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CASE REPORT

Tumour-induced Osteomalacia: A Case Report

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INTRODUCTION

Tumour-induced osteomalacia (TIO), also known as oncogenic osteomalacia, is a rare acquired paraneoplastic syndrome. Since the culprit tumour is difficult to localise using conventional anatomical imaging, functional imaging plays an important role in localisation. We present the case of a middle-aged male with TIO who underwent various imaging investigations with failure to localise the culprit tumour, where finally a ^{111}indium-pentetreotide scintigraphy (octreotide scan) located the tumour over his left foot. This case highlights the importance of covering the entire body when performing an octreotide scan in patients with suspected TIO so as not to miss any hidden tumour in the extremities.

CASE PRESENTATION

A 35-year-old man initially presented with right ankle pain. Magnetic resonance imaging revealed a non-traumatic stress fracture of the right distal tibia. One year later, the patient complained of increasing bone and joint pain. Bone scintigraphy, performed at an external centre, revealed multiple fractures of the ribs, bony pelvis and extremities, along with features of metabolic bone disease (Figure 1).

Biochemically, the patient was found to have a hypophosphataemia level of 0.48 mmol/L (normal range: 0.75-1.3) and an elevated alkaline phosphatase level of 852 U/L (normal range: 50-136). Further workup revealed normal calcium level of 2.28 mmol/L (normal range: 2.11-2.55) and parathyroid hormone level of 4.4 pmol/L (normal range: 1.6-6.9), low 1,25-dihydroxyvitamin D level of 4.9 pg/mL (normal range: 19.6-54.3), and elevated fibroblast growth factor 23 (FGF23) level of 252 RU/mL (normal range: <180). A presumptive diagnosis of TIO was made in view of his typical symptoms and biochemical profile. An extensive search for the culprit tumour by various imaging modalities was performed. Whole-body magnetic resonance imaging, octreotide scan (from vertex to mid-thigh) and ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) [from vertex to thigh] performed at external centres showed no suspicious lesion that could indicate TIO.

Two years later, the patient self-detected a lump over the first web space of his left foot. Contrast CT revealed a well-circumscribed lobulated isodense mass with avid heterogenous contrast enhancement at the first web

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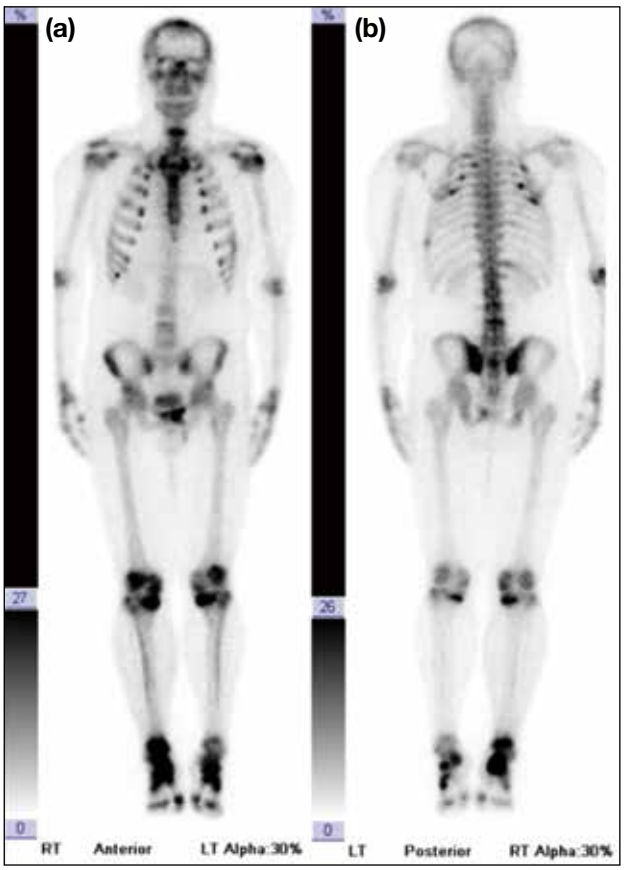

Figure 1. (a) Anterior and (b) posterior images of whole-body planar bone scintigraphy showing multiple fractures at bilateral ribs, pubic bones and lower limbs with features of metabolic bone disease, including diffusely increased tracer uptake in both axial and appendicular skeleton, as well as the presence of a hot sternum tie sign and rickety rosary beading at the costochondral junctions.

space. The nature of the lesion was non-specific but it was suspected to be the cause of TIO. The patient was then referred to our centre where whole-body octreotide scan revealed an octreotide-avid soft tissue mass at the first web space of the left foot. In the absence of any other suspicious lesion (Figure 2), this confirmed it to be the culprit tumour.

Subsequently, surgical resection of the tumour in the left foot was performed. Histological diagnosis revealed a phosphaturic mesenchymal tumour composed of spindle to short oval cells arranged in irregular bundles, characterised by a rich vasculature and mildly irregular or twisted outline with indistinct nucleoli. The phosphate level normalised 3 weeks after the surgery.

DISCUSSION

TIO is caused by a small benign tumour, most commonly classified histopathologically as phosphaturic mesenchymal tumour, mixed connective tissue type.[1] The tumour will secrete FGF23, a phosphaturic hormone that leads to inhibition of renal phosphate reabsorption. FGF23 also reduces the production of 1,25-dihydroxyvitamin D.[2] Eventually, these will result in hypophosphataemia.

