Pompe Disease Presenting with Supraventricular Tachycardia in the Early Neonatal Period: Case Report

Erken Yenidoğan Dönemde Supraventriküler Taşikardi ile Tanı Konulan Pompe Hastalığı

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ABSTRACT Pompe disease is a glycogen storage disorder with autosomal recessive inheritance which is caused by the deficiency of acid alfa-glucosidase enzyme. Clinical presentation can be fatal in infantile form, depending on the deficiency of enzyme level. Cardiac muscle hypertrophy induced by glycogen storage is the most significant finding. Early treatment with enzyme replacement therapy, especially for infantile cases, may improve clinical outcome. In this report, we present a newborn with supraventricular tachycardia in the delivery room and resting ECG showing Wollfs Parkinson White (WPW) pattern who was finally was diagnosed with Pompe disease on the basis of enzyme analysis. We also found optic atrophy on fundus examination and agenesis of the corpus callosum on cranial MRI along with the cardiac findings. Conclusion; Supraventricular tachycardia could be the early cardiac sign of Pompe's disease.

Key Words: Glycogen storage disease Type II; tachycardia, supraventricular; cardiomyopathy, hypertrophic

ÖZET Pompe hastalığı asit maltaz (asid alfa-glukozidaz) enzimi eksikliği sonucu ortaya çıkan otozomal resesif kalıtım gösteren bir glikojen depo hastalığıdır. İnfantil formunda klinik bulgular enzim seviyesinin çok düşük oluşuna bağlı daha ağır olabilir. Kalp kasında glikojen birikimine bağlı oluşan hipertrofi en önemli bulgusudur. Özellikle infantil vakalarda rekombinan enzim replasmanı ile erken dönemde tedaviye başlanarak olumlu sonuçlar alınmaktadır. Bu yazıda, doğum odasında supraventriküler taşikardi saptanan ve istirahat EKG'si Wollfs Parkinson White (WPW) ile uyumlu olan ve sonrasında enzim analizi ile Pompe hastalığı tanısı almış bir olguyu sunmaktayız. Kardiyak bulguların yanısıra fundus muayenesinde optik atrofi ve kraniyal MRG'de korpus kallozum agenezisi de saptadık. Sonuç; supraventriküler taşikardi Pompe hastalığının erken bir kardiyak bulgusu olabilir.

Anahtar Kelimeler: Glikojen depo hastalığı tip II; taşikardi, supraventriküler; kardiyomiyopati, hipertrofik

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Infantile Pompe disease is a glycogen storage disease presenting with hypotonia and muscle weakness. The disease has an autosomal recessive inheritance with an estimated frequency of 1/40 000.[1-3] The cardinal signs of the this disease include generalized myopathy, progressive cardiomyopathy and death in early infancy. Partial deficiency of the enzyme leads to a milder late onset phenotype. Data from the clinical trials show that the enzyme replacement therapy clears glycogen deposits from cardiac muscle and prolongs survival in patients. The best results are noted in in-

fants treated early.[1] Therefore, early diagnosis and prompt management of the disease is important. The clinical presentation of cardiomyopathy is variable. Generaly cardiomegaly develops during the follow-up period and cardiac insufficiency occurs gradually. However, rare cardiac presentations may also occur. Here, we present an infant who presented in the neonatal period with supraventricular tachycardia, secondary to hypertrophic cardiomyopathy.

CASE REPORT

Supraventricular tachycardia was noted in a neonate after physical examination in the delivery room. Her birthweight was 3000 g. She was hypotonic and her heart rate was 220/min. 12-lead Electrocardiography demonstrated narrow QRS tachycardia (Figure 1a). Following single dose of Adenosine (0.1 mg/kg, IV) her tachycardia improved. Chest X-ray was normal. 12-lead Electrocardiography showed ST elevation, short PR interval (0.08 sec), narrow QRS, sinusal rhythm and delta wave. These ECG findings were consistent with WPW (Figure 1b). Echocardiography demonstrated hypertrophic cardiomyopathy (Figure 2).

Laboratory investigation in the differential diagnosis of hypertrophic cardiomyopathy included complete blood count, liver and renal function tests, lactic acid, pyruvic acid, uric acid, ammonia, thyroid function, tandem mass spectrometry and abdominal ultrasonography were all normal. In the follow-up, optic fundus examination showed bilateral optic atrophy. Cranial magnetic resonance imaging showed corpus callosum agenesis.

