

Osteogenesis Imperfecta with pathological fracture shaft of femur: A case report

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Abstract: Osteogenesis imperfecta is a genetic disorder of connective tissue origin with the trademark clinical feature of bone fragility as evidenced by long-bone fractures. Other major clinical features may include skeletal deformity, blue sclerae, hearing loss and fragile, opalescent teeth. We are presenting here a case of a 6 years old boy presented with type III Osteogenesis Imperfecta with clinical features of large skull and wormian bones; pinched-lookin face, grey Sclerae, dentinogenesis imperfect, respiratory problem with old healed fracture in left proximal femur. Patient presented with acute history of pain right thigh which on radiography showed pathological fracture of proximal femur. Fracture reduced under sedation and kept in skin traction for 3 weeks and following that hip spica applied. Spica removed after 6 weeks. Pamidronate intravenous injection (single dose) was given as supportive treatment with calcitriol, calcium, vitamin C and vitamin D.

Conclusion: Osteogenesis Imperfecta type III is classical, but not the most common form of it, presents with multiple fractures since birth. It is sporadic or autosomal recessive in inheritance. Usually patient has poor quality of life, with few surviving to adulthood.

Key words: calcitriol, hip spica, Osteogenesis Imperfecta type III, pathological fracture, pamidronate.

I. Introduction

Osteogenesis Imperfecta is a genetic disorder of connective tissue with the trademark clinical feature of bone fragility as evidenced by long-bone fractures. Other major clinical features may include skeletal deformity, blue sclerae, hearing loss and fragility of bone leading to pathological fracture, opalescent teeth (dentinogenesis imperfecta(1). The so-called diagnostic triad of blue sclerae, dentinogenesis imperfecta and generalized osteoporosis in a patient with multiple fractures or bowing of the long bones usually is used clinically (2). It is now known that at least 90% of affected individuals have a defect in type I collagen formation. The disorder may be an autosomal dominant or may occur as a spontaneous mutation, or rarely, may be inherited as a homozygous autosomal recessive trait from both parents with an estimated incidence of 1 in 20 000(1). According to Silience (1981) it has 4 groups. Osteogenesis imperfecta type I is characterized by generalize osteoporosis with abnormal bony fragility, distinct blue sclerae throughout life and presenile conductive hearing loss. This is the most common type of osteogenesis imperfect. Type II Osteogenesis imperfecta is characterized by extreme bone fragility leading to death in the perinatal period or early infancy. The long bones are crumbled and ossification of the skull is markedly delayed. Osteogenesis imperfecta type III is characterized by qualitative and quantitative changes in type I collagen and may be inherited as an autosomal recessive or dominant negative trait. It is characterized by severe bone fragility, multiple fractures and progressive marked deformity of the long bones, and severe growth retardation. The sclerae are bluish at birth but become less blue with age. Osteogenesis imperfecta type IV is inherited as an autosomal dominant condition, and most patients have qualitative and quantitative changes in type I collagen. At birth the sclerae are of normal hue; if they are bluish, they become progressively less so with maturation and are normal in adolescence. The osteoporosis, bone fragility, and long-bone deformities are of variable severity (3). Healing of fractures and osteotomies usually is satisfactory in Osteogenesis imperfecta, although the healed bone may be no stronger than the original (2).

II. Case report:

We present a case of 6 year old boy presented to our Orthopaedics OPD with chief complaints of pain right thigh following a trivial fall 1 week back. Pain initially was mild in intensity but became severe with time, so as to limit his normal activities even to the extent of preventing him from standing up. Patient had a history of similar disease of the right leg about 3 years back, which was treated by applying plaster of paris. The patient often used to complain of pain in the limbs after walking for some distance. There was no such history in any relatives. He was delivered by normal vaginal delivery with no complications. The patient had achieved normal developmental milestones but following first 3 years of life had growth retardation in terms of gaining weight and height. On examination his height was 2.5 feet and weight was 7 kg indicating growth retardation. On systemic examination he had pallor and crepitus, in both lung fields. On local examination he had swelling and

