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Surgical management for tibial shaft fractures using flexible nailing in adult hypophosphatasia

Jay N. Patel, Priyal V. Bhagat, Li Sun, Juluru Rao

ABSTRACT

Introduction: Adult hypophosphatasia (HPP) is a rare inheritable metabolic disease affecting primarily the skeletal system resulting in decreased mineralization of bone. Hypophosphatasia has a variable inheritance pattern with the more severe form inherited as autosomal recessive. The diagnosis is based on decreased serum alkaline phosphatase (ALP) and an increased urinary phosphorylethanolamine (PEA). Patients with HPP suffer from multiple fractures, have limited mobility, rely on the use of assistive devices, and have a diminished quality of life. Case Report: A 47-year-old female was presented with a pathologic tibial shaft fracture that was treated with a flexible nail. Conclusion: Currently, there are no definitive treatment guidelines for fracture care in adults with HPP. Load sharing devices have been recommended due to their load-sharing properties and the osteoporotic bone quality in affected patients.

Keywords: Adult hypophosphatasia, Flexible nailing, Metabolic syndrome, Tibial shaft fracture, Trauma

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INTRODUCTION

Adult hypophosphatasia (HPP) is a rare inheritable metabolic disease affecting primarily the skeletal system. Hypophosphatasia caused by defective production of alkaline phosphatase (ALP) [1]. Alkaline phosphatase is a crucial enzyme in the mineralization process of the skeleton and can be found in chondrocytes, cartilage matrix, and teeth. It is essential in the catabolism of inorganic pyrophosphate (PPi) and other molecules. Decreased production of ALP leads to the endogenous accumulation and toxicity of PPi. The PPi accumulation causes defective skeletal mineralization manifesting as osteomalacia and development of articular chondrocalcinosis in affected adults [2, 3].

Hypophosphatasia affects males and females equally. It has a variable distribution worldwide with an increased frequency in Canada, with a prevalence estimated to be 1:100000 [4]. Mornet et al. [4] have proposed a genetic model concluding the prevalence of dominant mild HPP in the European population is about 1/6370 [5]. The ALP gene is located on the short-arm of chromosome 1. Hypophosphatasia can be inherited in an autosomal dominant or recessive pattern [6]. The severity of disease is correlated with the pattern of inheritance and is dependent on the large number of missense mutations.

Milder forms that reduce but do not completely suppress ALP activity can be inherited as either autosomal dominant or recessive [7, 8]. More severe forms of HPP are transmitted as autosomal recessive traits that suppress ALP activity almost completely.

Diagnosis is based on serum alkaline phosphatase assay of the liver/bone/kidney alkaline phosphatase gene [9]. In HPP patients >20 years old, ALP levels below 40 U/L is suspicious for HPP [10, 11]. The presence of phosphorylethanolamine (PEA) in the urine can also be used in diagnosing HPP [12]. The amount of urinary PEA excreted daily has been used to identify heterozygous carriers of the HPP trait. Though these patients excrete only 10–20% of the amount of PEA as their homozygotes counterparts, these levels are still three to five times higher than the normal population [13].

Hypophosphatasia is characterized by a variety of signs and symptoms. Individuals may present with a history of rickets during childhood or premature loss of their baby teeth. Patients may also present with chondrocalcinosis, pseudogout, joint inflammation, chronic bone pain, and other dental abnormalities [14, 15]. Frequently, affected individuals experience multiple fractures from low energy mechanisms, which in otherwise healthy individuals would not result in any injury. Most commonly, patients present with fractures of the femur and feet [16]. Decreased bony healing due to the PPi toxicity may lead to pseudofractures and bowing of the long bones [15].

CASE REPORT

A 47-year-old female presented to our institution after a mechanical fall trying to get onto her motorized scooter. The patient twisted her ankle and felt a sharp pain in the anterior aspect of her lower leg. Past medical history of the patient was significant for hypophosphatasia with multiple bilateral tibial shaft fractures treated conservatively. Patient was a non-ambulator who relied on the use of a motorized scooter to get around. At the time, the patient was not on any medical treatment regimen for her hypophosphatasia. On physical examination the patient was noted to have procurvatum and valgus deformities of both of her legs. X-ray of the patient showed a transverse fracture of the left distal third tibia and fibula with sclerotic fracture ends (Figure 1). Patient also had an ALP value of <20.0 IU on admission.

