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Paget's Disease of the Bone Mimicking Metastasis: Two Case Reports

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Abstract

Paget's disease of the bone (PDB) is a focal metabolic bone disorder generally asymptomatic which is characterized by excessive bone resorption followed by increased bone formation. The diagnosis of PDB requires a high index of suspicion, any condition characterized by sclerosis of bone, like metastasis from solid tumors, need to be excluded. We reported two cases of incidental diagnosis of this PDB in oncologic patients. The bone disorder, in these circumstances, is a challenge for timely radiographic diagnosis and histopathologic confirmation.

Keywords: Paget bone; Metastasis; Serum alkaline phosphatase

Introduction

Paget's disease of the bone (PDB) is a focal metabolic bone disorder characterized by the presence of localized areas with increased bone resorption associated with exuberant, but disorganized bone formation. The first description was in 1877 by Sir James Paget referred to this condition as osteitis deformans, due to the characteristic change in the shape and size of the bone [1]. Although almost any bone can be affected, PDB generally involves the axial skeleton; skull, spine and pelvis are the most frequent sites [2].

Two distinct forms of PDB do exist: Monostotic, if a single bone is involved, and polyostotic if several bone areas are affected [3]. The most representative microscopic feature of PDB is the presence of aberrant focal bone remodeling with the typical cotton wool appearance as radiographic sign, determined by high bone turnover and new irregular bone formation; the former is caused by an increase in the size and number of osteoclasts related to osteoclast activity; the latter is the expression of imbalance of the osteoblastic activity that generates an irregular tissue increased in volume but extremely weaker than the normal bone [4]. PDB is generally a benign asymptomatic disease, otherwise, at the onset, bone pain can drive the clinical suspicion whereas, in the late stage, the progression of the disease can lead to deformity, spinal stenosis, and complicated fragility fractures [5,6]. To date, few is known about the etiopathogenesis of the disease, with the exception that both genetic and environmental factors might be involved. Among the latter, essentially infections from parainfluenza viruses have been considered [7,8].

Noteworthy, cases of coexisting PDB and malignancies, have been reported. Indeed, since radiological features can mimic those of bone metastases, it may further represent a diagnostic dilemma during evaluation of patients affected by a cancer [9]. We report two cases of patients affected by cancer who presented with PDB of the bone.

Case Report

Case 1

A 69-year-old postmenopausal female with an history of 8 months intensive left pelvic and femoral walking pain presented at the outpatient clinic of Rheumatology.

The patient was previously diagnosed to have a left breast cancer (G2 N2) M0 ER 90% PR 60% and underwent surgery and radiotherapy. A pelvis X-ray showed a little irregular sclerotic lesion with mixed structural bone alterations in the left pelvic bone near the ischiopubic branch. Given the suspicion of a metastatic lesion, both a total body CT and a bone scan were performed for disease staging (Figure 1). Total body CT was negative for neoplastic lesion, whereas bone scintigraphy pointed out an increased radionuclide uptake in many areas such as the body of L2 and L3 vertebrae, the left sacroiliac synchondrosis, the acetabulum and the left ischiopubic branch. Since the possibility of a metastatic lesion could not be ruled out, an ago-biopsy of the left acetabulum area was carried out. The histological exam excluded any neoplastic process and documented the presence of trabecular rearrangement, focal intertrabecular bloodthirsty alongside to consensual focal peri trabecular fibrosis. Her serum calcium and phosphate levels were normal, and the serum alkaline phosphatase was slightly increased 174 U/L (normal values: 30–120 U/L). The histological were compatible with PDB and the diagnosis was done. Thus, patient started 100 mg neridronate for two consecutive days, accordingly to indications reported in technical schedule with calcium (1 gr/day) and vitamin D supplements- cholecalciferol (800 UI/day). The drug was well tolerated, pain and radiological extension of disease at the follow up, one year later, are under control.

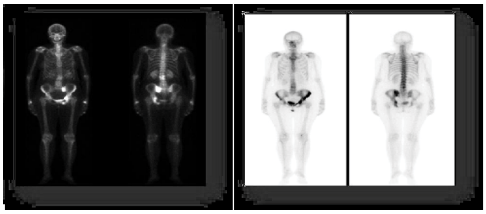

Figure 1: Bone scan (99mTc-HMDP) diffuse increase of the radionuclide uptake of the tracer at the left sacroiliac synchondrosis, and the left ischiopubic branch for patient 1 (Right) and left sacroiliac and the homolateral hemipelvis for patient 2 (Left).

