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ORIGINAL PAPER

Fractures in patients with osteopetrosis, insights from a single institution

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Abstract

Purpose Osteopetrosis is a hereditary skeletal disorder in which defective osteoclast function leads to abnormally hard and brittle bones. This study aims to describe the pattern of fractures occurring in this group of patients, possible complications, and strategies to avoid them.

Methods This is a case series of six osteopetrotic patients with a total of 12 fractures managed in our institution over a period of nine years. Patient records were also reviewed for complications both intra- and post-operatively.

Results The majority of the fractures involved the femur, with three of these being peri-implant in nature. Other bones involved include the tibia, humerus, patella, fifth metatarsal, and proximal phalanx of the toe. There was a high rate of complications while managing these patients: three patients had peri-implant stress fractures, three with retained broken screws, and one case each of delayed union, non-union, and surgical site infection.

Conclusion Osteopetrosis fractures present a unique challenge to the orthopedic surgeon. Careful pre-operative planning should be undertaken before proceeding with surgery in these cases.

Keywords Fractures · Osteopetrosis · Patients · Single institution

Introduction

Osteopetrosis is a rare heterogeneous group of inherited bone dysplasia characterized by diminished osteoclast mediated bone resorption leading to increased bone radio density. Also known as marble bone disease, it was first described by Albers Schönberg, a German Radiologist in 1904. This disorder is divided into three clinical forms [1], of which autosomal dominant osteopetrosis (ADO) is the most common. As many patients in this form are asymptomatic, the overall prevalence of the disease is underestimated. ADO has been further divided into two parts: type I and type II. ADO1 is no longer classified among the osteopetrosis [2]. ADO type II, characterized by rugger-jersey spine, endobone (bone within the bone), and an increased fracture risk [3], is the form originally described by Albers Schöberg in 1904. It is the most common form with an estimated prevalence ranging from 0.2/100,000 in Brazil to 5.5/100,000 in Denmark [4, 5]. The estimated genetic penetrance is about 75% and ADO has a tendency to skip a generation [6].

Currently, there is no accepted definitive therapy for ADO and thus for most patients with either recessive or dominant osteopetrosis, the treatment remains supportive [7, 8]. The most common clinical presentation of ADOII is frequent fractures in approximately 75% of the patients. Other manifestations include hip osteoarthritis, facial nerve palsy, and mandibular osteomyelitis [1]. However, 20–40% of the patients remain asymptomatic.

The fractures in patients with osteopetrosis most commonly affect the long bones [9] and are associated with significant complications; both intra-operative and post-operative. To add up, the variable healing response of the bone poses a significant challenge to the treating orthopaedic surgeon. Molecular defects in osteoclast cause an imbalance between bone formation by osteoblast and resorption by osteoclasts, leading to sclerotic brittle abnormal bone [10]. Absence of ruffled border in osteoclasts on electron microscopy explains the dysfunctional nature of osteoclasts in osteopetrosis [9]. As a consequence, there is absence of bone remodeling during union of

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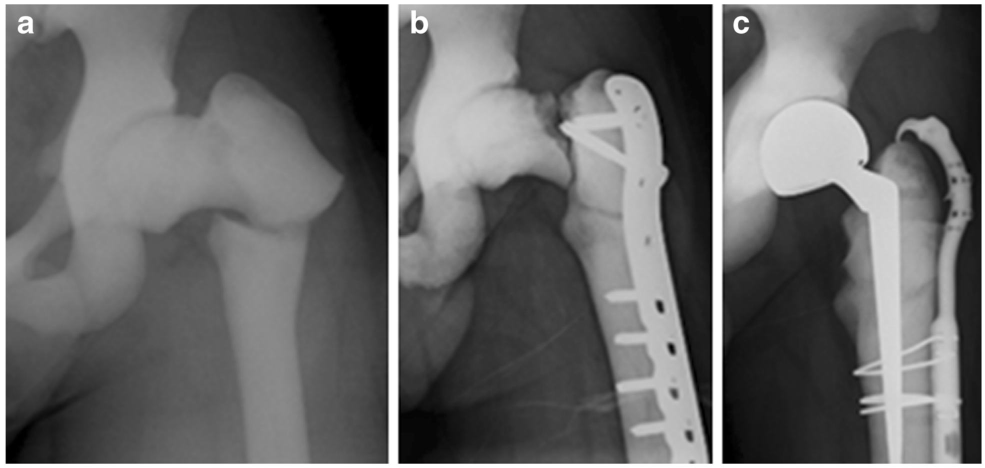

