CASE REPORT

Gaucher disease with pathological femoral neck fracture

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drbkizildag@gmail.com**SUMMARY**

Fractures of the femoral neck are rare and usually result from serious and high-energy trauma in the skeleton in young adults. Gaucher's disease (GD) is a lysosomal storage disorder that has progressive course and is rarely seen. Research has shown that a pathological femoral neck fracture with GD mostly emerges in childhood. But in adults, there are no reports of pathological femoral neck fractures with GD. We present a unique case of GD with a pathological femoral neck fracture in a 54-year-old woman who did not undergo surgery because of haematological problems including thrombocytopaenia.

BACKGROUND

Gaucher's disease (GD) is the most common lysosomal disorder, which is associated with β -glucocerebrosidase gene mutations more than 300.¹ Glucocerebrosidase that is formed as a consequence of mutations accumulates in the musculo-skeletal and reticuloendothelial system.² There are three types of GD; type 1 is the most common form and presents with hepatosplenomegaly, anaemia, thrombocytopaenia and bone pain or fractures. Neurological involvement does not occur in type 1.³ Type 2 accounts for fewer than 1% of cases and is the most severe form of GD.² Progressive neurological problems are predominant in the clinical presentation.³ There is no effective treatment, so most of these patients die before 2 years of age.² Type 3 is rare, begins in childhood and leads to moderate neurological symptoms. GD leads to some changes in normal bone turnover, therefore bone involvement ranges a wide spectrum from osteopenia and remodelling defects to lytic lesions and avascular necrosis.⁴ A few researches showed that pathological femoral neck fracture with GD is mostly emerges in childhood.⁵ But in adults, there are no reports about pathological femoral neck fractures in GD patients. In our report, we describe a very rare case of GD who was diagnosed 14 years ago, presented with pathological femoral neck fracture.

CASE PRESENTATION

A 54-year-old woman followed up with GD since 1998 was referred to the outpatient clinic with symptoms of limping, low back and the right hip joint pain. She had been visited the doctor in another clinic 6 months ago with similar symptoms. At this visit, a right-hip fracture was detected and operation was planned for the fracture. But she did not accept to undergo any operation. In her history, she had applied to hospital with epistaxis and

abdominal pain. Because she had massive splenomegaly, bone marrow biopsy had been performed and Gaucher cells had been showed. Then molecular genetic evaluation had determined N370S mutation and finally the patient had been diagnosed with type 1 GD in 1998 but she had not take any treatment since that time. She had attacks of quick bruising and occasional epistaxis during this time. She had two brothers with GD. She went to the previous clinic because of increased symptoms. Surgery was planned again, but she could not be operated due to low blood values. Then she was referred to our hospital. The results of the laboratory tests were leucocytes 3000/mm³, haemoglobin 9.6 g/dL and platelets 26 000/mm³. Folate 7.67 ng/mL, vitamin B₁₂ 1044 pg/mL, Ferritin 377 ng/mL. Erythrocyte sedimentation rate of, C reactive protein, liver enzyme levels and tests those show the normal kidney function tests. Biochemical bone markers were calcium 9.6 mg/dL (normal range 8.6–10.2 mg/dL), phosphorus 4.24 mg/dL (normal range 2.3–4.7 mg/dL), alkaline phosphatase 2110 U/I (normal range 35–129 U/I), parathyroid hormone 3396 pg/mL (normal range 9.5–75 pg/mL), 25(OH) vitamin D 19.2 ng/mL (normal range 20–120). Bone mineral densitometry revealed osteoporosis (T-score 3.1). The patient's X-ray (figure 1) and MRI of the hip (figure 2A,B) demonstrated a femoral neck fracture with surrounding areas of avascular necrosis (figures 1 and 2). In the right femur geographic contours of medullary bone infarcts, high signal on T2-weighted and low signal in T1-weighted images could be seen in proximal femoral head, neck, intertrochanteric region as well as proximal shaft. There was no bone marrow oedema probably due to the late phase of fracture. The medullary of all bones also revealed abnormal

Figure 1 X-ray showing right femoral neck fracture.

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Figure 2 MRI of the chronic medullar infarcts and femoral neck fracture line on the right hip.

T1-weighted and T2-weighted intermediate signals indicating red bone marrow infiltration. Orthopaedics department suggested surgery for fracture but asked for the correction of the blood values. Although the patient was given two units of erythrocyte suspension and three units of apheresis platelet before the operation, the patient's platelet counts only reached to 39 000/mm. We talked with the patient and explained the risks of surgery. Surgery was planned after correction of blood values with enzyme (imiglucerase) treatment because she did not admit any operation. She has been visited our internal medicine department for the past 6 months and received the enzyme treatment once in a month. Her number of platelets has reached to 87 000/mm. Control plain film of pelvis revealed partial union of the femur neck fracture after 6 months. Her right hip was no longer aching but she was walking slightly lame.

