Albers-Schönberg Disease (Marble Bone Disease) - A Clinical Case Report

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Abstract

Background: Albers-Schönberg disease (marble bone disease) is an adult autosomal dominant Type II osteopetrosis, caused by severe impairment of osteoclast-mediated bone resorption due to a mutation in CLCN-7 gene on chromosome 16q13.3; it is diagnosed incidentally based on the presence of a pathological fracture, which usually involves proximal femur and hip. A case of 21 years’ female patient who was brought to casualty with a subtrochanteric fracture of the left femur after a trivial trauma. History of fracture shaft of the right femur 7 years back diagnosed as pathological fracture due to osteopetrosis and treated surgically with plate and screws. In this case, open reduction internal fixation using dynamic hip screw (without autologous bone graft) was preferred over nonoperative modality for accurate reduction, stable fixation, early mobilization, fewer complications, and better functional outcome. Surgical treatment of fracture in these cases is a challenge to an orthopedic surgeon due to intraoperative difficulties and post-operative complications. Even though with intraoperative difficulties, operative modalities should be considered for a better outcome which requires proper pre-operative planning, with meticulous intraoperative skills and planned post-operative care.

Keywords: Osteopetrosis, Pathological fracture, Rugger-Jersey Spine, Dynamic hip screw, Femur.

Introduction

Osteopetrosis is a loss of osteoclastic bone resorption with preservation of osteoblastic bone formation with persistent primary spongiosa. It has three clinical forms based on the age of onset, inheritance pattern, and clinical features: (i) Infantile or malignant osteopetrosis (autosomal recessive), (ii) intermediate (autosomal recessive), and (iii) adult-onset or benign osteopetrosis (autosomal dominant) [3, 4, 5]. The first form is usually fatal in childhood, the second form is syndrome associated with renal tubular acidosis, whereas those with the autosomal dominant form generally have a normal lifespan [6] (Table 1). Adult autosomal dominant osteopetrosis (ADO) has two distinct phenotypic variants. ADO Type II (Albers-Schönberg disease, marble bone disease) is commonly called benign osteopetrosis but presents with an extremely heterogeneous course from asymptomatic to rarely fatal. The prevalence of the pathology has been estimated at 5 per 100,000 [7]. In Albers-Schönberg disease, clinical and radiological signs occur quite late in childhood or in the teens, although earlier occurring has sometimes been reported. Complications involve the skeleton [8]. Bone fractures occur in 80% of patients, with a mean of three fractures per patient. A few patients have had more than 10 fractures. The femur is the most fractured bone in this pathology, but fractures can occur on any long bones and even at the posterior arch of the vertebrae, which often leads to a spondylolisthesis [9, 10]. Common locations for fractures - inferior neck of the femur, proximal third of the femoral shaft, and the proximal tibia. Marble bone disease patients usually displayed osteosclerosis at the vertebral level (so-called sandwich vertebrae). Bone is grossly grayish-white on the section, as
hard as marble, brittleness of chalk with the obliterated medullary cavity. Osteoblasts are normal or increased in number. Histologically, mature osteopetrotic fracture callus contains no haversian organization and has a paucity of osteoclasts [11]. Radiographically, the bones have a dense, chalk-like appearance sandwich or rugger-jersey spine appearance, long bone shows marble-like appearance and Erlenmeyer's flask shape at their ends bowing of the bones due to multiple fractures, spondylolysis, or coxa vara. These various clinical manifestations ultimately are caused by genetic mutations affecting acidification of Howship's lacuna. There are case reports regarding treatment options of osteopetrosis-related fractures are available in the literature (Table 2). Internal fixation can be performed; however, intraoperative technical difficulties may be experienced due to increased bone density. Although many studies state that fractures in osteopetrosis heal at a normal rate, some studies report delayed union and non-union [12, 13, 14] (Table 2). The autologous bone graft is not available since osteoclasts of patients with osteopetrosis are dysfunctional. In this case report, we aimed to present an Albers-Schönberg disease-related subtrochanteric fracture of the femur with clinical and radiological findings in the light of comprehensive literature review. Informed consent is taken from the patient.

