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Intrapelvic mass causing femoral compression neuropathy in a patient with Gaucher disease: a case report

Gaucher hastalığında femoral kompresyon nöropatisine neden olan pelvis içi kitle: Olgu sunumu

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Gaucher disease is a lysosomal storage disorder in which glucocerebroside accumulates within the macrophages in any part of the body. Varying degrees of skeletal involvement may occur besides anemia, coagulation abnormalities and hepatosplenomegaly. Most of the factors influencing the quality of life in a patient with Gaucher disease are related to bone involvement. Gaucher cell deposits may extrude through cortical erosions and cause soft tissue masses around bones which are involved by the disease. We present a 38-year-old female patient with Gaucher disease who had a large intrapelvic mass originating from left iliac bone causing femoral compression neuropathy. The classification of disease is based on neurological involvement and if symptoms exist whether the symptoms are acute or subacute. The neurological impairment caused by compression by a tumor should be distinguished from the ones reported in neurogenic forms of the disease.

Key words: Femoral nerve; Gaucher disease; pelvic mass.

Gaucher hastalığı, glukoserebrositlerin, vücudun herhangi bir yerinde makrofajların içinde biriktiği lizozomal depo hastalığıdır. Anemi, koagülasyon anomalileri ve hepatosplenomegalinin yanı sıra farklı derecede iskelet tutulumu hastalığa eşlik edebilir. Gaucher hastalığında yaşam kalitesini etkileyen faktörler kemik tutulumu ile ilişkilidir. Hastalık kaynaklı Gaucher hücre birikintileri kortikal erozyonlardan kemik dışına çıkabilir ve kemiklerin çevresinde yumuşak doku kitleleri oluşturabilir. Bu makalede, sol iliyak kanattan köken alan femoral kompresyon nöropatisine neden olacak kadar büyük bir pelvis içi kitle oluşumu tespit ettiğimiz 38 yaşında kadın olgu sunuldu. Hastalık nörolojik tutuluma göre ve eğer nörolojik belirtiler varsa bunların akut veya subakut olmalarına göre sınıflandırılmaktadır. Tümör basısı ile ortaya çıkan nörolojik bir bozukluk, hastalık için tanımlanmış olan nörojenik formlardan ayırt edilmelidir.

Anahtar sözcükler: Femoral sinir; Gaucher hastalığı; pelvik kitle.

Gaucher disease (GD) is a lysosomal storage disorder. It is caused by an autosomal-recessive inherited deficiency of glucocerebrosidase activity. This deficiency causes accumulation of glucocerebroside within the macrophages in any part of the body. Anemia, coagulation abnormalities and hepatosplenomegaly are common pathologies in this disease.[1] Hematomas may occur spontaneously because of these afflictions.[2] Skeletal changes causing disabilities may also occur.[3] Soft tissue masses originating from Gaucher-cell deposits by cortical destruction, an extremely rare condition, may also be observed as a skeletal manifestation. These masses may mimic malignancies.[4-6] Management of a patient with GD, who has severe skeletal involvement and a giant intrapelvic soft-tissue mass is discussed in this paper.

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CASE REPORT

A 38-year-old female patient was admitted with a mass in her lower left abdomen, which was first noticed three years ago. Initially, it was a slow-growing and painless mass. During last year, an unbearable pain around the mass and a weakness of the left thigh muscles arose. She was scheduled for an incisional biopsy in another center but was referred to our hospital because of her haematological disturbances. She had a history of splenectomy because of splenomegaly 15 years ago, but there was the need of a definite diagnosis causing this splenomegaly. The patient had a history of gastrointestinal bleeding four years ago and intermittent generalized bone pain that had never been investigated.

On the physical examination, a firm and immobile mass sizing up approximately 15x15 cm was palpated at the left lower quadrant of the abdomen. There were no skin changes, pain, tenderness or thrill over the mass. A marked hepatomegaly was detected. Passive hip and knee motions were normal. There was motor and sensational deficit at the left femoral nerve distribution.

