

# DIAGNOSIS AND MANAGEMENT OF PAGET'S DISEASE OF BONE - SERIES OF 8 CASES

## DIAGNÓSTICO E MANEJO DA DOENÇA DE PAGET ÓSSEA - SÉRIE DE 8 CASOS

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### ABSTRACT

Paget's disease of bone is a chronic condition characterized by focal abnormalities of absorption and formation of bone, and it may lead to anatomical deformities, pain, fractures, and malignant transformation. It is common in the UK, Australia, New Zealand, and North America and has a strong hereditary component, affecting first- to third-degree relatives. The etiology remains unclear and treatment is based on control of the disease with bisphosphonates, with the aim of relieving symptoms and correcting laboratory abnormalities. Surgical treatment may also be necessary to correct deformities or treat pathological fractures. This study evaluated the management and course of 8 patients with Paget's disease of bone, followed in the Orthopedic Clinic of this hospital. Among these patients, 1 had concomitant advanced prostate carcinoma, highlighting the association between Paget's disease and secondary bone diseases that can affect the differential diagnosis. **Level of evidence IV, Study type: Case Series.**

**Keywords:** Paget's Disease. Osteitis Deformans. Neoplasm Metastasis.

### RESUMO

A doença de Paget Óssea é uma afecção crônica, caracterizada por distúrbio focal da absorção e formação ósseas, podendo levar a deformidades anatômicas, dor, fraturas e malignização das lesões. É frequente no Reino Unido, Austrália, Nova Zelândia e América do Norte. Mantém forte relação de incidência com parentes de primeiro a terceiro graus. Sua etiologia ainda permanece incerta e o tratamento se baseia no controle da doença, com uso de bisfosfonados, visando melhora dos sintomas e das alterações laboratoriais. O tratamento cirúrgico também pode ser necessário, para correção de deformidades ou para tratamento de fraturas. Este estudo compilou oito pacientes em acompanhamento pela doença de Paget Óssea, no Ambulatório de Ortopedia deste hospital, acerca do tratamento realizado e como evoluíram. Dentre os pacientes acompanhados, houve um caso de carcinoma de próstata concomitante ao Paget, chamando atenção para outras patologias ósseas que são diagnósticos diferenciais ou coexistem com a doença. **Nível de evidência IV, Tipo de Estudo: Série de Casos.**

**Descritores:** Doença de Paget. Osteíte Deformante. Metástase Neoplásica.

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### INTRODUCTION

As described by Sir James Paget in 1877, Paget's disease of bone is a chronic condition characterized by focal areas of excessive bone reabsorption accompanied by increased bone formation, resulting in anatomical and structural changes that can lead to pain, deformities, fractures, and progression to osteosarcoma or chondrosarcoma, among other complications.<sup>1,2</sup> Paget's disease predominantly occurs in males, with a male:female ratio of 1.8:1. It is rarely found in individuals under 50 years of age and is prevalent in approximately 2-4% of people over age 50.<sup>1</sup> It is more common in the UK, followed by Australia, New Zealand, and North America, reflecting the prevalence of British migrants in these areas. Conversely, it is rarely found in Scandinavian countries, Africa, and Asia.<sup>3</sup> The etiology of Paget's disease is uncertain, and there is a strong relation in its incidence among first-degree relatives.<sup>1,3</sup> Among those affected, mutations are found in sequestosome 1/p62, which plays an important role in the differentiation and response of

osteoclasts to RANK-L and interleukin-1 cytokines.<sup>1</sup> Some theories claim that environmental factors and viral infections may influence the onset of Paget's disease. There has been a gradual decline in disease incidence without the identification of contributory factors.<sup>1</sup>

### DIAGNOSIS

Paget's disease diagnosis is based on clinical features, such as bone pain, arthropathy, deformities, fractures, deafness, and neurological complications. Circumscribed osteoporosis, mosaic lesions, and bone deformities can be found on radiography and scintigraphy through hyperscanning of the affected areas. Laboratory tests may show changes in alkaline phosphatase and liver function tests, especially gamma-glutamyl transferase and vitamin D levels.<sup>1,3,4,5</sup>

### TREATMENT

Paget's disease is treatable, but not all patients require treatment. The main factor indicating drug treatment is bone pain at the affected site.

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Study was conducted at the Hospital das Clínicas of the Faculdade de Medicina de Botucatu, UNESP, Botucatu, SP, Brazil.

