CASE REPORT

Fibrodysplasia Ossificans Progressiva

Usman Rashid, Attia Bari, Amna Maqsood, Samia Naz and Tahir Masood Ahmad

ABSTRACT

Fibrodysplasia Ossificans Progressiva (FOP) is a rare autosomal dominant disorder characterized by postnatal progressive heterotopic ossification of connective tissue and congenital malformation of big toes. We report a 3-year male toddler with clinical and radiological features of FOP. He was born with bilateral hallux valgus and at the age of 3 years presented with hard swellings over back, scapular region and forehead that were initially inflammatory and then became bony hard. There is also tilting of neck towards the left due to calcification in neck region. The radiographs showed heterotopic ossification in thoracic region, neck, spine and region of hip joint.

Key Words: *Calcinosis. Fibrodysplasia ossificans progressiva. Progressive myositis ossificans. Heterotopic ossification.*

INTRODUCTION

Fibrodysplasia Ossificans Progressiva (FOP) is a rare autosomal dominant disorder. The worldwide prevalence is approximately 1/2,000,000.[1] FOP is a disease where a subject muscle and connective tissues, such as ligaments and tendons, are slowly replaced by bone through heterotopic ossification forming bone outside their skeleton, constraining their ability to move. The process of ossification usually starts during early childhood, beginning at the shoulders and neck and proceeds down into the limbs. The formation of extra skeleton causes a progressive loss of mobility. Congenital abnormalities of the big toes are associated with progressive heterotopic ossification of the connective tissue structures. Studies from Europe and United States concluded that the estimated incidence of FOP is 1 in 2 million births.[2] From Brazil, 3 have been published by Tonholo *et al*. in 1994, Nucci *et al*. in 2000 and Araujo *et al*. in 2005.[2,3]

Genetic analysis revealed that the FOP phenotype is linked to markers located at chromosome 4.[4] It is believed that a gene mutation causes an over-expression of a bone morphogenetic protein (BMP4).[5]

This report describes a rare condition in a male toddler.

CASE REPORT

A 3-year boy presented with multiple swellings on the body. These swellings had started at 4 months of age. Initially, these were inflammed and red, hot and tender but later on the signs of inflammation subsided and changed into bony hard swellings. Such swellings were on different regions of the body including back, forehead, and scapular region. There was also tilting of neck towards left side due to hard mass on right side of the neck.

Physical examination showed hard masses of 2 x 2 cm on the back, forehead and scapular region (Figure 1). These masses were tender and painful, but no warmth or inflammation was noted. The patient had bilateral hallux valgus but no other abnormality on any toes (Figure 1). His parents did not show any similar abnormalities on the physical examination.

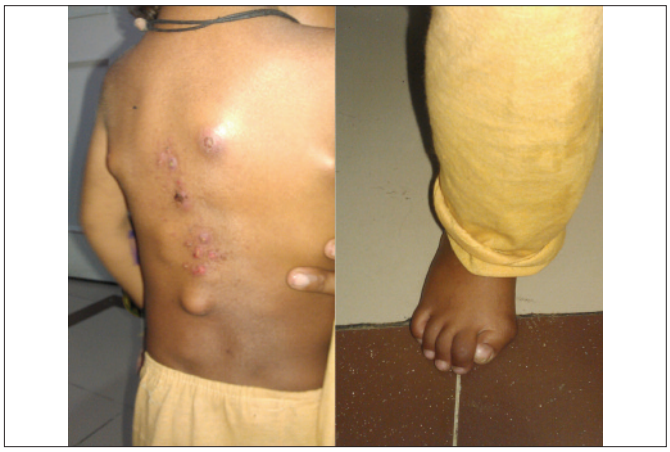

Figure 1: Calcified nodules on back and the typical hallux valgus deformity.