Fig. 1 (Case no. 2) **a** Pre-operative hip radiograph showing subtrochanteric fracture of the femur. **b** Hip radiograph showing peri-implant stress fracture of the left femoral neck proximal to the most proximal locking screw. Note the presence of the original subtrochanteric fracture line even after 2 years of index surgery suggesting fracture non-union. **c** Post-operative radiograph showing plate removal, bipolar hemiarthroplasty with cable plate augmentation

these fractures. According to a study by DePalma et al., the bone showed normal callus initially but united bone at one year showed unorganized tissue with no Haversian organization and absent cartilage islands or osteoclasts [11].

Hence, the fixation strategies need to be individualized for the fractures in these patients. These case series describe our experience and challenges faced in managing six such patients with 12 fractures. We also outline recommendations while treating these fractures and importance of informed consent highlighting prolonged treatment, multiple surgeries, and possible complications.

Case series

Six patients with osteopetrosis were managed in our institution over a nine year period from the period of 2007 to 2016. All of them had a history of multiple fractures, managed conservatively or surgically in other hospitals prior to management at our institution. All patients except case 6 were young males between the ages of 20–40 years of age. Case nos. 4 and 6 were siblings while the rest of the patients did not have any known family member with a diagnosis of osteopetrosis. There were a total of seven femoral fractures, one tibial, one fractured humerus, one patella fracture, and two fifth metatarsal fractures.

Case 1 sustained subtrochanteric fractures of both his femurs at an interval of one year. Both fractures were fixed with dynamic condylar screw (DCS) plates. The left side was managed in another institution but was later followed by us. It was complicated by delayed union for which bone grafting was performed.

Case 2 (Fig. 1a) had a subtrochanteric femur fracture which was fixed with a locking plate. Due to difficulty encountered in drilling through the bone, only short screws could be inserted in the proximal fragment. Three years later, he sustained a peri-implant femoral neck fracture proximal to the plate (Fig. 1b). A CT scan of the extremity confirmed non-union at the subtrochanteric fracture site. It was treated with implant removal and hip hemiarthroplasty augmented with allograft and cable plate fixation (Fig. 1c) [12]. A year later, he sustained a fracture of the proximal humerus shaft which was 5 cm proximal to a plate applied for a previous

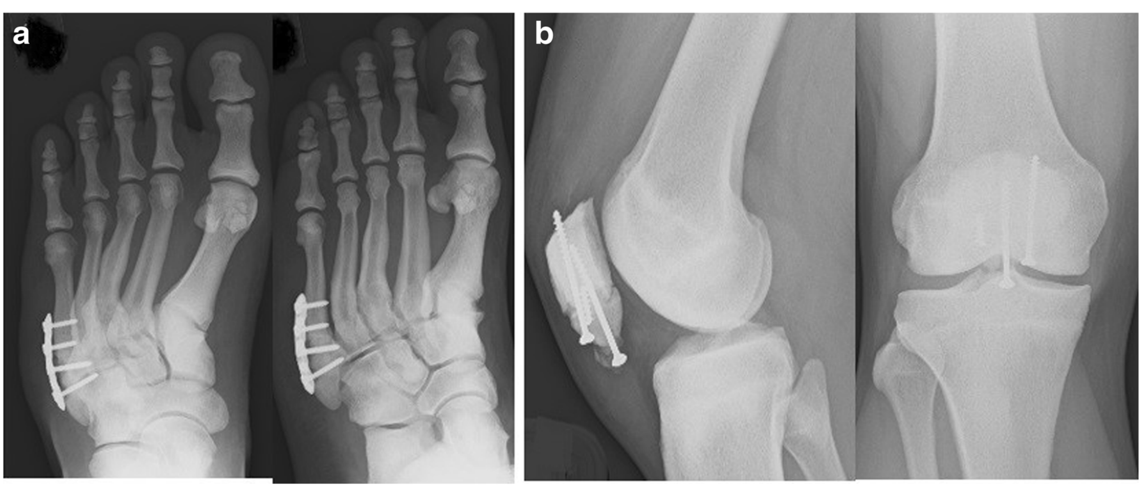

Fig. 2 (Case no. 3) **a** Post-operative radiograph foot-AP and oblique after fixation of fifth metatarsal base fracture. **b** Post-operative radiograph of knee-AP and lateral after surgical fixation of the patella. Note one broken screw and one partially inserted screw

