures (18). Screw fixation could be made by cannulated screws or malleolar screws. The surgeon selects the method depending on the type of the fracture, the size of the fragment, and bone quality, etc. (19). All these methods have successful rates. These fixation techniques are quite stable. In this case, we preferred open reduction for displaced fragment reduction and screw for stable fixation.

Of all the cases reported in the literature, tendon tears accompanying a medial malleolus fracture were diagnosed intraoperatively, and treated with the fixation of the medial malleolus and primary suture of the tendon (6). All the malleolar fractures previously presented were accompanied by posterior tibial tendon ruptures. Din reported a case of anterior tibial tendon injury associated with a closed midshaft tibial fracture (20). However, there have been no reports of medial malleolus fractures accompanied by anterior tibial tendon tears in the literature. In this case, the anterior tibial tendon tear was detected during surgery for the medial malleolus fracture. Depending on the shape of the fracture, this injury may occur due to trauma and direction of the forces applied to the foot. The tendon ruptured from its insertion site, unlike those presented in the literature, and was attached to the navicular bone using two anchor sutures after the stabilization of the medial malleolus fracture. No complications occurred and the patient had full movement of the ankle three months after surgery.

Although it is a very rare occurrence, anterior or posterior tibial tendon tears may accompany medial malleolus fractures. Lack of an early diagnosis can result in major complications. Thus, palpation of the tendons and checking for local tenderness are very important during the physical examination. Patients should be evaluated with ultrasound and MRI in addition to radiographs if required.

Authorship Contributions

Surgical and Medical Practices: S.H.B., E.S. Concept: S.H.B., E.S., M.Ç. Design: S.H.B., H.N.Ö. Data Collection or Processing: E.S., M.Ç. Analysis or Interpretation: S.H.B., H.N.Ö., A.B. Literature Search: S.H.B., A.B. Writing: S.H.B., H.N.Ö., A.B.

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Congenital Transmesenteric Hernia Without Bowel Strangulation in a Young Adult

Genç Erişkinde Barsak Strangülasyonu Olmadan Görülen Konjenital Transmezenterik Fıtık

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Abstract

Congenital internal hernia is a rare cause of bowel obstruction in adults and often presents with complications. A high index of suspicion, occasionally aided by appropriate radiological imaging, should lead to early surgical intervention and thus reduce morbidity and mortality. In this article, we describe a case of a 27-year-old man who presented with periumbilical and right lower quadrant pain. The patient who had undergone surgery for appendicitis was found to have an incidental mesenteric defect with herniating 30 cm-long small bowel segment on exploration. The mesenteric defect was repaired and the herniated bowel segment was reduced to prevent volvulus. The patient made an uneventful recovery.

Keywords: Internal hernia, mesenteric defect, small bowel

Öz

Konjenital internal fıtık, yetişkinlerde barsak tıkanıklığının nadir bir nedenidir ve sıklıkla komplikasyonlara neden olur. Bazen uygun radyolojik görüntülemeyle desteklenen yüksek bir şüphe, erken cerrahi müdahaleye sebep olup, morbidite ve mortaliteyi azaltabilmelidir. Bu yazıda, periumblikal ve sağ alt kadran ağrısı ile başvuran 27 yaşında bir erkek olgu sunuldu. Apandisit ön tanısıyla ameliyata alınan hastada, eksplorasyonda 30 cm'lik ince barsak segmentinin herniye olduğu, insidental mezenterik bir defekt görüldü. Bu mezenterik defekt onarıldı ve volvulusu engellemek amacıyla herniye olan barsak segmenti yerine konuldu. Hasta sorunsuz bir şekilde iyileşti.

Anahtar Sözcükler: İnternal fıtık, mezenterik defekt, ince barsak

Introduction

Transmesenteric hernia is a form of internal hernia through a congenital defect in the mesentery. The reported incidence of internal hernias ranges from 0.6 to 5.8% of all small bowel obstructions, and transmesenteric hernia accounts for approximately 5-10% of all internal hernias (1,2). There is no hernia sac in this situation but only a mesenteric defect, which is present at birth. As with other hernias, they may lead to intestinal obstruction, strangulation and subsequently, bowel gangrene with varying length of gangrenous intestine. Internal hernias may develop at different abdominal locations. They are generally in the paraduodenal area (50%), but may also be seen at transmesenteric, pericecal, intersigmoid and supravesical areas (1). Herniations to the foramen of Winslow, omentum, terminal mesoileum and broad ligament, or herniations to iatrogenic mesenteric defects are also possible. Although plain abdominal X-ray and computed tomography (CT) findings suggestive of an internal hernia have been described, the diagnosis of transmesenteric hernia is difficult, in part, because there

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are no radiographic or laboratory findings to confirm the suspicion. Diagnosis is frequently made at surgery (3-7). Herein, we report the case of a 27-year-old man who presented with symptoms of acute appendicitis and diagnosed to have approximately 30 cm-long small bowel segment herniated through a congenital transmesenteric hernia without bowel gangrene.