A stab incision was made on the lateral aspect of the proximal tibia, just below the tibial plateau. A drill bit was used to create an entry hole in the tibia. A 4 mm flexible nail was passed down the tibia to the fracture site. At the fracture site we encountered sclerotic fracture ends from the multiple previous fractures. This made it difficult to pass the 4 mm flexible nail down the tibial shaft. A mallet was used to tap the wire through the sclerotic ends, into the distal tibial shaft. A similar entry hole was made on the medial side of the tibia. A second 4 mm wire was too large to fit into the canal so smaller caliber flexible nails were attempted to be passed down the tibial canal. Due to the smaller size of the nails, they kept bending when we attempted to mallet them down the tibial shaft past the sclerotic fracture ends. The fracture site was not opened to clean out the sclerotic fracture ends because we did not want to disturb the blood supply around the fracture site with soft tissue and periosteal stripping. The fracture was found to be stable with a single 4 mm nail when stress was applied to the fracture site. The contralateral side was also found to be stable under fluoroscopic stress testing.

At first year follow-up, X-rays showed callus formation (Figure 2). The patient reported no pain at the fracture site. The patient was now able to bear weight on the operative leg and able to ambulate around her home using an assistive device. Previously, she was dependent on a motorized scooter and unable to walk even short distances. The patient reported no pain in her operative leg. It should be noted that recently, our patient has started enzyme replacement therapy with asfotase alfa to treat her HPP.

DISCUSSION

Weber et al. [17] investigated the patient-reported burden of disease and quality of life using two surveys in patients with HPP. Eighty-six percent of their patients had sustained at least one fracture and nearly 50% reported more than six fractures. At the time of their survey, 34% of patients reported currently using an assistive device to walk and 22% reported the use of a wheelchair. It is important to note that 69% of patients reported that their walking had worsened since their HPP diagnosis and that no patients reported improvement in walking. Furthermore, 32% of patients reported that they had to modify their homes due to HPP-related physical limitations. The burden of disease is high in adults with HPP, necessitating finding not only pharmacological

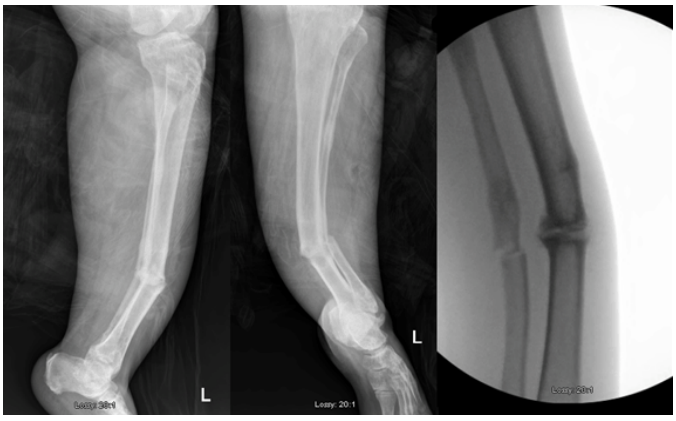

Figure 1: Preoperative and intraoperative radiographs demonstrating transverse tibial and fibular shaft fractures. Patient has procurvatum and valgus deformities of her tibia and fibula. Note the sclerotic fractures ends from multiple previous fractures in the same area.

