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Stone Man Syndrome : A Case Report and Review of Literature

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Abstract :

Fibrodysplasia ossificans progressiva (FOP) : Stone man's syndrome – A terminology truly justifying pictorial presentation of this entity. This entity is characterized by painful swelling of muscles and connective tissue in the early years of life, consequently leading to ossification at a mean age of 4-5 years. We report FOP in a 6year old boy presenting with hallux valgus deformity and palpable masses in the cervical, paraspinal and bilateral periscapular muscles. Hallux valgus a hallmark sign went unseen to the hawk eyes of the clinicians due to rarity of this entity. Clinically misdiagnosed as hematoma, FOP was proved only after clubbing imaging findings with retrospective clinical correlation. Undiagnosed for 3 long painful years, little could have can been done due to the lingering literary deficit of this entity. The fallacies and global unawareness of this rare dreadful entity is a harsh truth, has resulted in suboptimal knowledge of our specialists. A brief discussion on clinical presentation, differential diagnosis, radiological findings and management options after extensive review of literature is done, which may help concerned medical fraternity in early diagnosis. This case study is our attempt not just to add a pearl to the literature, but to create awareness as well.

Keywords: Fibrodysplasia Ossificans Progressiva; Hallux Valgus; Autosomal Dominant; stone man syndrome; Munchmeyer disease.

Introduction

Fibro dysplasia ossificans progressiva (FOP) or myositis ossificans progressiva also known as Munchmeyer's disease is a very rare autosomal dominant disorder with a worldwide prevalence of approximately 1 case in 2 million individuals. Begins in childhood, but most patients have a new mutation. Genetic analysis revealed that the FOP gene located on chromosome 4 and mutation in this gene causes an over expression of a bone morphogenetic protein (BMP4). This is characterized by proliferation of connective tissue in voluntary muscles, fascia's, tendons and ligaments resulting clinically as painful swelling of the muscles and connective tissue. This swelling subsides, then after approximately 6 months or more, ossification starts at some sites at the mean age of 4-5 years. Eventually, heterotrophic bone formation interferes with normal movement of the patient and most of them are confined to a wheel chair by the third decade. Mortality is related to restrictive lung disease (inability to expand the chest). Congenital malformations which are characteristically observed in the great toes at birth in almost all cases of FOP are the diagnostic hallmark.

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Case Presentation:

A 6-year-old boy presented with bilateral periscapular, cervical and upper back paraspinal tender masses. He was referred from pediatricians to our hospital (SSIMS & RC, Davangere, Karnataka) and subsequently admitted. He was the third child of 37-year-old mother delivered by normal vaginal delivery with good Apgar score, normal birth weight 2800gm), head circumference (HC) of 35cms and length of 54cms. His parents had non consanguineous marriage and family history was negative. The patient's two elder brothers show no similar features as the patient. Growth and development was normal for the first 3 years of life. Present disease began 3 year ago with painful swelling over nape of the neck after a mild trauma. Progressed to similar swelling in the arm and back. Later progressed to severe restriction of the shoulder joint movements within one year of disease initiation. Subsequently on hospital admission, he had paraspinal (neck and upper thoracic) and periscapular swelling which was painful and tender, without redness and inflammation over the skin (Fig. 1). The shoulder girdle had restricted movement. On physical examination of the limbs, bilateral hallux

valgus was observed (Fig. 2) and corresponding radiograph showed bilateral hallux valgus deformity(Fig.3)

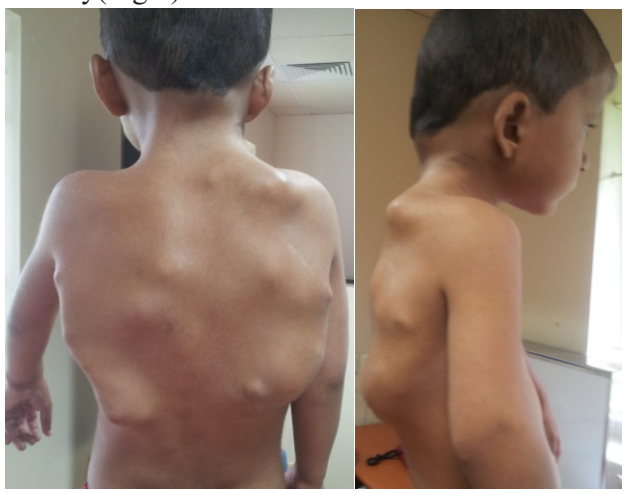

Fig. 1. A 6-year-old boy presenting with palpable masses in nape of the neck, bilateral pre scapular, para spinal and right frontal regions. Note the normal skin color without inflammation over the swellings.