Complete blood cell (CBC) counts and serum analyses were as follows: White blood cells (WBC) 13.7x103/μL (4.5-11), red blood cells (RBC) 2.29x106/μL (3.8-5.1), platelets 129x103/μL (150-400), hemoglobin (Hgb) 7.52 g/dL (11.7-15.5), hematocrit (Hct) 23.6% (35-45), erythrocyte sedimentation rate (ESR) 28 mm/h, C-reactive protein (CRP) 34.9 mg/L(<5), iron 55.5 μg/dL (49-151), total iron binding capacity 394 μg/dL (250-425), ferritin 1121 ng/mL (13-150), total protein 8.77 g/dL (6-8) and albumin 4.24 g/dL (3.4-4.8). Serum protein electrophoresis revealed 50.4% albumin (54-74), 14.7% β-Globulin (7.3-13.5) and 22.3% γ-Globulin (8.1-19.9).

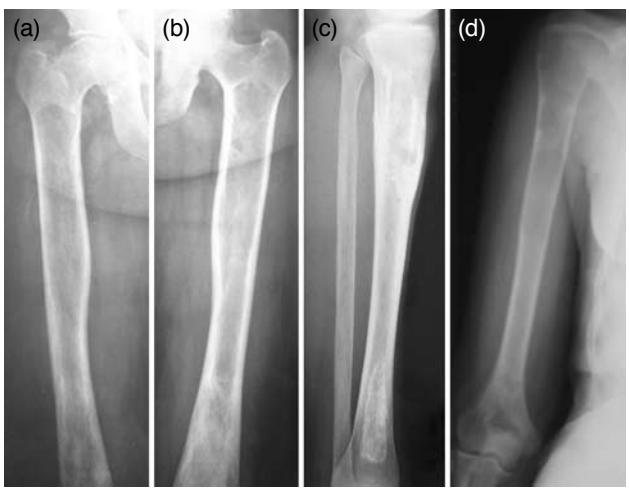

Figure 1. (a, b) Bilateral femoral osteopenia and expansion, avascular necrosis of the femoral head on right side and Erlenmeyer flask deformity on left side. **(c)** Medullary osteonecrosis on right tibia **(d)** Expansion and cortical thinning on right humerus.

The roentgenographic evaluation demonstrated a destructive lesion at the left iliac bone, lytic and sclerotic lesions on both humeral, femoral and tibial proximal metaphyses, Erlenmeyer flask deformity and avascular necrosis of the right femoral head (Figure 1).

The ultrasonographic evaluation revealed hepatomegaly and a solid mass in the lower left quadrant with distinct borders, extending to the contralateral side. In the computed axial tomography (CAT) scan, it was observed that the mass extended from the left iliac bone and filled the left pelvic space by destructing the inner wall (Figure 2). Magnetic resonance images revealed a mass with heterogeneous signal intensity. On the T_1W images, both low and high signal intensity areas could be demonstrated. On the T_2W images, the mass yielded high signal intensity. The images were not enhanced with contrast agent uptake. These findings were unable to rule out a malignant tumor.

A technetium-99m (Tc-99m) methylene diphosphonate (MDP) bone scintigraphy revealed minimally enhanced radioactive uptake irregularly at the left iliac bone and diffuse enhancement of uptake at proximal parts of both humeri and both tibiae (Figure 3). Other skeletal findings were normal.

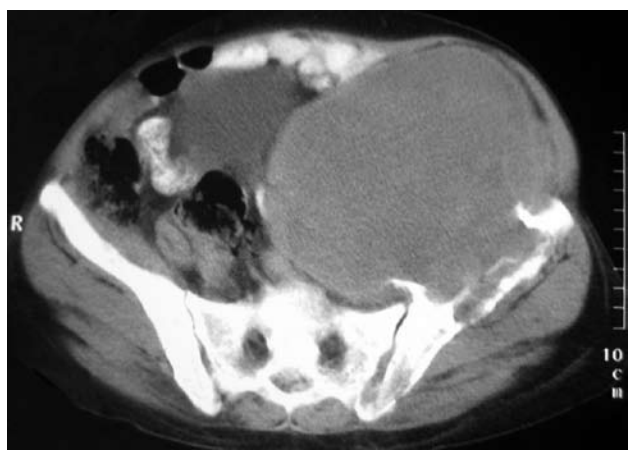

Figure 2. Huge soft tissue mass filling the left pelvic space originating from ilium.

