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SCIENTIFIC ARTICLE - CASE REPORT

PAGET'S DISEASE OF BONE: CASE REPORT

ANA JÚLIA LINHARES VOLPP[1]; LARA CHRISTINA RANGEL BRAGA[1]; RAUL KELLER AVELAR[1]; SEVERINO CORREIA DO PRADO NETO[1]

1 - Faculdade Morgana Potrich (FAMP) - Mineiros GO

ABSTRACT

Paget's Disease of Bone (PDB) is a complex condition that affects bone tissue and can lead to a series of complications if not properly diagnosed and treated. The classic symptoms of PDB, such as bone pain, deformities and neurological complications, can vary significantly in their clinical presentation. This case report illustrates an atypical patient, since the onset of manifestations and diagnosis occurred before the age of 50, a fact which occurs rarely. The importance of considering this condition in the differential diagnoses of pain and bone deformities is highlighted, even in younger patients, enabling early treatment of this morbidity.

Keywords: Paget's disease; Osteitis Deformans; Bone Remodeling.

INTRODUCTION

Paget's disease of bone (PDB) is a skeletal disorder characterized by increased bone remodeling, where osteoblasts and osteoclasts function excessively, resulting in increased bone components with sclerotic and lytic areas. The main affected sites are the vertebrae, long bones of the lower limbs (femur and tibia), pelvis, and skull. Men tend to be more affected than women, both at an older age, with it being rare before the age of 50. Family history also proves to be an important factor in patients with the disease, being positive in about 20% of cases, in which SQSTM1 is the main gene involved in pathogenesis[1-3].

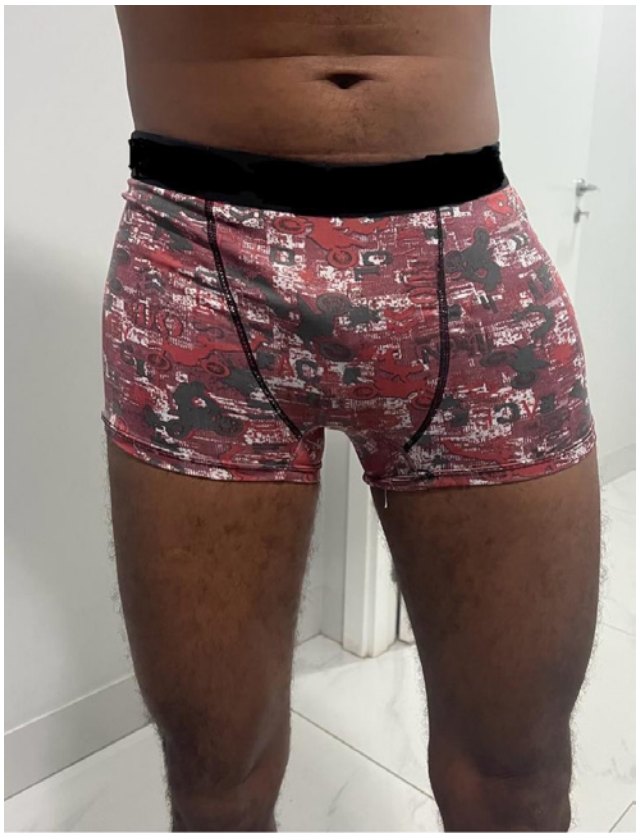
The clinical presentation of the disease is characterized by bone pain and deformities, an increased risk of stress fractures, and consequently, complete fractures. Additionally, hearing loss, basilar invaginations leading to cerebellar dysfunction, obstructive hydrocephalus, and aortic stenosis may occur[3,4]. Diagnosis is made through a combination of the patient's clinical presentation, imaging studies, and laboratory abnormalities. Among the tests, conventional radiography of the affected bone is notable, showing increased bone structure with osteolytic lesions resembling a candle flame, sclerotic changes, and cortical thickening[2].