tenderness right middle thigh with bowing of both legs and left thigh. Radiography revealed fracture shaft of right femur, upper third with old healed fracture of left femur and bowing of both tibia and fibula (Fig.1). He had opalescent teeth (Fig.5) and the teeth were fragile with caries, wearing down and fractured. There were 2 bluish grey patches on right sclera and one same patch on left sclera (Fig.6). Patient was diagnosed as a case of Osteogenesis imperfect type III on clinical and radiological finding and history of multiple previous fractures. Serum calcium and phosphorus levels were normal. Initially limb kept in Thomas splint (Fig. 2). The alkaline phosphatase level was elevated. Routine investigations were done. Bone mineral density done by DEXA scan showed osteoporosis. Patient was given single dose of intravenous pamidronate (7mg/kg) slowly after proper hydration. Calcitonin, calcium and vitamin C and vitamin D were given in oral formulations. Fracture was reduced under sedation with IITV guidance and skin traction with thomas splint applied. Traction kept for 3 weeks. After 3 weeks alignment of the fracture confirmed by radiography(Fig.3, Fig.4) hip spica applied(Fig.8). Patient discharged with medication and followed up in OPD every 2 weeks with serial radiographic monitoring. Spica was removed after 6 weeks. Follow-up bone mineral density test done, showing improvement in mineral density (Fig.7). After 6 months intravenous pamidronate repeated with supportive calcium, calcitonin and vitamin C and D. Parents were advised to take proper care of the patient to avoid fractures. Parents advised to attend OPD in regular interval.

III. Discussion:

Osteogenesis imperfect type III though classical but it is a rare form of Osteogenesis imperfecta. This variety of Osteogenesis imperfecta is also characterized by qualitative and quantitative changes in type I collagen and may be inherited as an autosomal recessive or dominant negative inheritance. It is characterized by severe bone fragility, multiple fractures and progressive marked deformity of the long bones and severe growth retardation. The sclerae are bluish at birth but become less blue with age. The most severely affected surviving patients often have this type of disease (3). The exact incidence of the various types of Osteogenesis imperfecta is uncertain. At present, the exact incidence of type III is unknown, but less common than type I in most clinical series. In Cole's review of the genetic defect and type I collagen anomaly in 200 patients, 28 patients had type IA (2 had type IB and 1 had IC), 49 had perinatally lethal type II (Cole subdivided this group into three types), 41 had type III, and 79 had type IV (3). The fundamental defect in Osteogenesis imperfecta is an absolute reduction in the amount of normal type I collagen in bone or its replacement with a poorly functioning mutant collagen (usually also reduced in quantity). That defect is manifested histologically in many ways. The formation of both enchondral and intramembranous bone is disturbed (3). In the severe congenital form (Sillence's type II), multiple fractures from minimal trauma during delivery or in utero cause the limbs to be deformed and short. This type is usually fatal, with death secondary to intracranial hemorrhage or respiratory insufficiency caused by incompetency of the rib cage; the infant is stillborn or lives only a short time. In the nonlethal forms of the disease (Sillence's types I, III, and IV), fragility of the bones is the most outstanding feature. In severely affected patients, fractures can occur after the slightest injury. The femur is more commonly fractured than the tibia. A pattern of repeated fractures can develop as the result of a combination of disuse osteopenia, progressive long-bone deformity. Growth may be arrested by multiple microfractures at the epiphyseal ends. Bowing results from multiple transverse fractures of the long bones and muscle contraction across the weakened diaphysis. Typically, an anterolateral bow or proximal varus deformity of the femur develops; an anterior or anteromedial bow of the tibia may develop. Severe spinal deformity may develop because of the combination of marked osteoporosis, compression fractures of the vertebrae, and ligamentous hyperlaxity. Hyperlaxity of ligaments with resultant hypermobility of Osteogenesis Imperfectants is common. The muscles are hypotonic, most likely because of the multiple fractures and deformities. The skin is thin and translucent, and subcutaneous hemorrhages may occur. Sclera in type III may be gray-blue at birth but become less blue with increasing age and are white in adulthood. The teeth are affected in patients with types IB and IVB disease, sometimes in type III patients. Both deciduous and permanent teeth are involved. They break easily and are prone to caries, and fillings do not hold well. Yellowish brown or translucent bluish gray discoloration of the teeth is common. Deafness may occur in osteogenesis imperfecta, usually beginning in adolescence or adulthood. Otosclerosis results from abnormal proliferation of cartilage, which on ossification produces sclerosis of the petrous portion of the temporal bone. Some patients, particularly those with type III disease, complain of excessive sweating, thought to be due to a resting hypermetabolic state. This excessive perspiration is associated with heat intolerance and difficulty tolerating orthoses and can lead to chronic constipation (3). Radiographically Type III patients have narrow diaphyses with increased flaring and enlargement of the metaphyses and epiphyses. Typically the long bones are deformed due to multiple fractures. Pelvic radiographs demonstrate protrusio acetabuli. Spine radiographs demonstrate platyspondyly, biconcave vertebrae, and varying degrees of scoliosis, kyphosis, or spondylolisthesis. Some patients will have cranial osteoporosis with wormian bones and flattening of the occiput (tam-o'-shanter skull) (4). In osteogenesis imperfecta, the results of routine laboratory investigations are normal. Specifically, serum calcium and