Case

An otherwise healthy 27-year-old man presented with a two-day history of severe periumbilical abdominal pain, multiple episodes of nausea without vomiting. The pain was acute in onset, severe, and continuous. The pain became prominent in the periumbilical area and localized in the right lower quadrant; it became worse over time. He had no other comorbid conditions and had not undergone any operations. On physical examination, he was lethargic with a pulse rate of 110/minute, blood pressure of 110/70 mmHg, temperature of 37.5°C and respiratory rate of 25/minute. Bowel sounds were audible. Results of laboratory investigations were normal except for a borderline elevated white blood cell count (WBC: 14000/mm^3). On abdominal ultrasonography, a moderate amount of fluid was detected between the intestinal segments. Since the patient was thought to suffer acute appendicitis, it was deemed unnecessary to take an abdominal CT prior to surgery. After initial resuscitation, the abdomen was explored through a McBurney incision. Approximately 0.5 liters of reactional peritoneal fluid was drained. On exploration, the appendix was found to be inflamed and edematous. Appendectomy was performed. Since the terminal ileum was also edematous, we continued exploration from the ileocaecal valve to the proximal intestine. We found a 30 cm-long herniated small bowel segment 90 to 120 cm distant from the ileocaecal valve. The segment was herniated through a large mesenteric defect (Figure). There was no bowel gangrene, and pulsations of mesenteric vessels were intact. The herniated bowel segment was reduced and the mesenteric defect was repaired with 2/0 silk sutures. Bowel function was resumed on the first postoperative day. Oral diet was initiated and tolerated well by the patient. He was discharged on the third postoperative day. On follow-up visit at 10 days, he was doing well. Histopathologic examination was interpreted as acute appendicitis despite the absence of a fecaloma in the appendix lumen on macroscopic examination. Patient's consent to publication was obtained.

Discussion

An internal hernia is formed by the protrusion of a viscus through a peritoneal or mesenteric aperture into a compartment of the abdominal cavity. It is estimated that internal hernias have an incidence of 0.2-0.9% and account for 0.6-5.8% of all cases of small bowel obstruction. Herniation can be congenital or acquired. Common sites of internal hernias are paraduodenal (50%), supra- and/or peri-vesical, intersigmoid, foramen of Winslow, omentum, postoperative mesenteric defects, and congenital mesenteric defects (8,9).

In 1836, Rokitansky reported the first case of mesenteric hernia, as an autopsy finding in which the cecum alone herniated through a hole near the ileocolic angle (10). The risk of developing a hernia in the presence of these defects is unknown (11). Mesenteric defects may be either congenital or acquired. Congenital defects are usually present in children and developmental defect is the likely cause, mainly in the mesentery of ileocaecal junction or ligament of Treitz. Various theories have been postulated to explain these developmental defects, including prenatal intestinal ischemia and subsequent thinning of the mesenteric leaves, intraperitoneal inflammation, trauma, partial development regression, and fenestration of the mesentery by the colon during the embryologic displacement into the umbilical cord. Transmesenteric hernia in adults is usually acquired resulting from previous abdominal surgery, particularly with Roux-en-Y anastomosis, as well as after abdominal trauma or intraperitoneal inflammation. These defects are found to be nearer to the ileocaecal junction or the ligament of Treitz (12).

Treves, in 1885, discovered a mesenteric region neighboring terminal ileum, which was wrapped by the junction formed by the ileocolic artery and the final branch of the ileal artery. This part was subsequently denoted as Treves' Field, which was free of fat, discernible vasculature, and lymph nodes, thus fairly prone to being damaged during development (13). Mesenteric defects have not been clearly explained from a pathogenetic aspect. One popular theory relates the cause to prenatal intestinal ischaemia and subsequent thinning of the mesenteric leaves because the prenatal intestinal ischaemia is associated with bowel atresia in 5.5% of the paediatric population (1). Whereas many views, such as dorsal mesenteric regression, rapid increase of the length of a mesenteric segment, and mesentery being compressed by the colon during foetal midgut herniation into the yolk sac, have been advocated in its pathogenesis, these causes may be caused by foetal environment. In contrast, transmesenteric hernia has been associated with other anomalies such as cystic fibrosis and Hirschprung disease, which raise the suspicion of a genetic aetiology (12). Mesenteric defects cause bowel loops to enter and to exit through the defect, which is the main cause of

obstructive symptoms of abdominal pain, distension, nausea, vomiting, and constipation. A herniated intestinal loop may distend, which may cause it to be incarcerated, strangulated, possibly culminating in shock. Patients with chronic defects may present with subtle and infrequent symptoms, making preoperative diagnosis fairly difficult. As such, bouts are thought to be due to peptic ulcer, biliary disease, or abdominal angina (2). Patients usually have a tender abdomen upon palpation. Eight percent of patients present with a palpable mass, while intestinal auscultation may yield no abnormality (14).

As there exist no radiological or biochemical signs or clues leading to diagnosis of mesenteric hernia, the latter is often difficult-to-diagnose. Although usually within normal range, leukocyte count may increase and metabolic acidosis may develop in the case of development of intestinal gangrene. The cases in the literature were generally admitted to hospital with symptoms of intestinal obstruction and strangulation and most of them needed a resection and anastomosis of bowel (15). However, in our case, the patient was admitted to the hospital with the symptoms of acute appendicitis. He had no symptoms of bowel obstruction, and at operation, no resection was needed.