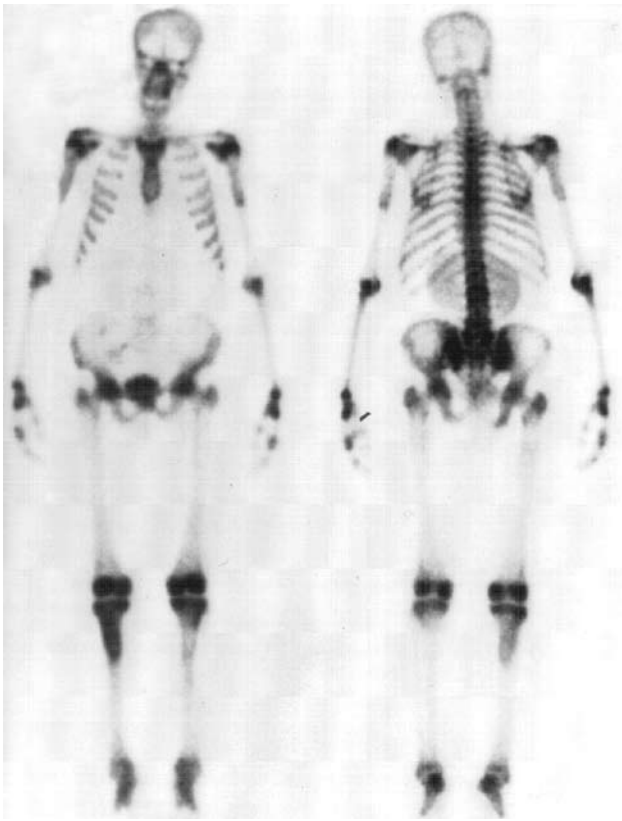

Figure 3. Note minimal irregular radioactive uptake at left iliac bone, diffuse enhancement of uptake at proximal parts of both humeri and both tibiae.

The histopathological examination results were reported as all the material containing necrotic tissue with no evidence of malignancy encountered, thus a marginal resection was employed. Just before the laparotomy, a double J ureteral catheter was introduced to the left ureter, which was pushed by the tumor to the opposite side, in order to prevent damage during the dissection. During the deep dissection, the femoral nerve was found to lie on the tumor; elongated and atrophied. After freeing the tumor from its surrounding soft tissues, the attachment to the left iliac bone was dissected. A geographic destruction at the inner wall of the ilium and a marginal elevation of the cortical bone around the tumor-ilium junction were observed. Also, a liver wedge biopsy was performed.

Macroscopic and microscopic findings

The mass was 15x16x12.5 cm in size, 1463 grams in weight, encapsulated and dark brown (Figure 4). On serial sections, the mass was generally necrotic, solid, soft and yellow-brown. Microscopic examination of the mass and iliac bone curettage material revealed hemorrhagia and necrosis. The liver biopsy specimen revealed puckered paper image on cytoplasms of Kupffer cells and hepatocytes around the central vein and the portal areas. Bridging fibrosis was evident on the portal areas (Figure 5). These findings of the liver biopsy were consistent with a liver involvement of Gaucher disease.

DISCUSSION

The symptoms, organ involvement and clinical course of GD vary among patients. More than 100 different mutations of the β-glucocerebrosidase gene, located on the chromosome 1, have been

