

PET/CT localisation of a scapular haemangiopericytoma with tumour-induced osteomalacia

Khadgawat R, Singh Y, Kansara S, Tandon N, Bal C, Seith A, Kotwal P

ABSTRACT

Oncogenic osteomalacia, or tumour-induced osteomalacia (TIO), is a rare paraneoplastic syndrome characterised by hypophosphataemia, phosphaturia, inappropriately low serum levels of 1,25-dihydroxyvitamin D for hypophosphataemia. TIO is caused by mesenchymal tumours that secrete phosphaturic substances, leading to increased renal wasting of phosphates. These tumours are very small in size and grow slowly. Localisation of these tumours has always been difficult with the available biochemical and imaging techniques. At times, despite all efforts, the tumour could not be localised. We report our experience with a 42-year-old woman with TIO where whole-body magnetic resonance imaging could not localise the tumour, a scapular haemangiopericytoma. PET/CT was helpful in the localisation of the tumour which, when surgically removed, resulted in the normalisation of biochemical parameters with clinical improvement.

Keywords: mesenchymal tumours, oncogenic osteomalacia, paraneoplastic syndrome, scapular haemangiopericytoma, tumour-induced osteomalacia

Singapore Med J 2009;50(2):e55-e57

INTRODUCTION

Oncogenic osteomalacia, or tumour-induced osteomalacia (TIO), is a rare paraneoplastic syndrome characterised by hypophosphataemia.⁽¹⁾ To date, only 120 cases of TIO have been described in the literature.⁽²⁾ TIO is caused by increased renal wasting of phosphates, secondary to phosphaturic substances secreted by certain mesenchymal tumours.⁽¹⁾ These tumours are very small in size and at times, are located at obscure sites. Localisation of these tumours has always remained difficult,⁽³⁾ and all available imaging modalities, such as computed tomography (CT) and whole-body magnetic resonance (MR) imaging, have been attempted for the localisation of these elusive tumours. There may be a long delay between the diagnosis of TIO and localisation of the tumour, ranging from five months to 16 years,⁽⁴⁾ with the longest gap

between the onset of symptoms and tumour localisation being reported as 16 years. In one instance, an extensive search could not localise the tumour for as long as 19 years after diagnosis.⁽⁵⁾ Recently, positron emission tomography (PET)/CT has been shown to be of use in the diagnosis and follow-up of one case of TIO.⁽²⁾ We report our experience with PET/CT in the localisation of a tumour in a case of TIO.

CASE REPORT

A 42-year-old woman presented with complaints of progressive and generalised muscle weakness and bone pains all over her body for the last five years. The bone pains initially started in the pelvic region, and later became generalised to involve the entire skeleton. As a result of bone pain and muscular weakness, the patient became largely confined to bed for the last two years, with minimal assisted mobility. She had fractured her right forearm two years ago and her left forearm one year ago, with minimal trauma. Her periods were regular with a total of four pregnancies. There was no significant family history of bone disease or fracture. Her general physical examination was normal except for a mild pallor. Cardiopulmonary system examination was also within normal limits. Musculoskeletal system examination revealed generalised bony tenderness, proximal muscle weakness (power 3/5 at shoulder and 4/5 at hip girdle) and positive rib and pelvic compression tests.

Investigations showed a normal haemogram except for mild hypochromic microcytic anaemia, normal liver and renal function tests, normal electrolytes and fasting blood glucose. Serum calcium was 8.5 mg/dL while serum phosphates were low at 1.6 (normal range of 3.5–5) mg/dL. Serum alkaline phosphatase was elevated at 448 (normal range < 225) IU. Serum intact PTH was 82 (normal range 7–53) pg/ml, while serum 25 vitamin D level was 27 (normal range 9–37) ng/ml. Tubular maximum reabsorption of phosphate (TMP–GFR) was calculated (n = 5) and it was consistently very low (1.3–1.6 mg/dL), with tubular resorption of phosphate ranging 94%–96%. Ammonium chloride loading test for distal renal tubular acidosis and bicarbonate loading test for proximal renal tubular acidosis were normal.

