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Case Report of Fibrodysplasia Ossificans Progressiva

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ABSTRACT

Fibrodysplasia ossificans progressiva is a rare genetic disease characterized by widespread soft tissue ossification and congenital stigmata of the extremities. We report a male patient who had bilateral hallux valgus since birth. Other noticed anomalies included multiple swellings over the back, stiffness of lower back area, multiple joints, restricting movement of spine, shoulders, elbows, and right hip and right knee. Patient was not able to bend forward, squat or turn head to either side. Patient also had multiple foci of ossification developed over left knee, and back region. All swellings and restrictions were painless.

Keywords: Fibrodysplasia ossificans progressiva, Myositis ossificans

Fibrodysplasia ossificans progressiva (FOP) is a rare, autosomal dominant [1-3] disease affecting all ethnic backgrounds [4]. It is particularly disabling in children and is characterized by two cardinal features: heterotopic progressive osteogenesis and congenital abnormalities of the great toes [5-6]. Patients are generally confined to wheel chair and live up to third to fourth decade.

The term fibrodysplasia ossificans progressiva is preferred to myositis ossificans because ectopic osteogenesis occurs in the connective tissue within muscles, fasciae, ligaments, tendons and joint capsules, rather than in the muscle fibers themselves. These may show nonspecific, possibly secondary pathological changes [6]. Recently, FOP has been considered a connective tissue disorder due to over expression of a bone morphogenetic protein, BMP 4 [7,8]. Since curative therapy is not available, management is conservative aimed at preventing abnormal ossification.

Therefore, an increased awareness of the disease among clinicians is of great importance. We report on a patient with FOP diagnosed at 13 years of age with progressive and painless restriction of multiple joint movements. Emphasis is placed on the adverse effects of simple surgical procedures, such as muscle biopsy, which may aggravate ectopic ossification and is not contributory for the diagnosis.

CASE REPORT

Patient was an 18 yr old boy, child of young healthy parents, born of a non-consanguineous marriage, by normal vaginal delivery after an uneventful full term gestation. The parents do not have any obvious clinical skeletal malformation. In neonatal period was uneventful with 2,500g birth weight. At the age of 7 years, parents noticed multiple swellings over the back but did not consult any doctor as they were painless. The patient came to orthopedic outpatient department for stiffness of right

shoulder at the age of 9 years. At that time, X-ray and MRI of shoulder joints were performed, which did not reveal any abnormality. The patient and parents were reassured and child was sent home. Gradually, patient observed progressive difficulty in the movements of neck and spine, shoulders, elbows, right hip and right knee joints.

He came to us at the age of 13 years with these complaints. Examination revealed a cooperative boy having normal intelligence with restricted mobility during walking, sitting and standing caused by a rigid axial musculature. Abduction of the shoulders, movements of elbows and mobility of the right hip and knee were severely restricted. Bilateral short hallux valgus was also observed.

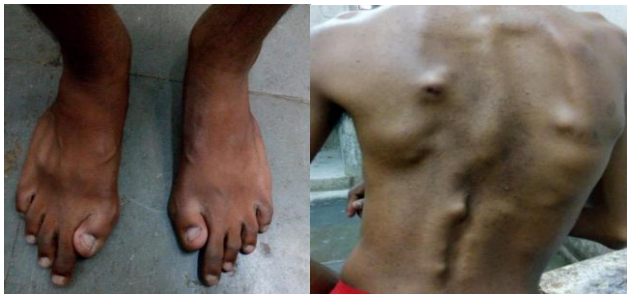

Figure 1 - Clinical photograph showing Bilateral Hallux Valgus and multiple swellings over the back

Laboratory investigations including complete hemogram, erythrocyte sedimentation rate, serum calcium, alkaline phosphatase, creatine phosphokinase, alanine and aspartate transaminases, routine urine analysis, and creatinine clearance were within normal limits. Antinuclear antibodies (ANA) and Anti Ds DNA were also normal and USG abdomen and of local part did not reveal any abnormality. Patient did not have any episodes of exacerbation yet but parents are counseled regarding the disease progression and its prognosis and advised to avoid sporty games, intramuscular injections, arterial puncture, and physiotherapy and to avoid any surgery to prevent such episodes.

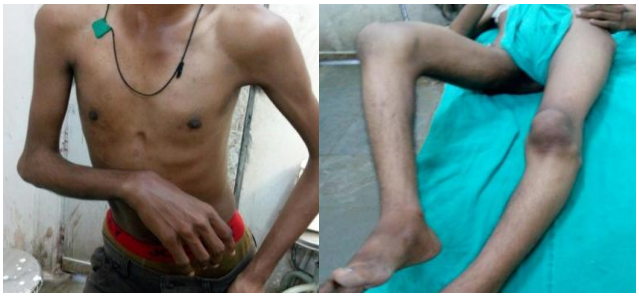

Figure 2 - Clinical photograph showing fixed contractures of shoulder, elbow, right hip and knee joints

