



# International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958  
P-ISSN: 2706-6630  
IJOS 2020; 6(4): 872-875  
© 2020 IJOS  
[www.orthopaper.com](http://www.orthopaper.com)  
Received: 06-08-2020  
Accepted: 12-09-2020

**Dr. Naresh Kumar**  
Senior Resident, Department of  
Orthopaedics, BPS GMC for  
Women, Khanpur Kalan,  
Sonapat, Haryana, India

**Dr. Raj Singh**  
Professor, Department of  
Orthopaedics, PGIMS, Rohtak,  
Haryana, India

**Dr. Jyotirmay Das**  
Senior Resident, Department of  
Sports Medicine, PGIMS,  
Rohtak, Haryana, India

**Dr. Akshay Lamba**  
Senior Resident, Department of  
Orthopaedics, Maharaja Agrasen  
Medical College, Agroha, Hisar  
Haryana, India

**Dr. Avik Kr Neogi**  
Senior Resident, Department of  
Orthopaedics, PGIMS, Rohtak,  
Haryana, India

**Dr. Ravi Sihag**  
Junior Resident, Department of  
Orthopaedics, PGIMS, Rohtak,  
Haryana, India

**Dr. Ankush Kundu**  
Junior Resident, Department of  
Orthopaedics, PGIMS, Rohtak,  
Haryana, India

**Dr. Urvashi Sharma**  
House Surgeon, Department of  
Medicine, PGIMS, Rohtak,  
Haryana, India

**Corresponding Author:**  
**Dr. Jyotirmay Das**  
Senior Resident, Department of  
Sports Medicine, PGIMS,  
Rohtak, Haryana, India

## Fibrodysplasia ossificans progressiva: A rare case report

**Dr. Naresh Kumar, Dr. Raj Singh, Dr. Jyotirmay Das, Dr. Akshay Lamba  
Dr. Avik Kr Neogi, Dr. Ravi Sihag, Dr. Ankush Kundu and Dr. Urvashi  
Sharma**

**DOI:** <https://doi.org/10.22271/ortho.2020.v6.i4m.2431>

### Abstract

Fibrodysplasia ossificans progressiva (FOP) is a rare autosomal dominant disorder characterized by gradual replacement of muscle and connective tissue by bone due to heterotopic calcification. We report on a fourteen year old girl with clinical and radiological features of FOP. Patient had bilateral hallux valgus at the time of presentation. There was significant decrease in range of motion in the spine and shoulder joint. The radiographs showed heterotopic ossification in the thoracic region. The disease course was persistent with severe reduction in movement at joints and restriction of breathing movements.

**Keywords:** Fibrodysplasia ossificans progressiva, myositis ossificans progressiva, myositis ossificans, heterotopic ossification

### Introduction

Fibrodysplasia ossificans progressiva (FOP) or previously called Myositis Ossificans Progressiva is a rare, autosomal dominant disease [1-3], is a severely debilitating inherited disorder affecting all ethnic backgrounds [4]. It is particularly disabling in children and is characterized by heterotopic progressive ossification of connective tissue like ligaments, tendons and muscles leading to permanent disability and congenital abnormalities of the great toes [5, 6]. Worldwide studies particularly from Europe and United state shows the incidence of FOP one in two million birth [7]. It has been found to be associated with overexpression of bone morphogenic protein due to genetic mutation, specifically BMP-4 [8, 9]. Genetic studies confirm the Autosomal Dominant inheritance of the disorder, from genetic analysis we find that FOP phenotype is linked to marker located on chromosome 4 [10] but most of cases of FOP are due to gene mutation. The term fibrodysplasia ossificans progressiva is preferred to myositis ossificans [5] because ectopic osteogenesis occurs in the connective tissue. These may show nonspecific, possibly secondary pathological changes [6].

### Case report

14 year old female present to our outpatients department of Orthopaedics at PGIMS Rohtak with complaints of stiffness of shoulder and neck movements with difficulty in eating. On details enquiry it was noted that first there was development of neck stiffness 3 years back without any pain or fever. The girl had no significant developmental milestone delay according to her parents. Gradually the stiffness in the neck progressed and it was not relieved by any exercises or medication prescribed by general physician. Afterwards there was appearance of stiffness in both shoulder joints. There was decrease in the range of motion in her bilateral upper limb joints. Stiffness gradually traversed down the spine and involved whole of the axial skeleton. Now there is decreased range of motion at bilateral hip joints. Patient also have difficulty in swallowing solid food.

