Case Report / *Olgu Sunumu*

A Case of Pfeiffer Syndrome Type 1

Pfeiffer Sendromu Tip 1'li Bir Olgu

Ali Karaman, Fuat Laloğlu*, Hasan Kahveci*, Remzi Arslan**

Department of Medical Genetics, Erzurum Nenehatun Obstetrics and Gynecology Hospital, Erzurum, Turkey
**Neonatal Intensive Care Unit, Erzurum Nenehatun Obstetrics and Gynecology Hospital, Erzurum, Turkey*
***Department of Pathology, Erzurum Nenehatun Obstetrics and Gynecology Hospital, Erzurum, Turkey*

Abstract

Pfeiffer syndrome is an autosomal dominant condition characterized by broad thumbs and great toes as well as craniosynostosis of the coronal sutures. Pfeiffer syndrome is very rare in the Asian population. Herein, we report the case of a male infant with Pfeiffer syndrome (acrocephalosyndactyly) who had acrocephaly, mild craniosynostosis of the coronal sutures and bilateral syndactyly of the toes. *(The Medical Bulletin of Haseki 2010; 48: 160-2)*

Key Words: Pfeiffer syndrome, craniosinositosis, syndactyly

Özet

Pfeiffer sendromu genellikle koronal sütürlerin kraniyosinositozu ve büyük ayak parmakları ve geniş başparmaklardan ibaret otozomal dominant bir durumdur. Pfeiffer sendromu Asya toplumunda çok nadirdir. Burada, Pfeiffer sendromlu bir erkek yenidoğan sunuldu. İnfantın, akrosefalisi, koronal sütürlerde hafif kraniyosinositozu ve ayak parmaklarında bilateral sindaktilisi vardı. *(Haseki Tıp Bülteni 2010; 48: 160-2)*

Anahtar Kelimeler: Pfeiffer sendromu, kraniyosinositoz, sindaktili

Introduction

In 1964, Pfeiffer described an acrocephalosyndactyly syndrome consisting of bicoronal craniosynostosis, midface deficiency, broad thumbs, broad big toes and partial and variable soft-tissue syndactyly of the hands and feet (1). Autosomal dominant inheritance with complete penetrance is characteristic, despite variable expressivity related to the presence or absence of syndactyly and its degree of severity. Based on the severity of the phenotype, Cohen proposed the division of Pfeiffer syndrome into 3 clinical subtypes (2). Classic Pfeiffer syndrome, designated type 1, involves individuals with mild manifestations, associated with normal neurological and intellectual development, generally has good outcome and can be found dominantly inherited. Type 2 consists of cloverleaf skull, Pfeiffer hands and feet, severe exorbitism, central nervous system involvement, elbow ankylosis or synostosis. Type 3 is similar to type 2 but without the cloverleaf skull. Types 2 and 3 have poor prognosis due to severe neurological compromise and various visceral anomalies, and they generally result in early death. To date, all cases of types 2 and 3 have only had sporadic occurrence.

We report a case of Pfeiffer syndrome type 1, with particular emphasis on the clinical presentation, differential diagnosis.

Case Report

The infant was the product of an uncomplicated, full-term gestation and normal vaginal delivery. The parents had a normal phenotype and were not consanguineous. The mother was 24 years and the father was 30 years old. The child had failure to thrive with a birth weight of 3.2 kg. On physical examination, acrocephaly, hypertelorism, antimongoloid slant of the eyes, flat nasal bridge, and low-set ears (Figure 1) were observed. The hands showed no abnormality. There was cutaneous syndactyly of the second and third toes bilaterally and the big toes were unusually broad.

Address for Correspondence/Yazışma Adresi: Dr. Ali Karaman
Department of Medical Genetics, Erzurum Nenehatun Obstetrics and Gynecology Hospital, Erzurum, Turkey Phone: +90 442 317 22 95 Fax: +90 442 317 22 94 E-mail: alikaramandr@hotmail.com

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(Figure 2A, B). Computed tomography of the skull and brain showed bicoronal mild craniosynostosis. According to the above-mentioned findings, diagnosis of Pfeiffer syndrome was made clinically.

