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CASE REPORT

A Gaucher Patient with Bilateral Total Femoral Lytic Lesions Mimicking Malignancy: a Case Report

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Abstract

Bone involvement in Gaucher disease can affect quality of life. Bone lesions of Gaucher disease can be confused with hematological diseases, infections, and malignancy. Our patient with bilateral femur involvement presented to us with a pathological fracture. After the fracture was treated with a long leg splint and healed, we performed a biopsy because of suspicious radiological findings. The pathology results confirmed Gaucher disease with bone infiltration during the time in which conservative follow-up was taking place, eventually leading to the patient's mobilization again. Bone findings of Gaucher disease indicate a difficult process requiring follow-up and treatment. It is crucial to scan patients periodically for possible vertebral and extremity symptoms. Vertebral and extremity fractures undoubtedly require experience on the part of the clinician as they can imitate malignant masses.

Keywords Gaucher disease · Pathological fracture · Diffuse osteopenia

Introduction

Gaucher disease is an autosomal recessive disease due to β-glucocerebrosidase enzyme deficiency; it is categorized as a lysosomal storage disorder [1, 2]. Gaucher disease affects multiple systems, including the skeletal system. Bone involvement in Gaucher disease may take different forms and affects quality of life [3]. Skeletal involvement requires treatment for patient mobilization and morbidity. In this case report, we present a pathological fracture due to bilateral diffuse femoral osteopenia that may mimic malignancy.

Case

An 8-year-old male patient who was followed up by the pediatric genetics and pediatric gastroenterology clinics with the diagnosis of Gaucher type-3 since birth was brought to our emergency department by his family due to bilateral thigh pain during genital cleaning.

The lower extremity motor examination could not be completed due to the patient's anterior thigh pain. The lower extremity sensory examination was normal.

Bilaterally, the hands and wrists had a full range of motion. Hand, wrist, flexor, and extensor muscle strength were 5/5, and the bilateral arm, forearm, and hand sensory examinations were normal.

X-ray imaging of the patient, who had bilateral proximal thigh pain and tenderness, showed lytic lesions nearly throughout the bilateral femur. In addition, minimally displaced fractures were seen in the right femural diaphysis and in the left femur close to the intertrochanteric area (Fig. 1). X-ray imaging of the bilateral humeral diaphysis showed lytic lesions without pathological fractures. The patient was

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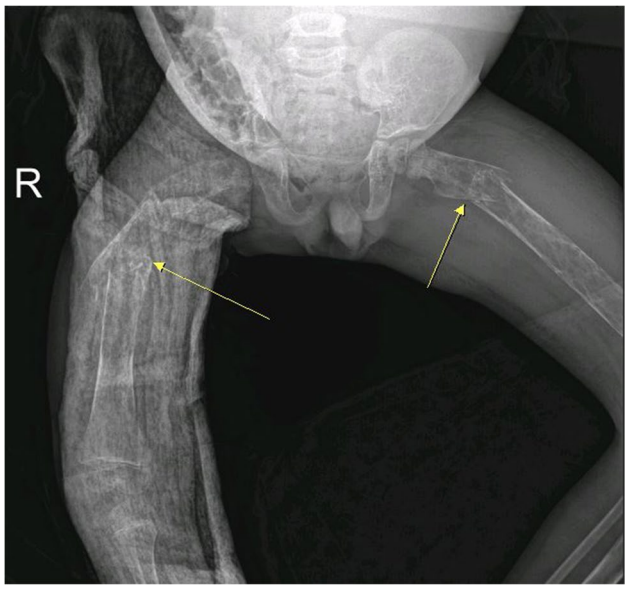

Fig. 1 The fracture line in the diaphysis area in the right femur and the fracture line close to the intertrochanteric area in the left femur are shown with an arrow. Diffuse osteopenia is seen in both femurs