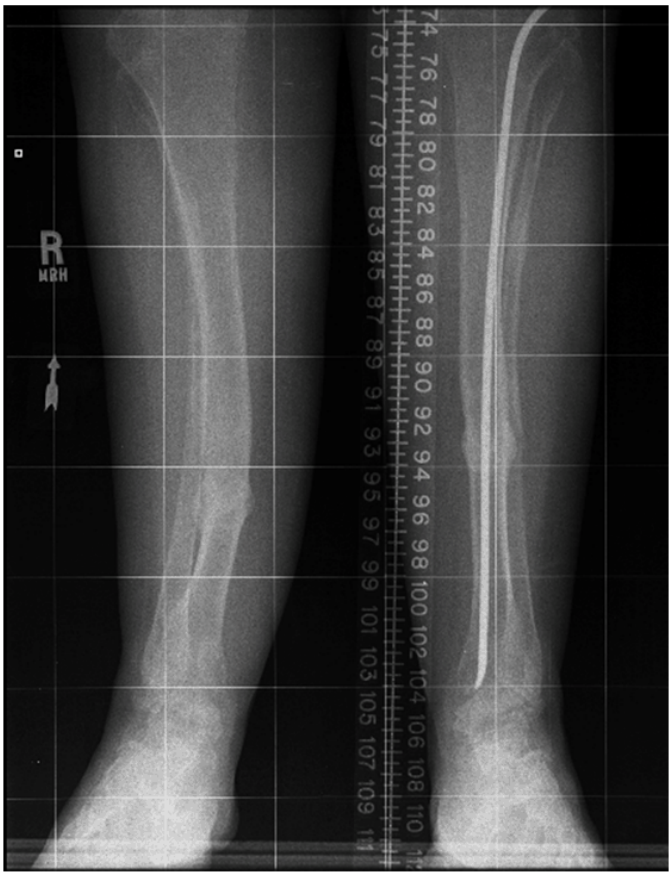

Figure 2: Radiograph at first year demonstrating healing of the tibial shaft fracture as well as correction of the patient's valgus deformity.

treatments but also surgical fixation strategies to help improve the quality of life in these patients. Currently, new pharmacologic treatment includes using enzyme replacement therapy with asfotase alfa to help replace ALP. Recent literature shows asfotase alfa to be effective in treating, decreasing the burden of disease, and improving overall survival of HPP patients [18, 19].

There is a paucity of literature on surgically treating fractures in adults with HPP. Treatment of these patients should be tailored to their preinjury level of functionality and ambulation. Due to our patient's preinjury ambulation status and wishes, we did not perform an osteotomy to properly correct the patient's procurvatum and valgus deformities. We felt the patient would benefit from stabilization using flexible nails and any correction we were able to achieve using manual traction, being prudent not to cause any iatrogenic fractures due to the bone quality.

In their series of femoral fractures and pseudofractures in HPP patients, Coe et al. [20] concluded that non-operative management cannot be relied upon to adequately relieve pain or to heal fractures/pseudofractures due to the underlying problems in skeletal mineralization. They recommended treatment with load-sharing devices. The decreased stress shielding properties of load sharing devices helps promote remodeling in patients with osteoporotic bone compared to load bearing devices. Flexible nails have been used since the 1930s in the treatment of fractures. Flexible nails work by providing multiple points of contact, depending on the number and their configuration, along the inner aspect of the cortex. The original flexible nails were stiffer and made out of stainless steel [21, 22]. Modern day flexible nails are made out of titanium, which has been shown in biomechanical studies to provide better rotational, and axial compression stiffness than their stainless steel counterparts [23].

DeLong et al. [24] had success with treating long bone fractures in adults with flexible, stainless steel nails. In their series, 41 out of 49 tibial shaft fractures healed within five months. The majority of these fractures was due to high-energy mechanisms and included open fractures. With the advent of modern day intramedullary nails, the use of the flexible nails for the treatment of long bone in fractures in adults has decreased. However, they still continue to be a good method of fixation in adults with length stable fracture patterns due to their cost and shorter surgical times [25–29]. Flexible nails may be a viable treatment option in adults with length stable, pathologic fractures in osteoporotic bone.

CONCLUSION

Overall, the burden of disease is high in adults with hypophosphatasia (HPP), resulting in limited mobility, use of assistive devices, and diminished quality of life. Loading sharing devices promote bone healing and callus formation and have decreased stress-shielding properties. Flexible nails can be a viable treatment option in adults with poor bone quality with length stable, pathologic fractures. Further long-term studies are needed on adult patients with HPP to make more definitive surgical treatment recommendations.

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Author Contributions

Jay N. Patel – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Priyal V. Bhagat – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Li Sun – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Juluru Rao – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Consent Statement

Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest

Authors declare no conflict of interest.

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