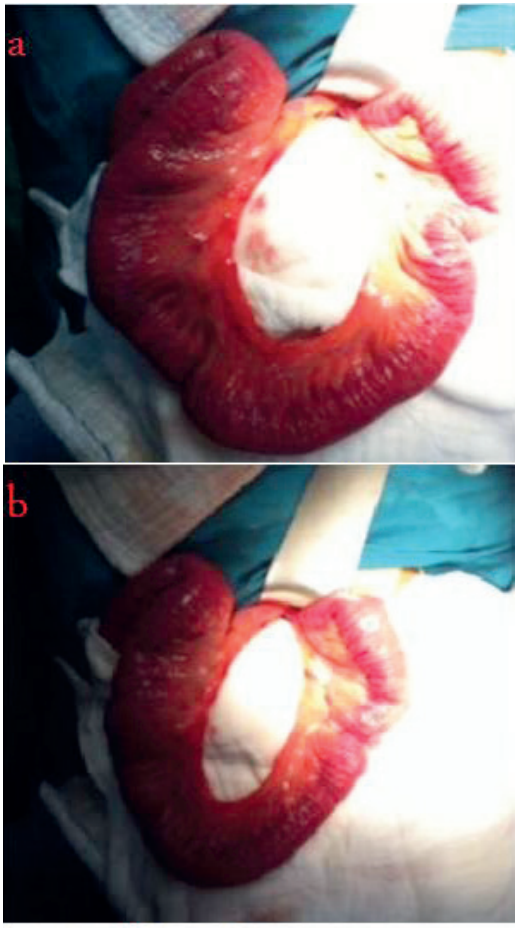

Figure. Intraoperative view of the mesenteric defect (a, b)

Most of the reports of congenital mesenteric hernia involve pediatric population, and adult cases are rare. The preoperative diagnosis of this congenital hernia is very difficult. The diagnosis is generally made at surgery (16). In our case, the preoperative clinical picture and laboratory data suggested acute appendicitis, not intestinal obstruction, and the accurate diagnosis was made during operation.

In conclusion, internal hernia usually manifests as acute intestinal obstruction that require early diagnosis and immediate surgery, but sometimes the clinical process is not obvious as seen in our case. Due to lack of specific signs and symptoms, the diagnosis is confusing. Therefore, possibility of such rare cases should be kept in mind.

Authorship Contributions

Surgical and Medical Practices: F.K., M.T.K., K.K. Concept: F.K., M.T.K., M.A.G., E.E. Design: F.K., M.T.K., M.A.G., K.K. Data Collection or Processing: F.K., K.K., E.E. Analysis or Interpretation: F.K., M.T.K., M.A.G., E.E. Literature Search: M.T.K. Writing: F.K., M.T.K.

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Case Report / *Olgu Sunumu*

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Intragastric Migration of Gastric Band Diagnosed During Surgery: A Case Report and Literature

Cerrahi Sırasında Tanı Konulan Gastrik Bandın İntragastrik Migrasyonu: Olgu Sunumu ve Literatür İncelemesi

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Abstract

Intragastric band migration (IGBM) is one of the major complications of gastric banding. In this report, we aimed to present a case of IGBM, which was diagnosed intraoperatively, and to review the relevant literature. A 59-year-old male patient was admitted to our outpatient clinic due to epigastric pain persisting for the past three months. The patient had a history of gastric banding surgery owing to obesity with open surgery nine years ago. Postoperative follow-up was not done properly and the patient had started to gain weight in the third postoperative year. Incisional hernia was found in physical examination and operation for gastric band removal and hernia repair was planned. During surgery, the band could not be found around the stomach, therefore, gastroscopy was performed and it was found that the majority of the band was placed in the stomach. The patient was intraoperatively diagnosed with IGBM and the band was removed through gastrotomy, and hernia repair was performed. The patient was discharged at postoperative 6th day without any complication. Although IGBM is rarely seen, it should be considered as a long-term complication in cases with dysfunctional gastric band and in patients who started to gain weight after operation. Treatment is the removal of the band review.

Keywords: Intragastric band migration, bariatric surgery, complication, obesity surgery

