CASE REPORT

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 child who had bilateral Hallux Valgus and firm swelling over lower back region since birth. At 3 years of age, he developed restriction of neck movement which gradually progressed and within 1 year duration involved multiple joints, restricting movement of hip, shoulder, spine and knee. Patient was not able to bend forward, squat or turn head to either side. Patient also had acyanotic congenital heart disease. Multiple foci of ossification developed over bilateral shoulder, right hip and lower back region. Patient has not developed episodes of crisis yet and all swellings and restrictions are painless. A review showed few similar case reports in the Brazilian literature. We revisited the criteria for diagnosis and the essentials of management and treatment.

Keywords: Fibrodysplasia ossificans progressive, myositis ossificans, muscle biopsy, rigid spine

INTRODUCTION

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]. The disease should be familiar to neonatologists, pediatricians, neurologists, orthopedic clinicians and surgeons, rheumatologists and ancillary personnel engaged in the diagnosis and management of neuromuscular conditions.

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 based on the principle of *primum non nocere*, particularly 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 4 years of age with progressive and painless restriction of multiple joint movements. We revisit the criteria for diagnosis, treatment and main rules for management. Emphasis is placed on the adverse effects of simple surgical procedures, such as muscle biopsy, which may propitiate ectopic ossification and is not contributory for the diagnosis.

CASE

A Hindu boy, child of a young healthy parents, born of a non-consanguious marriage,(father 22, mother 18) in 2008 by normal vaginal delivery after an uneventful full term gestation. The parents do not have any obvious clinical skeletal malformation and a younger sister of the patient is normal.

In neonatal period the condition was good, with 2,500g weight. An orthopedic consultation was done by parents because of malformation of the great toes and soft swelling over lower back region. A plain roentgenogram of the feet and MRI brain and spine was done by the doctor, which does not reveal any abnormality so parents were reassured and the child was discharged. Routine pediatric follow up elsewhere revealed cardiac murmur, although cyanosis was not a complaint. Psychomotor development was always within normal limits. The parents observed at 3 years of age, progressive difficulty in the child's neck extension and, multiple swellings over occipital and dorso-lumbar region, initially soft gradually becoming firm. 6 months later patient had fall down injury over shoulder and fracture clavicle following which parents noticed firm

swelling over bilateral shoulder and right hip area. All were painless with overlying skin normal. We examined patient at 5 year of age. Examination revealed a cooperative, normal intelligence boy with restricted mobility during walking, sitting and standing caused by a rigid axial musculature. Paraspinal muscles and Trapezeius were hard on palpation. Abduction of the shoulders and mobility of the hips were severely restricted, involving knee joint also to some extent. Clinodactyly of both fifth fingers and bilateral short hallux valgus were also observed.

Hemogram, erythrocyte sedimentation rate, serum calcium, alkaline phosphatase, creatine phosphokinase, alanine and aspartate transaminases, routine urinalysis, and creatinine clearance were within normal limits. ANA and Anti Ds DNA were also normal and USG abdomen and local part does not reveal any abnormality.

Patient did not have any episodes of exacerbation yet but parents are advised to make child avoid sporty games, I.M injections, arterial puncture, and physiotherapy and avoid any surgery to prevent such episodes.