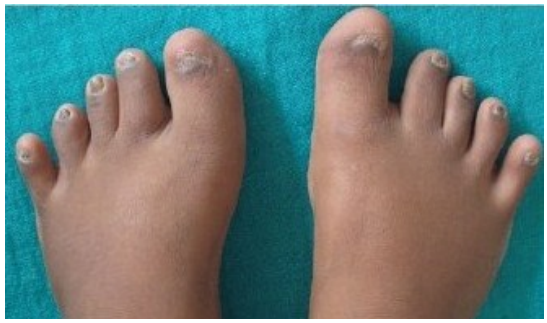

Fig. 2. Note the clinical photograph of feet showing laterally deviated great toes(bilateral hallux valgus deformity)

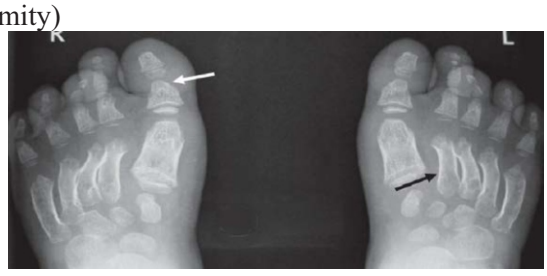

Fig.3. PA radiograph of the feet shows bilateral hallux valgus congenital malformation as a hallmark of FOP.

He was referred with the primary working diagnosis of multiple bony swelling. However routine blood tests were normal. Initial radiograph revealed extensive multiple ossified mass adhered to scapula and spine. Skeletal survey revealed bilateral hallux valgus deformity, extensive **extra skeletal ossification seen** in soft tissue connecting scapula and ribs on both side with pseudoarthrosis (Fig.4) and **extra skeletal ossification seen at the neck bridging between the skull base and scapula (Fig.5)**.

Further CT skull, neck, thorax and abdomen were performed. Skull CT images (Fig. 6), Neck CT images (Fig.7) chest CT images (Fig. 8)) and reconstructed CT images (Fig. 9) are shown below.

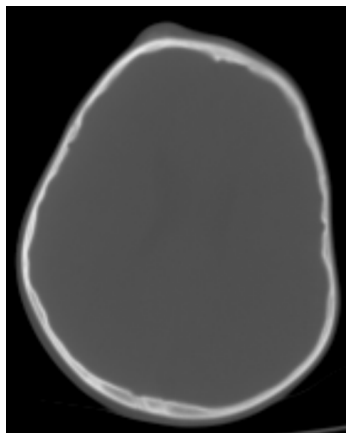

Fig. 6. Skull CT-scan of this patient indicating soft tissue mass(75-95 HU in density) without bone formation and calcification in the right frontal convexity.

An unnecessary initial biopsy was performed on the nape of the neck mass one year back, which may have lead to catastrophic disability. Without proper evaluation, the patient was discharged with non steroid anti-inflammatory drugs. The pathology report which was collected later, showed proliferation of fibro-connective tissue with large islets of compact cartilage cells and lacunars cells with blades and specula of bone and osteoblastic activation, compatible with fibro dysplasia ossificans progressiva

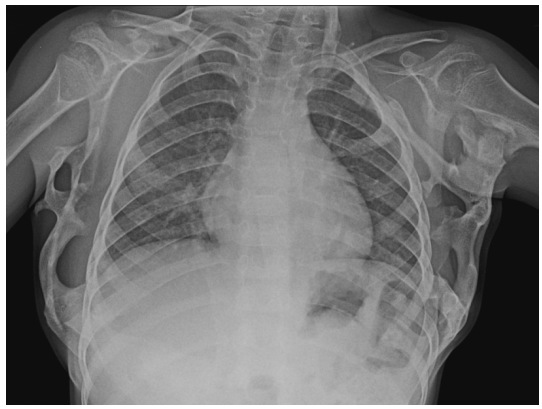

Fig. 4. Thorax radiography three year later at the age of 6 years shows extensive **extra skeletal ossification seen** in soft tissue connecting scapula and ribs on both side with pseudoarthrosis.