Discussion

The exact incidence of Pfeiffer syndrome is unknown, but is expected to be 1 in every 100 000 births in the Western population. Many cases had been reported in the literature (3,4). However, it is even rare in the Asian population, with few cases reported in Japan and Korea (5,6). Pfeiffer syndrome is known to be caused by mutations in exon IIIa or exon IIIc of the fibroblast growth factor receptor (FGFR)1 or 2 gene (7,8). Therefore, the disease is genetically heterogeneous. In Pfeiffer syndrome type 1, fresh mutations or autosomal dominance are the genetic disorders. In types 2 and 3, inheritance is sporadic. Pfeiffer syndrome type 1, which is named "classic," involves individuals with mild manifestations including brachycephaly, midface hypoplasia, and toe abnormalities. This type is associated with normal intelligence and generally good outcome. Pfeiffer syndrome type 2 consists of cloverleaf skull, extreme proptosis, finger and toe abnormalities, elbow ankylosis or synostosis, developmental delay, and neurologic complications. Type 3 of this syndrome is similar to type 2, but without a cloverleaf skull. It should be noted that clinical overlap between the three types may occur (2). They may have other congenital anomalies of the upper airway, cleft palate, cleft lip, choanal atresia, fused vertebrae, imperforate anus, hydrocephalus, and Arnold-Chiari malformation (6). Our patient had none of these malformations. Our patient had mild clinical manifestations in favor of Pfeiffer syndrome type 1, which is an autosomal dominant condition consisting of broad thumbs and great toes as well as craniosynostosis usually of the coronal sutures (6,9).

The diagnosis of the Apert syndrome is appropriate rather than Pfeiffer syndrome if a patient has broad thumbs and syndactyly with bony fusion (10) or syndactyly of the second, third and fourth web spaces (11). However, clinical differential diagnosis has been confusing until now in relation with genetic findings because Pfeiffer mutation has been reported to occur in a patient with Apert syndrome (12), and identical mutations in the FGFR2 gene could cause both Pfeiffer syndrome and Crouzon syndrome phenotypes (13), as illustrated by the demonstration of both phenotypes of Apert and of Pfeiffer syndrome in experimental mice (14). Some authors have attempted to revise the classification for Apert, Carpenter, Crouzon, Jackson-Weiss, Pfeiffer and Saethre-Chotzen syndromes on a genetic basis (15-17).

The prognosis depends on the severity of associated anomalies, mainly the severity of the central nervous system compromise. Patients with type 1 syndrome have, in general, a good prognosis. Patients with types 2 and 3 usually expire early in infant or childhood even though some may survive with aggressive medical and surgical management (6).

Figure 1. Face of the patient

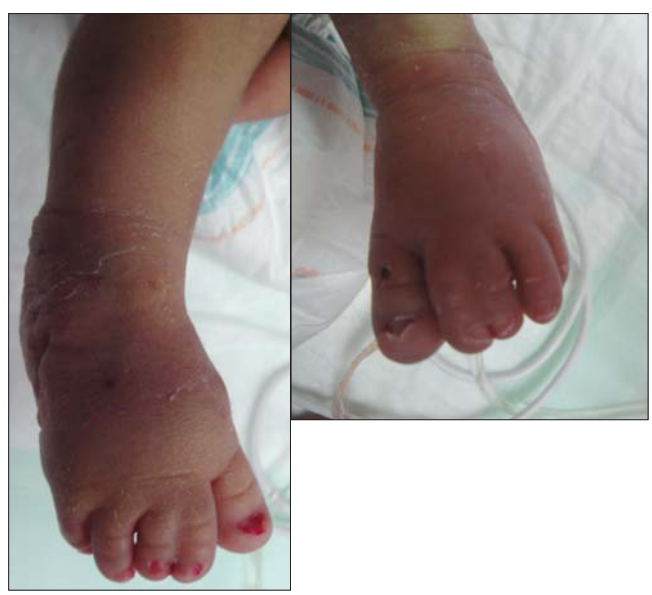

Figure 2 A, B. Feet of the patient showing broad big toes and partial syndactyly between second and third toes

