Tumour-induced osteomalacia

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Tumour-induced osteomalacia (also known as oncogenic osteomalacia) is an uncommon condition. The fibroblast growth factor-23 (FGF-23), a polypeptide secreted by mesenchymal tumours, causes phosphaturia, which in turn results in defective mineralisation. In addition, FGF-23 causes suppression of the enzyme 1α hydroxylase located in the proximal convoluted tubules of kidneys and responsible for final activation of vitamin D (from 25-hydroxy vitamin-D to 1,25-dihydroxyvitamin-D).[1] Once the tumour causing the osteomalacia is found, its excision usually results in complete remission of the bone disorder.[2] Herein, we report on a patient who presented to us with the features of oncogenic osteomalacia.

A 32-year-old woman born of non-consanguineous parents complained of gradually increasing proximal muscle weakness of both lower limbs over 1 year in February 2012. She also had pain in both hips while walking, which restricted her daily activities. She had no history of any chronic gastro-intestinal illness, and was not taking medication which might affect bone metabolism. Nor was there a family history of any similar illness. Clinical examination revealed severe proximal muscle weakness in both lower limbs. Active movements like external rotation and abduction at the both hips were painful. Otherwise the examination was unremarkable.

Biochemical evaluation revealed hypophosphataemia with phosphaturia (Table). Radiology of the hips showed bilateral femoral neck pseudofractures (Fig 1). These abnormalities favoured a diagnosis of hypophosphataemic osteomalacia. Further work-up yielded a high FGF-23 level and computed tomography of the paranasal sinuses showed a soft tissue tumour in the left ethmoidal sinus (Fig 2).

The patient was treated with phosphate supplements and underwent complete excision of the left ethmoidal sinus mass. Histopathological examination confirmed the diagnosis of a

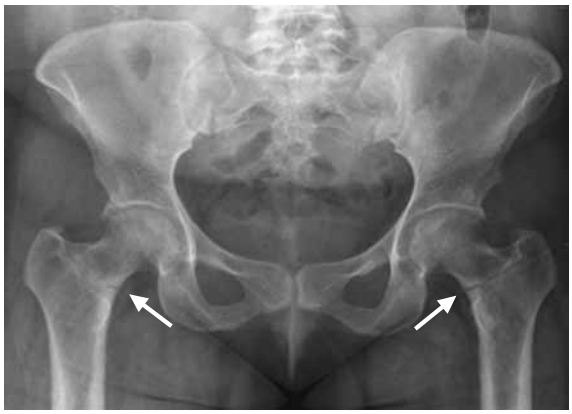

FIG 1. Pseudofractures seen in both femoral neck (arrows)

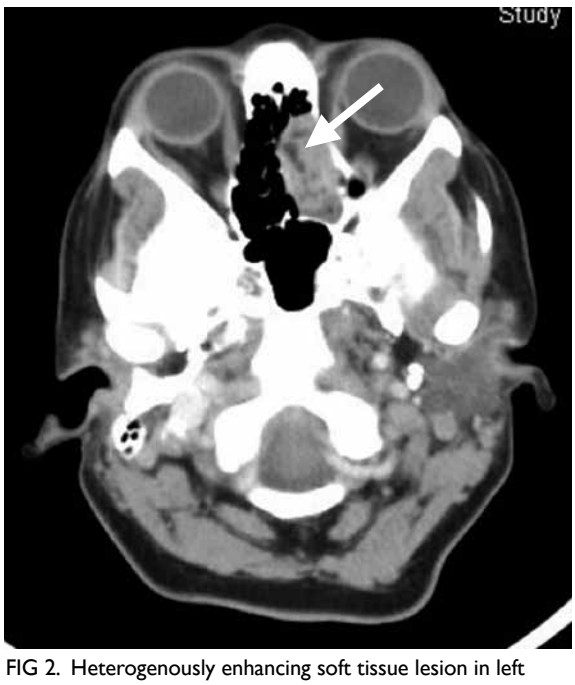

FIG 2. Heterogenously enhancing soft tissue lesion in left posterior ethmoid sinus (arrow)

TABLE. Biochemical parameters

Variable	Value	Reference range
Serum calcium (mmol/L)	2.29	2.10-2.55
Serum creatinine (μmol/L)	80	46-92
Serum phosphate (mmol/L)	0.45	0.80-1.45
Serum alkaline phosphatase (U/L)	105	40-125
Serum 25(OH) vitamin-D (ng/mL)	56	30-75
Serum parathyroid hormone (pg/mL)	58	8-74
Serum electrolyte (mmol)		
Potassium	4.2	3.5-5.0
Bicarbonate	24	22-29
Chloride	108	95-105
Serum albumin (g/L)	49	35-50
Plasma FGF-23 (RU/mL)	>2500	10-96

Abbreviation: FGF-23 = fibroblast growth factor-23

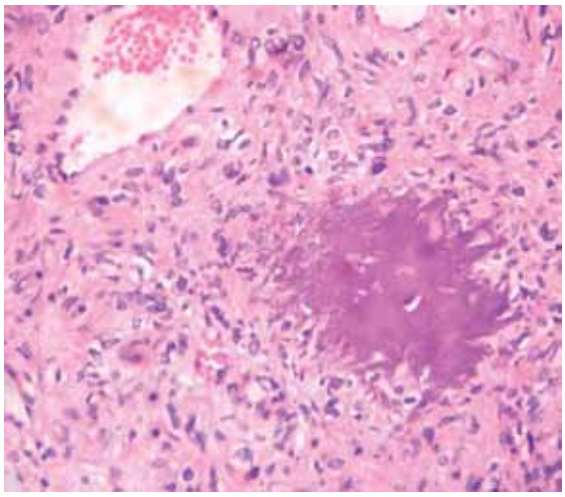

FIG 3. High-power view showing distinctive grungy pattern of matrix calcification with surrounding bland small round-to-spindle cells (H&E; original magnification, x 40)

phosphaturic mesenchymal tumour. The patient remained stable after surgery. Two months later she was asymptomatic, by which time her muscle weakness had resolved markedly. Respective serial serum phosphate concentrations were 0.9, 1.00, and 1.35 mmol/L at 1, 2 and 4 weeks after surgery. After surgery, her plasma FGF-23 levels were undetectable.

Phosphaturic mesenchymal tumours are rare mesenchymal tumours and mostly comprised of a single histological entity with mixed connective tissue (designated PMT-MCT). Such tumours can occur in the soft tissue or bone.[3] Most PMT-MCTs are histologically and clinically benign with rare instances of malignancy. Microscopically, PMT-MCTs are variable in appearance, usually being composed of small, bland round-to-spindle cells embedded in a vascular to myxochondroid matrix with variable amounts of mature adipose tissue (Fig 3). This matrix calcifies in an unusual 'grungy' fashion, inciting an osteoclast-rich and fibrohistiocytic response. A very prominent feature of PMT-MCT is its elaborate intrinsic microvasculature. Malignant PMT-MCTs resemble undifferentiated pleomorphic sarcomas or fibrosarcomas.[3] After complete excision of the tumour, most patients improve dramatically[4] and become symptomatically, biochemically, and radiologically better. Such results should prompt the physicians to search for such treatable and potentially curable causes, whenever they encounter hypophosphatemic osteomalacia.

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