



Mucopolysaccharidosis Type 3B in an Adult with Pancytopenia: A Rare Case Report

Pansitopenisi Olan Erişkin Mukopolisakkaridoz Tip 3B Olgusu: Nadir Bir Olgu Sunumu

Alparslan Merdin, Fatma Avcı Merdin, Mustafa Karaca, Nihal Güzelay*

Akdeniz University Faculty of Medicine Hospital, Department of Internal Medicine, Antalya, Turkey

*Akdeniz University Faculty of Medicine Hospital, Department of Neurology, Antalya, Türkiye

Abstract

Mucopolysaccharidoses are rare hereditary lysosomal storage diseases developing due to dysfunction or deficiencies in enzymes that metabolize long-chain carbohydrates and glycosaminoglycans. Patients are normal at birth, but with accumulation of damaged products in the tissues, clinical features begin to appear in early childhood and, generally lose their lives before reaching adulthood. Sanfilippo syndrome B is a mucopolysaccharidosis caused by the deficiency of the lysosomal enzyme alpha-N-acetylglucosaminidase. Herein, we report a very rare case of Sanfilippo syndrome B accompanied by pancytopenia in an 18-year-old female patient who has survived into adulthood. (*The Medical Bulletin of Haseki 2014; 52: 232-4*)

Key Words: Mukopolisakkaridoz Tip 3B, pansitopeni, erişkin yaş, San Filippo Sendromu Tip 3B

Özet

Mukopolisakkaridozlar (MPS) glikozaminoglikanların ve uzun zincirli karbonhidratların metabolizmasında rol alan enzimlerin yokluğunda veya fonksiyon bozukluğunda gelişen kalıtsal lizozomal depo hastalıklarıdır. Enzim eksikliği nedeni ile yıkılmayan ürünler lizozomlarda birikerek, hücrelere ve dokulara zarar verirler. Hastalık çok nadir görülmekle birlikte; hastalar sağlıklı doğarlar ama erken çocukluk döneminde klinik özellikler belirginleşmeye başlar ve yetişkin döneme değin de yaşamlarını kaybederler. Biz bu vakada 18 yaşında, yetişkin döneme değin yaşamını sürdürebilmiş ve pansitopeni eşlik eden çok nadir görülen bir Mukopolisakkaridoz Tip 3 olgusunu bildirdik. (*Haseki Tıp Bülteni 2014; 52: 232-4*)

Anahtar Sözcükler: Mucopolysaccharidosis 3 Type B, Pancytopenia, Adult age, Sanfilippo Syndrome B

Introduction

Mucopolysaccharidoses (MPSs) are a group of rare genetic disorders result from the deficiency of one of the lysosomal enzymes, causing an inability to metabolize complex carbohydrates (mucopolysaccharides) into simpler molecules. Glycosaminoglycans (GAGs) collect in the cells, blood and connective tissues due to failure of their metabolism. The collected GAGs in cells and tissues cause permanent, progressive cellular damage which affects appearance, physical abilities, organ and system functioning, and mostly mental development. There are seven distinct clinical types of MPSs (MPS 1, MPS 2, MPS 3, MPS 4, MPS

6, MPS 7, MPS 9). Of the seven MPSs, MPS Type 3 (MPS 3 or Sanfilippo syndrome) is the most common one (1). MPS-3 has been subdivided into four types: MPS-3 Type A, MPS-3 Type B, MPS-3 Type C, and MPS-3 Type D. The defective gene involves a different step and a different enzyme, in the deconstruction of the same GAG heparan sulfate, therefore, the excreted chemical is the same for all types of MPS-3. MPS-3 Type B is caused by the deficiency of the lysosomal enzyme alpha-N-acetylglucosaminidase and is a rare autosomal recessive lysosomal storage disease. Patients with Sanfilippo syndrome are born with no symptom and typically have normal development for the first 2 years of life. The median age at clinical and

biochemical diagnosis of MPS-3 type B has been reported to be 3.1 years (2). In all types of MPS-3, CNS disease, a salient skeletal and soft tissue involvement, is less frequent compared with the other MPSs. Herein, we report a very rare case of Sanfilippo syndrome B accompanied by pancytopenia in an 18-year-old female patient who has survived into adulthood.

Case

A 18-year-old female patient was referred to Akdeniz University Medical Faculty Hospital (AUMFH) because of anemia, leukopenia, and thrombocytopenia. The patient was accepted by the department of internal medicine to find the cause of her pancytopenia.

The patient had also been evaluated previously by the department of pediatrics at AUMFH in 2009 due to her skeletal abnormalities and abnormal appearance. She had mild facial dysmorphism and stiff joints. It was found that she had alpha-N- acetylglucosaminidase deficiency. Consequently, she had been diagnosed with MPS Type 3 B (Sanfilippo syndrome B). In the same period, she also had splenomegaly and mild pancytopenia, therefore, bone marrow biopsy procedure which revealed hypocellular bone marrow (lipid content 60%) had been performed in 2009 at the same department. Some of the megakaryocytes were small and close to each other (dysmegakaryopoiesis?). Erythroid cells could not be determined. Granulocytes were markedly decreased in number, but well matured.

