Progressive osseous heteroplasia: a rare case of late onset

Sir, Progressive osseous heteroplasia (POH) is a rare inherited ossifying disorder of infancy, characterized by diffuse cutaneous and deep connective tissue ossifications. We report a rare case of POH that appeared in adulthood.

In April 2001, a 52-yr-old woman, with no familial history of abnormal ossification, was admitted for pain and stiffness of the lower limbs. She first experienced symptoms in 1985, with knee, calf and ankle pains, and later suffered from lower limb stiffness.

Physical examination revealed subcutaneous ossifications of the lower limbs, hands and elbows, with impaired joint mobility, principally involving the left side. X-ray showed diffuse ossifications of all four limbs (Fig. 1A) and paravertebral muscles. Lower limbs computed tomography showed diffuse calcifications of the fascia, tendons, muscles and subcutaneous fat. Alkaline phosphatase and C-telopeptide of collagen 1 (CTX) levels were twice normal. Calcium, phosphate and parathyroid and thyroid hormones serum levels were normal. Bone scan showed multiple areas of enhanced isotope uptake (Fig. 1B). No dysmorphic or metabolic abnormalities were observed. POH was diagnosed on the basis of the patient’s clinical and radiological profiles, despite the absence of the GNAS1 gene mutation. Etidronate (1g) was administered intravenously in January 2002, with no improvement.

The patient was lost to follow-up until May 2005. Joint mobility had worsened, due to the progression of ossifications in areas of previous strong isotope uptake. Biological findings were similar to those obtained in 2001. Bone scan examination revealed persistent areas of technetium uptake. All these features were consistent with continuing active disease.

POH is the most recently described inherited ossifying disease with only a few reported cases [1–9]. POH was initially described in patients diagnosed with fibrodysplasia ossicifera progressiva (FOP), but displaying atypical features [1].

FOP is characterized by diffuse progressive heterotropic ossifications, associated with big toe deformities. POH can be distinguished from FOP by the presence of cutaneous ossifications, the absence of congenital musculo-skeletal malformations or inflammatory tumour-like swellings and an asymmetric distribution of lesions. Furthermore, POH intramembranous ossification, i.e. ossification of connective tissues by differentiation of mesenchymal cells into osteogenic cells, results in progression of ossifications from skin and subcutaneous tissue into skeletal muscle. Whereas, predominance of endochondral ossification in FOP, i.e. conversion of cartilage into bone, results in a proximal to distal extension.

According to the 19 previous reported cases, POH was more frequent in females (17/19). Ossifications were mainly located on the limbs (18/19), or even axial (9/19), and often displayed hemimelic predominance (12/19), as in our case. Usually, first symptoms occur in childhood (birth to 3 yrs). We describe the first case with onset and persistent progression during the adulthood. Mild cases of late-recognition have been described in families of severely affected patients, but are characterized by non-extensive subcutaneous ossifications with slower progression [9]. In patients with early disease onset, progression generally ceases by adulthood [1]. Our patient might have developed mild ossifications in childhood. However, as she was of normal size, with no inequality in limb length, we presume that the disease was quiescent during growth.
Mycophenolate mofetil for maintenance of remission in idiopathic retroperitoneal fibrosis

SIR, Retroperitoneal fibrosis (RPF) is a rare disease characterized by periaorttic inflammation and fibrosis that extends to adjacent abdominal structures. Early recognition and treatment is important to prevent secondary complications such as renal failure (secondary to ureteric obstruction). We have recently reviewed the epidemiology, clinical features and management of RPF in this journal [1]. Medical management consists mainly of use of steroids [2] and immunosuppressive drugs. Azathioprine [3], cyclophosphamide [3], methotrexate [4] and ciclosporin [5] have been used successfully for disease control associated with regression of the periaorttic mass. We report a patient with RPF (idiopathic type) who was treated with steroids, methotrexate and cyclophosphamide but disease control was eventually achieved with mycophenolate mofetil (MMF).

A 52-yr-old lady presented with a 5-month history of lethargy, profuse nocturnal sweating, weight loss, diffuse chest and abdominal pain. She was treated with atenolol for migraine. She smoked cigarettes for 15 pack years. Clinical examination was normal. Initial investigations revealed raised inflammatory markers: erythrocyte sedimentation rate (ESR) 130 mm/h and C-reactive protein (CRP) 190 mg/l. Full blood count, renal/bone/hepatic profile were normal. Infection screen was negative. Chest X-ray was normal. A contrast-enhanced computed tomography (CT) scan of her chest and abdomen (Fig. 1A) showed enhancing soft tissue around the abdominal aorta, proximal coeliac axis and superior mesenteric artery (SMA). There was no evidence of hydrenephrosis or spread to other structures. This appearance was suggestive of RPF (periaortitis). Temporal artery biopsy, ANA, ANCA, anti- phospholipid antibody, serum electrophoresis and VDRL were performed to exclude secondary causes and were normal.

She was treated with prednisolone 60 mg daily with a plan to gradually taper the dose and with this her symptoms and inflammatory markers improved (ESR 4 mm/h CRP 7 mg/l). Gradually prednisolone was reduced to 20 mg daily. Methotrexate 7.5 mg per week was added and prednisolone was reduced to 15 mg daily. Six months later she remained asymptomatic with normal inflammatory markers and her CT scan showed improvement (Fig. 1B). She was then started on mycophenolate mofetil (MMF) 2 g daily. She has been on MMF for 6 months and has remained asymptomatic with normal inflammatory markers. CT scan showed further improvement (Fig. 1C).

No further cases of RPF have been reported with the use of MMF. It is possible that MMF may have a role in the management of RPF. Further large studies are needed to confirm our findings.