PAGET'S DISEASE OF BONE AND ITS COMPLICATIONS DUE TO DELAY IN DIAGNOSIS

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Abstract

Paget's disease of bone is an osteometabolic focal disease characterized by defects in bone remodeling. It may be asymptomatic, but often is associated with bone pain, deformity, pathological fracture, secondary osteoarthrosis and deafness. The diagnosis is usually made by radiological and laboratory findings. This report describes a male patient, 74 years old, native of Amazon, without European ancestry, with polyostotic Paget's disease, with clinical, radiological and laboratory diagnosis after 30 years of disease. The authors emphasize several complications of Paget's disease due to delayed diagnosis and the rarity of the disease in this population group.

Keywords: Osteitis Deformans; Paget; Fractures, Bone; Bone Diseases.

Introduction

Paget's bone disease is a chronic focal non-inflammatory osteometabolic disease with a strong genetic background, with defects in bone remodeling affecting one (monostotic) or more points (polyostotic) of the skeleton. Recognized and described by Sir James Paget in 1877, it is typically found in people after the fourth decade of life, being slightly more common in caucasoid men. Its etiology remains unknown, although an autoimmune disorder associated with viral infections have been suggested. Long bones, pelvis, vertebral spine and skull are most often affected[1].

Paget's bone disease may run an asymptomatic curse, but often manifests as skeletal pain which may be related to disease activity or complications such as degenerative joint disease, fractures, osteosarcoma and neural impingement[2]. Four to nine years is the average lag time between the first symptoms and diagnosis[3,4], which is eventually made by the clinical history along with image and laboratorial finding[5], Herein, the authors report a case of a patient with Paget's bone disease with many complications related to delay in establishing the diagnosis.

Case Report

Male patient, 74 years old, brown skin, native of Amazon, retired driver, presented with a 30 years history of mild skeletal pain that has begun at the sacroiliac region, not continuous, which worsened with physical effort, and, sometimes, relapsed at night. Later, the skeletal pain has affected the lower limbs, diffusely, burning, associated with paresthesias. Deformities developed progressively in the left leg (arching) and in the vertebral spine. The patient walks with difficulty due to functional impairment caused by deformity and pain, with limitation for daily activities and work capacity.

The patient complained of bilateral hearing loss and intestinal constipation but had no weight loss. Previous diagnosis of congestive heart failure, systemic arterial hypertension and ischemic heart disease had been made. He had never been subjected to transfusions or surgeries. There was no history of familiar osteoporosis with fractures or other metabolic bone disease. He denied the use of corticosteroids or other drugs related to osteopenia. There was no personal history of renal failure, disease of the thyroid, hyperparathyroidism, hipogonadism or collagen-vascular disease. He

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smoked cigarettes, 50 packets/year, and consumed alcoholic beverages socially.

At physical examination, there was a paravertebral protuberance at the thoracolumbar region, warm bone deformities (bowing) at the lower limbs and an increased cranial circumference. He had small stature and walked with short steps and waddling gait. The range of motion was limited at the hips and knees, which impaired the performance of certain maneuvers, such as the evaluation of Lasegue sign. Patellar reflex was absent and there was reduced strength in extension and flexion of the hallux. The muscles of the lower limbs were hypotrophic, but proximal muscle strength and sensitivity were preserved.

Lab tests showed serum calcium: 9,0mg/dL (VR= 8,8 –11); Phosphorus: 4,0mg/dL (VR= 2,5-4,5); glucose: 92mg/dL; urine calcium: 32,9mg/24hs (VR=60-180); urine protein: 75mg/24hs; serum alkaline phosphatase: 1657U/L (VR= 644), C-Reactive protein: 12mg/dL; erythrocyte sedimentation rate: 34mm; lactic dehidrogenase: 181UI; prostatic specific antigen: 0,5ng/mL; uric acid: 4,0mg/dL.

A magnetic resonance study of the lumbar spine showed a partial collapse of the fourth vertebra, and low intensity lesions with T1 and heterogenic signal with T2, which captures contrast medium, spreaded along lumbar vertebras and the sacrum. There was bone destruction with collapse and soft tissues invasion at the twelfth vertebra, with backward projection of the posterior borders of the vertebral bodies of D11, D12, L1 and L4, narrowing the vertebral channel and compression the dural sac. A tomografic study of the pelvis showed a coarse thickening of bone trabeculae with an insufflated aspect, and sclerotic areas superposed on lytic lesions in pelvic bones (Figures 1 and 2). A tomographic study of the legs showed an expansive and insufflated lesion all along the left tibia, with diffuse and irregular thickening of cortical bone and disordered bone trabeculae (Figure 3). A tomographic study of toraco-lumbar spine showed destruction of vertebral bodies at D12, L1 and L2, with invasion of soft tissues, the medular channel and neural foramen at this level, and shrinking of intervertebral spaces at L3-L4 and L4-L5, with traces of air within the disks. Vertebral bone trabeculae were diffusely disarranged and showed a reactive zone (Figure 4). There was widespread inter-apophysary osteoarthritis. A radioisotope scanning showed excessive label capture at the abnormal bone, suggesting a metabolic disorder.

