Case Report 6

Fibrodysplasia Ossificans Progressiva : A Case Report

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Introduction

Fibrodysplasia ossificans progressiva, also known as myositis ossificans progressiva, stone man disease or Munchmeyer's disease is a rare connective tissue disorder characterized by heterotrophic ossification of extra skeletal sites such as muscles, ligaments and tendons resulting in severe disability.

Case Report

A fifteen-year-old girl presented with a history of episodic spontaneous swelling of the inter scapular region for two months duration. These lumps were associated with throbbing pain at onset which lasted a few days followed by resolution of the swelling leaving firm immobile mildly tender lumps of the size of about 3 cm. Ultrasound scan (USS) at this point revealed subcutaneous benign hypo echoic lesions without an increase in vascularity. Excision biopsy was carried out following which she developed painful neck and chest wall swelling. At this point USS scan and CT scans reveled inflammatory changes in trapezius, scalene anterior and sternocleido mastoid muscles with subcutaneous oedema. The histology revealed fibrotic muscle, vascular stroma, scattered lymphocytes and osteoclast like giant cells, immature bone formation surrounded by osteoblasts and injured myosites suggestive of myositis ossificans.

She further developed restricted movements of the left shoulder at which point she was referred for tertiary hospital for second opinion where she underwent a contrast enhanced CT which revealed coarse calcification at the origins of right latssimus dorsi at the inferior angle of the scapula, spinous process of T10 vertebra and ileac crest. There was also calcifications at the origin of serratus anterior at the 4-6 ribs and in the right scalene anterior at its insertion to the 1st rib. These findings were in keeping with dystrophic calcification seen following trauma or strain. With this she was offered a tenotomy of lattismus dorsi muscle to improve shoulder mobility. Histology at this procedure revealed skeletal muscle tissue with central area of fibrosis and foci of metaplastic cartilage with enchondral ossification which was again concluded as myositis ossificans.

She was referred to the rheumatology unit for further evaluation where she underwent screening for possible immune mediated myopathy (ESR 7mm/1st hr, CRP 1.9mg/dl, CPK 49u/l, ANA negative) and disorders of calcium metabolism (ALP was 132.2 U/l, AST 23.6 U/l, ALT 11.7 U/l, GGT 17.7 IU/l, Serum creatinine 50.1 µmoll, Serum Calcium 2.38 mmol/l, serum PTH 17.4 pg/ml, serum PO43- 0.99 mmol/l, Vitamin D level 21.8 nmol/l) all of which were normal except for low vitamin D levels. However as vitamin D deficiency does not give rise to this clinical picture it was excluded as the cause

for her presentation. Endocrine opinion was also taken at this point and it was concluded that this is unlikely to be a disorder of calcium metabolism.

With the given history of spontaneous myositis ossificans at multiple sites without a history of previous significant trauma with characteristic flare ups and with the presence of characteristic bilateral hallux valgus deformity (Figure 1) a diagnosis of Fibrodysplasia Ossificans Progressiva was made. She had a repeat CT scan at 5 months from the onset which showed extensive longitudinally extending dense calcifications in bilateral latissimus dorsi, serratus anterior, serratus posterior inferior, erector spinae, capitis and quadratus lumborum muscles which was in keeping with the diagnosis (Figure 2). Second opinion was taken from tertiary care rheumatologist who also agreed with the diagnosis and the management plan.

