Case Report

A Rare Case of Osteogenesis Imperfecta Type V

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Abstract

Osteogenesis imperfecta (OI) is a hereditary bone condition characterised by fragile bones to be more susceptible to fracture. We reported a rare case of a 6-year-old girl with OI Type V and hyperplastic callus formation. She presented with recurrent fractures since birth with no family history of a similar condition. Clinically, her height and weight were lower than the 5th percentile for her age. She had deformities with limitation of movement of elbows, kyphoscoliosis, a more extensive right thigh, and anterior bowing of both legs. Radiographic examination revealed interosseous membrane of forearm ossification, dislocation of the right radial head and hyper-callosity of both femurs during fracture healing. She was treated with intravenous pamidronate and had posterior instrumentation and fusion for scoliosis and intramedullary rodding for her femur fracture. On a recent follow-up at the age of 16 years, she was ambulating well with no progression of the spinal deformity.

Keywords: Hyper-callosity; interosseous membrane ossification; kyphoscoliosis; osteogenesis imperfect; recurrent fractures

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Introduction

Osteogenesis imperfecta (OI) was classified by Sillence et al. (1979) into four main clinical phenotypes: mild (type-I), intermediate (type-IV), and severe (type-III) disease (1). The type II disease is lethal perinatally. A dominant mutation of COL1A1 or COL1A2 genes result in abnormal collagen type 1 in about 90% of individuals diagnosed with OI (2). The expanded Sillence classification includes other newly discovered OI, such as V to IX (2). The diagnosis of severe or lethal OI can typically be made through prenatal ultrasound and then confirmed with magnetic resonance imaging (MRI), computed tomography (CT) and genetic tests (3).

OI type V was first described by Glorieux et al. (2000) and this condition is inherited in an autosomal dominant pattern (4). Approximately 4% to 5% of individuals diagnosed with OI are affected with OI type V (5). About 65% of individuals with OI type V may develop hyperplastic callus after surgery or fractures in long bones, which is the pathognomonic feature (5). Other features include the absence of blue sclera, dentinogenesis imperfecta, calcification of interosseous membranes of lower leg and forearm, radial head dislocation, sub-physeal metaphyseal radiodense line, abnormal histopathological pattern, and lack of mutation in COL1A1 and COL1A2 gene (2,4,5). It has been reported that heterozygous mutation of c.−14C>T of the 5'-untranslated region (5'-UTR) for a gene that encodes for interferon-induced transmembrane protein 5 (IFITM5) causes OI type V (2,6,7).

This case report highlighted a child with OI type V, which was rare in Malaysia. We have treated this child from the age of six years, and she is still on regular follow-up at skeletal maturity.

Case Report

A 6-year-old girl presented with a history of recurrent fractures since birth. She had a bilateral clavicle and right humerus fracture during delivery. She subsequently developed fractures of the left humerus, femurs, L3 compression fracture, right tibia, right radius and ulna. Her parents were non-consanguineous, and she had no family history of frequent fractures. She had no hearing or eye defects.
Her height and weight were lower than the 5th percentile for her age. Her sclera and teeth were normal. She had pectus carinatum and a right thoracic kyphoscoliosis. The kyphoscoliosis developed from the age of three years and progressively worsened, resulting in restrictive lung disease (Fig. 1). There was no associated neurological deficit. Her right radial head was dislocated with elbow flexion limited to 90° and limited forearm rotation (Fig. 2a). Her left elbow flexion was limited to 45°, and both legs were bowed anteriorly. The radiograph showed ossification of the interosseous membrane of the right radius and ulna (Fig 2b).

FIGURE 1: Clinical picture showed right thoracic kyphoscoliosis

She had intramedullary rod insertion after a right femur fracture at the age of seven years. Hyperplastic callus developed after intramedullary rodding of the femur fracture (Fig. 2c). She was given intravenous pamidronate treatment at the age of six years. Despite being treated with pamidronate, she still sustained a fracture yearly. Her biochemical profile was within normal range. Due to the worsening spinal deformity (Fig. 3a), she underwent posterior instrumentation and fusion of the spine at the age of 11 years. She can ambulate without walking aids and attends school. The latest follow-up at the age of 16 years shows no progression of the spinal deformity (Fig. 3b).