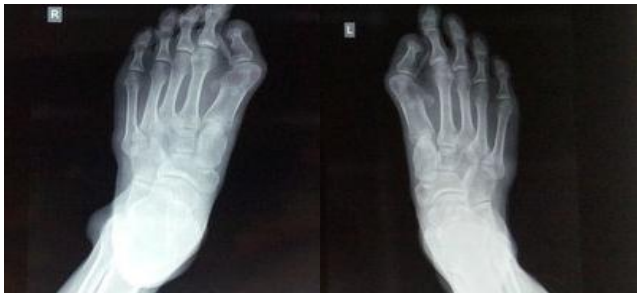

Figure 3 - X-ray of feet showing Hallux Valgus

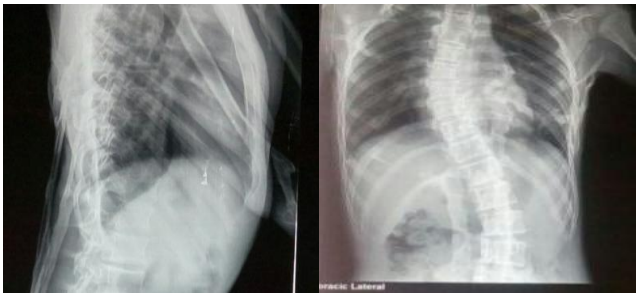

Figure 4 - X-ray of dorso-lumbar spine AP and Lateral showing calcifications around paraspinal muscles

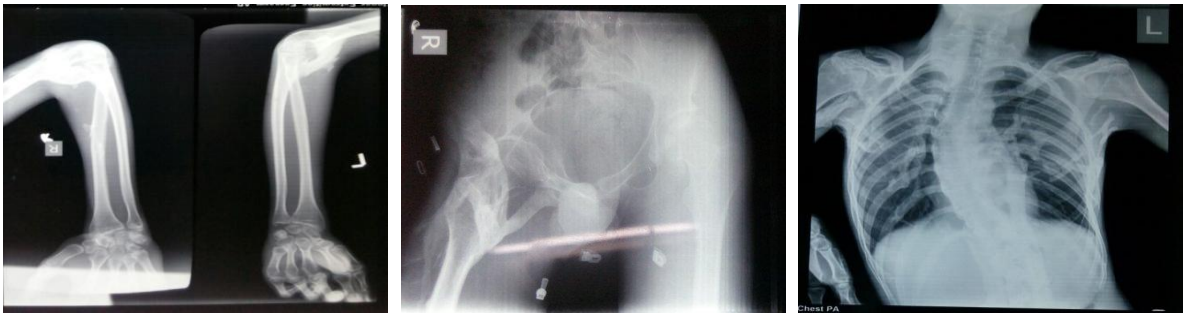

Figure 5 - X- rays of elbow, hip and shoulder showing calcified masses

DISCUSSION

Fibrodysplasia ossificans progressiva should be diagnosed as early as possible and noninvasively, based upon history, clinical and radiological findings. The mainstay of diagnosis is bilateral great toe anomaly present from birth, reported in 79 to 100% of patients in representative series [9-12]. The most characteristic deformity is microdactyly of both halluces due to a single phalanx in valgus position (type I deformity according to Connor and Evans). Three other subtypes of malformed big toes can be diagnosed up to the second decade, and this is where radiologic examination is especially important. Isolated congenital hallux valgus (i.e. not as part of FOP) is much rarer than FOP itself. Therefore, the finding of congenital hallux valgus must raise the possibility of FOP so that management should be early and adequate. Hand malformation is generally associated with, and proportional to the severity of hallux dysmorphism, and indeed is not seen in its absence. The most frequent anomalies are short first metacarpal and brachymesophalangy of the fifth finger with clinodactyly.

Ectopic ossification, another hallmark of disease, occurs lifelong, with records of its initial appearance at the mean age of three or five years [13]. In almost all patients, onset of the lesions was noted under 15 years of age. Ectopic ossification follows a well defined pattern, the axial body being compromised first and the most. Shoulder and hip regions are affected more than distal segments of the limbs. Deafness and baldness have been reported in up to one fourth of the cases, while mental retardation is rare. Exacerbation of FOP may occur spontaneously or be precipitated by trauma, such as intramuscular injections including vaccines [14], local anesthesia, especially truncular block near the temporomandibular joint, muscle biopsy and careless venepuncture.

Biopsy of calcified nodules is to be avoided if the diagnosis of FOP is clear on clinical and radiological grounds (foot and hand stigmata). Biopsy may result in recurrent ossification of the site, sometimes worse than the original lesion. Routine laboratory tests including calcemia and phosphatemia are usually normal or non contributory in FOP. Roentgenograms may aid in documenting minor osseous dysmorphism. Bone scintigraphy with 99mTc-MDP may demonstrate the heterotopic ossification early and aid in the assessment of the extent and progression of the disease. So far, no effective treatment for FOP is known. All management is conservative and based on the principle of avoiding conditions potentially provocative of abnormal ossification. Several types of treatment have been tried. Administration of calcium chelators such as sodium etidronate has been proposed since 1969 with variable results. In acute flare ups, oral corticosteroids and intravenous etidronate can be used simultaneously with promising results.

The phenotype and natural history of FOP are by now so well defined that differential diagnosis is limited. Other disorders of ectopic ossification may be considered, such as Albright hereditary osteodystrophy, pseudomalignant heterotopic ossification, progressive osseous heteroplasia and even osteosarcoma. In the recent Brazilian literature, three cases fulfill clinical and radiologic criteria for FOP. In the case of Tonholo-Silva et al., although there were ectopic ossifications they did not appear to be axial, and the characteristic skeletal stigmata of FOP were not mentioned. Garcia Filho et al. studied 25 cases of ‘heterotopic ossification’ including one of ‘progressive myositis ossificans’ which may represent an instance of FOP. It is hoped that the recent surge of knowledge on molecular genetics will lead to better understanding of the pathogenesis and to effective treatment for FOP.

CONCLUSION

This presents a case report of a very rare disease. In most cases there is history of any trauma or inciting factors in formation of myositis mass. This case however presented late with characteristic features of short great toe, multiple contractures and multiple ossifications so diagnosis was obvious. As patient presented with established myositis masses and flare ups bisphosphonates and corticosteriods were not given a trial.

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