Intramedullary nailing for adult hypophosphatasia: a case report

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ABSTRACT

Hypophosphatasia is a rare genetic metabolic disorder characterised by defective bone mineralisation secondary to serum and bone alkaline phosphatase deficiency. We report a 46-year-old woman who underwent multiple intramedullary nailings for fractures and deformities of 6 long bones over 13 years.

Key words: fractures, bone; hypophosphatasia

INTRODUCTION

Hypophosphatasia is a rare genetic metabolic disorder characterised by defective bone mineralisation, hypercalcaemia, ethanolamine phosphataemia, and ethanolamine phosphaturia, secondary to serum and bone alkaline phosphatase deficiency. We report a 46-year-old woman who underwent multiple intramedullary nailings for fractures and deformities of 6 long bones over 13 years.

CASE REPORT

In 1994, a 33-year-old woman presented with a fracture of the right proximal ulnar shaft and underwent an open reduction and internal fixation using a screw and plate. Three years later, she sustained a fracture of the left subtrochanteric femur and underwent a reconstruction nail fixation. She recovered uneventfully but relied on elbow crutches to assist walking because of bilateral leg pain. She was diagnosed with hypophosphatasia. Her serum alkaline phosphatase was low (7 IU/l) and her urinary phosphoethanolamine increased. She had poor dentition since childhood and had lost several permanent teeth by the age of 21 years.

In 2000, she sustained non-traumatic fractures of both distal tibias and fibulas and underwent long-leg...
casting. She also had a fracture of the left proximal ulna and underwent open reduction and plating. The left tibia and fibula developed a painful non-union with marked varus deformity and anterior angulation, but she refused a revision surgery.

In September 2006, she fell and sustained a transverse fracture of the left humeral shaft and a peri-implant fracture of the left proximal ulna (Fig. 1a), associated with a deformed non-union of the left distal tibia and fibula (Fig. 1b) and asymptomatic pseudofractures of the right humeral shaft.

To reduce the operating time and risks associated with reaming of multiple long bones, a 2-stage fixation was planned. Intramedullary nailing of both humeri (Fig. 2) and the left tibia (with excision of a 1.5-cm segment of the fibula) was performed. A cut-out of the tibial nail was encountered at the anteromedial aspect of the left tibia just above the non-union site (Fig. 3) because the curvature and deformity led to eccentric reaming. Two weeks later, screws and plates in both ulnas were removed and telescopic nails inserted (Fig. 4). The left tibia was osteotomised in order to straighten the tibia and reposition the nail.

Figure 1  (a) Stress fracture of the left ulna at the proximal end of the plate with screw loosening.  (b) Non-union of the left tibia and fibula with varus deformity and anterior angulation.

Figure 2  Intramedullary nailing of both humeri.

Figure 3  Cut-out of the intramedullary nail at the anteromedial aspect of the left tibia.

Figure 4  Telescopic intramedullary nails in the (a) right and (b) left ulnas.
This failed to centralise the nail at the non-union site, so a synthetic bone graft was used and the overall alignment improved (Fig. 5).

In January 2007, she complained of pain in her distal right tibia caused by anterior pseudo-fractures (Fig. 6a). She underwent a closing wedge osteotomy in the mid-shaft followed by intramedullary nailing (Fig. 6b). Anatomic alignment was restored and she was able to walk independently using a frame.

DISCUSSION

Only about 300 families have been reported to have hypophosphatasia worldwide. The incidence is estimated at approximately 1 in 100 000 live births. Most cases are from Canada. The incidence among the Mennonites of the state of Manitoba is 1 in 2500 births and up to 1 in 25 Mennonites is a carrier. There is gender predilection. The disease is caused by mutations in the alkaline phosphatase gene located on chromosome 1; both autosomal recessive and autosomal dominant variants exist. The disease manifests in one of 5 forms: perinatal, infantile, childhood, adult, and odontohypophosphatasia. Perinatal hypophosphatasia is invariably lethal whereas infantile hypophosphatasia has a 50% mortality rate with symptoms appearing within the first 6 months of life. The other forms are generally non-lethal. Common symptoms include bone malformations and pathological fractures. Both the adult and odontohypophosphatasial forms are marked by premature tooth loss. The adult form of hypophosphatasia is particularly rare. It is characterised by premature tooth loss, recurrent and multiple long bone fractures and pseudo-fractures.

The diagnostic criteria for hypophosphatasia are a very low tissue alkaline phosphatase and a high urinary phosphoethanolamine and a high inorganic pyrophosphate in both blood and urine and a high pyridoxal 5’-phosphate (a form of vitamin B6) in blood. It can be diagnosed prenatally by finding a high phosphoethanolamine in amniotic fluid and a low alkaline phosphatase in a placental biopsy, and by deoxyribonucleic acid analysis or ultrasonography (an unmineralised skeleton) in the early second trimester.

The diagnosis of familial hypophosphatasia should not be confused with familial hypophosphataemia, which is a form of rickets due to impaired proximal tubular re-absorption of phosphate in the kidney. Although both their clinical (e.g. short limbs, swollen knees and ankles) and radiological (e.g. osteopaenia, bowed long bones, and pseudo-fractures) features are similar, the biochemical parameters are different as the serum alkaline phosphatase level is low and the calcium level is high or normal in hypophosphatasia.
whereas in familial hypophosphataemia it is the reverse. Therefore, treatment for rickets, including calcium and vitamin D supplementation, may in fact be harmful in hypophosphatasia.

No effective medical therapy is currently available. Results of various treatments including zinc and magnesium are inconsistent. The effects of bone marrow transplantation are transient, and bone lesions may recur 6 months after the transplant. Enzyme replacement therapy using partially purified plasma enzyme achieves little clinical improvement.

Asymptomatic pseudofractures are easily missed because they are often masked by multiple bone pain or other acute fractures. Internal fixation is recommended for all pseudofractures even if asymptomatic. Pseudofractures may progress to complete fractures even after conservative treatments (with casts, braces or protected weight bearing). Prophylactic intervention should be performed before any progression. In our patient, the non-union with deformity in her left tibia might have been prevented if the fracture was managed initially with internal fixation instead of casting.

Intramedullary nails are preferred because of their load-sharing properties. Nails can span the whole length of long bones and avoid stress risers. Stress risers are inevitable at the ends and screw holes of plate fixation, and may lead to stress fractures. In our patient, a stress fracture developed at the left proximal ulna after plating. In the right ulna, plating was revised to intramedullary nailing as a prophylactic measure. Although conventional plating is the mainstay of treatment in forearm fractures because it facilitates better anatomic reduction and function, intramedullary nailing is a better choice for avoiding stress fractures after plating, despite not being widely available. Osteotomy and bone grafting may be necessary to facilitate nail insertion and prevent subsequent failure caused by delayed union, non-union or bone deformity.

Multi-disciplinary management of patients with hypophosphatasia should involve dentists, dieticians, occupational therapists, physiotherapists, psychologists, and social workers. Family screening, genetic counselling, and prenatal diagnosis are also essential.

REFERENCES