Treatment involves lifestyle modifications with physical activities and physiotherapy. Bisphosphonates are the treatment of choice for people with PDB, due to their high efficacy in suppressing bone resorption and consequently reducing bone pain. Zoledronic acid is more effective than other bisphosphonates, such as pamidronate and risedronate[5-7]. Orthopedic surgery may be necessary for correction of bone deformities, secondary degenerative arthropathy, and decompression of affected nerves[3,8,9]. Therefore, the objective of this study is to report a case of a patient diagnosed with PDB at a less common age, already presenting deformities at the time of diagnosis.

CASE DESCRIPTION

Male patient, 48 years old, born in Jacobina-BA, truck driver, presented to the Rheumatology outpatient clinic referred by the Orthopedics service for investigation of left thigh pain, even at rest and worsened with movement, starting 2 years before with worsening in the last 8 months, without local trauma. He did not present weight loss and had no other systemic complaints. He denied other symptoms, such as pain in other sites, craniofacial changes, or visual or auditory alterations. He had no previous comorbidities and did not use any continuous medications. He denied smoking and alcohol consumption and played soccer as physical activity. During the investigation of the family history, he mentioned a case of bone neoplasia but could not specify. On general physical examination, he did not present any significant alterations, including normal cardiac auscultation. During musculoskeletal evaluation, a bowing deformity was identified in the region near the left thigh (Figure 1), without local inflammatory signs and no crepitus during movement.

Figure 1. Bowing deformity in the region near the left thigh.



He brought the following complementary exams: alkaline phosphatase 997 U/L (reference range: 40-150 U/L); 25-OH vitamin D 24.3 ng/mL; normal complete blood count and liver enzymes. Additionally, he underwent a hip radiograph, visualized in Figure 2.

Figure 2. Conventional radiograph of the left femur showing an expansile appearance with cortical thickening (bone formation) and interspersed lytic areas (resorption).

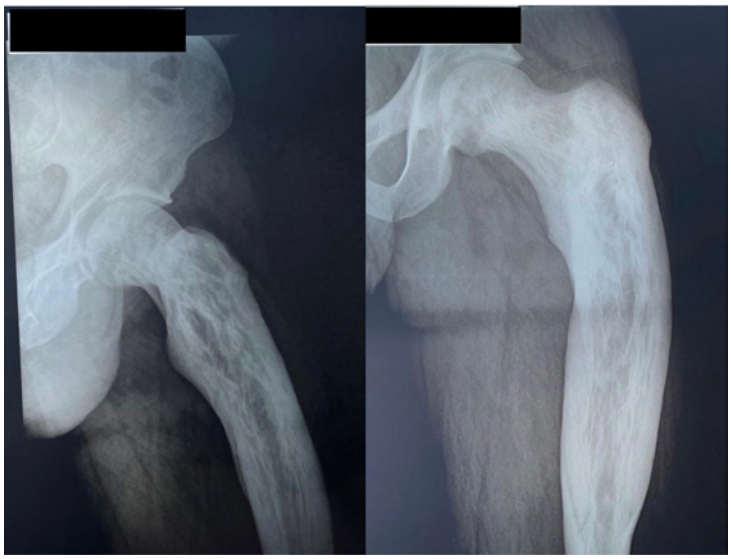
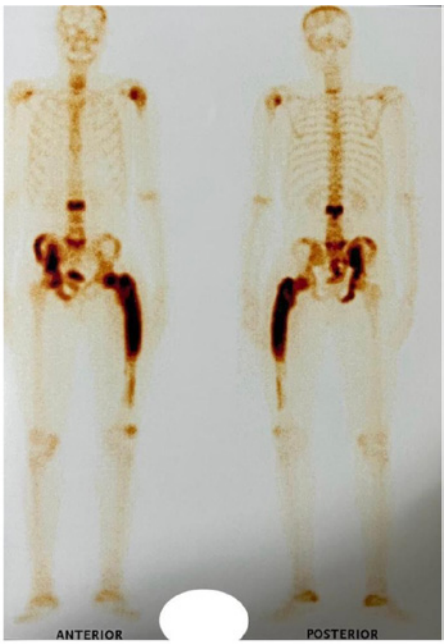


Table 1 lists the complementary exams requested for further investigation, with the bone scintigraphy shown in Figure 3.