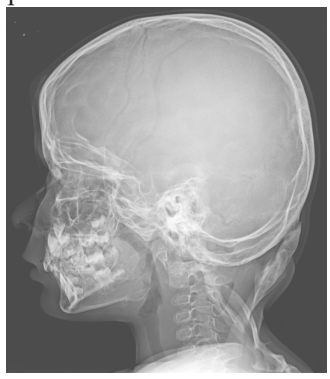

Fig. 5.

Skull/Neck radiography shows extra skeletal ossification at the neck bridging between the skull base and scapula.

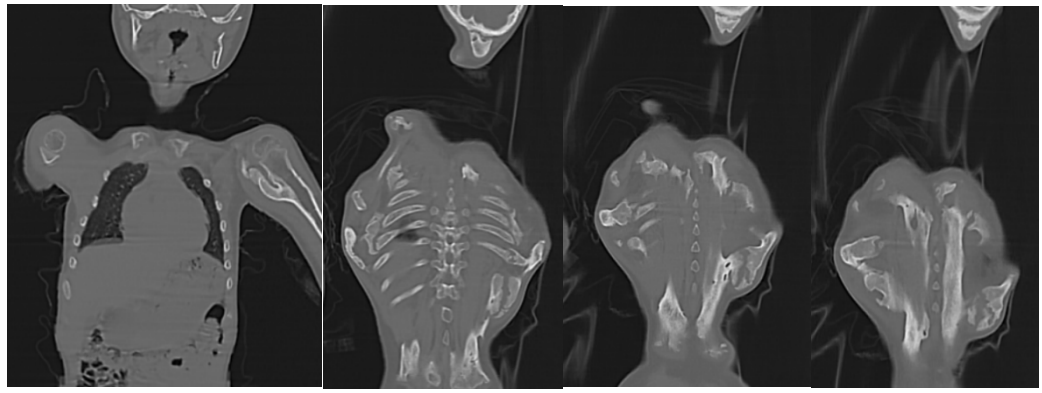

Fig. 7. Neck CT scan shows **extra skeletal ossification seen at right side of neck seen bridging between the skull base and right scapula** in the same case 1 year later at 6 years of age.

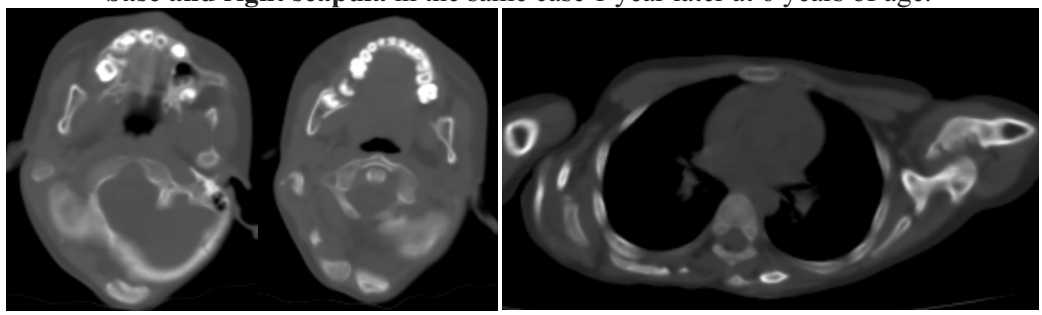

Fig. 8**.** Thorax CT scan shows extensive **extra skeletal soft tissue sheet like ossification seen in the back in subcutaneous plane extending in the 'V' pattern from either scapular region to para spinous region and extending inferiorly from the para spinous region almost upto the level of iliac crest. There is pseudoarthrosis between few of the ribs and sheet like calcification.**