On general physical examination no abnormality was found. Skeletal survey revealed bilateral mild hallux valgus deformity (Fig.1) and Kyphoscoliotic deformity in thoracic spine. There was multiple different sized nodules present over back (Fig. 2).



**Fig 1:** Clinical photograph showing the bilateral hallux valgus



**Fig 2:** Clinical photograph showing scoliotic deformity and nodules over back

On palpation these nodules were bony hard and adherent to underlying chestwall. There was severe kyphotic deformity in cervical spine and patient was unable to extend or laterally rotate her neck. There was also gross reduction in extension and lateral flexion of rest of the spine. Muscle tone was not increased but there were reduced movements in both shoulder joints.

Routine blood investigations were done and complete hemogram, erythrocyte sedimentation rate, urea, creatinine, uric acid, calcium, phosphorus, liver markers, serum proteins (albumin and globulin), alkaline phosphatase were within normal limits. Ultrasonography of abdomen revealed no significant abnormality. Ultrasonography of thigh revealed subcutaneous nodules. Clinical photograph of bilateral foot showed hallux valgus deformity, there were exostosis in distal femur, kyphoscoliotic curvature in upper thoracic and cervical spine (Fig.3, 4).



**Fig 3:** Radiograph showing scoliotic deformity in dorsal spine



**Fig 4:** Radiograph showing exostosis in distal femur

### Discussion

First case of FOP described by Guy Patin in 1692 in a young patient who “turned to wood” [11]. Sympson described the autosomal dominant genetic relationship of FOP in a case report [12]. Feldman *et al.* in 2000 described four affected families with markers located in the 4q27-31 [10].

FOP is a rare, hereditary, progressive connective tissue disorder characterized by progressive heterotopic calcification occurs mainly in the neck, chest, and back and there is congenital malformation of the great toes i.e. hallux valgus [13, 14].

The initial symptoms of FOP are painful and hard soft tissue swellings over the affected muscles later on that lead to heterotopic calcification of the soft tissue swelling. It usually occurs from birth to the second decade of life, following spontaneous or trauma-induced flare-ups [10]. Cervical paraspinal muscles are usually first to involve in heterotopic calcification and later it spreads from axial to appendicular, from cranial to caudal, and from proximal to distal sites. Asymmetric heterotopic ossification of bones connecting the trunk and pelvis lead to scoliosis which is common finding in FOP [15].

Conductive hearing loss is a common feature associated with this condition which due to fusion of ear ossicles [16, 17, 18]. Ankylosis of all major joints of the axial and appendicular skeleton occurs due progressive multiple flare-up episodes of heterotopic ossification, leads to restriction of movements at major joints. By the passing of second decade of life majority of the patient with FOP confined to wheelchair or bed [16, 19]. Cardiopulmonary failure is the most common cause of death in FOP resulting from thoracic insufficiency syndrome [20].

Diagnosis of FOP should be made as early as possible and by using non-invasive studies, by history, clinical symptoms and radiological findings. Mainstay of diagnosis is presence of three major criteria [18], congenital anomaly of bilateral great toe present since birth reported in 79 to 100% of patients in representative series [6, 21, 22, 23], progressive heterotopic connective tissue ossification and progression of the disease in well-defined anatomical and temporal patterns. There is discrete increase of ESR during the “flare -ups”. Imaging studies like radiographs and computed tomography shows the heterotopic bones and these radiographical studies are very useful to confirm the diagnosis.

Differential diagnosis to the FOP includes other genetic disorders those also cause the development of heterotopic ossifications, such as Albright hereditary osteodystrophy (AHO), progressive osseous heteroplasia (POH), osteoma

cutis, Still's disease, ankylosing spondylitis and Klippel-Feil-syndrome<sup>[18]</sup> so that FOP should be differentiated from these above conditions. Inflammatory processes of osseous tumors, and aggressive juvenile fibromatosis should be differentiated from the flare-ups period of the FOP.