phosphorus levels are normal. The alkaline phosphatase level may be elevated (3). Bone mineral density appears to be an indicator of disease severity and may be predictive of long-term functional outcome (5). Healing of fractures and osteotomies usually is satisfactory, although the healed bone may be no stronger than the original. Because of frequently frail and disabling bone and deformities and fractures that preclude ambulation, a comprehensive rehabilitation program with long-leg bracing has been suggested to result in a high level of functional activity with an acceptable level of risk of fracture in children with Osteogenesis imperfecta. The use of bisphosphonates has been shown to reduce osteoclast-mediated bone resorption. Intravenous administration of bisphosphonates, such as pamidronate, zoledronate, and risedronate, has been shown to decrease bone pain and incidence of fracture and to increase bone density and level of ambulation with minimal side effects. Recently, pamidronate has been recommended for use in combination with surgery both preoperatively and postoperatively. As pamidronate is depicted in bone and is detected years after treatment, the long-term safety and effectiveness of the drug in management of Osteogenesis imperfecta is not established yet. Hence it is important to consider treatment only in those with moderate or severe disease⁶ or those with milder disease but have spinal compression fractures⁽⁶⁾. Signs of bone pain usually disappears within days, and an increase in BMD was evident as early as 6 weeks after the start of treatment. Without exception, the gain in BMD was greater than the increase expected in healthy children (7) Surgical treatment with multiple osteotomies, realignment, and medullary nail fixation is the most successful surgical method of treating the deformities of osteogenesis imperfecta is based on the work of Sofield and Millar who used a method of multiple osteotomies, realignment of fragments, and medullary nail fixation for long bones. This operation and its modifications are now widely used (2).

IV. Conclusion:

Osteogenesis imperfect type III is a rare form of Osteogenesis imperfecta. There is no specific treatment to correct the basic mutant gene defect in Osteogenesis imperfecta. The treatment of osteogenesis imperfecta has been focused on maximizing patient's function, preventing deformity and disability as a result of recurrent fractures, correcting deformities that have developed, and monitoring potential complicating conditions associated with Osteogenesis imperfect⁽⁴⁾. The treatment of fractures in patients with Osteogenesis imperfecta is sometimes difficult. Fractures heal readily, often with exuberant callus, but this is plastic and easily deformed. As a result, bone deformities and shortening occur. Closed treatment is often used with lightweight splints or braces. Various reports have shown good result of using bisphosphonates in children with Osteogenesis imperfect. They inhibit osteoclastic resorption of bone, which is increased in patients with osteogenesis imperfecta. Aminohydroxypropylidene (pamidronate) has been studied extensively. This medication is administered intravenously in dosages ranging from 15 mg given every 20 days to 7 mg/kg/yr given every 4 to 6 months, with reported improvement in generalized bone pain and a reduced incidence of fractures. Oral form of bisphosphonates in management of Osteogenesis imperfecta in children is also available. When conservative treatment fails, intramedullary rodding is indicated. Multiple corrective osteotomies with intramedullary fixation have been accepted for managing recurrent fractures. Finally, though correcting the basic genetic defect by replacing the defective COL1A1 or COL1A2 gene with a normal one is theoretically the ideal treatment, but till date this modality of treatment does not exist.

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Fig.1 initial X-ray



Fig.2 in Thomas splint



Fig.3 reduced



Fig.4 reduced in thomas splint

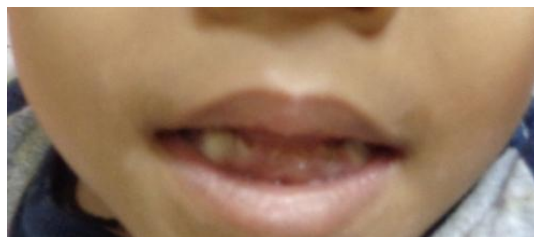


Fig.5 dental changes



fig.6 scleral spots



Fig. 7 in hip spica, union



Fig.8 hip spica



Fig. 7 in hip spica, union

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