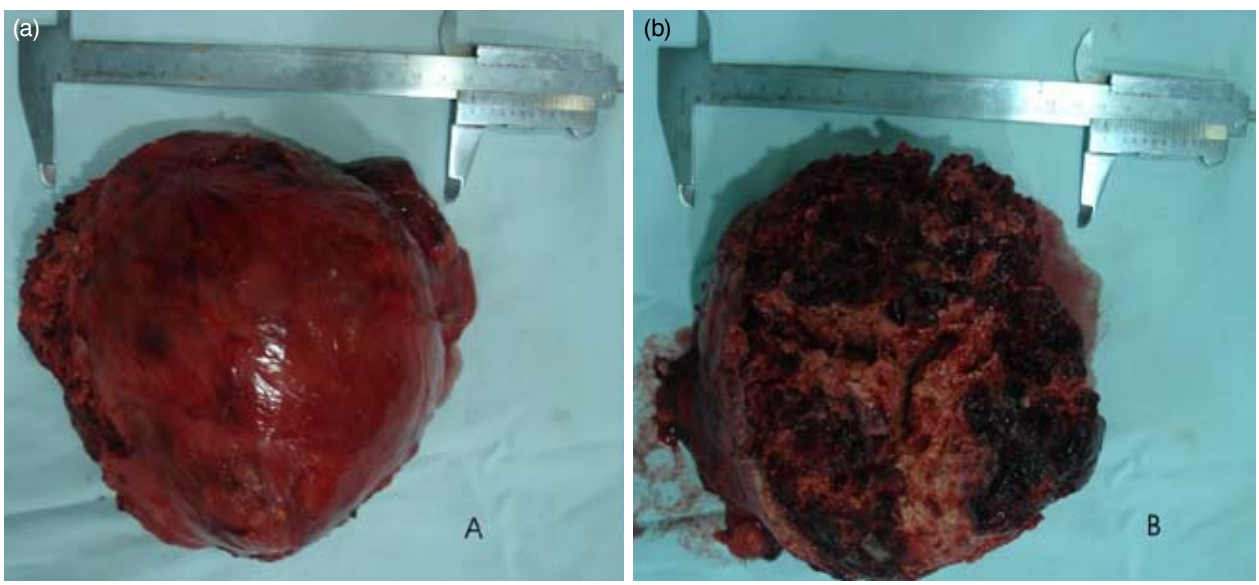

Figure 4. (a) Resected material, front view and **(b)** bone attachment side view.

identified and linked to β-glucocerebrosidase deficiency. The degree of the mutations and the neurological involvement distinguishes three basic clinical forms. Most patients with GD have the non-neuronopathic form, which is sometimes referred to as type 1.[1] The remainder of patients with GD have the acute neuronopathic form (type 2) or the subacute neuronopathic form (type 3).[7] In the acute neuronopathic form, the neurological symptoms may include cranial nerve and extrapyramidal tract involvement. Neurological deterioration progresses quickly, and death because of apnoea or aspiration usually occurs in early childhood.[8] With the subacutely neuronopathic form, the neurological symptoms can include myoclonic seizures or horizontal supranuclear gaze paresis.[9] The only neurological symptom in our patient was the paralysis of the left femoral nerve. It occurred slowly and its progress was in conjunction with the enlargement of the mass, so this neurological sign was considered a compression effect rather than a determinant of the disease. In other words, our patient had the type 1 (nonneuronopathic) GD.