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Asymptomatic cases should be individually managed, and treatment is recommended when there is a risk of fracture, especially in the femur, tibia, humerus, and spine, or, in the case of the skull base, to prevent deafness. Once there is a fracture, it will be difficult for the patient to respond to treatment. For young patients with the disease, treatment involving the joint areas in an attempt to prevent secondary arthrosis is also possible. However, evidence that these treatments prevent complications is limited, given the difficulty in conducting randomized studies of relatively rare diseases. The drugs most commonly used to treat Paget's disease are second- and third-generation bisphosphonates, such as alendronate, pamidronate, and risedronate, which have replaced the use of calcitonin and etidronate. Vitamin D deficiency should be corrected, and calcium supplementation should be prescribed to prevent hypocalcemia induced by bisphosphonates or secondary hypocalcemia due to hyperparathyroidism. Drug treatment aims to relieve bone pain, normalize alkaline phosphatase levels, and induce remission of osteolytic lesions. Surgery may be indicated for fractures, correction of deformities, spinal stenosis with neurological complications, and joint replacements due to arthrosis.<sup>1,4,5</sup>

## PATIENTS AND METHODS

This study describes the management, diagnostic approach, treatment, and recent clinical status of 8 patients with Paget's disease of bone who were examined at the Orthopedic Clinic of this hospital. The study was approved by Plataforma Brasil, with CAAE protocol number 53081416.2.0000.5411.

### Case 1

E.M., male, 62 years old. A monostotic lesion in the left humerus was discovered by chance after a radiographic study of the arm 19 years prior. He was administered alendronate at the time, but is currently asymptomatic and rarely has pain. He has impingement syndrome in the left shoulder secondary to bone deformities from Paget's disease. He is only followed up at the orthopedics department.

### Case 2

E.G.C., male, 78 years old, with a monostotic lesion in the right hemipelvis. He has been treated with alendronate for periods of 3-6 months, with 6-month intervals between treatment courses. He remains asymptomatic. He is monitored by urology for prostate adenocarcinoma and underwent radiation therapy in 2008 and orchiectomy in 2010. The prostate-specific antigen level remains <0.2. He had a stroke and has residual left hemiparesis. He is currently followed up at the orthopedics and urology departments.

### Case 3

J.A.P., 75 years old, male. While under treatment at the urology department for a urethral stricture, pelvic radiography identified local bone changes. Staging revealed polyostotic disease, with lesions in the skull, pelvis, and spine. With few symptoms, he did not undergo drug treatment for Paget's disease. He is followed up at the orthopedics and urology departments.

### Case 4

G.O.S., male, 46 years old. He had fallen from a height of <2 m in November 2014 and fractured the right femoral diaphysis. Changes on radiography were compatible with Paget's disease and a pathological fracture was diagnosed. Indirect reduction and internal intramedullary nail fixation led to good recovery. Although asymptomatic, alendronate

was started in March 2015, to be discontinued in November 2015. He is only followed up at the orthopedics department.

### Case 5

R. N. F., male, 89 years old. He had fallen from a height of <2 m in October 2014 and had a pathological fracture of the right elbow. Staging was compatible with a monostotic lesion in the right distal humerus. The fracture was treated with direct reduction and internal fixation, with good callus formation during recovery. The patient was asymptomatic before treatment and remains so. He took alendronate for 6 months after the fracture, and is only followed up at the orthopedics department.

### Case 6

Z.M.G.S., female, 50 years old. Bone lesions were found in the spine on imaging for low back pain. Staging revealed polyostotic disease in the right humerus, spine, left hemipelvis, skull, and left femur. She is otherwise symptomatic but has elevated alkaline phosphatase levels. Her condition is monitored by the orthopedics department, and she was referred to the endocrinology department in June 2015.

### Case 7

A.D.D., male, 49 years old. He sustained a pathological right intertrochanteric fracture in August 2015 after falling from a height of <2 m. Intraoperative pathologic diagnosis was compatible with Paget's disease of bone. He remains asymptomatic at the fracture site. Complete laboratory and imaging staging are pending to determine whether he has monostotic or polyostotic disease. He is only followed up at the orthopedics department.

### Case 8

L.B.C., female, 76 years old. Paget's disease was diagnosed because of a bone deformity in the left tibia, and complete staging is pending to determine whether the disease is monostotic or polyostotic. She has pain in the left leg unrelated to physical activity. Endocrinology recently initiated risedronate. She is followed up at the orthopedics and endocrinology departments.

## DISCUSSION

Paget's disease is routinely managed by the specialties of orthopedics and endocrinology. We believe that multidisciplinary follow-up is useful for diagnosis and staging as well as treatment. Because Paget's disease mainly affects people over the age of 50, it is important to evaluate the possibility of other primary and secondary bone diseases, such as malignant metastases and multiple myeloma, which are included in the differential diagnoses or may even coexist with Paget's disease. New drugs that modulate calcium metabolism, such as denosumab, may prove to be valuable in patients who cannot take bisphosphonates.<sup>6</sup> Paget's disease requires follow-up care and assessment for possible development of malignancy.<sup>2</sup>

## CONCLUSION

Paget's disease of bone is often diagnosed by chance on imaging studies for other diseases. Bisphosphonate treatment is effective in controlling pain and alkaline phosphatase levels in most patients. Because of the greater prevalence in older populations, it is important to consider Paget's disease in the differential diagnosis, in addition to the possibility of coexisting bone malignancies.

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