Myositis ossificans progressiva

Introduction

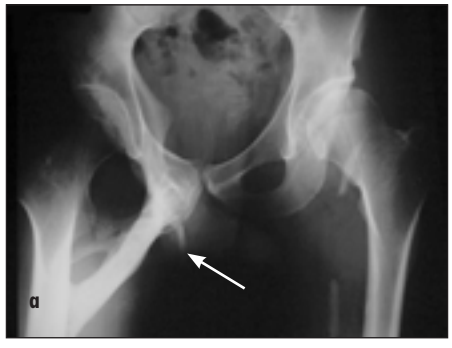
This article describes a case of myositis ossificans progressiva, also known as fibrodysplasia ossificans progressiva, from initial presentation to adulthood. Usually, there is a substantial delay before the correct diagnosis is made. Surgery, including biopsy, is hazardous because of the propensity for ectopic bone formation. However, limited surgery may be appropriate for certain lesions.

Discussion

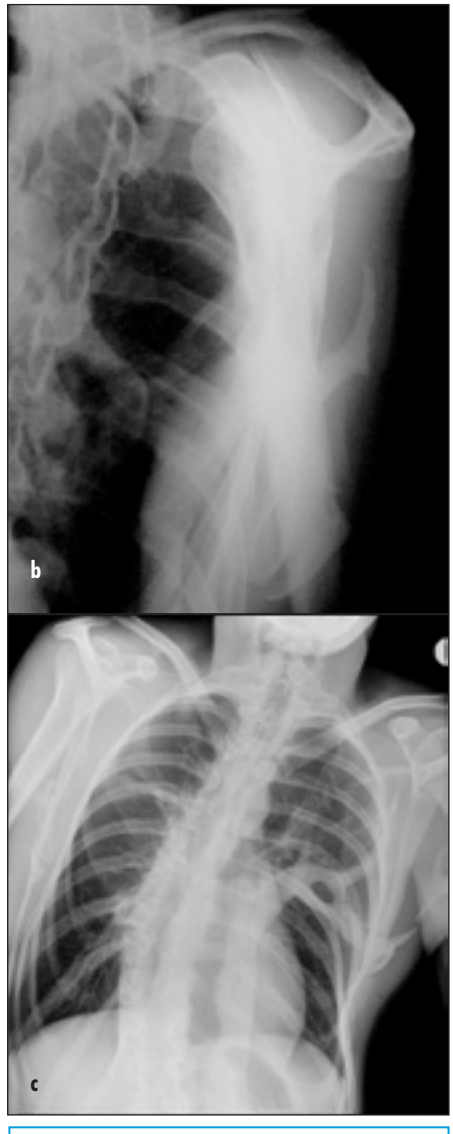
Myositis ossificans progressiva is a rare autosomal dominant condition with variable expressivity and complete penetrance occurring in about 1 in 2 million live births (Traore et al, 2004), with a point prevalence of 0.61 per million in the UK (Conner and Evans, 1982).

Onset is usually in childhood with the condition being diagnosed on clinical grounds. It is characterized by progressive heterotopic ossification of soft tissue (*Figures 1a–c*), with great toe microdactyly and hallux valgus (*Figure 2*). Other features include short thumbs, broad femoral necks (*Figure 1a*), fifth finger clinodactyly, malformed cervical vertebrae, scalp baldness, deafness and mild mental retardation. Soft tissue swelling of aponeuroses, fasciae and tendons of the neck, dorsal trunk and proximal limbs commonly precedes heterotopic bone formation and is often accompanied by pain and fever. In addition, surgical trauma, injury or deep soft tissue injection may be inducing factors (Ahn et al, 2003). This may occur as an exostosis (Bridges et al, 1994). Indeed an exostosis of upper medial aspect of the right tibia was the first sign of the disease in this case.

Figure 1. Radiographs showing sites of heterotopic ossification. a. Anteroposterior view pelvis. Note the ischiopubic spur (arrow), ischiofemoral bar and degenerative change at right hip. b. Lateral view left shoulder. c. Posteroanterior view chest.



Mandibular condyles are commonly flat and broad and the sternocleidomastoid is frequently involved. Cohen et al (1993) found the most common sites of early heterotopic ossification were the neck, spine and shoulder girdle. Following the tibial exostosis, successive sites of ossification in the patient in the authors' case were in the rectus femoris followed by the lumbar spine and shoulder girdle.