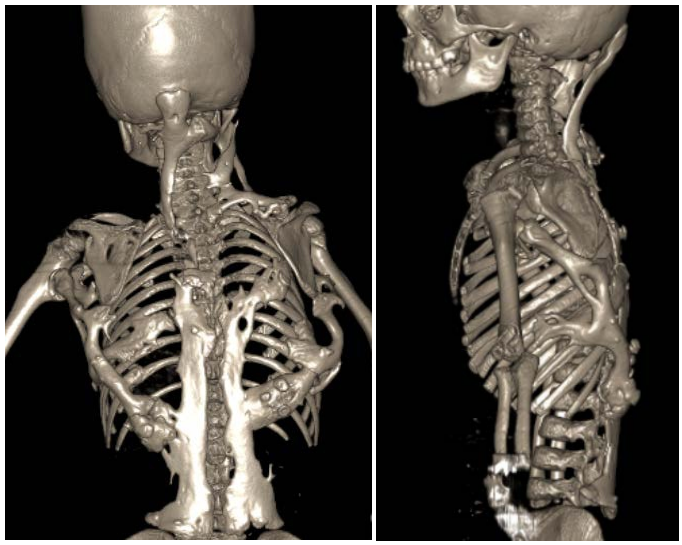

Fig. 9. VR and 3D reconstructed CT of thoracic bones shows ossification in the paravertebral, periscapular region, neck and the left arm in the same case at 6 years of age.

Discussion:

Fibro dysplasia ossificans progressiva (FOP) (Mendelian Inheritance in Man [MIM] #135100)[1] is a severely disabling heritable disorder of connective tissue characterized by congenital malformations of the great toes(hallux valgus, malformed first meta tarsal, and/or monophalangism) and progressive heterotopic ossification(HO) that form qualitatively normal bones in extra skeletal sites.

Gay patin first described this entity (FOP) in 1648 as a case that "turned to wood". No ethnic, racial, or geographic predisposition has been described[2].

Children who have FOP appear normal at birth except for congenital malformation of the great toes. Typically, during the first decade of life, sporadic episodes of painful soft tissue swellings (flare-ups) occur[3] and are commonly mistaken for tumors[4]. These soft tissue swelling transform skeletal muscles, tendons, ligaments, fascia, and aponeuroses through an endochondral process into heterotopic bone that renders movement impossible[5,6]. Progressive episodes of HO occur in specific anatomic patterns, and are typically seen first in the dorsal and axial and later distal regions[7]. Attempts to remove this heterotopic bone or minor soft tissue injury usually lead to episodes of explosive new bone formation. Immobility is cumulative and most patients are wheelchair-bound by the end of the second decade of life.

The diaphragm, tongue, extra-ocular muscles, cardiac muscle and smooth muscle spared in FOP. The cervical spine often becomes ankylosed resulting in neck stiffness early in life[8]. Other skeletal features associated with FOP are short malformed thumb, clinodactyly, short broad

femoral necks, and proximal medial tibial osteochondromas [9-11].

Life-threatening complications include severe weight loss following ankylosis of the jaw, as well as pneumonia and right-sided heart failure resulting from thoracic insufficiency syndrome (TIS) [12,17].

A large body of work has supported dysregulated bone morphogenetic protein (BMP) signaling in the pathogenesis of FOP. A single common heterozygous mutation (617G>A; R206H) has been identified in the cytoplasmic domain of activin receptor IA/activin-like kinase 2 (ACVR1/ALK2), a BMP type I receptor, in affected individuals of five small multigenerational families and in all sporadically affected individuals with the features of classic FOP [14]. All atypical FOP patients have heterozygous ACVR1 missense mutations in conserved amino acids [11]. Novel ACVR1 mutations have been described for FOP variants and in two cases of FOP plus [11]. To date, all ACVR1 mutations evaluated for enhanced BMP signaling are gain-of-function mutations [11,15]. Mounting evidence suggests that involvement of the inflammatory component of the immune system plays a critical role in FOP [16].