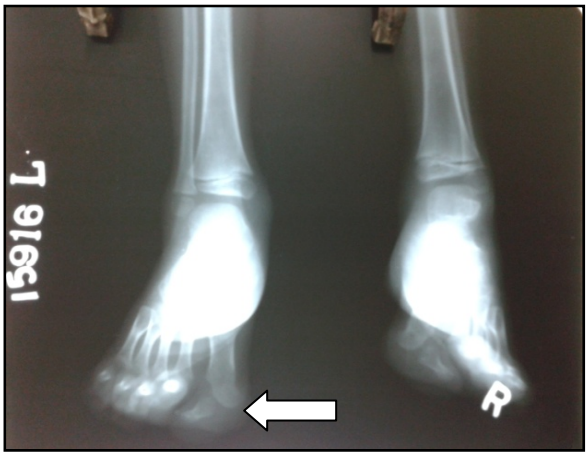

Fig A: AP View Radiograph of feet showing symmetrical 1st toe

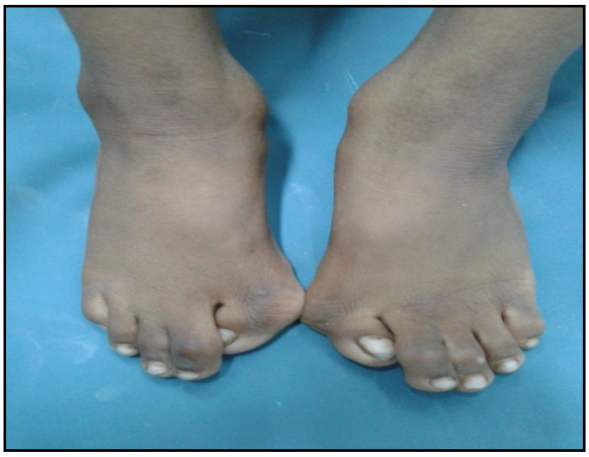

Fig B: Symmetric malformed great toes with hallux valgus deformity

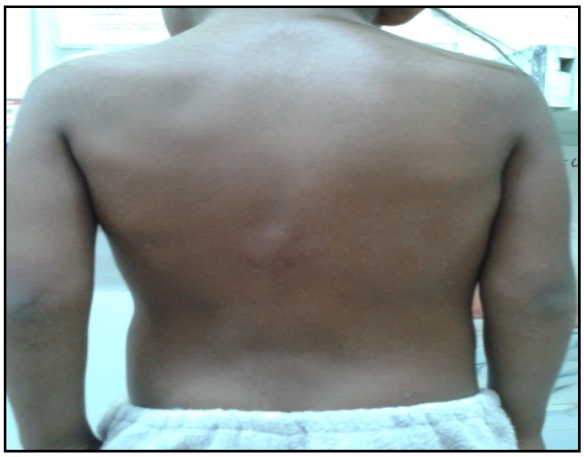

Fig C: Heterotopic Ossification (paraspinal muscle) presented as tumor like swellings over the back

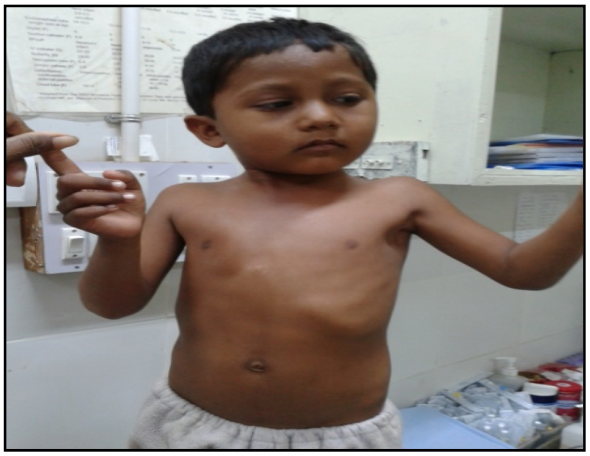

Fig D: Restricted shoulder abduction

DISCUSSION

FOP should be diagnosed as early as possible and non-invasively, based upon history, clinical and radiological findings[5]. 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[9-10] (type I deformity according to Connor and Evans[11]). Three other subtypes of malformed big toes can be diagnosed up to the second decade[11], 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[5]. 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[10]. The most frequent anomalies are short first metacarpal and

brachymesophalangy of the fifth finger with clinodactyly[10].

Ectopic ossification, another hallmark of disease, occurs lifelong, with records of its initial appearance at the mean age of three[11] or five years[13]. In almost all patients, onset of the lesions was noted under 15[9-13]. Ectopic ossification follows a well defined pattern, the axial body being compromised first and 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[11].

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[11], muscle biopsy[6] and careless venepuncture[11]. 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[11]. Another clinical expression of FOP is acute or chronic limb swelling, defined as an enlargement of the limb circumference at one or more locations with increased tissue turgor, the pathogenesis of which is multifactorial[14]. In the present case, fracture clavicle was followed on a short term by increased limitation of neck flexion, bending, arm abduction and hip flexion.

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 early the heterotopic ossification 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 primum non nocere, that is, 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. Controlled trials are thus encouraged.

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.

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