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

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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

Albers-Schönberg first described his eponymous description of the marked radiographic density of the bones ("hypersclerotic") in 1904 [1]. Approximately 22 years later, Karshner referred to the entity as osteopetrosis [2]. Osteopetrosis (osteo: Bone and petros: Stone) regroups a set of rare, heterogeneous, and inherited bone diseases characterized by increased bone mass. Osteopetrosis is, therefore, an osteocondensing disease. Osteopetrosis is known to result from defective osteoclast differentiation or function [3, 4]. The primary defect in 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

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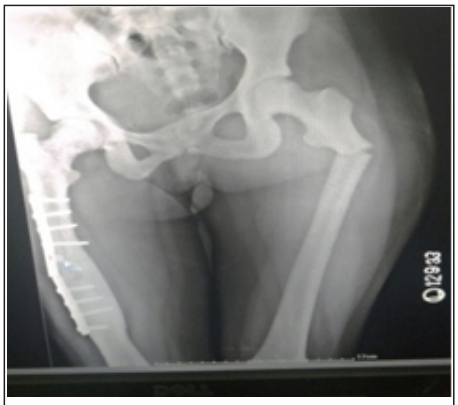

Figure 1: An anteroposterior view of the pelvis with the left-sided subtrochanteric fracture and right-sided healed shaft of femur fracture with broken plate in situ.

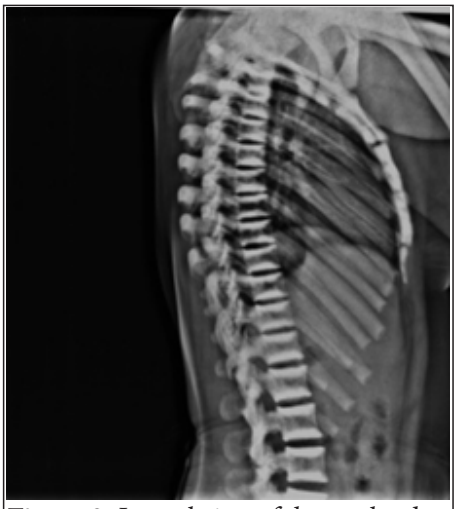

Figure 2: Lateral view of thoracolumbar spine showing rugger-jersey spine.

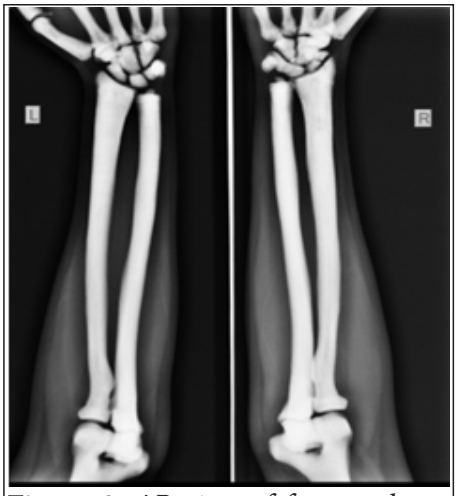

Figure 3: AP view of forearm bone showing no medullary cavity, i.e., chalk bones.

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 21years 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

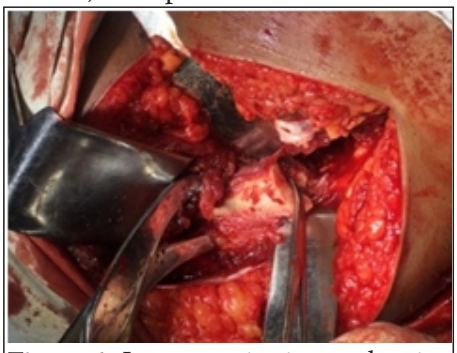

Figure 4: Intraoperative image showing narrow medullary cavity with thick cortex of femur.

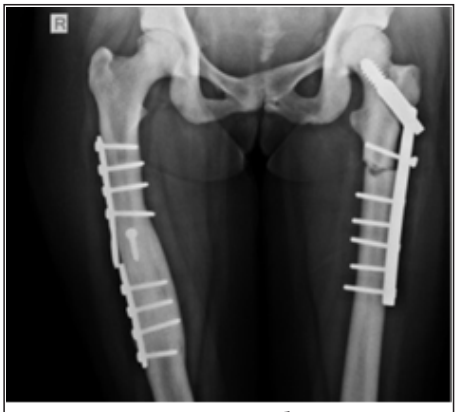

Figure 5: Post-operative day 1.

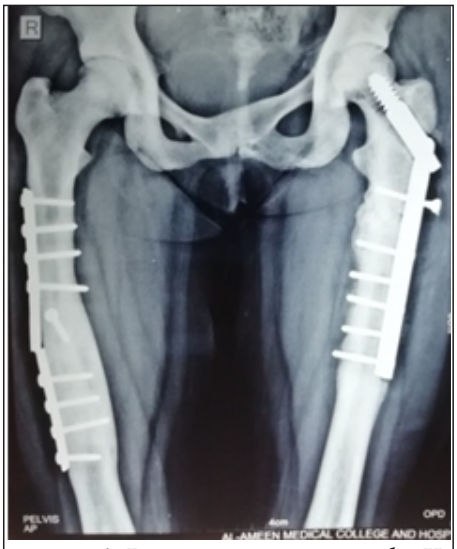

Figure 6: Post-operative 10 months X-ray showing good union.