Infantile Pompe disease was suspected because of hypotonia, cardiomyopathy, respiratory and swallowing difficulties and short PR on ECG. Although the muscle biopsy was normal, low leukocyte acid maltase activity was significantly reduced (0.2 μkat/kg protein, reference mean: 7.5 μkat/kg protein, normal: 4.8-13.3 μkat/kg protein). Enzyme replacement therapy (Myozyme; Genzyme Corporation, Framingham, MA, US, 20 mg/kg İV infu-

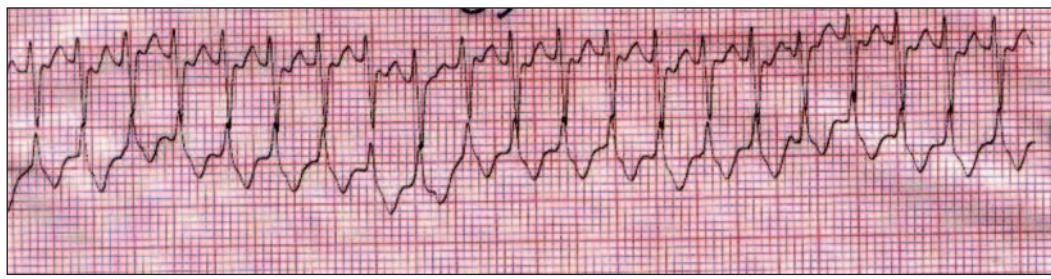

FIGURE 1a: Electrocardiography revealed supraventricular tachycardia in the derivations of DII and DIII.
(See color figure at http://www.turkiyeklinikleri.com/journal/journal-of-medical-research-case-reports/1300-0284/)

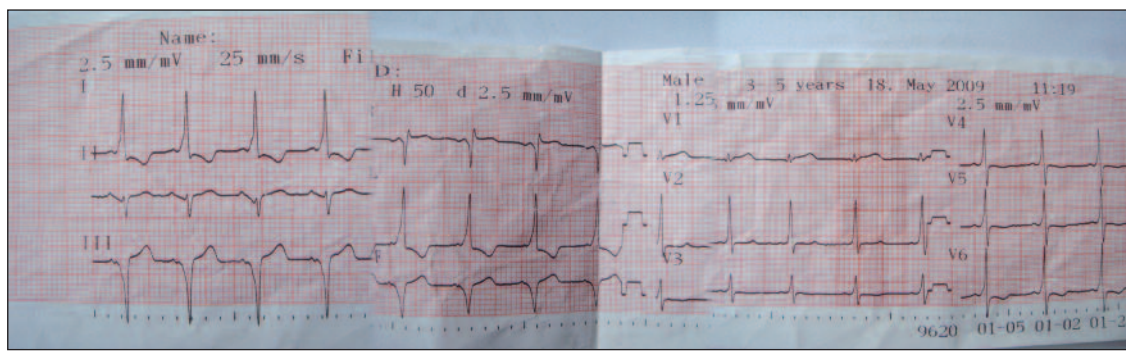

FIGURE 1b: 12 lead electrocardiography demonstrating left superior axis, short PR interval, narrow QRS, delta wave and ST-T changes.
(See color figure at http://www.turkiyeklinikleri.com/journal/journal-of-medical-research-case-reports/1300-0284/)

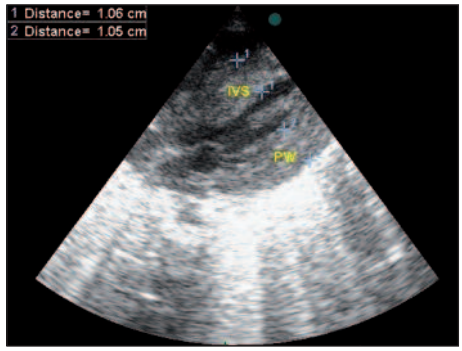

FIGURE 2: Echocardiography showing concentric hypertrophy in interventricular septum and posterior wall, there was no sign of left ventricular outflow obstruction.
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sion, 2 doses per month) was initiated. Propranolol 2 mg/kg bid, PO was added to prevent supraventricular tachycardia. In the follow-up, the patient remained free of dysrhythmias.