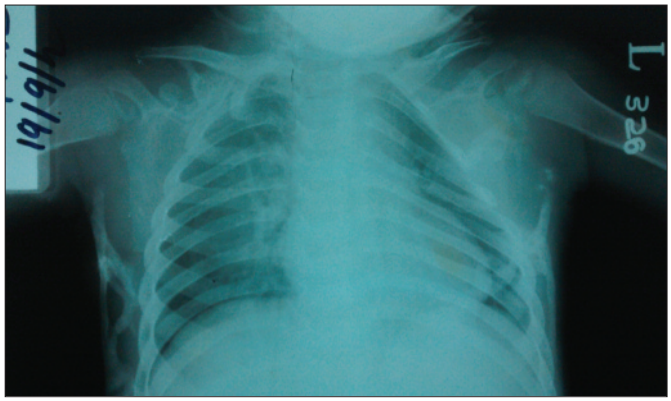

Figure 2: Soft tissue calcification in neck and lateral chest wall

Department of Pediatric Medicine, Children Hospital and Institute of Child Health, Lahore.

Correspondence: Dr. Usman Rashid, Department of Pediatric Medicine, Children Hospital and Institute of Child Health, Lahore. E-mail: drhero238@yahoo.com

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His blood (S/Ca, S/PO4) and urine tests turned out to be normal. Radiograph of boy showed heterotopic calcification in chest region bilaterally and also in neck, spinal, and hip joint region (Figure 2).

DISCUSSION

Guy Patin first described FOP in 1692 in a young patient who “turned to wood”.[6] The autosomal dominant inheritance of FOP was first described by Sympson in a case report of a 7-year-old boy with classic features of FOP whose father had the same congenital deformity of the great toes but no other characteristics of this disorder.[7] Genetic linkage analysis has shown that the FOP phenotype is heterogeneous linked to markers located in the long arm of chromosome 4. In 2000, Feldman *et al*. described 4 affected families with markers located in the 4q27-31.[4] In those cases, slight different chromosomal markers but abnormalities of toes was the common feature.

Abnormalities of the great toes were observed at birth in most cases of FOP (bilateral hallux valgus - microdactylia with hypoplasia or synostosis of the phalanges or both).

In our case, the parents reported that the patient had hallux valgus since birth. The initial symptoms of FOP are painful and hard soft tissue swellings over the affected muscles that lead to ossification. It usually occurs from birth up to the age of 16 years (mean age 4.6 years), following spontaneous or trauma-induced "flare-ups".[2,8] Heterotopic ossification usually begins in the cervical para-spinal muscles and later spreads from axial to appendicular, cranial to caudal and proximal to distal sites. Scoliosis is a common finding and is often the result of asymmetric heterotopic bones connecting the trunk and pelvis.[2]

Differential diagnoses include other genetic illnesses that also cause the development of heterotopic ossifications, such as Progressive Osseous Heteroplasia (POH), Albright Hereditary Osteodystrophy (AHO), osteoma cutis, ankylosing spondylitis, Still's disease and Klippel-Feil-syndrome.[2] The "flare-ups" of FOP must be differentiated from the inflammatory processes of osseous tumors, and aggressive juvenile fibromatosis.

Treatment of FOP is multifactorial and is based on injury prevention and clinical therapy. At present, there is no definitive treatment. Prevention of soft tissue injury and muscle damage, as well as the prevention of falls, are extremely important. Intramuscular injections, including vaccines, must be avoided. Moreover, in routine dental care, overstretching of the jaw and intramuscular local anesthetic injections should also be avoided.

Treatment of FOP is ineffective; as effectiveness of ACTH, glucocorticosteroids and calcium-binding agents has not been proven so far. Effects of sodium etidronate are controversial; however, it can be helpful in the prevention of ectopic bone formation after surgical procedures.[10] Kinesitherapy and physiotherapy are also used in these patients; treatment of recurrent pneumonias is also necessary. There are studies under way aimed at evaluating the usefulness of thalidomide, interferon alpha, angiostatin and endostatin in the therapy of FOP.

In our case as described above, pharmacotherapies with prednisone and nonsteroidal anti-inflammatory drugs were used. He was managed with motor rehabilitation and physical exercise to overcome the mobility problem and this helped us a little only. Strict advice was not to remove or do any surgical intervention to those calcified nodules as it would flare up the disease. Genetic counseling was done.

Fibrodysplasia ossificans progressiva is a rare and disabling disease that still does not have an effective treatment which can cure it or stop its progression. Physicians, healthcare professionals, patients and their families must be educated about the disease. Although drugs can be used to decrease some symptoms, the best approach is still the early diagnosis and prevention of trauma that can provide a better quality of life.

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