Table 1. Additional laboratory and imaging investigation

Laboratory Tests	**Results**
Total calcium	8.3
Creatinine	0.8
Protein electrophoresis (PEP)	0.83
Parathyroid hormone (PTH)	57
Imaging Exams	**Results**
Left hip computed tomography	- There is a significant corticoperiosteal thickening of the middle and proximal third of the femur with altered bone trabeculation, noting areas with fat attenuation coefficients interspersed with nonspecific appearance, but accepting Paget's disease as the main differential diagnosis, it is advisable to perform follow-up for evolution control. - Mild alteration of bone trabeculae in the body of the left iliac bone as well as in the last vertebra at the thoracolumbar transition; femoral bowing of probable chronic nature, with no evidence of fractures.
Bone scintigraphy with 99mTc	- abnormal increase in radiotracer concentration in the following regions: skull (left parietal bone); proximal left humerus; spine (C6, L2 with an expansile appearance, L5, sacrum); right hemipelvis with an expansile appearance; left femur with an expansile appearance; knees with mild involvement; and feet, specifically the calcanei. Conclusion: bone lesions suggestive of polyostotic Paget's disease of bone.

Figure 3. Abnormal increase in radiotracer concentration mainly in the skull, proximal humerus, spine with L2 showing an expansile appearance, right hemipelvis with an expansile appearance, and left femur with an expansile appearance.



After evaluating these clinical data, a diagnosis of polyostotic Paget's disease of bone was made, and supplementation with calcium and a single dose infusion of 5 mg zoledronic acid was indicated. After eight months, the patient returned without new complaints and with total improvement of previous painful symptoms. Additionally, alkaline phosphatase was 198 U/L, consistent with a good laboratory response.

DISCUSSION

Paget's disease of bone (PDB) was first described in 1877 by Sir James Paget. PDB is characterized by an increase in the activity of bone cells, leading to abnormal bone growth with sclerotic and lytic areas. The process begins with excessive resorption by abnormal osteoclasts, followed by disorganized bone formation by osteoblasts. This condition is the second most common osteometabolic disorder, after osteoporosis, yet still greatly underdiagnosed and undertreated[2,7].

PDB can affect a single bone (monostotic form) or multiple bones (polyostotic form). It is more prevalent among the elderly and slightly more common in men than in women, varying considerably by geographic region, with a higher incidence in populations of British descent, such as the United Kingdom, and rare in individuals under 50 years old[1,2]. The reported case is of a patient with an atypical presentation, characterized by symptom onset and diagnosis before the expected age range, already in the symptomatic phase of the disease and presenting considerable bone deformities.

The most affected sites include the pelvis, vertebrae, and femur, consistent with what was described in the case above, and can lead to complications such as bone pain and deformity, fractures, deafness, osteoarthritis, and osteosarcoma[5].

Genetic factors play an important role in the pathogenesis, as relatives of patients with the disease have an increased risk of developing it[1,3]. In Brazil, the highest rates of occurrence are in the Northeastern states, due to European colonization in the region[10].

The pathogenesis of PDB involves a loss of normal regulation of bone resorption and formation, occurring in three phases: a lytic phase, a mixed phase of lytic and blastic activity, and a sclerotic phase. Mutations in the SQSTM1 gene are common in cases with a positive family history[2]. This gene encodes the p62 protein involved in the NF-κB signaling pathway.

Mutations in SQSTM1 have been identified in patients with PDB, impairing the ability of p62 to bind to ubiquitin, leading to an increase in osteoclast activity[3]. Additionally, environmental factors, including viral infections, also appear to contribute to its pathophysiology[1-3].