DISCUSSION

GD is one of the lysosomal storage disorders that has a progressive course and is rarely seen.¹ Severe musculoskeletal system involvement can be seen in GD which can cause impaired mobility in 20% of patients due to unbalanced new bone formation and bone turnover.³ Deformities of the long bones besides the knee, distal femur and proximal tibia can develop³ in approximately 80% of patients with GD. Erlenmeyer flask deformity, insufficiency fractures due to osteopenia, pathological fractures, abnormal areas of sclerosis indicating bone marrow infiltration or bone infarcts are possible imaging findings. Erlenmeyer flask deformity is known as remodelling of the metaphyseal segments of tubular bones frequently occur in distal lateral region of the femur and proximal region of the tibia. Avascular necrosis (osteonecrosis) is the most important skeletal complication of GD. Secondary chronic infarction related ischaemia is the possible mechanism and it is unalterable. Involvement of the femur and humerus as well as vertebral bodies due to osteonecrosis induce collapse of the joint.^{6–8}

Despite the high prevalence of femoral fracture, a femoral neck fracture is very rare in patients with GD. To our knowledge, there are no reports of pathological femoral neck fracture with GD in adults. Arthroplasty of the joint is an important surgical treatment choice in GD patients. Preoperative haematological consultation is critical in these patients.⁹ Organ enlargement especially splenomegaly and hepatomegaly are common features of the GD. Splenomegaly can cause severe anaemia, leukopaenia, thrombocytopaenia and splenic infarction. Splenectomy may be alternative only to correct these haematological problems but does not any effect on the progression of the disease.¹⁰ Furthermore splenectomy can provoke the

exacerbation of pre-existing lesions in GD, particularly in the bones.² Ida *et al*¹¹ studied 35 Japanese patients with GD and in this study 57% of patients had severe bone diseases including avascular necrosis, pathological fractures as well as bone crisis.

Furthermore in this study, the frequency of severe bone disease was notably higher in patients undergone splenectomy than unsplenectomised ones. The preoperative assessment of haematological condition in patients with GD is very important. Lebel *et al*¹² suggested to perform some laboratory tests including coagulation factor levels and the amount of platelets that are particularly affecting variables and should be evaluated before surgery. They also showed that Gaucher patients had required more blood products postoperatively particularly in patients having low platelet values in preoperative period. These patients also had tendency for haematomas called as 'Gaucheromas' in adjacent muscles. Hence they commended that surgeons should pay more attention in order to avoid this complication. For these reasons Lebel *et al*¹² recommended to give erythropoietin preoperatively in Gaucher patients with anaemia and they also recommended to investigate the deficiencies of coagulation factors especially four factor XI and XIII preoperatively Gaucher patients are recommended to undergo echocardiographic evaluation for pulmonary hypertension. Symptomatic treatment of GD such as splenectomy, was performed until 1991.² Enzyme replacement therapy was a landmark in GD. Organomegaly and haematological abnormalities responded to this therapy within 1 year. Skeletal abnormalities of GD may respond slowly and can take up 4 years to remove.³ In our patient we detected avascular necrosis and osteoporosis together in the femoral bone neck which both caused neck fracture. Orthopaedic surgeons planned to perform total hip arthroplasty for femoral neck fracture. However, the patient did not undergo surgery because of haematological problems such as thrombocytopaenia. We decided to perform splenectomy before total hip arthroplasty despite the potential risk of increasing bone lesions, because the patient had lived for 6 months with a hip fracture. But she did not admit any operation, whereupon the surgery was postponed after the correction of blood values with enzyme (imiglucerase) treatment. In conclusion, patients with GD have progressive and irreversible changes to bone which reduce their quality of life. Despite children with GD have an increased incidence of femoral neck fractures, it was not reported in adults. As far as we know, our patient is the first case of GD with femoral neck fracture. Patients with GD should be managed properly preoperatively and postoperatively because they may have various haematological abnormalities such as hypercoagulation and bleeding tendency due to abnormal platelet function.¹²

Learning points

- ▶ Gaucher's disease (GD) is an inherited storage disorder resulting from lysosomal enzyme deficiency.
- ▶ Patients with GD should have musculoskeletal complications including osteopenia, medullary bone infarcts as well as avascular necrosis.
- ▶ Haematological abnormalities which can alternate therapeutic approach should be kept in mind in patients with GD.

Competing interests None.

Patient consent Obtained.

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