Case Report

A 23-year-old man with myositis ossificans progressiva was seen in the orthopaedic clinic with pain on sitting as a result of a bony spur extending caudally from the right ischiopubic eminence. The fragment of bone was mobile and exquisitely tender on palpation. There was a recent history of falling out of bed which was thought to be relevant to its onset. A pelvic radiograph (*Figure 1a*) showed an ischiopubic spur in conjunction with a substantial ischiofemoral bar that had effectively fused the right hip. He also had ectopic ossification deformities of the spine, left shoulder (*Figure 1b*) and thoracic cage (*Figure 1c*).

He initially presented at 6 years of age with a palpable exostosis of the proximal right tibia. Over the next 3 years he developed several haematomas with subsequent calcification often following minor trauma. By the age of 9 years, at which time the diagnosis was made, calcification was present at multiple sites and corresponding joint mobility was reduced. A maternal history of Addison's disease had prompted the exclusion of autoimmune disorders. Repeated coagulation screens were also normal. The diagnosis was eventually made on the basis of short hypoplastic halluxes (*Figure 2*) which are the classical dysmorphic markers of this condition. This was supported by biopsy, the tissue showing features of fibroblastic proliferation. Unfortunately the biopsy site was further affected by ossification. He was commenced on a course of etidronate and physiotherapy.

It was decided to proceed with limited surgery to excise the ischial spur. The patient accepted the possibility of recurrence or exacerbation following the procedure, the rationale being that any subsequent ossification was unlikely to form such a sharp spur (*Figure 1a*). Following surgery discomfort has been dramatically reduced and he is able to sit without pain.

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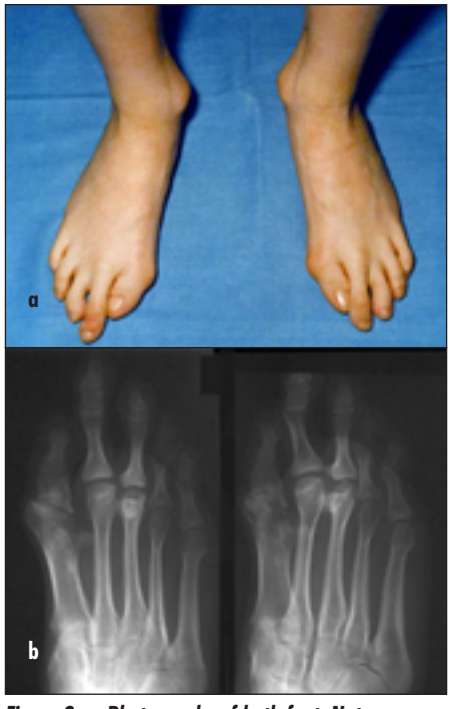

Figure 2. a. Photographs of both feet. Note hypoplastic short hallux. b. Radiographs (anteroposterior and oblique) of right foot.

Differential diagnosis includes rigid spine syndrome, arthrogryposis multiplex congenita, extraskeletal osteomyelitis and calcinosis universalis (Traore et al, 2004). Smith et al (1996) found that the original diagnosis was usually wrong and that the mean delay in correct diagnosis after initial ectopic ossification was 2.7 years (range 0–14 years). In this patient's case the time to correct diagnosis was 2.6 years.

Bone morphogenetic proteins (BMPs) are signalling molecules, belonging to the transforming growth factor-beta superfamily, involved in skeletogenesis (Wozney and Rosen, 1998). BMP-4 messenger ribonucleic acid (mRNA) and protein are uniquely over-expressed in lymphocytes and lesion cells of myositis ossificans progressiva patients, although the BMP-4 gene is not mutated.

Ahn et al (2003) found paresis of a BMP-antagonist response suggesting a defect in the negative feedback loop regulating skeletogenesis. They hypothesized that this may contribute to increased BMP-4 activity in myositis ossificans progressiva. This could lead to the development of targeted therapies for patients with myositis ossificans progressiva.

Although there is no effective treatment, Brantus and Meunier (1998) suggested some benefit from treatment with intravenous etidronate during an acute exacerbation. Death commonly occurs in the second or third decade as a result of pulmonary complications.

It is important to recognize the clinical features of this condition to prevent unnecessary and potentially harmful biopsies – indeed in this patient inflammation adjacent to the area of biopsy had reoccurred within 2 years. However, on the basis of the authors' experience, limited surgery – with meticulous attention to haemostasis – may be justified in certain situations. **BJHM**

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