

# Telangiectatic osteosarcoma, a rare complication of Paget's disease of bone

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## Introduction

Paget's disease of bone (PDB) is the second most common metabolic bone disease. This condition, characterised by abnormal bone remodelling, has a prevalence of 5-8% in patients of European ancestry over the age of 55 years.<sup>1-4</sup> The majority of patients are asymptomatic. Diagnosis is based on the distinct radiological picture or on the elevation of serum alkaline phosphatase (ALP). Malignant sarcomatous degeneration is a rare (< 1%) and often fatal complication of PDB.<sup>5-8</sup> Osteosarcoma is considered to be a rare and devastating complication of PDB. We report on a confirmed case of very rare telangiectatic osteosarcoma in monostotic PDB.

## Case study

A 60-year-old female patient of mixed ancestry presented with a 6-12 month history of progressively worsening left hip and pelvic pain, which increased in severity at night and at rest. Conventional pelvic X-rays revealed classical features of PDB, involving the left iliac and pelvic bone (Figure 1 a and b).

However, significant weight loss (> 10% body weight in three months), an elevated erythrocyte sedimentation rate of 65 mm/hour, and radiological evidence of progressive destruction of the left superior pubic ramus prompted further investigation. Biochemical analysis showed a moderate elevation of ALP of 227 IU/l (normal reference range 35-120 IU/l). However, other more sensitive biomarkers of bone resorption (urinary deoxypyridinoline and the creatinine ratio) and bone formation (osteocalcin) were not elevated.

Although sarcomatous degeneration or unrelated metastatic disease in PDB was a distinct possibility, the initial biochemical and standard radiological evaluation was not definitive. Alternative and more benign conditions were also considered, including a giant cell tumour of bone or an aneurysmal bone cyst.

Skeletal scintigraphy suggested that the PDB was active and monostotic. However an unusual photopenic area was localised to the left iliac bone. This phenomenon was described as the "doughnut sign" by Sangle and Layfield et al.<sup>9</sup> It proved to be decisive in supporting the eventual diagnosis (Figure 2). Magnetic resonance

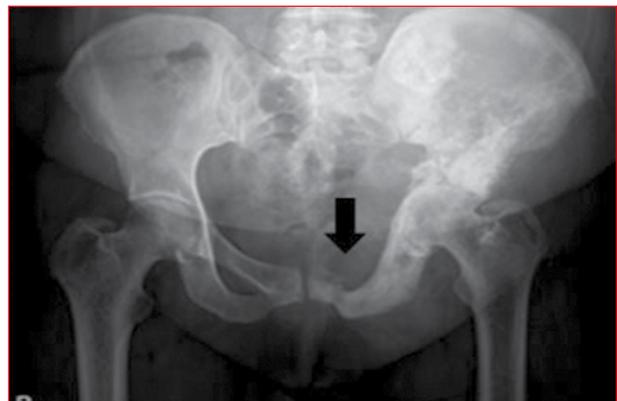
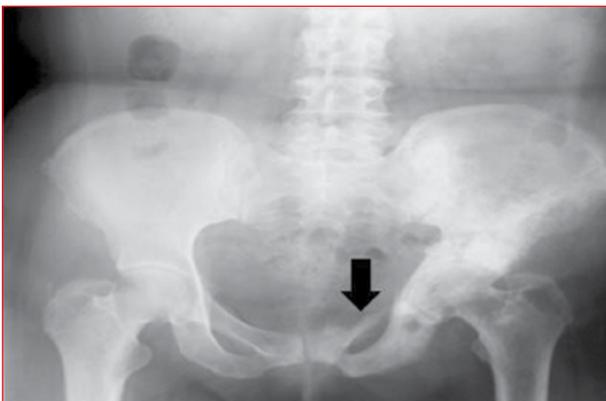


Figure 1 a (left) and b (right): Conventional pelvic X-rays show characteristic features of Paget's disease of bone, including thickening of the ileopectineal line, bone expansion and coarse trabeculations. Additional findings included mixed sclerotic and lytic changes within the left iliac bone, accompanied by protrusio acetabuli. The arrows indicate progressive erosion and eventual destruction of the left superior pubic ramus. The date for Figure 1 a was December 2011. The date for Figure 1 b was March 2012.