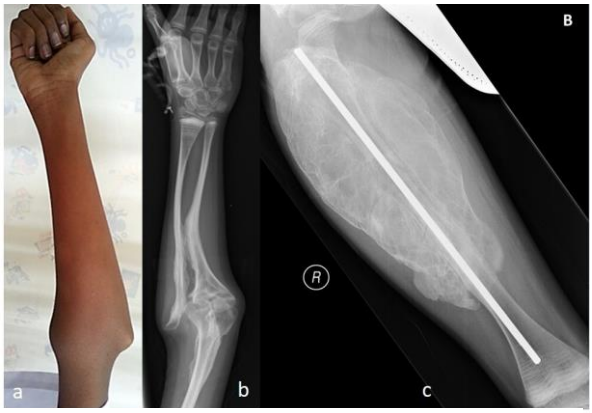

FIGURE 2: Clinical picture (a) and radiograph of right elbow (b) showed the dislocated radial head and calcification of the interosseous membrane. Hypercallosity after intramedullary rodding of the right femur fracture (c). Adapted from Joseph 2015

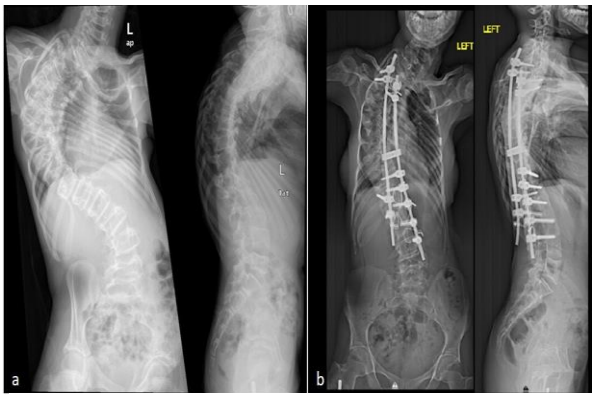

FIGURE 3: Radiograph of spine before surgery (a) and at the age of 16 years old showed no progression of the deformity five years after posterior instrumentation and fusion (b)

Discussion

OI is a hereditary bone disorder with an increased fracture risk secondary to reduced collagen and abnormal type 1 collagen production. Individuals with OI exhibit varying degrees of deformities, short stature, ligamentous laxity and spinal deformities, including scoliosis and kyphosis.

Hyperplastic callus is a remarkable feature of OI type V and usually manifests as a painful, warm, and hard swelling that can be misdiagnosed as inflammation or sarcoma. The size of the callus may remain unchanged for many years after rapid growth (4). Qualitative histological examination of iliac biopsy specimens in individuals with OI type V showed that lamellae were irregularly arranged or had a meshlike appearance (4).

This patient was diagnosed with OI type V based on her typical clinical and radiographic features as well as the pattern of gene mutation. A genotype-phenotype study revealed that our patient has c.-14C>T mutation of interferon-induced transmembrane protein 5 (IFITM5) (7). This finding is consistent with other studies by Semler et al. (2012) and Cho et al. (2012), which reported that heterozygous mutation of c.−14C>T in the 5'-untranslated region (5'-UTR) of a gene that encodes the IFITM5 which then causes OI Type V (2). The IFITM5 plays a vital role in osteoblast formation-recurrent mutation in IFITM5 results in abnormal cortical and trabecular bone formation, leading to fragile bone and osteopenia.

Histomorphometric and biochemical studies of bone in OI revealed increased osteoclastic activity and reduced new bone formation (8). Bisphosphonate inhibits bone resorption, reduces bone turnover, and has a role in treating OI. Improvement of bone mineral density, decrease of fracture rates, reduction of chronic pain and fatigue, enhanced mobility and ambulation have been described following to treatment with bisphosphonate (9).

Glorieux et al. (1998) showed that pamidronate therapy in OI individuals reduced bone resorption, as evidenced by reduced excretion of calcium and type I collagen N-telopeptide in urine and serum alkaline phosphatase concentrations (8). The administration of cyclical intravenous pamidronate in OI type V patients was reported to be successful in remitting symptoms, improving bone mineral density, and reducing fracture rates (10). The patient had an improved energy level, better well-being, and a marked reduction in pain. Based on remarkable health improvement in the subject of their study, the authors recommended bisphosphonate therapy in the overall treatment of OI type V patients (10).

Surgical intervention with intramedullary rodding is indicated in children with severe bowing and recurrent fractures. The surgery will improve function and ability to walk and stand, reducing pain and fracture incidence (11). The intramedullary rod is preferred because it facilitates early protected ambulation and rehabilitation of children.

Conclusion

The case report highlighted a rare OI with specific clinical features. By identifying this patient group will help us for better understanding and management of the affected patients.

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