

Case Report

Gaucher Disease Diagnosed During Adolescence

Ergenlik Döneminde Teşhis Edilen Gaucher Hastalığı

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ABSTRACT

Gaucher's disease (GD) is an autosomal recessive lysosomal lipid storage disorder caused due to insufficient activity of the enzyme beta-glucocerebrosidase. Type 1 GD may present at any age but manifests in childhood in more than half of patients. In this case report, an adolescent who applied to our gastroenterology outpatient clinic with dyspeptic complaints and was diagnosed with type 1 GD is presented to draw attention to rare metabolic diseases. A 14-year-old girl complaining of abdominal and bone pain was admitted to the hospital. Erlenmeyer flask deformity was detected on the direct knee radiograph of the patient, as well as thrombocytopenia, ferritin elevation and hepatosplenomegaly. A preliminary diagnosis of Gaucher disease was considered upon detection of low levels of beta glucocerebrosidase enzyme for our patient. The homozygous variant was detected in the GBA gene NM_000157.4:c.1226A>G (p.Asn409Ser) and diagnosed as Type 1 GD. When evaluating patients, it is important to remember that some rare metabolic diseases can be observed in older children. Our patient was diagnosed with Type 1 GD at an adolescent age, and treatment was started. Currently, improvements in clinical manifestations can be achieved with existing treatments. Therefore, it is crucial to diagnose the disease at an early stage and begin the necessary treatment.

Keywords: Gaucher's disease, adolescence, metabolic disease

ÖZET

Gaucher hastalığı (GH), beta-glukoserebrosidaz enziminin yetersiz aktivitesine bağlı, otozomal resesif geçişli lizozomal lipit depo hastalığıdır. Tip 1 GH, erişkin tip olarak tanımlanmaktadır ancak klinik semptomatik infantlardan, asemptomatik erişkinlere kadar geniş bir yelpazede görülebilir. Bu olgu sunumunda, dispeptik şikayetlerle gastroenteroloji polikliniğimize başvuran ve Tip 1 GH tanısı alan adolesan olgu nadir metabolik hastalıklara dikkat çekmek amacıyla sunulmaktadır. 14 yaşında kız hasta karın ağrısı ve kemik ağrısı şikayeti ile başvurdu. Hepatosplenomegali saptanan hastanın trombositopenisi, ferritin yüksekliği ve direkt diz grafisinde Erlenmayer deformitesi saptandı. Sfingolipidoz gen panelinde homozigot NM_000157.4 (GBA):c.1226A>G (p.Asn409Ser) varyantı GBA geninde tespit edildi ve Tip 1 GH tanısı aldı. Hastaları değerlendirirken bazı nadir metabolik hastalıkların büyük çocuklarda görülebileceği unutulmamalıdır. Olgumuz adolesan yaşta Tip 1 GH tanısı alabilmiş ve tedavisi başlanmıştır. Günümüzde mevcut tedavilerle klinik bulgularda iyileşme sağlanabilmektedir. Bu nedenle hastalığı düşünmek ve erken dönemde tanıyı koyup tedaviyi başlamak önemlidir.

Keywords: Gaucher hastalığı, adolesan, metabolik hastalık

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INTRODUCTION

Gaucher's disease (GD) is a rare autosomal recessive lysosomal lipid storage disorder caused due to insufficient activity of the enzyme beta-glucocerebrosidase (1). Along with the accumulation of glucocerebrosides in monocytes and macrophages, liver, spleen and bone marrow involvement can be observed. GD is divided into three main types. Type 1 is the most common form, accounting for up to 90% of all cases. Unlike other types, it has no neurological involvement. Type 2 is called the infantile or acute neuropathic form, and type 3 is called the juvenile subacute neuropathic form. Type 1 GD is defined as an adult type, but its clinical manifestations can be observed in many individuals, from symptomatic infants to asymptomatic adults (2).

In this case report, an adolescent who was admitted to our gastroenterology outpatient clinic with abdominal pain and dyspeptic complaints and diagnosed with type 1 GD is presented to draw attention to rare metabolic diseases and raise awareness.