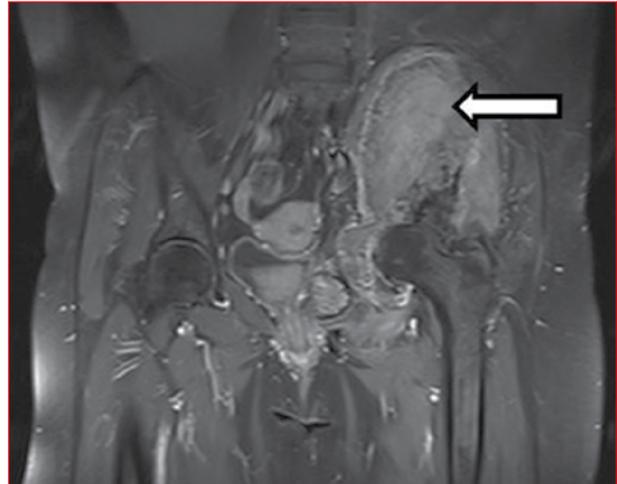


**Figure 2:** Skeletal scintigraphy. Note the central photopenic area in the left iliac bone (arrow). This "doughnut sign" is pathognomonic of telangiectatic osteosarcoma, and represents cystic haemorrhagic components surrounded by increased uptake in the septa and peripheral solid areas

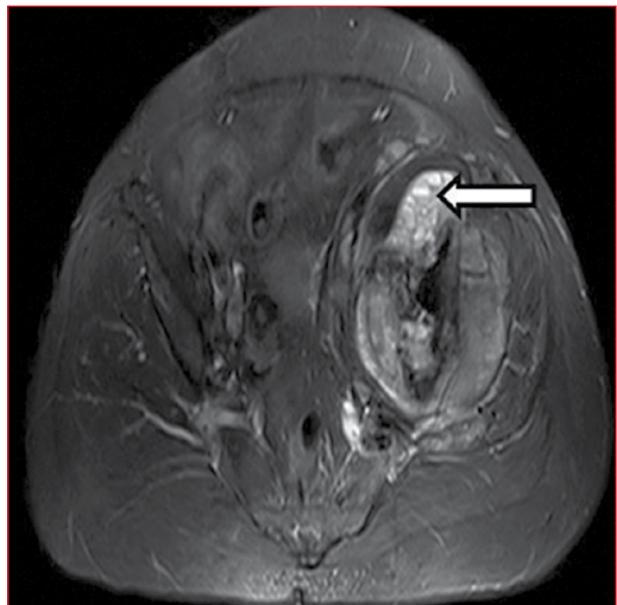
imaging delineated the extent of the tumour and showed the hallmarks of fluid-fluid levels, in keeping with the final histopathological diagnosis (Figures 3-4). The macroscopic features of a haemorrhagic tumour were described at the time of biopsy. Microscopic sections of the tissue obtained confirmed the diagnosis of telangiectatic osteosarcoma in PDB (Figure 5). The tumour consisted of osteoid-producing atypical cells with pleomorphic nuclei, an increase in mitotic figures and a moderate amount of cytoplasm. Multinucleated giant cells were also seen diffusely scattered throughout the tumour. The atypical cells lined large telangiectatic spaces filled with red blood cells.

### Discussion

PDB is a common metabolic bone disease characterised by increased bone turnover, an imbalance in bone remodelling and distorted bone microarchitecture.<sup>1-4</sup> The disease process itself involves various stages of lysis and sclerosis. The initial phase is described as osteolytic, followed by a mixed lytic or sclerotic phase. As the disease progresses, bone



**Figure 3:** Magnetic resonance imaging T1 post-gadolinium (coronal view). Large soft tissue mass in left hemipelvis originating from pelvic and iliac bone, and displacing adjacent structures

