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Fibrodysplasia Ossificans Progressiva

Report of a case

Abstract: Fibrodysplasia ossificans progressiva (FOP) is a rare, dominantly inherited connective tissue disorder, characterized by congenital malformations of the great toes and thumbs and progressive heterotopic ossification of soft tissues of the trunk and extremities.

The ossifications typically appear within the first decade of life and result in progressive ankylosis of the joints and severe disability. So far, more than 600 cases have been reported worldwide and presently there is no effective treatment or prevention. During the early phase, particularly prior to the development of calcifications, it is often mis-diagnosed as soft tissue sarcomas or fibromatoses, which considerably delays the diagnosis, and therefore leads to unnecessary and perhaps life threatening treatments. Herein, we present a case of a 21-year-old male with FOP diagnosed late in the course of his disease.

Keywords: Myositis Ossificans, Musculoskeletal Diseases, Muscular Disease.

Case Presentation

The patient was a 21-year-old man referring for surgical treatment of restricted jaw movement. His major complaint was progressive inability to open his mouth for the past two years so that he could only take liquids. The attending surgeons requested a preoperative chest radiogram. This showed large chunky calcifications, raising the possibility of fibrodysplasia ossificans progressiva (FOP). As a consequence, further imaging studies were recommended.

His past medical history was significant for a painful subcutaneous mass in his supraclavicular region at the age of five. The mass was surgically resected, but it recurred four months later. This was followed by appearing of additional masses in paraspinal, posterior cervical, and left gluteal regions and also posterior aspect of the chest wall bilaterally.

As these masses underwent ossification, ankylosis of the nearby joints developed resulting in severe limitation of movement. During this period, he underwent two more surgical operations to restore the decreased range of motion in his neck and shoulders. The results of his surgical biopsies were interpreted as desmoid fibromatosis. Unfortunately, the procedures performed had resulted in only temporary relief of his symptoms and ultimately, the restriction of jaw movement ensued.

There was no positive family history. The parents were not related. When the patient returned for additional work-up, a physical examination revealed multiple firm non-tender subcutaneous masses, malformation of the great toes, mild scoliosis and reduced range of motion in multiple joints. Laboratory studies were all normal.

Radiographic examination of the chest showed mature bars of ossification bridging the overlying soft tissues along the postero-lateral chest walls, right supra-clavicular region, and right sternocleidomastoid muscle. There was also irregularity of the lower ribs near the attachment of ossifications (Figure 1).

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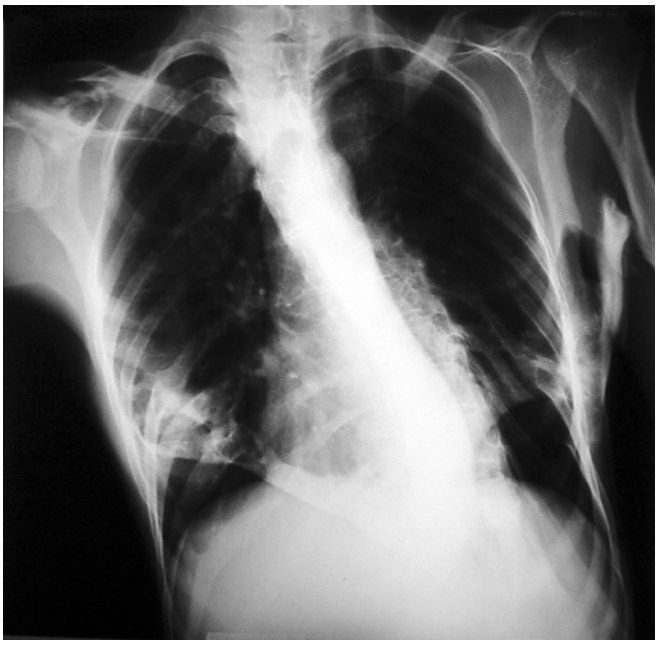

Figure1: PA chest radiography shows soft tissue ossification in postero-lateral portion of chest wall, right supra-clavicular region, and SCM muscle with some lower ribs deformity around ossified masses.