DISCUSSION

Pompe disease (Glycogen storage disease type II, GSDII, Asit maltase deficiency) is characterized by inadequate levels of alpha-glucosidase which lead to progressive accumulation of glycogen inside the lysosome and many tissues.[2,4] However, major clinical manifestations are seen in cardiac and skeletal muscles. The disease presents as a continuum of clinical phenotypes. In severe forms of disease, the symptoms occur in the first months of life and death results from cardiac and respiratory failure within the first years of life.[2] Mean age at presentation was reported as 1.6 to 1.9 months. Affected infants undergo progressive debilitation and most present at a mean age of 6 and 7.7 months and almost all die by 2 years.[3,4] Early diagnosis is highly crucial to start enzyme replacement therapy immediately.[5,6] Enzyme replacement therapy may improve the prognosis.[7]

The heart in Pompe's disease is grossly enlarged; fibroelastic thickening of the endocardium develops in approximately 20% of patients with Pompe's disease.[8,9] The infantile form of type II GSD is a generalized and habitually fatal disease of infancy, characterized by massive cardiomegaly caused by glycogen accumulation in the myocardial cells in the first weeks of life.[10] Juvenile and adult form of GSD type II show mostly skeletal muscle involvement simulating muscular dystrophy even if cardac involvement may occur. The reason why the heart in these forms is less commonly affected is attributable to limited dependence of the myocardium to glycogenolysis and glycolysis.[10] Echocardiography confirms severe concentric biventricular hypertrophy which initially resembles hypertrophic cardiomyopathy and may be associated with left ventricular outflow tract obstruction.[10] The case presented here had an unusual clinical presentation. She had tachycardia on the first day of her life. Electrocardiography demonstrated supraventricular tachycardia and echocardiographic examination demonstrated hypertrophic cardiomyopathy. In literature, there are case reports with atypical cardiac presentations of patients with Pompe disease. Venugopalan reported an infant who presented in the neonatal period with cardiac failure secondary to hypertrophic cardiomyopathy.[11] The boy subsequently progressed to show features of a metabolic disorder with multisystem involvement and was diagnosed to have Pompe's disease. Fung et al. also reported a Chinese infant with Pompe's disease.[12] The patient had an unusual presentation of supraventricular tachycardia and subsequently died of ventricular fibrillation. However, our patient experienced supraventricular tachycardia which responded to intravenous adenosine.

Biventricular hypertrophic cardiomyopathy induced short PR duration, wide QRS complexes and ST-T changes on ECG may occur in Pompe disease. Enzyme replacement therapy may stop or diminish cardiac hypertrophy and intracellular glycogen storage. Improvement in systolic function, reduction in left ventricular mass and increase of PR duration are indicators for response to therapy.[13] Short PR interval may be attributed to enlargement of cells in conduction system, which might be due to excessive glycogen storage.[14] PR duration lengthens as glycogen storage in cells decreases. Supraventricular tachycardia in our case is possibly caused by both cardiac hypertrophy secondary to glycogen storage and short PR interval

which is related to an increase in the cells of conduction system. Coexistence of supraventricular tachycardia episodes with Wolff-Parkinson White syndrome (WPW) and Pompe disease were previously reported.[13] In this case, we also observed the co-occurrence of Pompe disease and WPW syndrome presenting with supraventricular tachycardia.

Glycogen storage may involve the special cells of the conduction system, particularly the AV node and the His bundle cells, demonstrating the histological setting of classical electrocardiographic abnormalities in Pompe disease such as short PR and delta waves. The pathogenesis of ventricular preexcitation (Wolff Parkinson White syndrome) is unknown. However, Arad et al. provided an anatomical explaination for electropyhsiological findings observed in Pompe disease and other glycogen storage disorders. They concluded that the preexcitation pattern does not reflect the presence of an accessory pathway as in the classical WPW.[15] In our case, we observed delta waves in D I along with short PR.

In conclusion, infantile Pompe disease may have different clinical presentations. It should be kept in mind that patients with infantile Pompe disease may exhibit tachycardia and cardiomegaly in the first days of life. This case was presented to emphasize the rare presentation of supraventricular tachycardia in the neonatal period of infantile Pompe disease. In the differential diagnosis of supraventricular tachycardia in the neonatal period metabolic myocardiopathies, especially infantile Pompe disease should be considered.

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