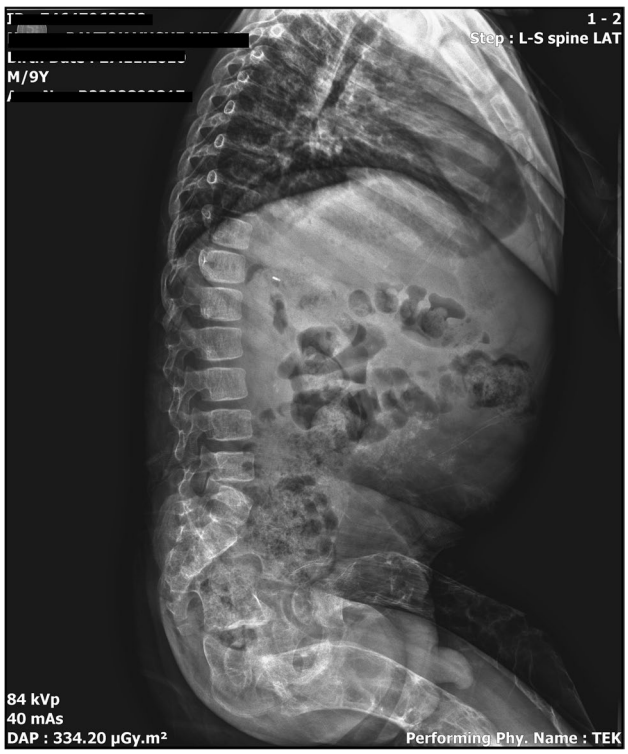

Fig. 2 There is no evidence of Gaucher disease-related spinal involvement

suffering from chronic low back pain without any significant spinal deformities. Bone pathology and deformity were not seen in the spine radiography (Fig. 2). Bone densitometry performed one year before was consistent with a 1–4 lumbar *Z* score of − 3.4.

The patient received 3 doses of imiglucerase enzyme therapy two years before; he developed hepatosplenomegaly that did not respond to enzyme replacement therapy and was followed up by the pediatric surgery clinic.

The patient's laboratory results measured at the time of the fracture were as follows: hemoglobin 13.1 g/dl (normal (N)), aspartate aminotransferase 33 U/l (N), alanine aminotransferase 4 U/l (N), alkaline phosphatase 58 U/l (N), prothrombin time 19.1 s (high (H)), activated partial thromboplastin time 31.1 s (N), phosphorus 1.9 mg/dl (low (L)), magnesium 2 mg/dl (N), calcium 8.7 mg/dl (L), and 25-OH Vit D 7.45 µg/l (L). In addition, the amount of urinary calcium was 109 mg/dl (H).

Conservative treatment was decided on because the fracture was stable and the fragments were not displaced. A bilateral long leg splint with pelvic support was applied with the knees at 15 degrees of flexion.

The patient was evaluated in the outpatient clinic at 2 weeks. His neurovascular examination was normal. It was determined that new bone formation and union had begun (callus tissue) in the fracture area.

Since mature callus formation was seen at the 4-week check-up, the splint was removed and passive exercises were started.

After 3 months of follow-up, both knee extensions of the patient were limited by 10°, but the knee flexion muscle strength was 5/5. There were 100 degrees of flexion and − 10 degrees of extension in both hips of the patient. A total range of motion of 20° was observed in both hips. Pain was reported during the FABER and FADIR tests.

Magnetic resonance imaging was recommended due to the diffuse lytic lesions in both femurs on computed tomography imaging (Fig. 3). A femur biopsy was planned for the patient with suspected malignancy on contrast-enhanced magnetic resonance imaging. A percutaneous bone biopsy was performed under general anesthesia. At the same time, a splenectomy was also performed by the pediatric surgical team, because of massive splenomegaly and thrombocytopenia despite enzyme replacement therapy.

Phagocytic cells were diffusely observed in the bone marrow biopsy and splenectomy material. These cells, which were found to be PAS positive and immunohistochemically CD68 positive, were evaluated as Gaucher cells by morphological findings (Fig. 4).

At 3 months postoperatively, the examination of both hips of the patient was completely pain-free. After 20 sessions of physiotherapy, a significant decrease in spinal pain was achieved. One year after the pathological fracture, the patient came to the check-up completely without support. X-ray imaging showed complete union accompanied by minimal varus (Fig. 5).

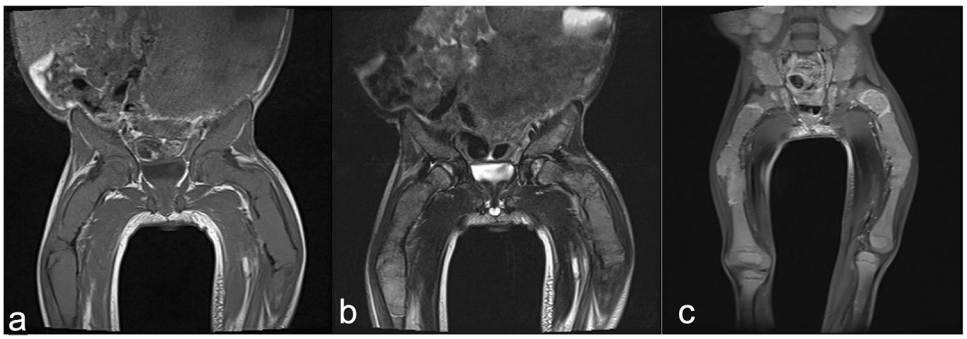

Fig. 3 **a** Coronal T1-weighted image shows diffuse involvement of the bone marrow with intermediate signal change. There is diffuse expansion in both femora and pelvic bones. Cortical destruction is present. Deformity is present in both femora. **b** Coronal T2-weighted images show heterogeneous signal change in the bone marrow. **c** Postcontrast images show slight enhancement at the fracture site in the left proximal femur. There is also slight enhancement in the left ilium. There is little to no enhancement in other parts, probably due to high cellularity of the bone marrow