Öz

İntragastrik band migrasyonu (IGBM) gastrik band yerleştirilmesinin nadir gözüken majör komplikasyonlarından biridir. Bu yazıda intraoperatif tanı koyulan IGBM olgusunu sunmayı ve IGBM konusundaki literatürü derlemeyi amaçladık. Elli dokuz yaşında erkek hasta üç aydır olan epigastrik ağrı nedeni ile polikliniğimize başvurdu. Öyküsünde obezite nedeni ile dokuz yıl önce açık yöntemle gastrik band uygulandığı öğrenildi. Operasyon sonrası takipleri düzgün yapılmamıştı ve postoperatif üçüncü yıldan sonra tekrar kilo almaya başladı. Fizik muayenesinde insizyonel hernisi olan hastaya gastrik bandın çıkartılması ve herni tamiri nedeni ile operasyon planlandı. Operasyon sırasında band mide etrafında bulunamayınca intraoperatif gastroskopi yapıldı ve bandın büyük bir kısmının mide içinde olduğu tespit edildi. Hastaya operasyon sırasında IGBM tanısı konuldu ve band gastrotomi ile çıkartıldı, herni tamiri yapıldı. Postoperatif takiplerinde problem olmayan hasta altıncı günde taburcu edildi. IGBM nadir gözükmesine rağmen işlev görmeyen gastrik band durumlarında ve kilo almaya tekrar başlayan hasta gruplarında uzun dönem komplikasyon olarak akılda bulundurulmalıdır. Tedavisi bandın çıkartılmasıdır.

Anahtar Sözcükler: İntragastrik band migrasyonu, bariatrik cerrahi, komplikasyon, obezite cerrahisi

Introduction

Surgical treatment of obesity has become quite common during the last decade and it has been increasingly performed. Different surgical techniques have been used for treating obesity in years. Among these techniques, adjustable gastric banding (AGB) has been frequently used due to its easy applicability and relatively low complication rates (1). Although intragastric band migration (IGBM)

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among the complications of this technique is rarely seen, it is a complication which may cause serious consequences (2,3).

In this study, we aimed to present a case of IGBM identified during operation in a patient who underwent dysfunctional gastric band removal and to review the literature.

Case

A 59-year-old male patient was admitted to the general surgery outpatient clinic at our hospital with epigastric pain persisted for the past three months. In anamnesis, it was found that he had undergone open gastric banding due to obesity with a body mass index (BMI) of 49.2 about nine years ago and also underwent re-operation due to early preoperative distal band slippage for fixation of the band to the stomach. During following years, the patient's BMI had decreased to 34, however, he had started gaining weight and the patient dropped out of his follow-ups. The patient was 120 kg and his BMI was 42.9 on admission. An incisional hernia arising from the supra-umblical median incision healed with a bad scar tissue was present and the area around the port was hyperemic. The patient stated that this area had frequently become hyperemic and hyperemia resolved after antibiotic therapy. An operation for incisional hernia repair and removal of the dysfunctional gastric band was planned. The patient did not require another bariatric procedure. Endoscopic examination of the upper gastrointestinal system (GIS) was not performed in his previous follow-up period.

During the operation performed through supra-umblical incision under general anesthesia, a connector providing connection between gastric band and port was followed for reaching the band around the stomach, however, the band could not be seen around the stomach.

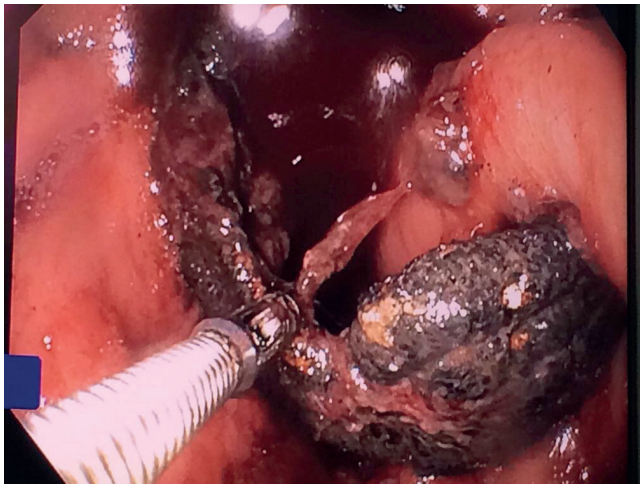

Figure 1. Intraoperative endoscopic view of intragastric migration of gastric band

Considering the possibility of IGBM, intraoperative upper GIS endoscopy was performed and the gastric band was found as mostly placed in the stomach; especially on the proximal stomach (Figure). Then, the entrance point of the band to the stomach was identified by following the connector. Gastrotomy was performed on this area on the lesser curvature at proximal stomach; and band was cut and excised. Gastrotomy was closed with sutures. There was no other perforation or fistula origin in the stomach. Additionally, hernia repair was performed with primary sutures. The patient was discharged at postoperative 6th day without any complication. There was also no problem in follow-ups after discharge; and BMI and weight of the patient were recorded at postoperative 18th month as 42.9 and 126 kg, respectively. Informed consent was obtained from the patient for all treatment process and also for the publishing of the results.

IGBM prevalence and diagnosis/treatment approaches in different series in the literature are summarized in Table. The rate of complication associated with laparoscopic AGB (LAGB) and IGBM have been reported to be 8-50.4% and 0.24-2.85%, respectively. Pars flaccida was the most common technique and laparoscopy was most commonly chosen approach as treatment modality. In addition, cases treated with excision through open surgery have also been reported.