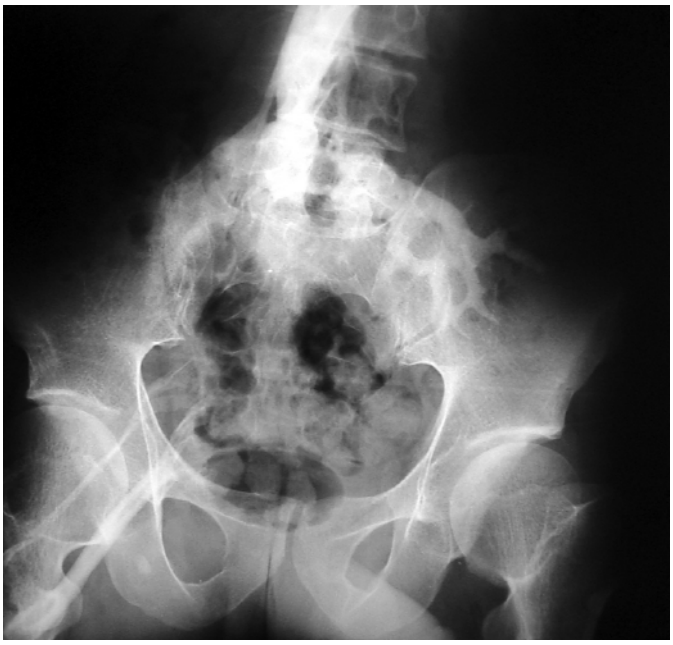

Figure 2: Pelvic X-ray shows linear ossification in the right paraspinal region, supromedial part of left iliac wing and in right iliopsoas region with the femoral neck broadening.

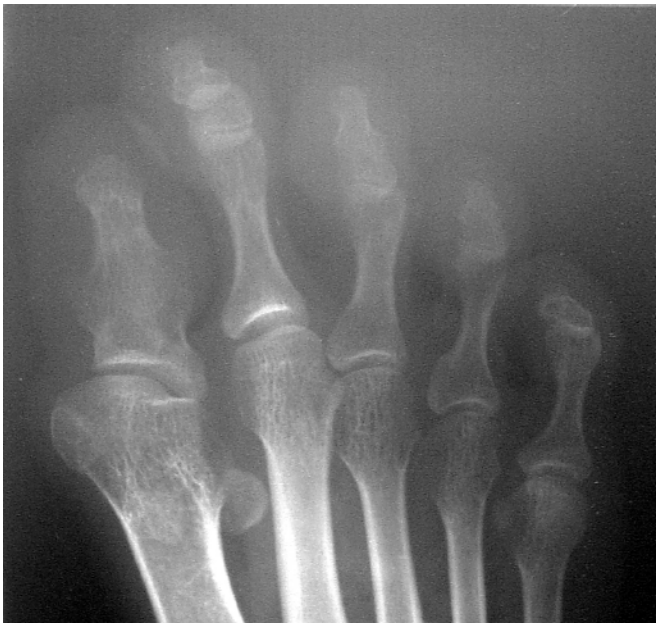

Figure 3: Graphy of forefoot shows hallux valgus and fusion of the phalanges of the great toe.

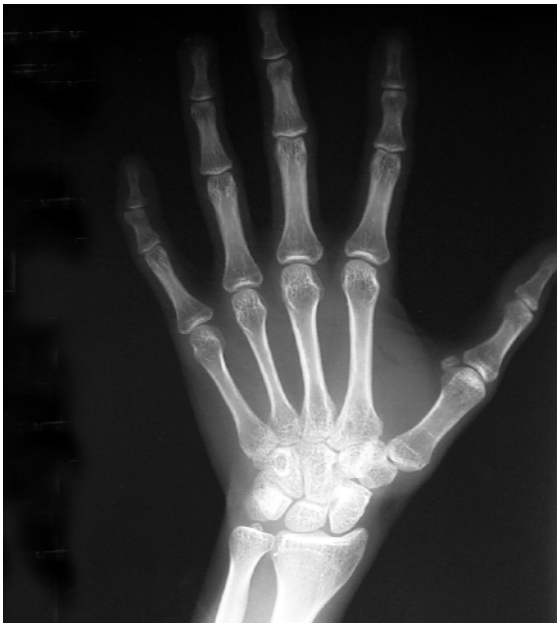

Figure 4: Hand X-ray shows, clinodactily of the fifth finger

A skeletal survey was performed to prove the initial radiological impression of FOP. Pelvic radiology showed linear ossifications in right paraspinal region, supromedial port of the left iliac wing, and right iliopsoas region (Figure 2). Forefoot radiography showed hallux valgus deformity and fusion of phalanges of the great toe (Figure 3). Radiography of hand showed clinodactily of the fifth finger (clinically apparent) and shortening of the middle phalanx (Figure 4).

Similar ossifications were noted in the nuchal ligament, apparent on the lateral cervical X-ray.