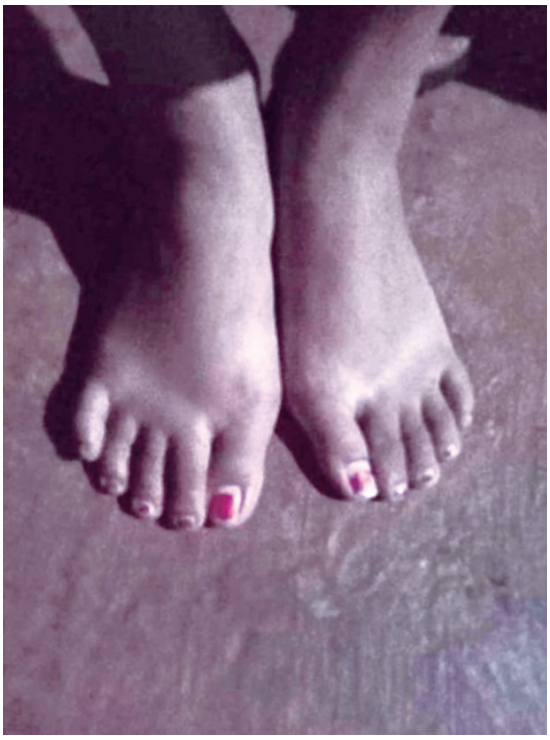

Figure 1

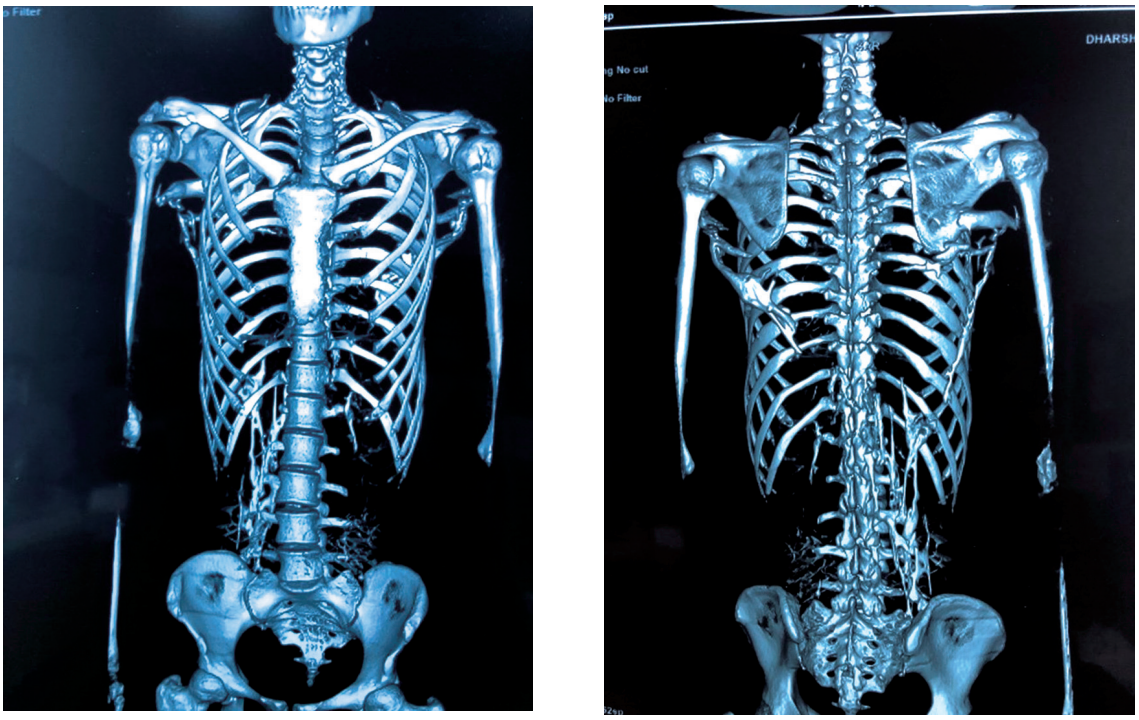

Figure 2

She was started on Celecoxib 200mg bd, Vitamin C 400 mg daily, Montelucast 10 mg daily and desloratadine 5m daily. Flare ups (acute attacks with new onset lumps) were treated with Prednisolone 1mg/kg/day for 4 days. Her vitamin D was corrected with oral D3 200000IU 2 doses two weeks apart followed by 2000 IU daily. She was given IV pamidronate 1mg/kg/day for 3 days for one flare up which did not respond to steroids. She was advised to avoid falls, injuries, exposure to infections, surgical procedures and IM injections. She was advised

to take prednisolone 1mg/kg/day for 3 days following trauma, surgical or dental procedures as prophylaxis. Her immunization was up to date and she was given Covid 19 pfizer vaccine subcutaneously. She was offered occupational therapy and gentle physiotherapy to aid her with the activities of daily living. After 8 months of onset she had limited mobility of left shoulder and neck movements and continued to get flares once every three to four months.