Discussion

Surgical treatment methods for weight loss by restricting calorie intake or reducing absorption or combination of both of them are named bariatric surgery. Although it was first performed during 1950s; it has gained popularity in the last two decades. In spite of differences between the chosen methods in time; LAGB, Roux-en-Y gastric bypass, and sleeve gastrectomy have been the most frequently performed methods. Although LAGB method has lower success rate in weight loss when compared with other techniques, it has been a preferred technique due to low complication rates and lower risks of malnutrition and vitamin deficiency. It was defined as a safe method, however, different complications, such as gastric perforation, gastrogastric fistula, band slippage, pouch dilatation, esophageal dilatation, gastric volvulus, and IGBM, associated with gastric banding have been reported (6). In this paper, we presented a case of IGBM occurred late after gastric banding and aimed to evaluate different diagnostic and treatment approaches towards IGBM reported in the literature.

The incidence of IGBM has been reported to be lower than 1% in centers specified in obesity surgery with high patient volume; and as high as 10-20% in centers at the

Table. Intragastric band migration prevalence, diagnosis and treatment approaches in published patient series

	Year	Duration of follow-up	Number of patients	Migration rate	Approach	Mortality	Complication	Tratment
Nocca et al. (3)	2005	60 (max)	4236	1.6% (45)	Both	0%	8%	44 L 1 O
Carelli et al. (4)	2010	60 (max)	2965	0.24% (7)	Pars flaccida	0.06% (2)	12.2% (363)	NA
Brown et al. (5)	2013	NA	2986	2.85% (85)	Both	0%	NA	NA
Mittermair et al. (6)	2009	36 (med) 120 (max)	785	6.5% (51)	NA	0%	50.4% (396)	44 L 7 NA
Cherian et al. (7)	2010	NA	865	1.96% (17)	NA	NA	NA	16 L 1 O
Kurian et al. (8)	2010	NA	2437	0.57% (14)	Pars flaccida	NA	NA	NA
Abu-Abeid et al. (9)	2005	NA	754	2.1% (16)	Pars flaccida	NA	NA	16 L
Belachew et al. (10)	2002	48 (min)	763	0.92% (7)	Perigastric	0.1% (1)	16.1% (123)	NA
Favretti et al. (11)	2002	84 (max)	830	0.5% (4)	Perigastric	0	24.9% (210)	4 L
Abu-Abeid et al. (12)	2003	35 (med) 13 (min) 67 (max)	1480	1.14% (17)	Perigastric	NA	NA	16 L 1 O
Kohn et al. (13)	2012	NA	2097	2.53% (53)	Both	0%	NA	3 operated in another center 1 refused removal of the band 49 L
Hussain et al. (14)	2014	72 (max)	1149	0.17% (2)	Pars flaccida	0%	NA	NA
Watkins et al. (15)	2008	NA	2411	0.12% (3)	Pars flaccida	0.04% (1)	10% (241)	NA
Angrisani et al. (16)	2003	72 (max)	1893	1.1% (21)	NA	0.53% (10)	10.2% (193)	2 L, 1 O 5 deflation 14 followed

max: Maximum, min: Minimum, med: Median, NA: Non-available, L: Laparoscopic surgery, O: Open surgery

start of learning curve (1,3,4,17). In addition, migration incidence is higher during the first two years of surgeon's practice in a technique (5,7,18). It is remarkable that rates of IGBM occurrence and experience of the surgeon are associated parameters when the rates in centers with high patient volume and experience were evaluated.

Epigastric pain, weight gain and port infection are the most common symptoms observed in patients with IGBM (7,19). Feeling of hunger, lack of satiety, non-specific abdominal pain, dysphagia, and rarely peritonitis and abscess are other symptoms, however, patients may present without any clinical findings or with fatal and unexpected clinical conditions such as hematemesis (18,20). Time of IGBM occurrence may range between postoperative 3rd month and postoperative years. In our case, inflammation which had intermittently occurred around the port area and responded to antibiotics and the complaint of weight gain started three years after the first operation. The complaint of weight gain was present for many years and it was considered to be related with dysfunctional gastric band and dropped-out follow-ups. It has been criticized that the diagnosis has been made earlier if complaints had been carefully examined and additional tests such as abdominal tomography or gastroscopy had been performed during preoperative period.

AGB can be performed as open or laparoscopic surgery. Although open surgery was chosen in this patient, the more acceptable method is now minimally invasive surgery which has been increasingly used during the last decades. Two major surgical techniques, such as perigastric and pars flaccida, have been used in LAGB. Various complications, especially slippage and perforation have been more frequently reported in patients treated using the perigastric approach whose dissection is closer to the stomach. A significant decrease in complication rates has been observed with the pars flaccida technique which was defined later (5,9,21). Although general practice is tended to choose the pars flaccida technique, there are also other

practices which predominantly favour perigastric approach owing to its successful outcomes (10,11). There was no information related with which method the first operation had been performed on this patient.

Keeping in mind the possibility of the IGBM in patients with the history of gastric banding is the most crucial part of diagnosis. First diagnostic modality must be upper GIS endoscopy and diagnosis can be made with endoscopic examination without any other imaging modality in many cases (5). Ultrasonography and computed tomography are more beneficial in patients with predominant non-specific symptoms (5). It may be suggested that performing preoperative endoscopic or radiological examination in patients scheduled for band removal may reduce the risk of unexpected intraoperative conditions as happened in the presented cases; and be more reasonable approach. The criticism in the present case is that avoidance of preoperative gastroscopy resulted in a long duration of the surgical intervention because of intraoperative endoscopy. Moreover; if we could not have seen the band during intraoperative gastroscopy because of a possible totally intramural location, we would not finish the operation with success.