FOP exacerbates spontaneously or may be precipitated by any type of trauma such as intramuscular injections<sup>[24]</sup> including vaccines, local anesthesia, muscle biopsy<sup>[7]</sup> and venipuncture<sup>[23]</sup>. Biopsy of the ossified swelling should be avoided if diagnosis is made by clinical or radiological studies because it may aggravate ossification of the site and worsen the lesion<sup>[23]</sup>. Another clinical expression of FOP is Acute or chronic limb swelling is another clinical symptom that appears in FOP, in it there is enlargement of the limb circumference at one or more locations with increased tissue turgor, the pathogenesis of which is multifactorial<sup>[25]</sup>.

Multifactorial treatment therapy should be started in FOP and is based on injury prevention, analgesic, physical therapy and surgical excision. Prevention of any type of injury to the body i.e. soft tissue injury and muscle damage, as well as the prevention of falls, is extremely important. FOP flare up episodes may occur spontaneously or may be caused by any type of injury i.e. intramuscular injections, including vaccines and muscle biopsy, must be avoided. Moreover, in routine dental care, overstretching of the jaw and intramuscular local anesthetic injections should also be avoided<sup>[26]</sup>.

Surgical excision of calcified mass is considered when there is excessive pain, joint limitation, or nerve compression is present. Surgical excision is done when calcified mass is mature and is identified by radiological imaging and serum alkaline phosphatase level and ESR.

Patients with FOP may have an additional risk of "flare-ups" after influenza-like illness. Thus, a subcutaneous influenza vaccine could help these patients, particularly those who have severe restrictive disease of the chest wall and are at a greater risk of presenting complications of respiratory infections that are a frequent cause of death<sup>[27]</sup>.

Kaplan *et al.* initially published the guidelines for drug treatment for FOP<sup>[28]</sup> and currently on the new guidelines published by the same authors<sup>[29]</sup>. Patients received corticosteroids in the acute phases of the disease and a long term treatment using a combination of a leukotriene inhibitor and a Cox-2 inhibitor.

When corticosteroid is discontinued, a non-steroidal anti-inflammatory drug or a Cox-2 inhibitor may be used symptomatically for the duration of the "flare-up". None of these drugs avoided the progression of the disease in our patient. Non-steroidal anti-inflammatory drugs like ibuprofen and indomethacin can be used. Leukotriene inhibitors may reduce the downstream effects of released mast cell mediators that are involved in the pathological process of heterotopic bone formation<sup>[28]</sup>.

Fibrodysplasia ossificans progressiva is a rare and disabling progressive disease, till date there is no definitive treatment that stops the progression of disease or cures it completely. Although drugs are available that decrease or reduce the symptoms due to disease. Multifactorial treatment therapy is the best approach and early diagnosis and prevention of injury to the body can provide a better life. Treating doctor should explain the prognosis of disease and educate the patient and their family members.