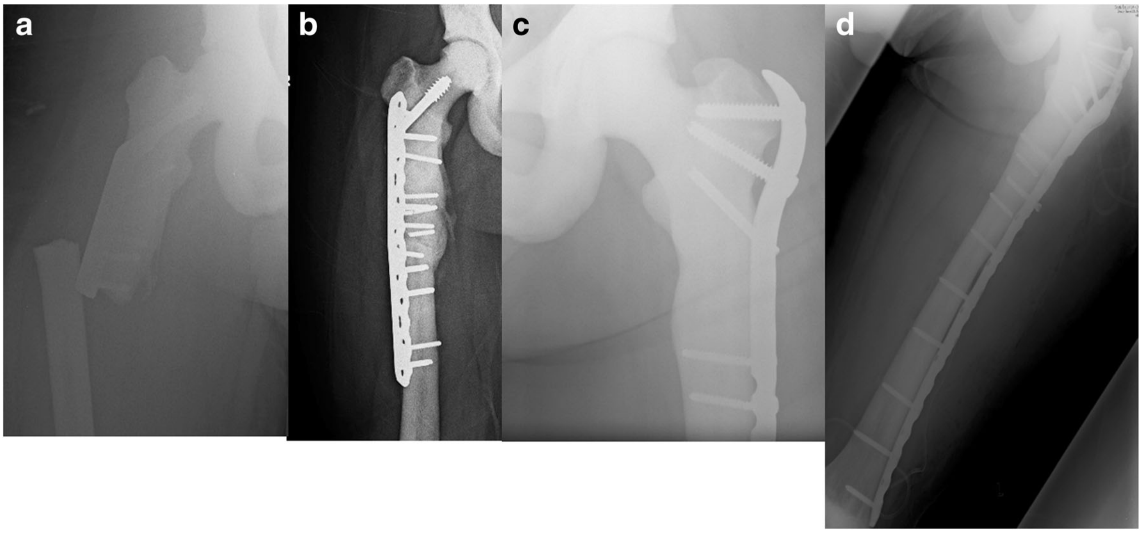

Fig. 3 (Case no. 4) **a** Pre-operative radiograph of the right femur showing a peri-DHS fracture distal to the plate. **b** Post-operative radiograph showing plate removal and locking plate fixation. Note retained compression screw and multiple broken screws on X-ray. **c** Pre-operative radiograph of left femur with LCP. There was no fracture noted on X-ray, but the distal locking screws were broken at the screw-plate junction. **d** Post-operative radiograph after plate removal and longer plate fixation. Note retained broken screws on X-ray

humerus shaft fracture. This was in turn fixed with a long proximal humerus locking plate.

Case 3 (Fig. 2) developed a minimally displaced fracture of his right patella with intact extensor mechanism after a fall during skiing. Three weeks later, he sustained an undisplaced fifth metatarsal base fracture after a twisting injury to his left foot [13]. Both his fractures were managed non-operatively for two months after which they were surgically fixed as there was no evidence of healing in both the fractures. The patella fracture was fixed with non-cannulated screws instead of standard tension band wiring in view of the anticipated difficulty in drilling K wires through the hard sclerotic bone. The surgery was complicated with one screw breakage and one partially inserted screw. The fifth metatarsal fracture fixation developed a delayed wound infection five months after index surgery. It was treated with wound debridement, six weeks of intravenous antibiotics followed by prolonged antibiotic suppression until implant removal which was performed at one year.

Case 4 (Fig. 3) had previously fixed bilateral proximal femur fractures in childhood from another hospital. He was referred to us for a peri-implant fracture of his right femur. Many of the distal screws were broken and buried inside the bone. The Richard compression screw could not be extracted during the surgery and left in situ. The fracture was then fixed with a locking compression plate after removal of the previous plate. A few months later, he was seen for pain in his contralateral left thigh. X-ray showed broken distal screws in the previously applied locking plate. In view of an impending peri-implant fracture, his old plate was removed and he was prophylactically fixed with a long locking compression plate spanning the whole femur.

Case 5 had a pre-existing anterior bow deformity of his tibia due to an old fracture. He sustained a minimally displaced tibial shaft fracture, which was managed conservatively in a cast.