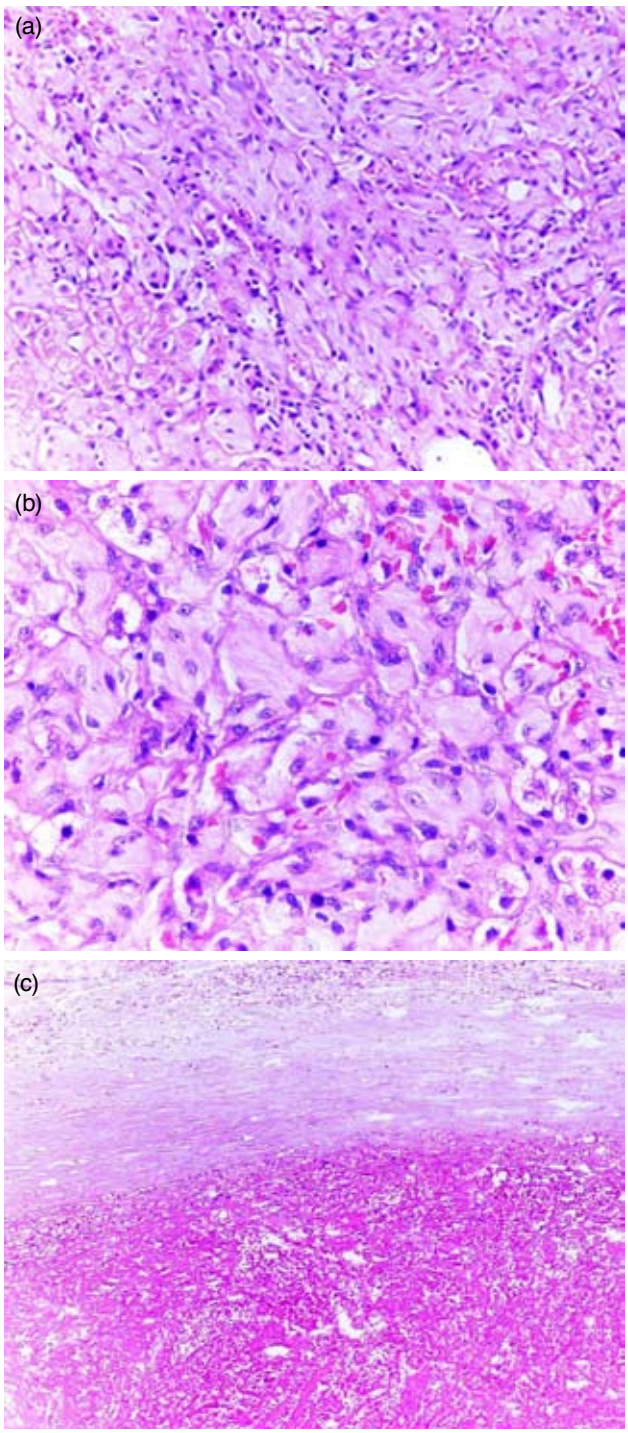

Figure 5. (a) Liver paranchime including Kupffer cells with puckered paper appearence (H-E x 200). **(b)** Hepatocytes with puckered paper appearence (H-E x 400). **(c)** Hemarogia and necrosis areas surrounded by fibrotic capsule (H-E x 100).

Systemic symptoms are more common than neurological involvement in patients with GD. The organs affected by GD include spleen, liver, lung, kidney, bone and bone marrow, and patients may exhibit hepatosplenomegaly, anaemia, thrombocytopenia and skeletal and bone marrow pathology.[1] Our patient had a history of splenomegaly treated by a splenectomy. Marked hepatomegaly and puckered paper image on cytoplasms of Kupffer cells and the hepatocytes around the central vein and the portal area on microscopic evaluation of the liver biopsy were the supporting findings of our diagnosis. Our patient also had haematological disturbances, anemia and thrombocytopenia.

The effects of GD on the skeleton are the most disabling results of the disease and they have a negative impact on the patient's quality of life. The skeletal aspects of GD include symptomatic and radiological findings. Bone pain is common among patients with GD and it varies in severity, can be acute or chronic, and may not correlate with the radiological findings.[10] Our patient had been suffering from intermittent pain episodes like bone crises fort the last 10 years, especially in the lower extremities. Erlenmeyer flask deformity, osteolyses, osteopenia, osteosclerosis, osteonecrosis and osteoarthrosis may be observed in the radiological examinations of the patients with GD.[3] In our patient, we saw lytic and sclerotic areas of bone, osteopenia, Erlenmeyer flask deformity and avascular necrosis of the right femoral head.

Although expected, it is not a rule to observe a correlation between the roentgenographic findings and the radionuclide bone scintigraphy (using Tc-99m MDP) in Gaucher disease, as was the case in our patient. This condition may be explained throughout the natural course of the bone scans: Determination of a decreased uptake of the radionuclide agent at the involved region initially during a bone crisis, increased uptake several weeks later around the area where previously the uptake was decreased, and a few months later, a return of the radionuclide bone scan to normal. The Tc-99m sulfur colloid scans could be more useful in determining the extent and severity of bone marrow involvement in our patient.[11]

A similar case of GD with severe skeletal involvement and extraosseous extension of the Gaucher cells from the left iliac bone, in which monoclonal gammopathy was evident, was reported by Kaloterakis et al.[5] Our patient also had higher percentages of β-Globulin (14.7%) and γ-Globulin (22.3%) compared to the normal values on the protein electrophoresis. The most important difference between this patient and our case was on the microscopic evaluation of the tumor where we did not see the expected signs of GD. We think that the extreme size of the mass caused the vascular insufficiency and necrosis. Although the elevation of the cortices around the tumor-ilium border is a sign of a pathology originating from the bone, infiltration of the soft tissue by the accumulative Gaucher cells and a chronic organizing hematoma originating from the periosteum might be the causes of this finding. Coagulation abnormalities in GD are generally due to thrombocytopenia and/or poor platelet function, as well as the concomitant coagulation factor deficiencies.[12] Our patient had low platelet counts on CBC but we do not know if this finding is the reason of such a large chronic hematoma. Barone et al.[4] stated that the extension of the Gaucher cells into the soft tissue might be associated with focal haemorrhagic events. Reactive fibrous tissue proliferation may lead to a huge soft tissue extension as was seen in our patient.

Previously reported contributing factors to the quality of life in GD type 1 are splenectomy, advanced age and GD-related bone manifestations such as chronic bone pain, necrosis, fracture and joint replacement.[13] In addition to most of these factors, our patient had femoral compression neuropathy that worsened her functional status.

In conclusion, patients with GD, especially those with severe skeletal involvement, may present with huge masses apart from any malignancies and their quality of life may be worsened by the local compression effects.

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