Doi: 10.17944/mkutfd.41900

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2016; 7(27): 76-78

OLGU SUNUMU/CASE REPORT

ASSOCIATION OF GAUCHER'S DİSEASE WITH HYPOPARATHYROIDISM: CO-INCIDENCE OR A NOVEL ASSOCIATION?

Gauche Hastalığı ve Hipoparatiroidizm Birlikteliği: Rastlantısal ya da Yeni Bir Birliktelik?

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ABSTRACT

Gaucher's disease-related hypoparathyroidism is a condition that hasn't been previously described. Here, we presented a ten years old boy referred to our clinic due to hypocalcemic convulsion who was found to have splenomegaly, bicytopenia and hypoparathyroidism. Gene muatation analysis was result in two mutation; (c.(1192C>T); (1226A>G) and p.(Arg359Term); (Asn370Ser). In the context of this patient with Gaucher's disease, we will discuss whether this association is co-incidence or a novel finding.

Key words: Gaucher's diease, hypoparathyroidism, child

ÖZET

Gauche hastalığına bağlı hipoparatiroidi daha önce tanımlanmamış bir durumdur. Hipokalsemik konvülsiyon nedeniyle değerlendirilen; splenomagali, bisitopeni ve hipoaratiroidi saptanan on yaşındaki erkek hastayı sunacağız. Gen mutasyon analizinde Gaucher hastalığı ön tanısı ile istediğimiz gen mutasyon analizi çalışmasında iki yeni mutasyon (c.(1192C>T); (1226A>G) and p.(Arg359Term); (Asn370Ser) saptanarak Gaucher hastalığı tanısı alan bu hasta üzerinden, hipoparatirodi ve gaucher hastalığı birlikteliğinin sadece bir koinsidans mı yoksa yeni bir bulgu mu olduğunu tartışacağız.

Anahtar Kelimeler: Gaucher hastalığı, hipoparatiroidi, çocuk.

Gönderme tarihi / Received: 27.10.2015 **Kabul tarihi / Accepted:** 30.11.2015
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INTRODUCTION

Gaucher's disease (GD) is the most common form of lysosomal storage diseases. It is characterized by accumulation of glucosylceramide in lysosomes due to glucocerebrosidase enzyme deficiency. It is one of the rare diseases in which enzyme replacement is possible. It results from mutation in glucocerebrosidase gene located in chromosome 1q21 and is inherited in autosomal recessive fashion (1,2). Although it is classified into 3 clinical subtypes, it is also suggested that GD should be considered as a spectrum of symptoms rather than a disease with distinct subtypes, since there are shared characteristics among clinical subtypes and diversity in symptoms (3). Here, we presented this case with association of GD and hypoparathyroidism due a case not previously reported.

CASE PRESENTATION

A 10-years old boy was referred to our center with seizure. It was found out that he had had seizure when he was 6-months old. It was also found that he had no recurrent seizure or history of antiepileptic therapy. In addition, he was evaluated in 2 distinct centers for splenomegaly; however, etiology was unclear and follow-up was recommended for splenomegaly. In his family history, there was no chronic disease or consanguinity between parents. On physical examination, weight and height was measured as 27 kg (25-50 percentile) and 132 cm (25-50 percentile), respectively. There was no abnormal finding other than hepatosplenomegaly (spleen was 5 cm palpable; liver was 3 cm palpable) on physical examination. Initial laboratory findings were as follows: Calcium 6.7 mg/dL; phosphor 9.07 mg/dL; alkalen phosphatase 274 U/L; parathormone 14.4 pg/mL; magnesium 1.9 mg/dL; urinary calcium: creatinine ration, 0.07; leukocyte count, 3200 /µL; Hb12.5 g/dL; platelet count 56,000/µL. TORCH panel and Brucella assay were found to be negative. Bone marrow aspiration excluded malignant disease. ß-glucosidase enzyme activity was found to be low (6.09 pmol/spot 20 h [200-2000]). Gene muatation analysis was result in two mutation; (c.(1192C>T); (1226A>G) and p.(Arg359Term); (Asn370Ser).

Electrocardiography was found to be normal. Also, there was no pathological finding on brain MR imaging and electroencephalography. DEXA Z score was found as -1.2 SDS on dual-energy X-ray absorptiometry.

DISCUSSION

There is a great variation in age of onset and clinical severity in GD. Typically, adynamia, loss of appetite, bleeding diathesis, increased susceptibility to infection and complaints about bone can be seen in adolescents and adults, while many patients presents with hematological findings or splenomegaly without hematological findings in early life (4,5). Hepatomegaly is a common finding. Liver failure and cirrhosis are rarely seen in GD. Skeletal involvement is frequent, while pain and limitation in mobility have significant impact on quality of life (6,7).

The most common presentation is anemia or thrombocytopenia during complete blood count which is performed due to loss of appetite and bleeding. In some cases, it is diagnosed by incidentally. Leucopenia is also common. Although it is generally secondary to hypersplenism, infiltration of bone marrow by

Gaucher's cells also contributes. GD leads to bleeding diathesis independent from thrombocytopenia by causing impaired platelet function or coagulation factor deficiency (7). Corneal lesions have been also reported in GD. Although cardiac involvement is uncommon, severe calcifications in cardiac valves and aortic arc are defined as characteristic of patients with homozygote D409G (1342C) mutation (8). Severe pulmonary involvement is extremely rare. In the shed of these data, there was thrombocytopenia, hepatomegaly and leucopenia but not bleeding diathesis or history of frequent infection in our patient. Splenomegaly and thrombocytopenia, two most common presentations of GD, were present in our case. Echocardiography was normal. No abnormal finding was detected in ocular examination and there was no pulmonary involvement.

Diagnosis of GD is confirmed by decreased glucocerebrosidase activity. In addition to above-mentioned findings, extremely low ß-glucosidase activity in peripheral leucocytes and two mutation (c.(1192C>T);(1226A>G) and p.(Arg359Term);(Asn370Ser)) were compatible with GD. However, our patient presented with hypocalcemic convulsion, an unusual manifestation, and hypoparathyroidism was detected in the patient.

CONCLUSION

Hypoparathyroidism is a finding that hasn't been reported in GD. The association of GD with hypoparathyroidism may be co-incidence but it may also be a manifestation of GD. There is insufficient data to think that this finding is associated with the GD. Further investigations are needed to elucidate if this finding are part of GD.

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