Case 6 had a history of previous multiple femur fractures managed surgically in another hospital during her childhood. She was referred for an internal rotation deformity of her left femur post-fixation. She then sustained an undisplaced fifth metatarsal shaft which was managed conservatively.

A summary of the patients are compiled in Table 1.

Discussion

Great caution has to be exercised while fixing fractures in patients with osteopetrosis. The fractures most commonly involve long bones, namely the femur, tibia, humerus, and foot bones though uncommon locations like clavicle [14], olecranon [15], distal humerus [16], and cervical and lumbar spine [17–20] have been described as well. As it is an uncommon disease, there is a paucity of literature on adequate management of fractures in osteopetrosis with most of the studies being case reports and very few series. In this series, we have shared our experience of managing 12 fractures in six patients in our institution. To the best of our knowledge, this study has the largest number of surgically fixed fractures in patients with osteopetrosis managed by a single institution. Bhargava et al. [15] described a series of seven patients but only three of them were managed surgically with a total of six operations. Gupta et al. [21] shared their experience of managing seven femoral fractures in five patients over two decades and highlighted the importance of high clinical suspicion and pre-operative

Table 1 A summary of the patients including age at presentation, fracture sustained, management, and complications with difficulties encountered

Case no.	Fracture	Age at fracture (in years)	Treatment	Complications
1.	Right subtrochanteric femur fracture	39	ORIF with DCS	Nil
	Left subtrochanteric femur fracture	40	ORIF with DCS	Delayed union
2.	Left subtrochanteric femur fracture	35	ORIF with LCP	Non-union of fracture Peri-implant stress fracture
	Left peri-implant femoral neck fracture	38	Plate removal and bipolar hemiarthroplasty	Nil
	Left humerus shaft fracture	39	ORIF with Philos plate	Nil
3.	Left patella fracture	40	ORIF with screws	Broken screw Incompletely inserted screw
	Right fifth metatarsal base fracture	40	ORIF with LCP	Surgical site infection and osteomyelitis
4.	Peri-implant fracture right femur	23	Plate removal and ORIF with LCP	Retained and broken screws
	Peri-implant stress injury left femur	24	Plate removal and LCP	Broken screws
5.	Left tibial shaft fracture	31	Non-surgical	Nil
6.	Malunited left femur fracture	22	Expectant	Nil
	Left fifth metatarsal shaft and left big toe proximal phalanx fracture	22	Non-surgical	Nil

ORIF, open reduction internal fixation; *DCS*, dynamic condylar screw; *LCP*, locking compression plate

planning. Armstrong et al. [6] conducted a survey of the Pediatric Orthopaedic Society of North America describing the experience of 79 osteopetrotic fractures managed by 59 surgeons.

Seven out of the 12 fractures managed by us involved the femur, which is consistent with the literature. All our patients were young adults in their third to fifth decade when they sought treatment at our institution. All except one were male. As the disease transmission is autosomal dominant/recessive, no sex predilection has been described for these patients. Armstrong [6] had a predominantly male population (3:2) while Bhargava [15] (6:1) and Gupta [21] (3:2) had more female patients. All our patients sustained trivial trauma and had a transverse fracture configuration compatible with the pathological nature of fracture.

The femoral neck fracture in our patient (case 2) was managed with hip hemiarthroplasty in view of the pathologic nature of the bone and the high Pauwel's angle [12]. Insertion of a femoral stem is always difficult when performing hip arthroplasty in osteopetrosis due to the absence of a medullary canal [22, 23]. An industrial tungsten carbide drill bit [12, 24] was thus used to fashion the medullary canal to facilitate insertion of the stem. This was further supplemented with allograft and cable plate fixation.

We also found a high incidence of delayed union and non-union in our series. Though most of our patients showed good bone healing, the patient with the patella fracture did not show any appreciable callus formation or bone healing despite being asymptomatic and returning to his premorbid activity at one year [13]. Although in our series, no autogenous bone grafting was performed at our institution; it is foreseeable that the bone grafting procedure may also be complicated by difficulty in accessing and obtaining viable cancellous bone from the donor sites as well as fracture of the harvest site [19].

Osteomyelitis is also common in these patients because of the absence of white cell function and diminished vascular supply [6]. Our case number 3 developed abscess formation with osteomyelitis of the fifth metatarsal. The implants were stable and hence retained during the debridement. The implants were eventually removed after a year when the fracture had healed. This case illustrates the risk of infection in this group of patients.