Discussion

Fibrodysplasia ossificans progressiva (FOP) is a heritable disease inherited in an autosomal dominant pattern. However, most of the cases are sporadic. It is caused by a mutation of ACVR1/ ALK2 gene encoding a bone morphogenetic protein type 1 receptor1. The prevalence of this condition is 1 in 2 Million2.

Usually, patients develop clinical signs and symptoms during the first decade of life. They present with episodic painful soft tissue swelling (flare ups) which may resolve or result in ribbon like ossification of underlying muscles, ligaments, tendons and aponeuroses. Neck, back and shoulders are the first sites to be involved. The swelling typically shows three stages: first painful stage (first few weeks) followed by painless induration phase and the late phase (after 12 weeks) which shows radiographic ossification3. Flare ups are triggered by injury, viral infection, surgical procedures, muscle stretching and intramuscular injections. The heterotrophic ossification progresses and spans across joints leading to limited mobility. This is a progressive disease which leads to severe disability including feeding difficulty caused by ankylosis of the jaw and respiratory insufficiency due to reduced mobility of the thoracic cage. The average life expectancy is 40 years.

The patient with FOP has characteristic bilateral hallux valgus deformity with malformed first metatarsals and fused interphalengeal joints. They may also have short malformed thumbs, clinodactyly and neck stiffness. Hearing loss may be associated in about 50% of the cases3,4.

Typically, biochemical studies are normal in these patients however alkaline phosphate maybe elevated during heterotrophic ossification phase of flare ups. Characteristic radiographic findings include soft tissue ossification, malformed first metatarsals and fused interphalangeal joints. There may be medial tibial osteochondromas, fusion of posterior elements of cervical spine and malformation of thumbs.

Diagnosis can be confirmed by genetic testing. Genetic testing was not carried out in our patient due to unavailability, however her clinical features were in keeping with the diagnosis with characteristic great toe malformations and sites of heterotrophic ossification and the presence of characteristic flare ups.

Other condition that needs to be excluded in the presence of progressive soft tissue ossification is progressive osseous heteroplasia (POH). In POH ossification starts from cutaneous tissue and extends to involve deep connective tissue , lacks flare ups and the great toe abnormalities.

Aggressive juvenile fibromatosis can present with rapidly growing soft tissue swelling but can be differentiated from FOP in the absence of great toe malformations and heterotrophic ossification.

Extensive calcinosis cutis (Calcinosis universalis) can rarely be seen in autoimmune connective tissue diseases like juvenile dermatomyositis and systemic sclerosis. Typically calcinosis start in limbs and is associated with other clinical features of connective tissue disease and auto antibodies. Histological findings are that of dystrophic calcification and differ from that seen in myositis ossificans.

There is no definitive management for FOP. The current treatment considerations by The international clinical council for FOP (ICC) and consultants (2022) include management of flare ups with steroids (prednisolone 1-2mg/kg/day) for3- 4 days, steroid prophylaxis (prednisolone 1mg/kg/day for 3 days) following blunt muscle trauma, surgical and dental procedures and Cox 2 inhibitors to ameliorate pain5.

IV Bisphosphonates6, ascorbic acid 7 and mast cell stabilizers have been used to achieve some improvement in disease course. Patient education on avoidance of precipitants, supportive care with occupational therapy, gentle physiotherapy (avoiding passive muscle stretching), addressing mental health issues, orthotics, addressing respiratory health and prevention of viral infections play an important role in the management.

Conclusion

It is important to consider FOP in the differential diagnosis of children presenting with progressive soft tissue swelling and look for characteristic clinical features to minimize surgical procedures which would lead to rapidly worsening of the condition.

References

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