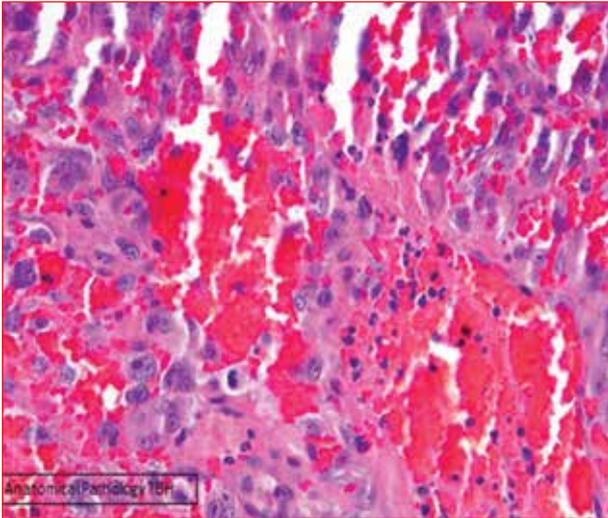


**Figure 4:** Magnetic resonance imaging T2 (axial view). Characteristic radiological feature of telangiectatic osteosarcoma histological variant. Mass with different-sized multicystic spaces within it, containing fluid-fluid levels (arrow).

formation predominates, resulting in sclerotic bone overgrowth and deformity.<sup>5</sup> Elevation in ALP, urinary deoxypyridinoline and osteocalcin typically reflects these increases of bone turnover. Sarcoma that arises in PDB is rare and presents with increasing age.<sup>6</sup> This case report highlights some unique features which deviate from the norm and warrant clarification.

Firstly, PDB is infrequently reported in patients who are not of European descent, but the geographical variation of PDB may be influenced by migration.<sup>2</sup>

Secondly, the moderate elevation in serum ALP is not congruous with the marked elevation that is typical of osteosarcoma or active PDB. However, osteosarcoma may not always be associated with very high-serum



**Figure 5:** Histopathology. Multinucleated giant cells diffusely scattered throughout the tumour. Atypical cells line large telangiectatic spaces filled with red blood cells

ALP.<sup>6,8</sup> The biomarkers of bone turnover may be normal in PDB, suggesting a quiescent or "burnt out" phase of the disease, less extensive (monostotic) involvement, or previous exposure to bisphosphonate therapy.<sup>8</sup> Skeletal scintigraphy showed significant increased uptake in the left hemipelvis in our patient. Pagetic osteosarcoma is said to arise most commonly in the mixed lytic or sclerotic phase of the disease.<sup>5</sup> However, in this case, the predominant destructive or osteolytic nature of the underlying tumour may have been an additional confounding factor, and could explain the apparent discrepancy between activity and limited changes in bone turnover markers. Telangiectatic osteosarcoma is described as an extremely vascular tumour, and increased uptake on skeletal scintigraphy may reflect the increased perfusion of the tumour, rather than increased osteoblastic activity.

Thirdly, osteosarcoma is a rare and devastating complication of PDB, arising in less than one per cent of affected individuals. Traditionally, it is thought to occur in patients with extensive (polyostotic) and long-standing disease who are older than 65 years of age. However, as evident from current literature relating to osteosarcoma in PDB, this complication should not be discounted in the absence of long-standing disease and regardless of the site or stage of presentation.<sup>5-7</sup>

Finally, various subtypes of osteosarcoma are described, based on the predominant cellular component, including osteoblastic, fibroblastic or chondroblastic.<sup>5,7</sup> Telangiectatic osteosarcoma, a rare histological variant of osteosarcoma, is described in 2-12% of all osteosarcomas.<sup>5,9,10</sup> Historically, first recognised by Paget in 1853 and classified as a distinct variant of osteosarcoma by Ewing in 1922, telangiectatic osteosarcoma predominantly affects male patients (male to female ratio of 2:1), and is seen more often in younger patients.<sup>10-12</sup> When considering

the clinical, radiological and histopathological features of telangiectatic osteosarcoma, it is important to differentiate it from an aneurysmal bone cyst and giant cell tumours of the bone.<sup>12,13</sup> Distinguishing pathological features of this case were the destructive growth pattern (cortical destruction and infiltration of soft tissue), gross appearance (predominantly cystic lesion filled with blood), and the presence of malignant cells on microscopic examination.<sup>9-12</sup> Despite advances in neoadjuvant chemotherapy, the prognosis remains poor in the setting of all secondary osteosarcomas arising in PDB (a five-year survival rate of 10%). The poor outcome of osteosarcoma in this clinical setting suggests a different biological potential which may relate to underlying genetic susceptibility or environmental factors.<sup>7,14</sup>

### Clinical outcome

Surgical intervention was not considered to be a viable option in this patient. Palliative radiotherapy was initiated, but unfortunately discontinued owing to increased patient discomfort. Supportive management was limited to adequate pain relief and intravenous zoledronic acid.

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