Case 2

A 64-years-old postmenopausal woman recently diagnosed with right typical carcinoid lung cancer (pT1a G1 pNx) was referred from her oncologist to our bone outpatient clinic, because of the finding at the staging total body CT of diffuse bone structure alterations in the left iliac bone and pain at the same site. The patient was asymptomatic, and

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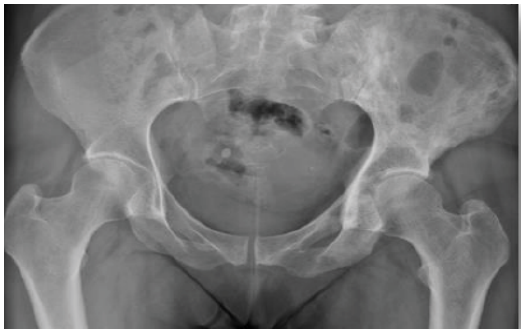

Figure 2: Pelvis X-ray for patient 2 revealed both osteolysis and osteosclerosis in the left sacral wing and the left iliac bone typical cotton wool lesion suggestive for PBD.

the clinical examination did not reveal any abnormal sign, in addition the bone resorption markers such as serum collagen type I cross-linked C-telopeptide (CTX) and urine N-terminal telopeptide resulted in normal range and the bone formation tests were normal, particularly serum alkaline phosphatase (103 U/L, normal values: 30–120 U/L). A pelvis X-ray revealed both osteolysis and osteosclerosis in the left sacral wing and the left iliac bone (Figure 2), and the technetium bone scan (99mTc-HMDP) demonstrated a marked increased tracer uptake in the left sacroiliac and the homolateral hemipelvis. Analysis of both two exams leaded to PDB; however, given the oncologic history of patient, also a percutaneous tissue biopsy was taken. The pathologist excluded any neoplastic process and described the presence of diffuse foci of bone remodeling together with an increased number of enlarged multinucleated osteoclasts.

The results were consistent for PDB. Also, this patient was treated with neridronate with calcium 1 gr/day and cholecalciferol 800 UI/day.

Discussion

PDB is a disorder of unknown etiology characterized by focal lesions of osteoclastic bone resorption and increased and disorganized bone formation associated with marrow fibrosis, and increased vascularity [10]. Both genetic and environmental factors seem to be involved in the pathogenesis, but very few is still known about it [11]. Although, as for patient 1, bone pain is the most common presenting symptom, in the majority of the patients, PDB can be asymptomatic and only incidentally is revealed by elevated serum alkaline phosphatase levels, radiographic skeletal exams or radionuclide bone scan, as it happened for patient 2. Such patients may also present with pathological fractures or bone deformities; others, with hearing difficulties, high output heart failure, arthritis, and headache [12].

PDB localization has a strong predilection for the skull, thoracolumbar spine, pelvis, and long bones of the lower extremities. Polyostotic PDB tends to have right-sided predominance and is more often asymmetrical in distribution. It involves the cranium (25% to 65%), vertebral column (30% to 75%), sacrum (30% to 60%), pelvis (30% to 75%), femur (25% to 35%) and tibia [13]. The first case presented a multiple localization involving the vertebrae, the left sacroiliac synchondrosis, the acetabulum and the left ischiopubic branch, whereas the latter was a monostotic presentation affecting the right hemipelvis. The diagnosis of PDB is generally made on clinical and imaging evidences with the support of serum elevated bone turnover markers. Of note in these cases they were within limits (ALP), probably due to the limited bone extension of the disease. PDB may be associated with other benign and malign conditions.

Breast, prostate, lung, lymphoproliferative, colorectal, and renal neoplasms are the most frequently described together with PDB. There are few reports showing this association, Sa Pinto et al., describe an incidental case of monostotic PDB at the scapula in lung cancer; [14] Shimoyama et al., colleagues in a gastric cancer with pelvic localization confirmed by biopsy a PBD [15] and a rare coexistence of myeloma and Paget disease is also reported by Maryam Pourabdollah and Hong Chang [16]. In oncologic situation, clinician often reflect on this diagnostic dilemma, since the firm diagnosis of PDB in patients with cancer, and the assurance that there is no metastasis, may save them from further unnecessary examination and aggressive therapy. Bone scan is often helpful in the diagnosis because of the characteristic distribution patterns and the scintigraphic images. The sensitivity and specificity of bone scintigraphy in bone metastases are, respectively, 66.7% and 86.8%. It has a positive predictive value of 10% and a negative predictive value of 99.2% with accuracy of 86.3%. Nevertheless, bone scintigraphy appears to be insensitive for detecting early bone or bone marrow metastasis and differentiation between malignant or benign lesions through bone scintigraphy is problematic, even for experienced nuclear physicians [17,18].

Typical features of Pagetic bone lesions at the microscope slides are characterized by focal increases in osteoclastic bone resorption with an increased and disorganized bone formation associated with marrow fibrosis, and increased vascularity of bone.

Conclusion

In conclusion, these two cases offer various points to ponder. First, although X-rays follow up in neoplastic patients remain a test of paramount importance, it could potentially make erroneous diagnosis. Secondly, possible diagnosis of PDB should not be excluded also in the presence of low concentration of typical biochemical markers. Finally, when oncological patients present history, physical examination and laboratory and imaging tests suggestive of bone disease, microscopic data are mandatory to make the correct diagnosis.

Informed Consent

An informed consent was released by both patients for the publication.

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