Table 1: Types of osteopetrosis [3, 4, 5]

Type	Genetic transmission	Gene	Mutation type	Protein
ARO	Autosomal recessive	*TCIRG1*	Loss of function	α 3 subunit V-ATPase
		CLCN7	Loss of function	Chloride channel 7
		OSTM1	Loss of function	Osteopetrosis associated transmembrane protein
		PLEKHM1	Loss of function	Pleckstrin homology domain containing family M, member 1
		SNX10	Loss of function	Sorting nexin 10
		TNFSF11	Loss of function	Receptor activator for nuclear factor κ B ligand
		TNFRSF11A	Loss of function	Receptor activator for nuclear factor κ B
IRO	Autosomal recessive	*CAII*	Loss of function	Carbonic anhydrase II
ADO Type I-Type II (Albers-Schönberg disease)	Autosomal dominant	*CLCN7*	Dominant negative	Chloride channel 7

ARO: Autosomal recessive osteopetrosis, IRO: Intermediate recessive osteopetrosis, ADO: Autosomal dominant osteopetrosis

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

Table 2: Comprehensive illustration of published operated cases of the osteopetrosis in literature

Study	Age (years)	Sex	Fracture location	Treatment	Complications	Follow-up
Kleinberg [27]	35	M	Left peritrochanteric	Plate and screw, cortical allograft	Plate breakage and angulation	Union
de Palma et al. [11]	27	M	Right peritrochanteric	Jewett plate	Union, removed plate at 1year, refractured and fixed with DCP	Union
Armstrong *et al*. [12]	6–16 (n=3)		Femoral neck	Pins/compression screw		Union
	6–16		Femoral neck	Non-weight-bearing/pins	Non-union treated at the 6th month with pins	Union
	Adult (n=3)		Peritrochanteric	Nail plate/compression screw plate		Union
	8–30		Peritrochanteric	ORIF		Non-union
	8–30		Peritrochanteric	ORIF		Union at 6 months
	31	M	Peritrochanteric	Blade plate		Union at 12–16 weeks
Chhabra *et al*. [13]	22	F	Left, peritrochanteric	DHS revision after prior Jewett nail	Infection	Infection, non-union
	22	F	Right, peritrochanteric	DHS	Hardware failure	Pullout, non-union
	41	F	Left, peritrochanteric	Kuntscher nail	Rod migration with exchange rodding	Union 2 months, rod removed at 6 months
	42	F	Left, peritrochanteric	Kuntscher nail		Union
	45	F	Right, peritrochanteric (3 years later)	Kuntscher nail		Union
	42	M	Right, peritrochanteric	Proximally locked intramedullary nail		Union at 2 months
Kulkarni *et al*. [28]	22	M	Left shaft	Plate-screw	Unspecified	Unspecified
	47	M	Right subtrochanteric	Plate-screw	Unspecified	Unspecified
Kumar *et al*. [29]	45	M	Bilateral subtrochanteric	DHS	None	11 months
Amit *et al*. [14]	35	F	Right subtrochanteric	Locking plate	Contralateral stress fracture	23 weeks
	38	F	Left subtrochanteric	Locking plate	Delayed union	21 weeks
Sen *et al*. [30]	26	4 M 1 F	Four subtrochanteric (one of them bilateral)	Locking plate	None	3 months

DCP: Dynamic compression plate

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 harbors 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.