**Case Report**

A 21 years old short statured female, was brought to our casualty with complaints of left side hip pain, deformity, swelling over proximal thigh and inability to walk or bear weight after a history of fall from height of 4 feet. Physical examination showed diffuse swelling over proximal 1/3rd of thigh, tenderness over proximal 1/3rd of left femur and abnormal mobility, and shortening of 3 cm. On oral examination, she had crowding of teeth, tooth caries, and high-arched palate, surgical scar was present over lateral aspect of the right thigh. Other systemic examinations were normal. Plain X-ray pelvis with both hips and full length femur showed transverse displaced subtrochanteric fracture of the left femur. She had a history suggestive of fracture shaft of the right femur.
operated 7 years back with plate and screw, which on X-ray showed united but angulated fracture site, with broken plate in situ (Fig. 1). Femur had thick cortex and reduced medullary cavity. Thomas splint was applied and fracture was immobilized. The patient was hospitalized with preliminary diagnosis of osteopetrosis and pathological femoral fracture. Clinical, radiological, and laboratory evaluation was done. Mild anemia and moderately elevated levels of alkaline phosphatase were seen. Radiographically, thoracolumbar spine showed sandwich or rugger-jersey spine appearance (Fig. 2), long bones of forearm have a dense, chalk-like appearance, and long bone shows marble-like appearance (Fig. 3). After appropriate planning of surgical management, under spinal anesthesia patient was placed in supine position. Following standard antiseptic precautions for hips and lower limbs, through a standard lateral straight
incision open reduction was done. Then, osteosynthesis with internal fixation was performed using 8-HOLED dynamic hip screw (DHS). Drilling was very difficult, drilling of bone was so hard that even with saline irrigation a lot of heat was generated. Intraoperative successful reduction and fixation were confirmed under fluoroscopic guidance. The patient had no post-operative complications, partial weight bearing was started on the 2nd post-operative day and staple removal was done on the 12th post-operative day, and the patient was discharged. The patient was followed up in our hospital and follow-up period was uneventful (Figs. 4 and 5) at the 10th month of follow-up, X-rays were done which showed complete union at fracture site with implant in situ (Fig. 6).

Discussion
Osteopetrosis is a disease of osteoclasts that result in failure of bone remodeling. The autosomal dominant form is identified radiographically by universal osteosclerosis and has been divided into two subtypes based on the location of this osteosclerosis. Osteosclerosis of the cranial vault is evident with the first type, whereas end-plate thickening of the vertebrae (rugger-jersey spine) and endobones (bone within bone) in the pelvis are evident with the second type. The second type (Albers-Schönberg disease) [6,15] is associated with increased fracture frequency in the autosomal dominant population. Serum levels of alkaline phosphatase are reduced in Type I and increased in Type II. In addition, Type I does not present with increased risk of fracture; however, fractures may develop, particularly in long bones, after even minor trauma. Although rare in Type I, the incidence of trigeminal neuralgia, facial nerve paralysis, and optic nerve compression is higher in Type II. Furthermore, short stature may result from diminished longitudinal growth in patients with Type II disease. Other conditions which may be accompanied by ADO Type II include hepatosplenomegaly, anemia, renal tubular acidosis, and pancytopenia [16,17,18,19,20]. About 70% of patients affected by Albers-Schönberg disease harbor heterozygous dominant-negative mutations of the CLCN7 gene. In the remaining ~30% of cases, no mutations in CLCN7 gene sequences were found, suggesting involvement of further genes in the pathogenesis of this form of osteopetrosis [10]. The mutation responsible for Albers-Schönberg disease has been localized to two possible chromosomal locations, 1p21 and 16p13.3 [21,22]. In a study including 42 patients with osteopetrosis tarda, Bénichou et al. [4] reported a fracture rate of 78%. The mean number of fractures was 4.4 and the most common fracture localization was the femur. Both operative and non-operative modalities are available in literature for the treatment of pathological fracture in osteopetrosis. There are case reports in which various implants (e.g., locking plates, cannulated screws, dynamic condylar screw, DHS, and intramedullary nailing) were used during surgery in the light of the methods of osteosynthesis for the surgical treatment of osteopetrotic femoral fractures (Table 2). Osteosynthesis has been the primary method for the surgical treatment of femoral osteopetrotic fractures (Table 2). Despite increased risk for implant failure during the follow-up period, we suggest that osteosynthesis is the primary treatment of choice in the treatment of osteopetrotic femoral fractures. Several surgical-related complications, on the other hand, have been reported in the literature. Several complications such as delayed union, non-union, broken plates or screws, recurrent fractures, coxa vara deformity, and infection may be observed [4,19,23,24]. Technical difficulties associated with operative treatment include bending of drill bits or screws during surgery due to hard-fragile sclerotic bones and a narrow medullary canal. Slow-speed high-torque electric drills as well as frequent cooling with physiological saline, clearance of drill grooves, and the use of staggered drill system have been recommended. The treatment success is based on the appropriate selection of internal fixation and meticulous approach during surgery [19,25,26]. In our case, the patient has short stature, crowed teeth, tooth carries, high-arched palate, and no neurological deficit, and laboratory tests were within normal limits, alkaline phosphatase was on higher end of normal range. X-rays showed characteristic features of osteopetrosis. After pre-operative planning and workup, a standard lateral straight incision was used for open reduction. Then, osteosynthesis with internal fixation was performed using 8-HOLED DHS. Drilling was very difficult, drilling of bone was so hard that even with saline irrigation a lot of heat was generated.

Conclusion
With this case report and review of literature, we suggest that surgery is an effective treatment modality in patients with osteopetrotic fractures, although technical difficulties may be experienced and fracture healing is slower than normal. Technical challenges and complications may occur during surgery; however, we believe that osteopetrotic femoral shaft fractures can be successfully treated with plate-screw systems without using any graft. Orthopedic surgeons should be aware of intraoperative technical difficulties and possible post-operative complications during the follow-up period.
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References


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How to Cite this Article