Polyostotic Paget's disease

Doença de Paget poliostótica

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Abstract

Polyostotic Paget's disease is an uncommon condition, affecting middle-aged or elderly people. The etiology is related to genetic factors, viral infections and production of IL-6 by osteoclasts. Diagnosis is based on images, pathologic findings, and bone-specific alkaline phosphatase level. The main features include joint pains, bone fractures/ deformities, neurologic or cardiac changes; whereas secondary osteoarthritis or sarcomas have been described as associated conditions. The sites more often involved are pelvis, skull and spine with abnormal shape and trabecular pattern. Bony metastases and lymphoma, fibrous dysplasia, hyperostosis frontalis interna, and primary sarcoma should be ruled out. The purpose is to enhance the suspicion index of about this entity.

Keywords: Diagnosis; Paget's disease; Polyostotic Disease.

Resumo

A doença de Paget poliostótica é uma condição incomum, afetando pessoas de meia-idade ou idosas. A etiologia está relacionada a fatores genéticos, infecções virais e produção de IL-6 por osteoclastos. O diagnóstico é baseado em imagens, achados patológicos e níveis elevados de fosfatase alcalina óssea específica. As principais características incluem dores articulares, fraturas e deformidades ósseas, e alterações neurológicas ou cardíacas; enquanto osteoartrite secundária ou sarcomas são descritos como condições associadas. Os locais mais envolvidos são a pelve, o crânio e a coluna, com deformidades e alteração no padrão trabecular. Metástases ósseas e linfoma, displasia fibrosa, hiperostose frontal interna e sarcoma primário devem ser descartados. O objetivo é melhorar o índice de suspeita sobre esta entidade.

Palavras-chave: Diagnóstico; Doença de Paget; Doença Poliostótica.

Introduction

Paget's disease of bone (PDB) is an osteometabolic disease mainly of individuals over 50 years of age, with increased and disorganized bone turnover.[1-5] It was found in a Tanzanian dinosaur, but its first description

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by James Paget was in 1877.[4] Although often asymptomatic, this condition is classically characterized by bone and joint pains, fractures, deformities, neurologic and heart disorders, and secondary osteoarthritis or sarcomas.[1-4] As PDB more often evolves unsuspected by many years, it is usually incidentally diagnosed.[4] This condition is also called *osteitis deformans*, predominates in people of European ancestry, and may be monostotic or polyostotic, accordingly with the number of the involved bones. Differential diagnosis includes blastic bony metastases; lymphomatous bone involvement; fibrous dysplasia of bone; hyperostosis *frontalis interna*; and primary osteogenic sarcomas. The etiology has been related to genetic factors, viral infections and production of IL-6 by osteoclasts.[1,3,4] PDB is diagnosed with base on radiological images or pathologic features, and bone-specific alkaline phosphatase level is additional tool for management.[3] First- and second-line treatments for PDB are respectively bisphosphonates and calcitonin; whereas zolendronic acid, calcium, vitamin D, NSAIDs and analgesics have been also utilized.[1-3,5]

Castro GR et al. evaluated 50 patients with PDO, 60% females, mean age of 66.32 ± 8.65 years; 74.2% of them had polyostotic disease, and 29% had positive familial history.[2] They reported past (56.9%) or current (32.3%) bone pains, deformities (19.4%), physical impairment (12.9%), and osteoarthritis (32.3%) in the studied group of patients.[2] As other authors, they concluded that these changes adversely affect the quality of life.[2,3] Kang H et al. reviewed data of eight patients with PDB and pelvis, skull and spine were the more often affected bones, with changes in shape and trabecular pattern causing bowing of lower extremity, osteoarthritis, compression fracture of spine, and enlargement of skull.[3] The mean age was 55.4 (39-67) years, 75% were females, alkaline phosphatase (AP) level was elevated in 50% of the cases, and all patients were treated with bisphosphonates.[3] Disease activity was assessed by serum AP, and bisphosphonate controlled well the enzyme levels.[3]