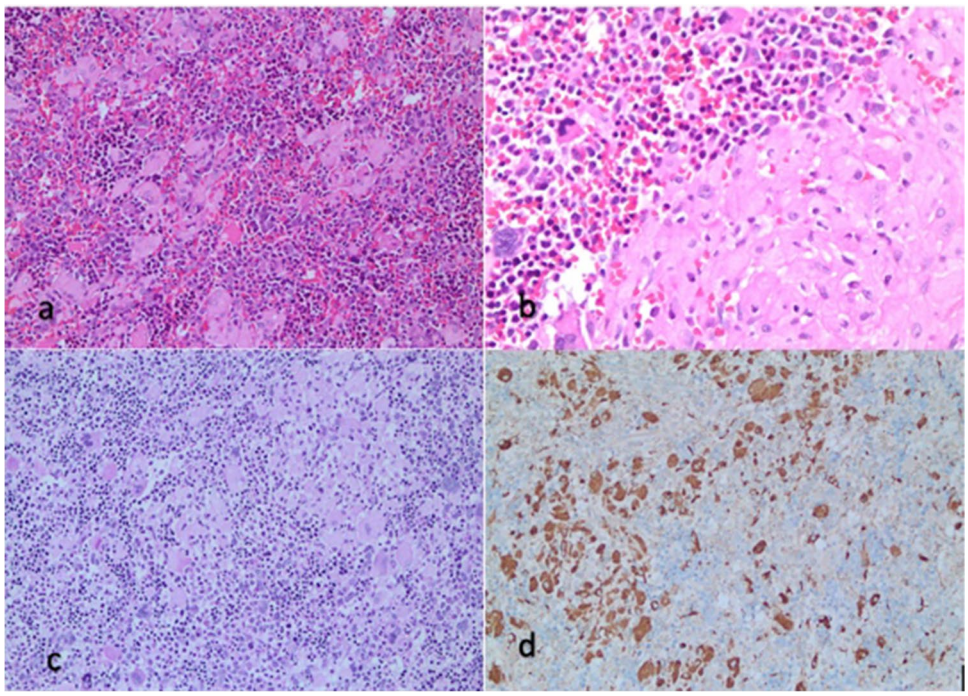

Fig. 4 **a** Gaucher cells in the bone marrow biopsy are plump macrophages characterized by their cytoplasmic appearance of crumpled tissue paper due to glucocerebroside accumulation. **b** Gaucher cells under high magnification. **c** PAS positivity in Gaucher cells. **d** CD68 immunoreactivity in Gaucher cells

Discussion

There are six different bony manifestations of Gaucher disease: bone marrow infiltration, avascular necrosis, bone crisis, pathological fractures, lytic lesions, and osteomyelitis [3]. Our patient had such a large lytic lesion that pathological fracture was inevitable. To the best of our knowledge, such a large lesion has not been reported in the literature. In Gaucher disease, the bones have a less perfect structure than normal bones and are exposed to a higher pathological fracture rate than in the normal population [4, 5]. This means our patient will experience the risk of fractures repeatedly throughout life [6]. It is essential to inform the family about this issue.

The orthopedic problems that develop in type 1 and 3 diseases vary among patients [7, 8]. Trabecular resorption develops as a result of bone marrow infiltration, cellular necrosis, and fibrous proliferation. These findings are reflected in radiographs as focal radiolucent areas in the bone and cortical thinning. In our case, a widespread radiolucent area caused by trabecular resorption was seen in both femurs. Axial skeletal involvement, epiphyseal involvement, and Erlenmeyer deformity are common in Gaucher patients, but we did not encounter any of them in our patient.