CASE REPORT

A 14-year-old girl was admitted to our paediatric gastroenterology outpatient clinic with complaints of weakness, nausea, burning in the stomach and abdominal pain in the epigastric region. It was learned that the frequency of complaints of the patient had been increasing for the last year. When her history was evaluated in detail, she described weakness and pain in her entire body, especially in the kneecap, heel and fingers. It was learned that there was a first-degree kinship between the patient's parents with no known disease in the past.

The patient's body weight and height were at the 90-97th percentile and 97th percentile, respectively. On physical examination, it was observed that Traube's space was closed, the spleen was palpable 1 cm below the left costal margin, the liver was palpable by 2 cm, and epigastric tenderness was present. The neurological examination and other physical examination findings of the patient, who had tenderness in the knee and elbow joints and fingers by palpation, were within the usual limits.

The following were also detected: 12,4 g/dL haemoglobin, 9900/mm³ leukocyte count, 96000 mm³

platelet count, 1312 ng/mL ferritin, 36 U/L aspartate aminotransferase and 30 U/L alanine aminotransferase. Hepatitis B, C and HIV serology were negative. Moreover, a peripheral blood smear test showed 60% polymorphonuclear leukocytes, 32% lymphocytes, 8% monocytes, and clusters of 6-7 platelets, some of which were large in appearance. No atypical cells were observed.

Direct radiography of the femur revealed Erlenmeyer flask deformity (Figure 1), and abdominal MRI revealed signal changes in the liver parenchyma consistent with hemochromatosis. Bone densitometry (lumbar and femoral neck) was compatible with osteopenia.

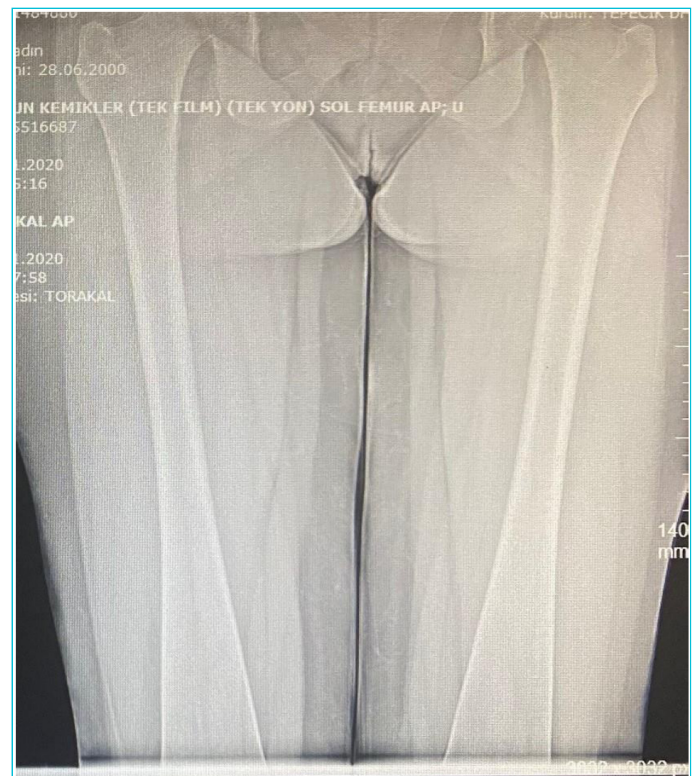


Figure 1. Radiograph of the Erlenmeyer flask deformity, showing the triangular outline of the metaphysis of the distal end of the femur.

In a liver biopsy, mild inflammatory cell reactions, including lymphoplasmacytic cells in portal areas, focal balloon degeneration in hepatocytes, nuclear glycogenation, regenerative changes, and mild (Grade 2/4) iron accumulation with a Prussian blue stain were reported (Figure 2). Bone marrow biopsy showed Gaucher cells.