## References

1. Connor JM, Skirton H, Lunt PW. A three generation family with fibrodysplasia ossificans progressiva. *J Med*

- Genet 1993;30:687-689.
2. Kaplan FS, McCluskey W, Hahn G, Tabas JA, Muenke M, Zasloff MA. Genetic transmission of fibrodysplasia ossificans progressiva: report of a family. *J Bone Joint Surg* 1993;75A:1214-1220.
  3. Janoff HB, Tabas JA, Shore EM, *et al.* Mild expression of fibrodysplasia ossificans progressiva: a report of three cases. *J Rheumatol* 1995;22:976-978.
  4. Delatycki M, Rogers JG. The genetics of fibrodysplasia ossificans progressiva. *Clin Orthop Rel Res* 1998;346:15-18.
  5. Buyse G, Silberstein J, Goemans N, Casaer P. Fibrodysplasia ossificans progressiva: still turning into wood after 300 years? *Eur J Pediatr* 1995;154:694-699.
  6. Smith R. Fibrodysplasia (myositis) ossificans progressiva: clinical lessons from a rare disease. *Clin Orthop* 1998;346:7-14.
  7. Brooke MH. Myositis ossificans progressiva. In Brooke MH. *A clinician's view of neuromuscular diseases*. 2Ed. Baltimore: Williams & Wilkins 1986:239-242.
  8. Lanchoney TF, Olmsted EA, Shore EM *et al.* Characterization of bone morphogenetic protein 4 receptor in fibrodysplasia ossificans progressiva. *Clin Orthop* 1998;346:38-45.
  9. Shafritz AB, Shore EM, Gannon FH, *et al.* Overexpression of an osteogenic morphogen in fibrodysplasia ossificans progressiva. *N Engl J Med* 1996;335:555-561.
  10. Feldman G, Li M, Martin S, *et al.* Fibrodysplasia ossificans progressiva a heritable disorder of severe heterotopic ossification, maps to human chromosome 4q27-31. *Am J Hum Genet* 2000;66:128-135.
  11. Goldman AB. Heritable diseases of connective tissue, epiphyseal dysplasias, and related conditions. In Resnick D, (ed) *Diagnosis of bone and joint disorders*. Philadelphia: W.B. Saunders 2002:4409-4415.
  12. Delatycki M, Rogers JG. The genetics of fibrodysplasia ossificans progressiva. *Clin Orthop* 1998;346:15-18.
  13. Wei J, Jia Y, Liang B. Myositis ossificans of the serratus anterior as a rare complication of massage: a case report. *J Med Case Rep* 2015;9:143.
  14. Kaplan FS, Xu M, Glaser DL *et al.* Early diagnosis of fibrodysplasia ossificans progressiva. *Pediatrics* 2008;121(5):e1295-300.
  15. Mahboubi S, Glaser DL, Shore EM, Kaplan FS. Fibrodysplasia ossificans progressiva. *Pediatr Radiol* 2001;3:307-14.
  16. Lanchoney TF, Olmsted EA, Shore EM, *et al.* Characterization of bone morphogenetic protein 4 receptor in fibrodysplasia ossificans progressiva. *Clin Orthop Relat Res* 1998;346:38-45.
  17. Levy CE, Lash AT, Janoff HB, Kaplan FS. Conductive hearing loss in individuals with fibrodysplasia ossificans progressiva. *Am J Audiol* 1999;8:29-33.
  18. Delatycki M, Kantanie S, Santilli C *et al.* Fibrodysplasia ossificans progressiva: a hereditary illness of multidisciplinary interest. *Rev Bras Ortop* 2004;39:205-213.
  19. Talbi S, Aradoini N, Mezouar IE, Abourazzak FE, *et al.* Myositis ossificans progressiva: case report. *Pan Afr Med J* 2016;24:264.
  20. Kaplan FS, Zasloff MA, Kitterman JA, Shore EM, *et al.* Early mortality and cardiorespiratory failure in patients with fibrodysplasia ossificans progressiva. *J Bone Joint Surg Am* 2010;92:686-91.

21. Rogers JG, Geho WB. Fibrodysplasia ossificans progressiva. A survey of forty-two cases. *J Bone Joint Surg* 1979;61A:909-914.
22. Schroeder HW, Zasloff MA. The hand and foot malformations in fibrodysplasia ossificans progressiva. *Johns Hopkins Med J* 1980;147:73-78.
23. Connor JM, Evans DA. Fibrodysplasia ossificans progressiva: the clinical features and natural history of 34 patients. *J Bone Joint Surg* 1982;64B:76-83.
24. Lanchoney TF, Cohen RB, Rocke DM, Zasloff MA, Kaplan FS. Permanent heterotopic ossification at the injection site after diphtheria-tetanus-pertussis immunizations in children who have fibrodysplasia ossificans progressiva. *J Pediatr* 1995;126:762-764.
25. Moriatis JM, Gannon FH, Shore EM, Bilker W, Zasloff MA, Kaplan FS. Limb swelling in patients who have fibrodysplasia ossificans progressiva. *Clin Orthop Rel Res* 1997;336:247-253.
26. Cohen RB, Hahn GV, Tabas J *et al.* The natural history of heterotopic ossification in patients who have fibrodysplasia ossificans progressiva. *J Bone Joint Surg Am* 1993;75:215-219.
27. Kussmaul WG, Esmail NA, Sagar Y *et al.* Pulmonary and cardiac function in advanced fibrodysplasia ossificans progressiva. *Clin Orthop* 1998;346:104-109.
28. Kaplan FS, Shore EM, Glaser DL, *et al.* The medical management of fibrodysplasia ossificans progressiva: current treatment considerations. *Clin Proc Intl Consort FOP* 2003;1:1-81.
29. Kaplan FS, Shore EM, Glaser DL, *et al.* The medical management of fibrodysplasia ossificans progressiva: current treatment considerations. *Clin Proc Intl Clin Consort FOP* 2005;1:1-71.