Numan MS et al. emphasized that the elevated levels of IL-6 and interferon-gamma are similar to various osteoimmunological disorders, and the RANKL-NF-κB signaling play a major role in osteoclast differentiation and activation in people diagnosed with PDB.[5] These authors suggested that the control of PDB may also benefit from current progresses in osteoimmunology-targeted therapies, mainly by the RANKL and IL-6 signaling inhibition.[5]

In this setting, we comment the case of a 65-year-old woman with progressively growing bone pains that had been affecting the

skull, left femur and right hand for a decade. Except for the discrete to moderate bone pains, she considered herself as a previously healthy woman, who had 12 normal pregnancies and her menopause occurred at the age of 50 years. She was not sedentary, denied smoking, alcohol abuse, and illicit drug consumption. Medical antecedents were mild episodes of bronchial asthma and many viral infections during infancy. Physical examination showed a eutrophic non-febrile woman, with pale mucosae, BP: 130/80 mmHg, HR: 80 bpm; she was edentulous, and had *varus* deformity in lower extremities. Laboratory data: elevated level of bone-specific alkaline phosphatase, hemoglobin 11.6 g/dl, hematocrit 36%, platelets 143,000/mm^3, leukocytes 5,500/mm^3, albumin 4.3 g/dl, and globulins 2.4 g/dl; calcium, phosphate, beta-2 microglobulin, C-reactive protein, erythrocyte sedimentation rate, tumor markers, ALT, AST, DLH, uric acid, glucose, glycated hemoglobin, urea, creatinine, lipid profile, and thyroid function tests were within the normal ranges. The panel of serological tests including syphilis and HIV infection resulted negative. Total skeleton X-ray evaluation showed characteristic features of Paget's disease (Figure 1).

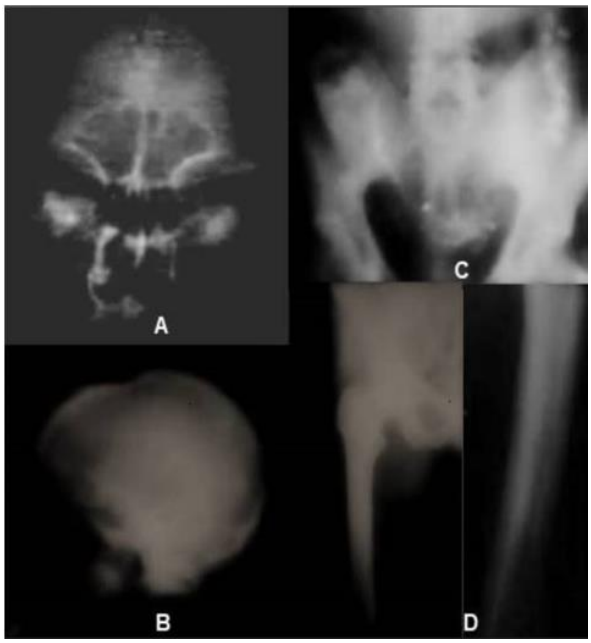

Figure 1. (Plain radiographic images consistent with polyostotic Paget's disease) **A** and **B**: thickened skull bone tables, mixed osteolytic and osteosclerotic lesions, and disordered new bone deposition like "cotton-wool patch"; **C**: predominant sclerotic lesions in pelvic bones, in proximal femora and in lumbar vertebrae, as well as expanded size of the left femur head; and D: femora with a bowing convex aspect, proximal osteosclerosis

and new bone formation, increased circumference, and a distal osteolysis progressing proximally like an inverted V.

Histopathological analysis of iliac bone biopsy samples revealed thickened trabeculae with osteoblastic and osteoclastic activity with a disorganized pattern, without malignant changes. Therefore, the diagnosis of PDO was established and she started using oral bisphosphonates. Worthy of note, significant improvement was confirmed after two years of routine controls.

The aim of this paper is enhance the suspicion index in primary health scenery about a bone disorder that very often evolves unsuspected and underreported, or even misdiagnosed.

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