ABSTRACT X-Linked Hypophosphataemia is an X-linked dominant disorder caused by the phosphate-regulating neutral endopeptidase gene sequence mutation. The classical presentations are short stature and dental abscesses, with radiographic evidence of rickets and osteomalacia. It is also strongly associated with X-linked familial history. We described a case of a middle-aged woman who presented with a femur fracture. Physical examination shows that the patient is overweight, short stature, with bowing of legs. Trident fingers, frontal bossing depressed nasal bridge and maxillary hypoplasia were not present. She underwent dynamic locking of the intramedullary nail of the right femur. The patient recovered well and had no postoperative complications.

KEYWORDS XLH, Fracture, Dynamic locking intramedullary nail

Highlights
This case report highlights the lack of suitable implants for patients that present with a fracture and an underlying skeletal deformity. We discuss the biomechanical challenges and how routine procedures do not apply to these patients.

Summary
This case uniquely presents with a simple transverse fracture but was further complicated by an underlying disease which skewed the usual tangent of care to a more complicated one. XLH, in our case, has complicated the routine operation, post-operative care and recovery. Clinically this case was a challenge to manage with an interlocking nail. The clinical decision and dilemma made this case interesting to manage. Literature on using dynamic locking for XLH is scarce. Some literature performed on XLH patients suggests favourable results in similar cases [10].

Introduction
The diagnosis of skeletal dysplasias can often be confusing to clinicians. These conditions are usually made when the patient is young [1, 2]. In adults, these conditions are sometimes difficult to diagnose, and the sequelae of the misdiagnosis or delayed diagnosis may continue to add barriers to the management of the patient [2]. X-linked hypophosphatemia (XLH) can be easily mistaken as the disease pattern shows similar features in autosomal dominant hypophosphatemic rickets (ADHR) and achondroplasia [1, 2, 3]. Presentations such as short stature and genu valgum are common presentations among the 3. Similar presentation such as renal inorganic phosphate wasting is shared between XLH and ADHR. Complications from skeletal dysplasias may occur. Thus, the clinical dilemma to understand the underlying cause of a complication is crucial [2]. XLH is the most common type of hereditary rickets, with the prevalence of 1 in 20,000 live births worldwide. However, the prevalence is still generally unknown in Malaysia [4, 8]. This, therefore, adds to the difficulty in the management of XLH in Malaysia from its rarity. We described a middle-aged woman who experienced a transverse midshaft fracture of the femur with an underlying condition of XLH. The management of such fracture and outcomes of the surgery was discussed.
Case

A 45-year-old Indian lady fell on her right hip in the bathroom. She presented with a localised sharp pain on her right thigh that does not radiate. The patient was unable to bear weight with a pain scale of 8/10. She had a medical history of hypertension and childhood rickets. Since the age of 10, she underwent surgical intervention to correct her bowing deformity with plates and screws on both femurs. After a few years, the right-sided implant was taken out. Upon further history taking, her family showed extensive hereditary rickets. Nine of her family members, including direct and indirect family members, are affected by familial rickets. The family pedigree shows that her familial rickets is X-linked dominant (Figure 1). Figure 2 shows one of her daughters who came and visited the patient. The physical examination of her daughter showed similar traits to the patient with genu valgum and of short stature. Otherwise, the rest of her history was not significant.

Figure 1 Pedigree of affected family members shows strong X linked involvement from the patient's generation of sisters only and then passing down to the third generation to both genders

Figure 2 Daughter of the patient presents with short stature and obvious genu valgum. Consent obtained from daughter

On physical examination, our patient was overweight, short in stature with genu varum. She had no frontal bossing, depressed nasal bridge, trident fingers or maxillary hypoplasia. Other findings were unremarkable, and her vitals were stable. However, she could not move her right leg due to pain, and there was swelling and deformity over her right thigh. Her preoperative blood investigations were normal. Her plasma alkaline phosphatase was 142 U/L (44-147 U/L), and plasma calcium was 2.25 mmol/L (2.12-2.52 mmol/L). X-ray of the right femur showed bowing deformity, closed, transverse mid-shaft fracture, posteriorly displaced, and with no angulation according to her femur axis (Figure 3).

Figure 3 Midshaft fracture of right femur with minimal angulation according to the patient femur axis

Differential Diagnosis

ADHR presents similarly to XLH as it has very similar pathogenesis of phosphate wasting by the kidneys. Achondroplasia was also suspected in this patient, but it is unlikely from most of the absent physical signs. Given the extensive X-linked nature from the pedigree, XLH was diagnosed as the underlying condition with a primary condition of a closed transverse midshaft fracture of the right femur.

Treatment and Outcome

Interlocking nail fixation was done on the right femur. However, the proximal screws were not placed because of the bowing of the femur (Figure 4). The patient was not treated with phosphates or calcium supplements. Although an interlocking nail was done, the patient was kept on traction. Weightbearing was not recommended with only the distal screws for the interlocking nail. The patient was kept on skin traction for 2 weeks and was sent home in a wheelchair. Postoperative recovery was uneventful. One year later, there was callous formation seen around her fracture site (Figure 5).