The clinical presentation of PDB can vary from asymptomatic patients to bone pain, deformities, fractures, neurological complications such as nerve compression, and hearing loss. Osteoarthritis can also be associated with this condition[2,6,7]. The symptoms and signs in the clinical case were typical, such as bone pain and deformity, which likely contributed to the diagnosis in a patient of divergent age from the literature.

The diagnosis of this condition usually occurs incidentally during evaluations for other health conditions and is confirmed by X-rays and bone scintigraphy. Performing bone scintigraphy with radionuclides is useful for assessing the extent of the disease and identifying possible asymptomatic sites, as in the reported clinical case where the patient had a polyostotic form but was symptomatic only in the proximal femur region. Radiographic changes reflect pathological changes over time. To assess disease activity, bone remodeling markers such as alkaline phosphatase are often used[1,3,7,8].

Bone remodeling markers are highly sensitive to detect Paget's bone changes, although they cannot completely exclude the disease in normal concentrations. These markers have shown moderate to strong correlation with scintigraphic indices before treatment with bisphosphonates. The marker P1NP shows higher correlation with disease activity, being an attractive option for monitoring treatment response. However, the limited availability and high cost of this marker seem to limit its use. Therefore, the measurement of total alkaline phosphatase is considered a useful marker for assessing disease activity after treatment, considering its availability and moderate correlation with bone scintigraphy data[1].

Despite remodeling markers being widely recommended for therapeutic monitoring, we should also value aspects related to the quality of life of patients. Although generally considered a benign disease, some individuals may present significantly severe complications. This justifies the need for more effective methods of early detection of the disease before irreversible bone damage occurs[4].

Non-surgical treatment involves lifestyle modifications, physiotherapy, and medications. Surgical modalities are used in refractory cases for corrections of deformities or complications of the disease[6,9].

Regarding drug treatment, attention should be paid to controlling painful symptoms using analgesics, nonsteroidal anti-inflammatory drugs, and antineuropathic agents, in addition to specific anti-Paget's treatment involving the use of osteoclast inhibitors to reduce bone remodeling. Bisphosphonates are considered the treatment of choice for PDB[3,5,8]. Long-term results of treatment with bisphosphonates, particularly zoledronic acid, show lasting suppression of bone remodeling and improvement in quality of life[2,8]. Zoledronic acid rapidly normalizes biochemical markers of PDB. Furthermore, this medication is highly safe for use in patients with PDB, with adverse events being rare, particularly when compared to osteoporosis[3]. As therapeutic alternatives, denosumab and salmon calcitonin are available, although

there is less evidence regarding the efficacy of these medications[2,3].

The patient reported in the case was treated with a single dose of 5 mg intravenous zoledronic acid, along with calcium supplementation, showing clinically significant improvement with resolution of painful symptoms. Additionally, there was a significant decrease in total alkaline phosphatase levels, consistent with a satisfactory laboratory response. These results are in line with current literature, which highlights the importance of bisphosphonates in the treatment of PDB.

CONCLUSION

Patients are advised to seek early medical help when experiencing symptoms. For healthcare professionals, it is important to recognize classical symptoms even in patients younger than those mentioned in current literature, as well as the efficacy of zoledronic acid in controlling symptoms and rapidly normalizing disease activity biomarkers.

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ANA JÚLIA LINHARES VOLPP - http://lattes.cnpq.br/4748117368922835 - https://orcid.org/0009-0006-8832-1790

LARA CHRISTINA RANGEL BRAGA - http://lattes.cnpq.br/8678730475123454 - https://orcid.org/0009-0003-5097-9763

RAUL KELLER AVELAR - http://lattes.cnpq.br/7754313191643110 - https://orcid.org/0009-0007-8768-559X

SEVERINO CORREIA DO PRADO NETO - http://lattes.cnpq.br/2843540709610403 - https://orcid.org/0000-0002-3998-1251

ADDRESS

SEVERINO CORREIA DO PRADO NETO
Avenida 3, Q07, Lts 15-19, Setor Mundinho – CEP 75832-009- Mineiros – GO
E-mail: severinopradoneto@gmail.com

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