References

1. Albers-Schonberg H. Roentgenbilder einer seltenen knochennerkrankung. Munch Med Wochenschr 1904;51:365.
2. Karshner R. Osteopetrosis. Am J Roentgenol 1926;16:405-19.
3. Sobacchi C, Schulz A, Coxon FP, Villa A, Helfrich MH. Osteopetrosis: Genetics, treatment and new insights into osteoclast function. Nat Rev Endocrinol 2013;9:522-36.
4. Stark Z, Savarirayan R. Osteopetrosis. Orphanet J Rare Dis 2009;4:5.
5. Sly WS, Hewett-Emmett D, Whyte MP, Yu YS, Tashian RE. Carbonic anhydrase II deficiency identified as the primary defect in the autosomal recessive syndrome of osteopetrosis with renal tubular acidosis and cerebral calcification. Proc Natl Acad Sci U S A 1983;80:2752-6.
6. Bollerslev J, Mosekilde L. Autosomal dominant osteopetrosis. Clin Orthop Relat Res 1993;294:45-51.
7. Bollerslev J, Henriksen K, Nielsen MF, Brixen K, Van Hul W. Autosomal dominant osteopetrosis revisited: Lessons from recent studies. Eur J Endocrinol 2013;169:R39-57.
8. Bénichou OD, Laredo JD, de Vernejoul MC. Type II autosomal dominant osteopetrosis (albers-schönberg disease): Clinical and radiological manifestations in 42 patients. Bone 2000;26:87-93.
9. de Vernejoul MC, Kornak U. Heritable sclerosing bone disorders: Presentation and new molecular mechanisms. Ann N Y Acad Sci 2010;1192:269-77.
10. de Vernejoul MC, Schulz A, Kornak U. CLCN7-related osteopetrosis. GeneReviews 2007;???:???.
11. de Palma L, Tulli A, Maccauro G, Sabetta SP, del Torto M. Fracture callus in osteopetrosis. Clin Orthop Relat Res 1994;308:85-9.
12. Armstrong DG, Newfield JT, Gillespie R. Orthopedic management of osteopetrosis: Results of a survey and review of the literature. J Pediatr Orthop 1999;19:122-32.
13. Chhabra A, Westerlund LE, Kline AJ, McLaughlin R. Management of proximal femoral shaft fractures in osteopetrosis: A case series using internal fixation. Orthopedics 2005;28:587-92.
14. Amit S, Shehkar A, Vivek M, Shekhar S, Biren N. Fixation of subtrochanteric fractures in two patients with osteopetrosis using a distal femoral locking compression plate of the contralateral side. Eur J Trauma Emerg Surg 2010;36:263-9.
15. Bollerslev J, Andersen PE Jr. Fracture patterns in two types of autosomal-dominant osteopetrosis. Acta Orthop Scand 1989;60:110-2.
16. Osuna PM, Santoz-Guzman J, Viellela L, Garcia A. Osteopetrosis-calcification beyond the skeletal system. A case report clinical case. Bol Méd Hosp Infant Méx 2012;69:109-13.
17. Rysavy M, Arun KP, Wozniak A. Fracture treatment in intermediate autosomal recessive osteopetrosis. Orthopedics 2007;30:577-80.
18. Özcan AÜ, Ocak FŞ, Ratip S. A rare case of osteopetrosis tarda: Radiographic signs. Acıbadem Üniv Sağlık Bilimleri Derg 2012;3:79-81.
19. Kumbaraci M, Karapinar L, Incesu M, Kaya A. Treatment of bilateral simultaneous subtrochanteric femur fractures with proximal femoral nail antirotation (PFNA) in a patient with osteopetrosis: Case report and review of the literature. J Orthop Sci 2013;18:486-9.
20. Khan MN, Datta PK, Hasan MI, Hossain MA, Patwary KH, Ferdous J, et al. Osteopetrosis. Mymensingh Med J 2011;20:715-8.
21. Bénichou O, Cleiren E, Gram J, Bollerslev J, de Vernejoul MC, Van Hul W, et al. Mapping of autosomal dominant osteopetrosis Type II (albers-schönberg disease) to chromosome 16p13.3. Am J Hum Genet 2001;69:647-54.
22. Van Hul W, Bollerslev J, Gram J, Van Hul E, Wuyts W, Benichou O, et al. Localization of a gene for autosomal dominant osteopetrosis (albers-schönberg disease) to chromosome 1p21. Am J Hum Genet 1997;61:363-9.
23. Ihde LL, Forrester DM, Gottsegen CJ, Masih S, Patel DB, Vachon LA, et al. Sclerosing bone dysplasias: Review and differentiation from other causes of osteosclerosis. Radiographics 2011;31:1865-82.
24. Rafiq I, Kapoor A, Burton DJ, Haines JF. A new modality of treatment for non-united fracture of the humerus in a patient with osteopetrosis: A case report. J Med Case Rep 2009;3:15.
25. Şar C, Pınar H, Demirhan M, Yazıcıoğlu Ö. Bilateral femoral neck fracture in a case of osteopetrosis. Acta Orthop Traumatol Turcica 1994;28:56-8.
26. Martínez FL, Zenteno CB, Rodríguez RS. Subtrochanteric fracture in autosomal dominant osteopetrosis Type II. A case report. Acta Ortop Mex 2006;20:30-2.
27. Kleinberg S. Osteopetrosis. Am J Surg 1954;87:50-62.
28. Kulkarni JV, Bengali R, Jewalikar S, Joshi A. Osteopetrosis-a challenge in rare situation. Case report. J Evol Med Dent Sci 2012;1:532-7.
29. Kumar D, Jain VK, Lal H, Arya RK, Sinha S. Metachronous bilateral subtrochanteric fracture of femur in an osteopetrotic bone: A case report with technical note. J Clin Orthop Trauma 2012;3:103-6.
30. Sen RK, Gopinathan NR, Kumar R, Saini UC. Simple reproducible technique in treatment for osteopetrotic fractures. Musculoskelet Surg 2013;97:117-21.

Conflict of Interest: NIL
Source of Support: NIL

How to Cite this Article

Ahmed O, Patil M S. Albers-Schönberg Disease (Marble Bone Disease) - A Clinical Case Repor. J Kar Orth Assoc. Jan-April 2019; 7(1): 34-38.