Question of how surgeon should approach after IGBM diagnosis is made involves many different treatment algorithms. Although there are no ideal answers for questions like when or which methods, the treatment is removal of the band (3). There are groups suggesting immediate removal of the band right after identifying migration due to possibility of peritonitis and abscess in IGBM cases, however, there are also substantial amount of practices preferring elective operation after close monitoring (3,11,19). The less invasive method is gastroscopic removal of the band and there are special devices developed for this purpose (gastric band cutter) (9,11,19,20). In gastroscopic method which can even be performed under sedation, presence of arch of the gastric band in the stomach is important for utilization of the method. Laparoscopic surgery may also be added when endoscopy is not adequate alone (20).

Although gastroscopic method is less invasive, long hospitalization period, frequent gastroscopy need and high cost of this method have made laparoscopy the most preferred method (3,12). In the laparoscopic method, a little gastrotomy incision is usually required for easier removal of the band, and repair of this created gastrotomy defect with an omental patch or primary closure are recommended (12,13). However, there are cases in which the gastric bands were removed without gastrotomy according to migration level of the band. Open surgery is the alternative approach when laparoscopic removal is not possible. A classification according to the amount of migration guides us to choose which removal method to use (3). In this classification, gastroscopic approach is recommended in cases of migration of most of the band whereas laparoscopic approach or gastroscopic approach is recommended in cases with little migration of the band after close monitoring until progression to migration. Additional techniques may be required for the treatment of obesity after band removal. Consensus between the patient and the doctor on whether surgery will be performed in same operation or in different session is the most accurate approach (5,8). In our case, open surgery was preferred due to planned incisional hernia repair and scar revision; and no additional intervention was performed due to the patient's refusal of bariatric procedures.

IGBM is a rarely seen complication after gastric banding surgery. It should be kept in mind that the band may migrate into the stomach in patients with a history of gastric banding and, in case of suspicion, the diagnosis should be confirmed with upper endoscopy, then endoscopic or surgical removal should be considered.

Authorship Contributions

Surgical and Medical Practices: M.U., R.Y., A.G. Concept: M.U, R.Y., K.T., M.S.B., S.T., S.T.A., A.G. Design: M.U., R.Y., K.T., M.S.B., S.T. Data Collection or Processing: M.U., R.Y., K.T., M.S.B., S.T., S.T. Analysis or Interpretation: M.U., R.Y., K.T., M.S.B., S.T., A.G. Literature Search: M.U., R.Y., K.T., S.T., S.T. Writing: M.U., A.G.

Conflict of Interest: No conflict of interest was declared by the authors.

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Radiological and Clinical Manifestations of Metastatic Pulmonary Calcification in a Patient with Parathyroid Hyperplasia

Paratiroid Hiperplazili Olguda Metastatik Pulmoner Kalsifikasyonun Radyolojik ve Klinik Bulguları ile Birlikte Değerlendirilmesi

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Abstract

Metastatic pulmonary calcification (MPC) is the deposition of calcium salts in the walls of the alveoli and small blood vessels in normal tissue. MPC may be associated with end-stage renal disease, primary and secondary hyperparathyroidism, diffuse skeletal malignancy, intravenous calcium therapy, massive osteolysis from metastases, and multiple myeloma. We present a case of a 53-year-old-man with end-stage renal disease and primary hyperparathyroidism presented with hip and chest pain. Computed tomography of the chest revealed multiple, ground-glass opacities associated with poorly defined centrilobular nodules and numerous calcific nodules, consistent with MPC.

Keywords: Computed tomography, hyperparathyroidism, metastatic pulmonary calcification, parathyroid adenoma

Öz

Metastatik pulmoner kalsifikasyon (MPK) alveol duvarlarında ve normal dokuların küçük kan damarlarında kalsiyum tuzlarının birikimidir. MPK, son dönem böbrek hastalığı, primer ve sekonder hiperparatiroidi, diffüz iskelet malignitesi, intravenöz kalsiyum terapisi, metastaza bağlı masif osteoliz ve multipl miyelom gibi hastalıklarda ortaya çıkabilir. Biz burada son dönem böbrek hastalığı ve primer hiperparatiroidi ile birlikte kalça ve göğüs ağrısı bulunan 53 yaşında erkek hastanın bilgisayarlı tomografide izlenen multipl, buzlu cam dansitesinde sentrilobüler nodüller ve kalsifik nodüller ile karakterize MPK görünümünü ilgili literatür eşliğinde sunmayı amaçladık.