Patients with TIO present with muscle weakness, bone pain, and multiple fractures.[3] Characteristic biochemical features are hypophosphataemia and hyperphosphaturia. Other common biochemical features include normal calcium, parathyroid hormone and low-to-normal 1,25-dihydroxyvitamin D level, and elevated alkaline phosphatase and FGF23 level.[3] Nonetheless the non-specific nature of the symptoms often leads to underdiagnosis with a consequent delay in management, often years after initial presentation.[1]

With a consistent clinical history and typical biochemical features establishing the diagnosis of TIO, localisation of the culprit tumour is the next important step in management. Nonetheless this often presents another major challenge that delays curative treatment. The culprit tumour is typically small and can present anywhere in the body but more commonly in the lower extremities or craniofacial region.[4-6] There is no specific pattern or pathognomonic feature of the culprit tumour on conventional anatomical imaging,[1] rendering tumour localisation difficult.

Culprit tumours of TIO frequently express somatostatin receptors (SSTR), evidenced by avid uptake on somatostatin analogue imaging.[3] Therefore, ^{111}In-octreotide scintigraphy and ^{68}Ga-DOTA–conjugated SSTR-targeting peptide PET/CT (SSTR PET/CT) are useful for tumour localisation. Due to possibly obscure locations of culprit tumours, they are easily missed if a whole-body scan is not performed. Whenever a patient is suspected to have TIO, it is vital to ensure that the entire body is included in the scan range so as not to miss any hidden tumour in the extremities or craniofacial region.

In recent years, SSTR PET/CT imaging has gained popularity due to its lower radiation exposure, shorter acquisition time, and improved spatial resolution compared with ^{111}In-octreotide scintigraphy.[7,8] Previous studies have shown that SSTR PET/CT imaging exhibits the highest sensitivity and specificity among different functional imaging studies for localising the culprit tumour of TIO.[8,9] A recent systematic review and

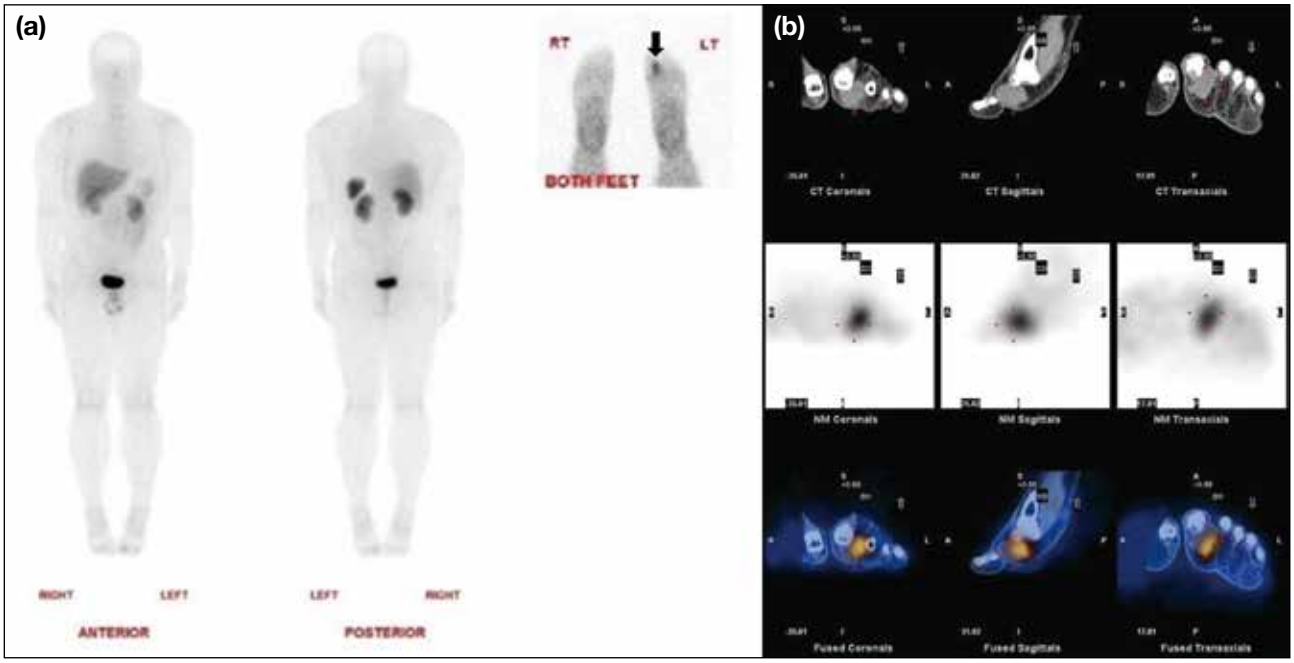

Figure 2. (a) Anterior (left) and posterior (right) view of whole-body planar image of ^{111}In-octreotide scintigraphy showed an octreotide-avid lesion at the left foot (arrow). (b) Single-photon emission computed tomography/computed tomography showing an octreotide-avid soft tissue lesion at the first web space of the left foot.

meta-analysis showed a pooled detection rate of 87.6% for culprit tumour localisation using SSTR PET/CT imaging.[10]

Definitive treatment for TIO is surgical resection of the culprit tumour. This usually results in rapid resolution of hypophosphataemia.[1]

CONCLUSION

TIO is a rare but devastating disease. One of the major challenges is localisation of the culprit tumour and subsequent curative surgical resection. Somatostatin analogue imaging, including ^{111}In-octreotide scintigraphy and ^{68}Ga-DOTA-SSTR PET/CT, is useful in localising the culprit tumour. It is worth noting that coverage of the entire body in the scan range is mandatory to avoid missing any hidden tumour in the extremities.

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