On physical examination of the patient, splenomegaly (5 cm) and hepatomegaly (2 cm) were palpated below the rib, but there was no peripheral lymphadenopathy. There was facial features of the syndrome (Figure 1). The patient was conscious, however, was with no orientation and cooperation, besides, she could not communicate. She did not have hyperactivity, she had severe mental retardation. Body temperature was 36.8 Celsius. She was taking levetiracetam 250 mg twice daily due to convulsion.

Clinical laboratory measurements revealed the following results: CRP (C-Reactive Protein): 0.37 mg/dl; LDH: 166 U/L; creatinine: 0.38 mg/dl; ALT: 24 u/L (0-41); albumin: 4.1 g/dl (3.9-4.9) ; ferritin: 72.4 ng/mL (13-150); vitamin B12: 353.6 pg/mL (197-866); folate: 6.4 ng/mL (4.6-18.7); serum transferrin: 225 mg/dL (200-360); serum iron: 27 µg/dL (33-193) and total iron binding capacity: 284 µg/dL (228-428). Blood tests revealed a leukocyte count of 2480/mm³, a neutrophil count of 1520/mm³, a hemoglobin count of 11.2 g/dl (12-16), and a platelet count of 65000/mm³. Other laboratory findings were within normal limits. There were not any atypical cells or blast cells seen in peripheral blood smear. Erythrocytes had normochromic and normocytic appearance in peripheral blood smear. The number of the all blood cells was found to be decreased.

The patient's general condition was good during the follow-up period and there was no obvious symptom. Her pancytopenia was evaluated as a part of MPS and bone marrow biopsy was not performed again. She was discharged with replacement therapy plan in case of symptomatic anemia or progressive severe pancytopenia.

Discussion

Mucopolysaccharidosis Type 3 B is a very rare disease. Meike et al. reported the prevalence of MPS 3B to be 1 in 211.000 live births (1). Kılıç et al. reported that MPS Type 3 was the most common form of MPSs in Turkey (3). Neurologic degeneration usually begins in children with MPSs at age 6 and death may not occur until after puberty. Affected individuals can have severe neurological symptoms, including progressive dementia, aggressive behavior, hyperactivity, seizures, deafness, loss of vision, and inability to sleep for more than a few hours at a time (4). However, our patient has survived into adulthood. but she is well in general except for her syndromic characteristics. This is a very rare opportunity for Sanfilippo syndrome B.

Enzyme replacement therapy (ERT) is an effective treatment in MPSs. Laronidase is an analogous with human alfa-L-iduronidase approved by the FDA in 2003 for MPS Type 1. Hematopoietic stem cell (HSC) gene therapy is also a potentially curative treatment modality for storage disorders. Genistein supplementation has been proposed as a potential therapy for the reduction of substrates in patients with these disorders (5). Genetic



Figure 1. Adult Mucopolysaccharidosis Type 3B (Sanfilippo Syndrome B), typical physical appearance

counseling is recommended for prospective parents with a family history of Sanfilippo syndrome.

There are many causes of pancytopenia, such as leukemia, myelofibrosis, metastatic bone marrow tumors, paroxysmal nocturnal hemoglobinuria, and hypersplenism. Pancytopenia might accompany MPSs especially due to hypersplenism that might be seen in MPSs. Our patient had also mild hepatosplenomegaly. But she had mild pancytopenia and hypocellular bone marrow. To the best of our knowledge, this is the first patient presented with Sanfilippo syndrome Type B accompanied with pancytopenia secondary to decreased bone marrow function. Consequently, lysosomal storage diseases and Sanfilippo syndrome B should also be considered in the etiology of pancytopenia.

References

1. Meikle PJ, Hopwood JJ, Clague AE, Carey WF. Prevalence of lysosomal storage disorders. *JAMA* 1999;281:249-54.
2. Delgadillo V, O'Callaghan Mdel M, Gort L, Coll MJ, Pineda M. Natural history of Sanfilippo syndrome in Spain. *Orphanet J Rare Dis* 2013;8:189.
3. Kılıç M, Kalkanoğlu S, Tokatlı A, Dursun A, Coşkun T. Mukopolisakkaridozlar: 3 Yıllık Hacettepe Deneyimi *J LSD* 2010;2:83.
4. Mucopolysaccharidoses Fact Sheet. National Institute of Neurological Disorders and Stroke Website. February 16, 2010; http://www.ninds.nih.gov/disorders/mucopolysaccharidoses/detail_mucopolysaccharidoses.htm. Accessed 4/14/2010.
5. Delgadillo V, O'Callaghan Mdel M, Artuch R, Montero R, Pineda M. Genistein supplementation in patients affected by Sanfilippo disease. *J Inherit Metab Dis* 2011;34:1039-44.