Discussion

Endochondral osteogenesis is the formation of new bone tissue in an attempt to unite the fracture site by secondary healing [5]. The bone-forming cells osteoblasts form hard crystal hydroxypatite, namely calcium phosphate crystals. The hydroxypatite then undergoes mineralization which turns into structurally stable skeletal bone. For mineralization to happen, adequate calcium and phosphates ions are crucial in the process [5]. XLH is a mutation of the phosphate-regulating neutral endopeptidase
bone contact is unequally distributed with high force on the medial aspect of the fracture. This led to a clinical decision to keep the patient warded with skin traction. This helps to relieve pain and to reduce unequally distributed bone contact. Callus formation was seen after 1 year of follow-up, which showed a good sign of recovery for the patient. The callus formed had vague contours with turbulent structures (Figure 5). This was not surprising as it was previously described in the dynamic locking of intramedullary nails [6]. Although phosphate and calcitriol supplements were recommended in the literature, our patient was not given supplements. This was because her follow up phosphates and calcium ions were within normal range.

Strengths and Limitations to this case

We found that our patients with XLH can form new bone tissue regardless of its pathogenesis. Normal calcium and phosphate levels may have contributed to an uneventful recovery. However, we were limited by the lack of proper guidelines in fracture management in XLH. More studies are needed to produce guidelines for the fracture management of XLH.

Conclusion

XLH is rare in Malaysia. However, this case highlights the importance of taking a detailed history and physical examination to investigate the type of skeletal dysplasias. Understanding the underlying co-morbidities can allow better clinical treatment decisions and improve overall patient outcomes. Dynamic locking of femoral intramedullary nails can promote callus formation in patients with XLH. More implant designs are needed to cater to these patient groups at risk of fractures.

Take-away lessons

1. Dynamic locking intramedullary nails are feasible for patients who experience uncomplicated fractures with an underlying XLH. However, it may not recover as fast as a normal adult would.

2. The callous formation was possible in our patients with XLH. However, they provided that their calcium and phosphate levels were normal.

3. A shorter interlocking nail could have been a better choice for locking the proximal nail in place instead of a dynamic lock.

Abbreviations

X-Linked Hypophosphataemia - XLH
Autosomal dominant hypophosphataemic rickets - ADHR
Patient informed consent
The patient has pre-signed informed declarative consent for examination and treatment. The photo of the patient’s child has also been signed by the parent accompanying the child.

Conflict of interest
There is no conflict of interest to declare by any of the authors of this study.

Funding
This work did not receive any grants from funding agencies from the public, commercial, or not-for-profit organizations.

Author’s contribution
All authors have equally conceptualized the study, acquired data for this study, drafted the manuscript and approved the reviewed final manuscript before submitting this case report.

Acknowledgements
We want to acknowledge Dr Surinder Singh from the Orthopaedics department for his invaluable consult on this case on the patient’s disease presentation and management plan.

References
1. Linda SN, Mahajan P, Joshi A, Kamat D. Rickets: Not a disease of the past. Am Fam Physician 2006; 74 (4): 619-626.

2. Carpenter TO, Imel EA, Holm IA, Beur SMJ, Insogna KL. A clinician’s guide to X-linked hypophosphatemia. J Bone Miner Res 2011; 26 (7): 1381–1388.

3. Gummadapu S, Nuthlapati P, Meka PVP, Lakshmi CR, Bhavana SM, Thabusum DA. Hypophosphatemic Rickets in Siblings. Case Reports in Dentistry 2016; 2016: 1-8.

4. Pereira CM, Andrade CR, Vargas PA, Coletta RD, Almeida OP, Lopes MA. Dental alteration associated with X-linked hypophosphatemic rickets. J Endod 2004; 30 (4): 241-245.

5. Bonjour JP. Calcium and phosphate: a duet of ions playing for bone health. J Am Coll Nutr 2011; 30 (5): 438-448.

6. Omerovic D, Lazovic F, Hadzimehmedagic A. Static or Dynamic Intramedullary nailing of femur and tibia. Med Arch 2015; 69(2): 110–113.

7. Skrinar A, Dvorak-Ewell M, Evins A, Macica C, Linglart A, Imel EA, et al. The lifelong impact of X-linked Hypophosphatemia: Results from a burden of disease survey. Journal of the Endocrine Society 2019; 3(7): 1321-1334.

8. Radlovc V, Smoljanic Z, Radlovc N, Lekovic Z, Ristic D, Ducic S, et al. X-Linked Hypophosphatemic Rickets: Case Report. Srp Arh Celok Lek 2014; 142(1-2): 75-78.

9. Robinson ME, AlQuorain H, Murshed M, Rauch F. Mineralized tissues in hypophosphatemic rickets. Pediatr Nephrol 2020; 35(10): 1843-1854.

10. Kocaoglu M, Bilen FE, Sen C, Eralp L and Balci HI. Combined technique for the correction of lower limb deformities resulting from metabolic bone disease. Bone Joint J 2011; 93(1): 52-56.