A skeletal survey showed multiple rib fractures, pseudofracture of the medial border of the scapula and

Department of
Endocrinology and
Metabolism,
All India Institute of
Medical Sciences,
Ansari Nagar,
New Delhi 110029,
India

Khadgawat R, MD, DM
Assistant Professor

Singh Y, MD, DM
Senior Resident

Kansara S, MD
Senior Resident

Tandon N, MD, PhD
Professor

Department of
Nuclear Medicine

Bal C, MD
Professor

Department of
Radiology

Seith A, MD
Assistant Professor

Department of
Orthopedics

Kotwal P, MS
Professor

Correspondence to:
Dr Rajesh Khadgawat
Tel: (91) 11 2659 3237
Fax: (91) 11 2658 9386
Email: rajeshkhadgawat
@hotmail.com

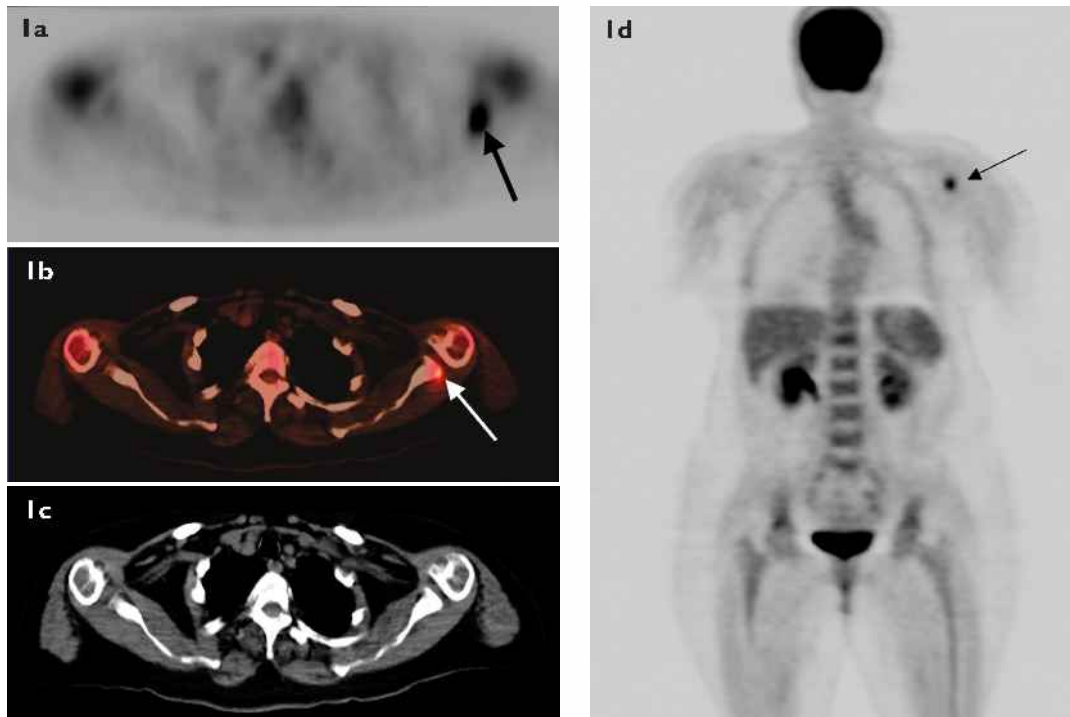


Fig. 1 (a) 18F-FDG PET image, (b) 18F-FDG PET- CT fusion image, (c) CT image, and (d) coronal 18F-FDG PET image all show increased uptake in the region of the neck of the left scapula (arrows).

pubic rami, partially-united old left forearm fracture and diffuse osteopenia. ^{99m}Tc methylene diphosphonate (MDP) bone scan was suggestive of metabolic bone disease. Bone mineral densitometry (BMD) by dual energy X-ray absorptiometry (DXA) showed osteopenia at the spine and femoral neck with osteoporosis in the forearm. Parathyroid ^{99m}Tc sestamibi scan and whole-body ^{99m}Tc -RBC blood pool scan were also normal. A diagnosis of hypophosphataemic osteomalacia, possibly oncogenic, was considered and phosphate supplementation was started along with calcium and vitamin D, while all efforts to localise the tumour were made. Sequential whole-body MR imaging was done, but no lesion was found except for a few enlarged lymph nodes which were biopsied and found to be non-specific.

As we could not find any lesion, the patient was discharged with calcium, vitamin D and phosphate supplementation. She showed some symptomatic relief but developed diarrhoea, which restricted more frequent phosphate supplementation. With therapy, serum phosphate levels increased but did not normalise. She continued treatment for the next one year but without any clinical improvement. Meanwhile, the PET facility had become functional in our institute. She was admitted and biochemical reevaluation was consistent with previous diagnosis. Whole body PET/CT (10 milli Cu F-18 FDG injected intravenously after one hour of rest) (Biograph Duo, Siemens, Germany) showed increased uptake in the region of the neck of the left scapula (Fig. 1). Selective

coronal, oblique and sagittal contrast-enhanced MR imaging of this region showed a well-defined lobulated 2.7 cm \times 1.2 cm \times 1.5 cm lesion in the soft tissue in the region of the neck of the left scapula (close to the posterior glenoid rim), which was hypointense on T1, hyperintense on T2, with homogeneous solid enhancement and evidence of restricted diffusion, suggestive of a vascular tumour (Fig. 2) The tumour mass was excised surgically and histopathological examination showed a haemangiopericytoma. Postoperatively, the serum phosphate returned to normal by the second postoperative day without any supplementation and remained within the normal limit for the next 14 days, when she was discharged from the hospital. Re-evaluation six months after surgery showed marked clinical improvement with normal levels of serum calcium and phosphate. By this time, the patient was able to conduct all her routine daily activities without any assistance.