FOP should be diagnosed as early as possible based on history, clinical and imaging findings. The guide of diagnosis is bilateral anomaly of the great toes, hallux valgus deformity on plain radiography present from birth, reported almost in 100% [21,22] of the patients. Ultrasonography of early lesions may show sonolucent soft tissue masses[18,19]. In early disease before ossification, CT demonstrates fascia plane edema and swelling and mesenchymal mass like lesion in the muscle. In late disease after ossification and calcification, these findings could be seen in the muscles, fascia and connective tissue, especially near bones[18,20]. MRI finding of a pre osseous lesion and masses spreaded along the fascial planes are the features that confirms the diagnosis. Bone scintigraphy with TC-MOP demonstrate heterotrophic ossification in the early stage and helps in the assessment of the extent and progression of the disease.[22]

FOP must be distinguished from other genetic conditions of heterotopic ossification (HO), and nonhereditary (acquired) HO. Progressive osseous heteroplasia (POH) is a rare genetic condition of progressive HO defined clinically by cutaneous ossification that usually presents during childhood and progresses to involve subcutaneous and deep connective tissues, including muscle and fascia, in the absence of multiple features of Albright hereditary osteodystrophy (AHO) or hormone resistance[23]. FOP is differentiated from POH by congenital malformation of the great toes, pre osseous inflammation or “flare-ups” and the lack of cutaneous ossification.

Acquired HO commonly follows severe trauma, and can be observed at any age but is rare in young children[24]. Acquired HO tends to occur at peri articular sites or at sites of blunt trauma or localized injury. FOP is commonly misdiagnosed as aggressive juvenile fibromatosis, lymphedema, or soft tissue sarcoma[4]. Other diagnostic considerations are lymphoma, desmoids tumors, isolated congenital malformations, brachydactyly (isolated), and juvenile bunions.

Genetic counseling is important and in most cases of FOP arises as a result of a spontaneous new mutation. Genetic transmission is autosomal dominant and can be inherited from either parent. Within a family, inherited FOP can show variable expression. If a parent has FOP, the chance that a child will inherit FOP is 50%. There are substantial life-threatening risks to both the mother and child that women with FOP might encounter during pregnancy and at delivery; there should be a team skilled in resuscitation of high risk infants. Prenatal testing is not routinely available for FOP.

Management including treatment: Acceptable modification of activity, improvement in household safety and use of protective headgear are all strategies to prevent falls and minimize injury when falls occur. Prophylactic measures to reduce respiratory infection and Intramuscular injections must be avoided [25]. Surgical attempts to remove heterotopic bone will provoke explosive new bone growth and should not be attempted. Corticosteroids are indicated as first-line treatment at beginning of flare-ups. A non steroidal anti-inflammatory drug (NSAID) may be used symptomatically for the duration of the flare-up. The use of mast cell inhibitors and amino bisphosphonates and muscle relaxant can be used at the physician's discretion. For a complete description of medications refer to the current treatment guidelines at the International Fibro dysplasia Ossificans Progressiva Association website [26].

Prognosis : The median lifespan is approximately 40 years of age [27]. Most patients are wheelchair-bound by the end of the second decade of life and commonly die of complications of thoracic insufficiency syndrome [27].

After a combined multidisciplinary approach which involved paediatric, radiological and pathological assessment of our case, we arrived at our diagnosis of fibro dysplasia ossificans progressive which helped better symptomatic management. It was however not possible for us to retrieve the specimen slides.

From our extensive literature review, only 700

confirmed cases of FOP have been seen across the globe. This case report is not just an effort to add another pearl to the literature, but also to enlighten our collogues in and outside our speciality about the existence and further management of this rare entity.

Conclusion:

Fibro dysplasia ossificans progressive is a rare disease. Early recognition of this autosomal dominant disorder by summing up history, clinical and imaging findings is of utmost importance for genetic counseling, nursing the child, preventing trauma leading to painful flare ups and its devastating complications.

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