On coronal CT scans of paranasal sinuses, ossification of the lateral pterygoid muscle was noted on the right side (Figure 5) which resulted in the fusion of mandible to the lateral pterygoid process.

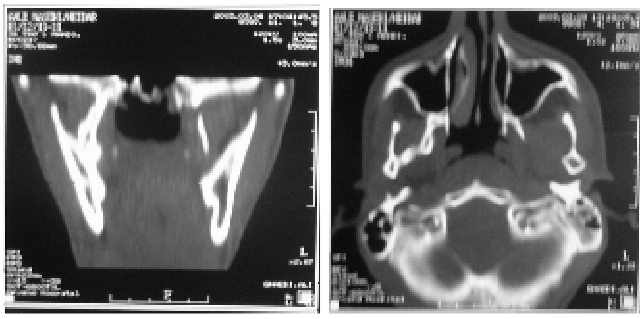

Figure 5: Axial and coronal cuts in CT scan of paranasal sinuses without contrast shows ossification of right lateral pterygoid muscle and fusion of the mandible to the right lateral pterygoid process.

Discussion

FOP is a rare autosomal dominant hereditary disorder.[1] Most cases are due to spontaneous mutations.[2]

Guy Patin first described this disorder in 1648.[2] So far, more than 600 cases have been reported worldwide.[1] The defected gene has recently been mapped to human chromosome 4q27-31.[3] Despite the unique clinical features, afflicted patients are frequently misdiagnosed in childhood.

The mean delay in reaching the correct diagnosis after the onset of ectopic ossifications was found to be about 3 years (range 0-14) in different reports.[1]

FOP can be suspected at birth, before any soft tissue lesions occur, if the typical congenital skeletal malformations, especially short great toe are recognized

The most characteristic skeletal malformation is the shortening of great toes[3] due to synostosis of the phalanges[2] and hallux valgus deformity. Many children also have similar malformations of thumbs.[3] Malformations of great toe occur in more than 95% of cases,[1] as was apparent in our patient (Figure 3).

The earliest symptom is appearance of painful subcutaneous nodules and masses, particularly around the head and neck. Dorsal paraspinal muscles, shoulders and elbows also could be first involved. Later on, pelvic girdle and lower extremities are affected. Subsequently, extensive ossification of muscles, ligaments, tendons and fascias of the thorax, along with encasement of large joints of extremities (*e.g.*, shoulders and hips) ensues, which leads to clumsy gaits, falling, fracture, restricted chest expansion and ventilatory problems, and subsequent pneumonia.[6]

Additional radiographic findings include shortened broad femoral necks pseudo-exostoses[2], delayed skeletal maturation, prominent calcaneal spur, large epiphyses, due to hypotonia and rarely enchondromas. Furthermore, an association of the disease with synovial chondromatosis has been reported.[3]

Facial musculature, smooth muscles of the tongue, larynx, gastrointestinal tract (including viscera) and diaphragm are spared.[6]

Bone scans are abnormal, before any ossifications can be seen by plain radiography. Gallium 67 citrate and Tc-99-diphosphonate bone imaging agents are localized in myositis ossificans.

CT scanning and MR imaging detect early swelling of muscular fascial sheets earlier than plain radiography. Ultrasound shows increased echogenic material in the soft-tissue mass lesions within muscles and connective tissue. However, these imaging modalities are more expensive than conventional radiology.

The radiographic differential diagnoses of patients with progressive mineralized masses include dermatomyositis, tumoral calcinosis, some bone and soft-tissue sarcomas and fibromatoses.[2]

The growth restriction of antero-posterior diameter of vertebral bodies, especially in the neck, confuses the picture with that of Klippel-Feil syndrome.[6]

The earliest histopathological finding is an intense perivascular lymphocytic infiltration, followed by death of skeletal muscle and its replacement with a highly-vascular fibroproliferative soft tissue.

The soft tissue rapidly matures through an enchondral process to form heterotopic bone[3] but mistaken histologic diagnoses such as soft tissue sarcoma or fibromatosis could lead to inappropriate treatment.[4]

There is no established treatment for this disorder. Corticosteroids, non-steroid anti-inflammatory drugs, etidronate, warfarin, radiotherapy and surgery have been used. Nonetheless, none of them has been proved effective.

Early diagnosis precludes unnecessary biopsies which exacerbates heterotopic ossification at sites remote from the operative field. Once FOP is diagnosed, intramuscular injection and local anesthetics for dental blocks should be avoided[3,5] and the patient should be protected from injuries.[3]

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