Anahtar Sözcükler: Bilgisayarlı tomografi, hiperparatiroidi, metastatic pulmoner kalsifikasyon, paratiroid adenoma

Introduction

Metastatic pulmonary calcification (MPC) is a deposition of calcium salts in normal alveoli, interstitium, and bronchovascular tissue (1). MPC may be associated with end-stage renal disease (ESRD) and other disorders, such as hyperparathyroidism, diffuse skeletal malignancy, massive osteolysis from metastases, and multiple myeloma as well as intravenous calcium therapy (1,2). Chest X-rays can be used for the diagnosis of MPC, however, the findings are often normal since they are not sensitive. Computed tomography (CT) is a highly sensitive and useful imaging technique for the diagnosis of MPC. Calcifications can be detected easily. Also, CT shows calcification of the trachea, bronchi, blood vessel walls, and myocardial calcifications and other accompanying pathologies (1). We present the case of MPC in a patient with ESRD who presented with femoral neck fracture, as well as a brief literature review, including clinical and imaging findings.

Case

A 53-year-old male presented to the hospital with the complaints of left hip pain and chest pain for the preceding month. Anterior posterior pelvic and lateral hip X-rays were taken and showed left femur neck fracture. Physical

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exam was grossly unremarkable except for left hip pain, and vital signs were stable. He had a history of 70 pack/year smoking and chronic renal failure. He underwent hemodialysis three times per week for 16 years. The following serum levels were recorded (normal values in parentheses): creatinine: 8.64 mg/dL (0.40-1.40), calcium: 10 mg/dL (9.0-10.2), phosphor: 4.58 mg/dL (2.3-4.7), and parathyroid hormone: 3.259 pg/mL (<50 pg/mL). Cervical ultrasonography (US) (Toshiba Medical Systems Corporation, Otawara, Japan) was performed due to the high level of parathyroid hormone. On US, there was homogeneous, hypoechoic well-defined 2-cm diameter nodule adjacent to the lower pole of the left thyroid lobe. A technetium-99m methoxy-isobutyl-isonitrile (99mTc-MIBI) scan was performed for detection of the parathyroid adenoma, and 99mTc-MIBI accumulation was detected in the adjacent structures of the lower pole of the left thyroid lobe. Chest X-ray revealed numerous diffuse confluent nodular opacities with poorly defined margins (Figure 1). Chest CT was performed without history of dust exposure and malignancy. Chest CT revealed ground-glass opacities associated with poorly defined centrilobular nodules and numerous calcific nodules (Figure 2a, b). Also, circumferential calcification of the trachea, bronchi, and bronchioles was detected. A homogeneous, hyperdense, well-defined 2-cm-diameter nodule adjacent to the lower pole of the left thyroid lobe was detected (Figure 3). Osteoporosis and lytic lesions were seen in all of the bony structures of the thorax. MPC was considered in the differential diagnosis of pulmonary calcification. Imaging findings and medical history were compatible with MPC. The patient underwent parathyroidectomy. Histolopathological examination demonstrated parathyroid hyperplasia. The creatinine level was 2.35 mg/dL (0.40-1.40) and calcium

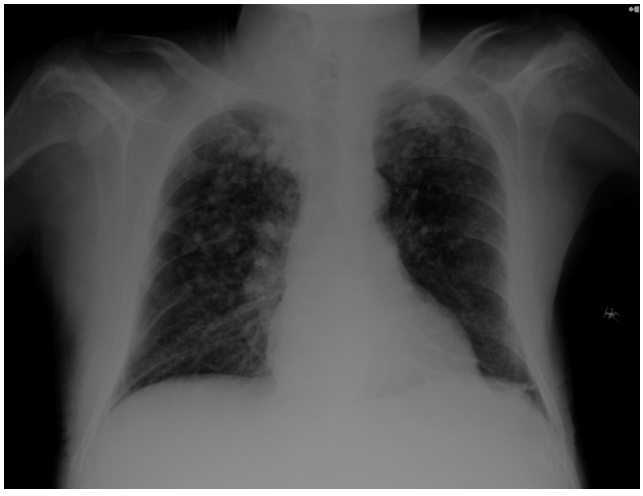

Figure 1. Chest X-ray shows numerous diffuse confluent nodular opacities with poorly defined margins, predominantly in the upper zone

Figure 2a, b. Axial contrast enhanced computed tomography with (a) mediastinal and (b) parankimal windows reveal ground-glass opacities associated with poorly defined centrilobular nodules and numerous calcific nodules

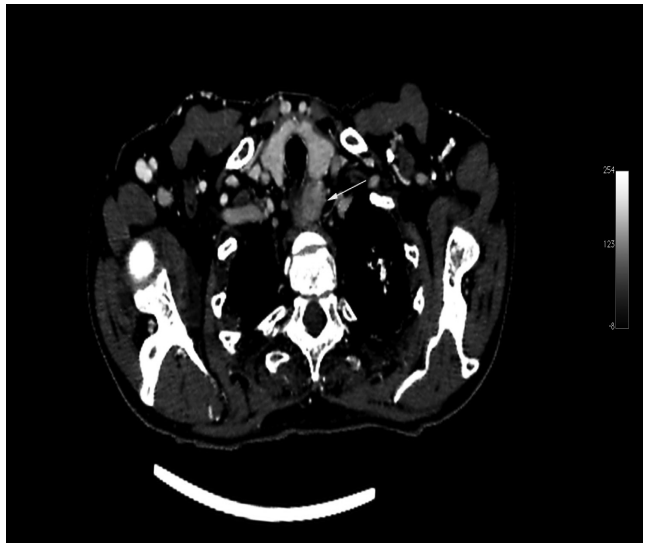

Figure 3. Axial contrast enhanced computed tomography shows homogeneous, hyperdense, well-defined 2-cm-diameter nodules (arrow) adjacent to the lower pole of the left thyroid lobe

level was 9.9 mg/dL (9.0-10.2) four months after surgery. Informed consent was obtained from the patient.