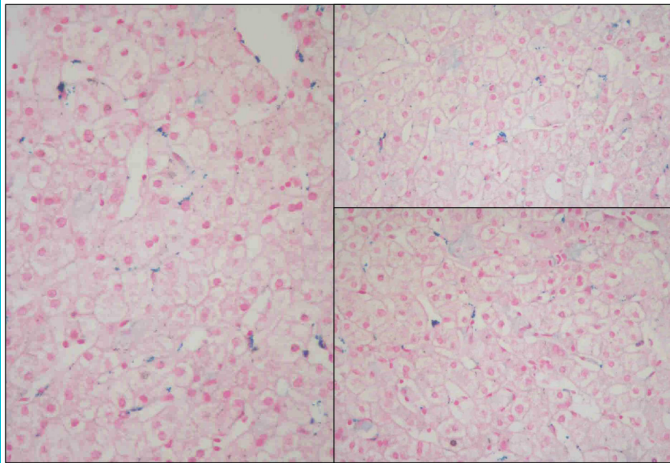


Figure 2. x400, Prussian blue histochemical staining. Iron accumulation in the cytoplasm of Kupffer cells and hepatocytes is observed.

Genetic tests for hemochromatosis were normal in the case. The homozygous variant NM_000157.4:c.1226A>G (p.Asn409Ser) was detected in the GBA gene. Neurological and eye examinations were normal, and we started imiglucerase treatment on the patient after the diagnosis of type 1 GD. She has been taking imiglucerase treatment at a dose of 30 IU/kg for two years. The homozygous mutation was also found in one brother with family screening. The consent from the parents' of the participant was obtained in this case study.

DISCUSSION

Gaucher's disease is a lipid storage disease with an incidence ranging from 1/4000-1/10000 (3). It was first described by Ernest Gaucher in 1882. Type 1 non-neuropathic GD, the most common of the three types of disease, may occur at any age. Our patient was admitted with dyspeptic complaints at the age of 14 and was able to get a diagnosis when she was evaluated in detail with the history and physical examination findings in our clinic. Hepatosplenomegaly, haematological disorders and bone lesions are the main pathologies in patients with type 1 Gaucher disease. The earlier the age of onset of symptoms, the worse the prognosis. The prognosis is negatively affected due to neurological involvement in type 2 and type 3 GD, and both types have a deficiency of the beta glucocerebrosidase enzyme, but their mutations are different (4,5,6).

The hallmark of Gaucher disease is the presence of lipid-laden Gaucher cells in organs, such as bone marrow, spleen and liver. Although these cells seem unique

in morphologic features and metabolism, their exact role in the pathology of GD remains largely unknown (7). Phenotypic changes may be observed depending on the age of manifestation of symptoms (8). Hepatosplenomegaly on physical examination in a patient with bone pain as a starting symptom and the detection of anaemia and thrombocytopenia in laboratory studies are stimuli for diagnosing GD. Cases where massive splenomegaly was detected in childhood, splenectomy was performed due to hypersplenism and GD was diagnosed in adulthood were also reported (3,9). Dyspeptic complaints at the forefront, bone pain, hepatosplenomegaly on physical examination and thrombocytopenia found through laboratory tests made the patient think she had GD, and further examinations were performed.

Although bone involvement is most common and severe in type 3 GD, bone involvement is also common in type 1 GD. The most common of these is the Erlenmeyer flask deformity of the distal femur, which is seen as cortical thinning and loss of concavity in the distal femur (2). More rarely, osteopenia, bone necrosis and bone infarcts can also be observed. (4, 10, 11). In our patient, the detection of Erlenmeyer flask deformity in the femur, which is suggestive of GD, was a guide regarding diagnosis.

Iron accumulation is observed in GD for unclarified reasons. Studies have shown that mild chronic inflammation in patients may lead to high ferritin levels, increased hepcidin transcription and subsequent storage of ferritin in macrophages (12). Ferritin levels were high in the examinations of our patient, and iron accumulation was observed in the histopathological examination of the liver biopsy.

When evaluating patients, it should be noted that some rare metabolic diseases can be observed in older children with different clinical manifestations. As a result of a detailed evaluation of our case, we were able to diagnose type 1 GD at an adolescent age and begin enzyme replacement therapy for our patient. Significant improvement in hepatosplenomegaly, haematological disorders and skeletal findings can be achieved with current treatments (2). Therefore, it is important to think about the disease, determine the diagnosis at an early stage and begin treatment.

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Patient Consent Form / Hasta Onam Formu

The parents' of this patient consent was obtained for this study.

Conflict of Interest / Çıkar Çatışması

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

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