Fractures in osteopetrosis have been treated nonsurgically historically in view of the many challenges associated with surgical management. There is a high incidence of breakage of instruments and implants during the surgery due to the hardness of the bone. The use of external fixation has been described in a tibial osteotomy of an osteopetrosis patient with unicompartmental osteoarthrosis [25]. Intramedullary fixation has been recommended because of its load bearing mechanics and long-term strength. However, finding the medullary canal in an osteopetrotic long bone is a very tedious process and involves opening of the canal with progressively larger drill bits followed by cutting reamers [26]. This procedure may be associated with breakage of multiple drill bits [26, 27], takes two to four hours longer than a standard intramedullary nailing, and is associated with a significantly higher amount of blood loss. Conventional

Table 2 Summary of challenges and recommended strategies

	Challenges	Recommended solutions
Pre-operative	Diagnosis	High index of suspicion based on: low energy trauma, X-ray findings of increased bone density, obliteration of medullary canal; other non-orthopedic manifestations; positive family history
	Consent	Patient should be warned about prolonged surgical time; increased blood loss; possible retained or broken implants; delayed and non-union; infection and osteomyelitis
	Anesthesia	Be prepared for prolonged surgery and preference for general anesthesia; close hemodynamic monitoring and blood products
	Surgical inventory	Multiple new drill bits, metal cutting burrs Air-operated drills Self-drilling and self-tapping screws
Intra-operative	Drilling through sclerotic bone	Use of new drill bit for each drilling Industrial tungsten carbide drills Avoid low-powered battery-operated drivers Saline cooling to avoid thermal necrosis
	Intramedullary nailing	Careful pre-operative planning and sizing Use of progressively larger drill bits Cutting reamers Have smaller diameter nails ready
	Brittle bones	Be wary of intra-operative fractures Avoid mallet usage Avoid bending or torsional forces
	K wire insertion	Pre-drilling before inserting wires Avoid smaller gauge wires that may bend or break
	Plate fixation	Use of locking plates preferred as unicortical self-tapping screws may be advantageous Span the whole bone to reduce possibility of stress fractures Screws may not be able to penetrate opposite cortex Do not use torque limiting screw driver to insert locking screws
Post-operative	Delayed and non-union	Close follow-up required
	Stress fractures	High index of suspicion Look for any stress response at end of implants Investigate for loosening or breakage of implants
	Osteomyelitis	Debridement and long-term antibiotics Removal of implants when feasible Early consultation with Infectious Disease Specialist

plate fixation has enjoyed limited success as the screw holes and plate ends create areas of increased stress that are prone to fracture [21]. In addition, load bearing components are prone to failure because of the increased demand placed on them during delayed union [28]. Titanium locking plate can be used as an alternative because it is a less rigid implant system and hence may be less prone to peri-implant fracture. The technical difficulties associated with an intramedullary nail can thus be obviated as well. An example is the use of reverse LISS plating that has been used in subtrochanteric fractures in these patients [29, 30]. Also, locking plates by using self-tapping screws avoid an extra step of tapping the screw thread thus minimizing the chance of instrument breakage. We used locking plates in most of our fractures (five cases). However, we found a high incidence of peri-implant fractures that may be explained by the high stresses next to locking plates as well. We noted that all our peri-implant fractures were next to a short plate applied on the proximal femur. As the stresses passing through proximal femur are very high [31], any implant that ends in this region creates a stress riser at the end of plate in these bones. Use of longer plates to span the whole bone can be considered as an option to prevent peri-implant fractures. We also experienced that a torque limiting screw driver could not be used for inserting locking screws as the force needed to insert the screw was much higher than the torque required to lock the screws. As a result, most of the locking screws were inserted using the standard screw driver. We used new drill bits for drilling every new hole and did not encounter any drill breakage during our surgery. It is our practice to avoid battery-operated power in fixing these fractures as they are not as powerful as air-operated drills.

Table 2 summarizes the potential challenges in the surgical management of osteopetrotic patients, as well as our recommended strategies.

Conclusion

Complications associated with fixation in patients with osteopetrosis must be taken into account when managing these fractures. Plates are technically easier to do with less intra-operative problems but are associated with a higher incidence of peri-implant stress fractures. Longer plates that span the entire bone should be used in such cases. Inability to use the torque limiting screw driver when using locking screws should also be considered. Risks and benefits of each fixation modality should be considered when planning surgical management of fractures in these patients.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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