Discussion

Metastatic calcification is a deposition of calcium salts in normal tissue. It occurs most commonly in the lungs, kidneys, gastric mucosa, heart, and vessel walls (3). MPC can be caused by chronically elevated serum calcium-phosphorus levels, as in chronic renal failure, primary and secondary hyperparathyroidism, hypervitaminosis D, milk-alkali syndrome, or diffuse myelomatosis (2,3).

In addition, MPC is a complication of ESR failure and its treatment (1). The process is often undiagnosed in antemortem, however, commonly at autopsy in patients with renal failure. Most patients are asymptomatic, although some patients may present with fulminant respiratory failure and early death. Also, dyspnea and chronic, non-productive cough can be seen (4). Calcium salts often accumulate in alveolar walls and less often in bronchiole walls, pulmonary arteries, and veins (1). Apical segments are more affected than basal segments. The degree of respiratory distress usually is not associated with the degree of macroscopic calcification. Patients with extensive calcification may be asymptomatic. Also, mild calcification can cause severe respiratory failure (4).

Small calcifications cannot always be seen clearly on chest X-rays. Therefore, chest X-rays are often normal in patients with MPC (4). However, sometimes confluent or patchy airspace opacities may be seen on chest X-rays. This appearance can be simulated pneumonia, or infarction or pulmonary edema (5). Additionally, on chest X-ray, diffuse interstitial patterns or discrete or confluent calcified nodules can be seen in patients with MPC (1).

CT is very sensitive for the detection of small calcifications. Thus, it is the most preferred imaging modality in the diagnosis of MPC (3). Numerous patterns have been described on CT. These are multiple diffuse calcified nodules that are either distributed throughout the whole lung or show a predilection for the apices, diffuse or patchy areas of ground-glass opacity or consolidation, and confluent high-attenuation parenchymal consolidation. In addition, calcifications can be seen in the bronchial wall, myocardium, and the vessels of the chest wall (4). In our case, CT demonstrated multiple symmetrical, centrilobular, calcified nodules and patchy areas of ground-glass opacity throughout both lungs, especially the upper and middle lobes. Additionally, calcification was seen in the bronchial and tracheal walls.

The main differential diagnosis for MPC is dystrophic calcifications. Dystrophic calcification is the deposition of calcium salts in dead cells or tissue damaged by infections (tuberculosis, fungal infections, and chickenpox pneumonitis), silicosis, sarcoidosis, metastatic tumor, rheumatic mitral stenosis, microlithiasis, and broncholithiasis (5). Parenchymal calcified nodules are located mainly in the subpleural areas of the middle and lower zones in diffuse parenchymal amyloidosis. Also, hilar lymphadenopathy, interlobular septal thickening, consolidation, and ground-glass opacities can be seen in amyloidosis. The calcified pulmonary nodules in alveolar microlithiasis are smaller and typically seen in the lower zones and the paracardiac regions. Besides, apical bullae and subpleural cysts may be seen in alveolar microlithiasis (4). Miliary tuberculosis show multiple tiny discrete nodules randomly distributed in both lungs. Rarely, nodules can be calcified (4). Metastatic calcification tends to involve mainly the upper lung zones. Calcifications can also be seen in the myocardium, walls of the bronchioles, and the vessels of the chest wall (4). In our patient, pulmonary calcifications occurred due to hypercalcemia related to primary hyperparathyroidism and chronic renal failure. There are many reported cases of MPC related to chronic renal insufficiency and secondary hyperparathyroidism in the literature. However, cases of MPC related to primary hyperparathyroidism are limited in the literature (6).

Pulmonary calcification associated with renal failure is potentially reversible, and may resolve after parathyroidectomy, renal transplant, or adequate dialysis. (4). However, irreversible lung damage and respiratory failure can develop in untreated patients (3).

Chest CT is a valuable imaging modality in the diagnosis of pulmonary calcifications. It is very sensitive for identifying renal calcifications. Also, other mediastinal pathologies, such as tracheobronchial and myocardial calcifications, can be detected with CT as in our case. Primarily, MPC should be considered in differential diagnosis with these imaging findings. Diagnosis of MPC prevents unnecessary biopsies. Respiratory failure and irreversible lung damage can be avoided with early treatment.

Authorship Contributions

Concept: A.T.S, M.E. Design: A.T.S. Data Collection or Processing: A.T.S. Analysis or Interpretation: A.T.S, D.S. Literature Search: A.T.S. Writing: A.T.S

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