References

1. Pfeiffer RA. Dominant Hereditary Acrocephalosyndactylia. Z Kinderheilkd 1964;90:301-20. [Abstract]
2. Cohen MM Jr. Pfeiffer syndrome update, clinicalsubtypes, and guidelines for differential diagnosis. Am J Med Genet 1993;45:300-7. [Abstract]
3. Plomp AS, Hamel BC, Cobben JM et al. Pfeiffer syndrome type 2: further delineation and review of the literature. Am J Med Genet 1998;75:245-51. [Abstract] / [PDF]
4. Jones KL. Smith's Recognizable Patterns of Human Malformation. 6th ed. Philadelphia, WB Saunders Company, 2006,472-3.
5. Nagase T, Nagase M, Hirose S, Ohmori K. Japanese sisters with Pfeiffer syndrome and achondroplasia: a mutation analysis. J Craniofac Surg 1998;9:477-80. [Abstract]
6. Park MS, Yoo JE, Chung J et al. A case of Pfeiffer syndrome. J Korean Med Sci 2006;21:374-8. [Abstract]
7. Muenke M, Schell U, Hehr A et al. A common mutation in the fibroblast growth factor receptor 1 gene in Pfeiffer syndrome. Nat Genet 1994;8:269-74. [Abstract] / [PDF]
8. Teebi AS, Kennedy S, Chun K et al. Severe and mild phenotypes in Pfeiffer syndrome with splice acceptor mutations in exon IIIc of FGFR2. Am J Med Genet 2002;107:43-7. [Abstract] / [Full Text] / [PDF]
9. Wilkie AO, Patey SJ, Kan SH, et al. FGFs, their receptors, and human limb malformations: clinical and molecular correlations. Am J Med Genet 2002;112:266-78. [Abstract] / [Full Text] / [PDF]
10. Wilkie AO, Patey SJ, Kan SH et al. FGFs, their receptors, and human limb malformations: clinical and molecular correlations. Am J Med Genet 2002;112:266-78. [Abstract] / [Full Text] / [PDF]
11. Martsolf JT, Cracco JB, Carpenter GG et al. Pfeiffer syndrome: an unusual type of acrocephalosyndactyly with broad thumbs and great toes. Am J Dis Child 1971;121:257-62. [Abstract]
12. Panthaki ZJ, Armstrong MB. Hand abnormalities associated with craniofacial syndromes. J Craniofac Surg 2003;14: 709-12. [Abstract]
13. Passos-Bueno MR, Sertie AL, Zatz M et al. Pfeiffer mutation in an Apert patient: how wide is the spectrum of variability due to mutations in the FGFR2 gene? Am J Med Genet 1997;71:243-5. [Abstract] / [PDF]
14. Rutland P, Pulleyn LJ, Reardon W et al. Identical mutations in the FGFR2 gene cause both Pfeiffer and Crouzon syndrome phenotypes. Nature Genet 1995;9:173-6. [Abstract] / [PDF]
15. Nagase T, Nagase M, Hirose S et al. Japanese sisters with Pfeiffer syndrome and achondroplasia: a mutation analysis. J Craniofac Surg 1998;9:477-80. [Abstract]
16. Hajihosseini MK, Wilson S, De Moerlooze L et al. A splicing switch and gain-of-function mutation in FgfR2-IIIc hemizygotes causes Apert/Pfeiffer-syndrome-like phenotypes. Proc Natl Acad Sci USA 2001;98:3855-60. [Abstract] / [Full Text] / [PDF]
17. Chun K, Teebi AS, Jung JH et al. Genetic analysis of patients with the Saethre-Chotzen phenotype. Am J Med Genet 2002;110:136-43. [Abstract] / [Full Text] / [PDF]