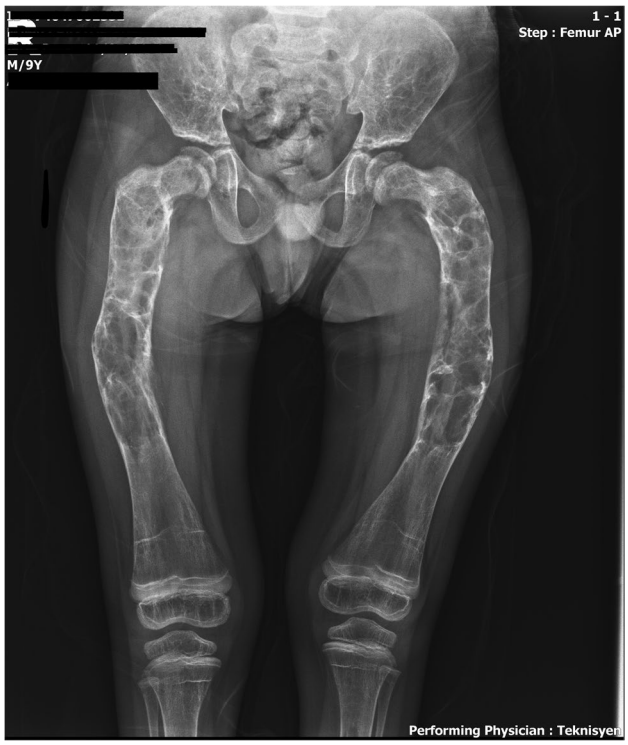

Fig. 5 Bilateral femur remodeling in the first year of fracture development

Serum calcium, phosphorus, and parathyroid hormone levels are normal in most patients. Urine calcium and hydroxyproline levels are generally normal as well [9]. The high urinary calcium excretion explains the osteopenia and large lytic lesion in our patient.

X-ray imaging is the first imaging modality to be used, as it provides quick and easy identification of fractures and lytic lesions. After the fracture, X-rays were used to determine the amount of displacement and level of union and in the follow-up of our patient. However, when we evaluated our patient at our tumor council, we decided to perform a biopsy since we could not distinguish the common lytic lesion on MRI from a lytic lesion formed by malignant tumor tissue [10].

The incidence of neoplastic disorders such as lymphoproliferative disease appears to be more common in Gaucher disease patients than in the general population [11]. Nevertheless, lesions of benign etiology that mimic these aggressive processes should be considered in the differential diagnosis, when cortical destruction with coexisting soft tissue is the main finding in these patients [12]. This suspicious appearance in Gaucher patients makes orthopedic surgeons unsure about the treatment process. Öztürk et al. presented a lesion mimicking a bone tumor in proximal tibia involvement accompanied by Erlenmeyer deformity in the distal femur [13].

Although there are different treatment models in the literature, conservative treatment is the most reliable for treating pathological fractures in Gaucher patients. The existing difficulty in avoiding anesthesia complications, as well as performing surgery on poor quality bone, indicates that it is safer to immobilize and follow-up with a splint and plaster. Pathological femoral fractures of patients can heal with conservative treatment. Varus angulation is an uncommon complication that may develop [14]. When we first encountered the fracture, we had a number of options: follow-up with a splint, follow-up with a hip spica cast, closed reduction and percutaneous fixation or open reduction fixation with or without graft. Considering the patient's age and fracture displacement, the decision to conduct conservative follow-up was more reasonable, and saved the patient from a long hip spica cast process by applying a splint. If we performed surgery, the lytic lesion in the distal area could be the reason for implant failure. Additionally, the patient had not yet been evaluated in terms of malignancy. Fixation methods without resection to malignant bone tissue make resection very difficult.

Conclusion

The bone findings of Gaucher disease indicate a difficult process that requires follow-up and treatment. It is crucial to scan patients periodically for possible vertebral and extremity symptoms. Vertebral and extremity fractures undoubtedly require experience on the part of the clinician as they can imitate malignant masses.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s42399-021-01082-0.

Author contribution Yavuz Şahbat: conceptualization, methodology, visualization, supervision, project administration, writing—original draft, writing—review and editing. Ahmet Hamdi Akgülle: methodology, formal analysis, data curation, writing—review and editing, visualization, supervision. Onur Buğdaycı: validation, writing—original draft, writing—review and editing. İpek Erbarut Seven: validation, writing—original draft, writing—review and editing, visualization, project administration. Beyza Keskin: project administration, writing—original draft, writing—review and editing.

Data Availability All information and data is available for review by the Editor of this journal.

Code Availability Available.

Declarations

Conflict of Interest The authors declare no competing interests.

Ethics Approval The authors declare that all investigations were conducted in conformity with ethical standards.

Consent to Participate Informed consent was obtained from the mother of the patient due to mild cognitive delay in the patient.

Written Consent for Publication Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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