DISCUSSION

In TIO, a rare syndrome characterised by hypophosphataemia, hyperphosphaturia, low plasma 1,25-dihydroxyvitamin D concentrations and osteomalacia, all biochemical and pathological abnormalities disappear after excision of the tumour.⁽¹⁾ These tumours are thought to secrete some phosphaturic substances that inhibit renal tubular reabsorption of phosphate. Fibroblast growth factor 23 (FGF23) is considered to be a major phosphaturic factor secreted by these tumours, although other factors, such as matrix extracellular phosphoglycoprotein and

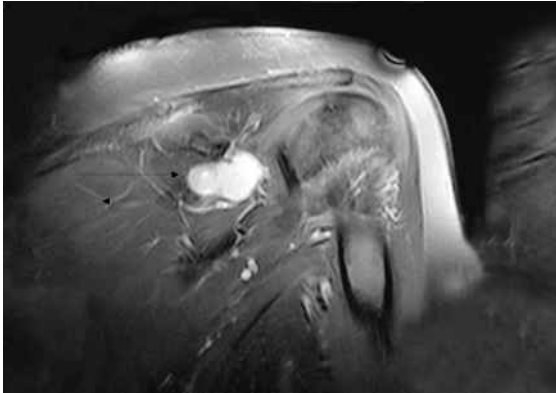


Fig. 2 Contrast-enhanced coronal T1-W MR image shows a well-defined, ovoid, homogeneously-enhancing mass lesion adjoining the posterior glenoid rim (black arrow).

secreted frizzled-related protein 4, have also been found to be involved in the pathogenesis of TIO.⁽⁶⁾ Our patient had typical clinical and biochemical manifestations of TIO, but the causative tumour could initially not be localised with the available facilities, including a whole-body MR imaging. Once PET/CT localised the lesion, site-specific MR imaging picked up the lesion, which was 2.7 cm × 1.2 × cm × 1.5 cm, a size which should not have been missed by MR imaging. Since previous MR imaging was performed one year before, it is possible that during this period the tumour had increased in size, enabling its detection. Once operated, the patient was completely cured of symptoms, with normalisation of serum phosphate levels.

Localisation of these tumours has always remained difficult because of their small size, very slow-growing nature, frequent location in unusual anatomical sites and their resemblance to common benign lesions.⁽³⁾ As a consequence, others have reported delays of more than 15 years in tumour localisation.^(4,5) Various modalities that have been used for tumour localisation are routine radiographs, ultrasonography, CT, MR imaging,⁽³⁾ whole-body ^{99m}Tc sestamibi scanning,⁽⁷⁾ ¹¹¹In-pentetreotide or octreotide scintigraphy,⁽⁸⁾ body ²⁰¹Tl scintigraphy and ^{99m}Tc MIBI SPECT.⁽⁹⁾ Despite their use, there are reports of the tumour still not being able to be localised. Using an innovative approach, Takeuchi et al successfully used selective venous sampling for FGF23 with MR imaging to confirm that a localised tumour in the inguinal region was producing FGF23.⁽⁵⁾

F-18 FDG PET/CT works on the principle of increased uptake of radiolabelled glucose by lesions with increased glucose utilisation or increased blood supply. The tumours commonly reported to be responsible for TIO include phosphaturic mesenchymal tumour, mixed connective tissue type (PMT/MCT, approximately 70%–80% of all the mesenchymal tumours) subtype,

and haemangiopericytomas, which are the most common PMT/MCT.⁽¹⁰⁾ As these tumours arise from haemangiogenic tissue and are very vascular, they should have a high probability of being identified by PET/CT. Such localisation by PET/CT was first reported by Dupond et al in 2005.⁽²⁾ In this case, localisation was initially attempted with total body tomodensitometry (TDM), MR imaging and ¹¹¹In-octreotide with negative results. F-18 FDG PET/CT was able to localise the tumour under the left gum between the 37th and 38th tooth. Surgical removal of the tumour resulted in the normalisation of serum phosphate and clinical improvement. Histopathology was consistent with a haemangiopericytoma-like pattern. Recently, two more cases of PET/CT localisation of phosphaturic tumour have also been reported.^(11,12) Our report reinforces the utility of PET/CT in the detection of phosphaturic tumour where other attempts at tumour localisation have failed.

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