During the 30 years of disease, because of insidious mild pain, despite the major deformities, the patient was consulted only during periods of pain exacerbation, in the emergency room, not pursuing a diagnosis. Difficulty of access to a public health specialist also contributed to delay in diagnosis. In 2005, he consulted an orthopedist, when the first radiographs were taken and Paget's

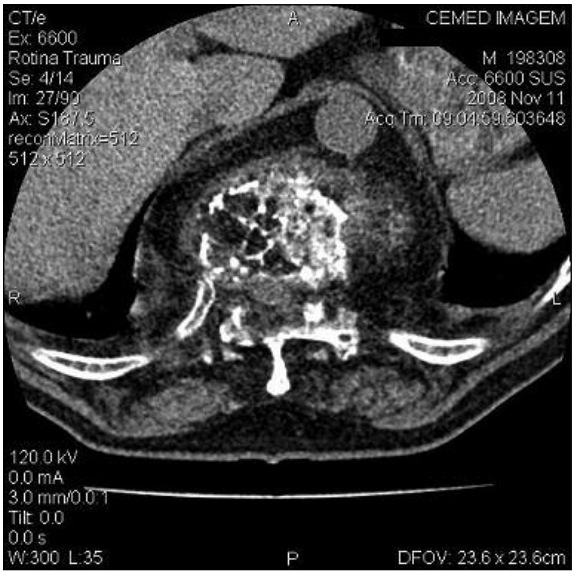

Figure 1. Tomographic study of pelvic bones showing lytic images

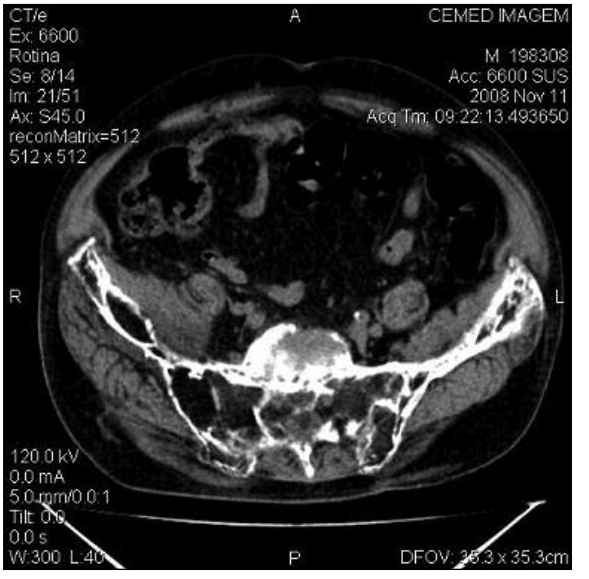

Figure 2. Tomographic study of pelvic bones showing lytic images

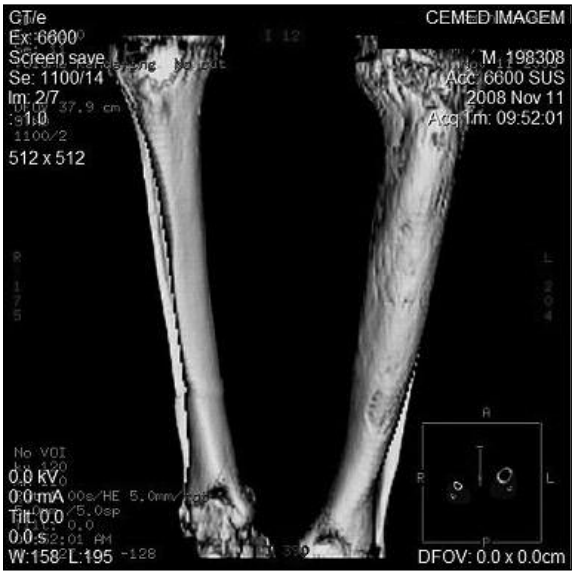

Figure 3. Tomographic study showing lytic images and thickening of cortical bone

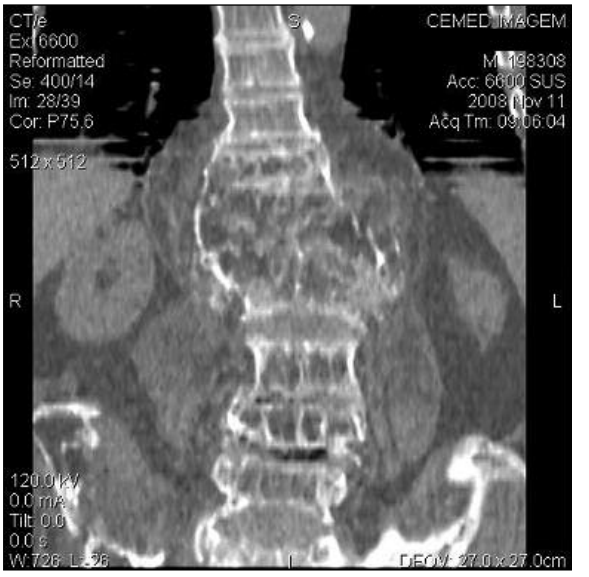

Figure 4. Destruction of multiple vertebrae with lytic lesions and areas of repair (reactive zone).

disease was suspected. Subsequently, he was referred to a rheumatologist, but he came to our Department of Rheumatology only in 2010. After a thorough clinical and laboratory evaluation, the diagnosis of Paget disease of bone was established, and specific treatment with zolendronic acid was tried, but the patient still could not get the medication because of financial reasons. Thus, alternatively, alendronate 40mg/day was used with gradually reduction of alcaline phosphatase: 1283 UI/ /L after three months and 1083 UI/L after six months of starting treatment.

Discussion

Paget's disease is the second most common metabolic bone disease, second only to osteoporosis. It is difficult to estimate its impact because, in most cases it is asymptomatic[6], but is more frequent in Countries of European and Anglo-Saxon extraction and is rare in the Americas[5,7]. In Latin America, 1149 cases were reported in the last 30 years, and the fact common to these patients is that the vast majority have European ancestry[8]. In Brazil, most cases are found in the city of Recife, owing to its peculiar mixed European colonization over approximately four centuries[9] and for being a reference center for Paget's disease in the country. The patient reported is native of Amazon, without European ancestry, which makes the case interesting due to the rarity in this population. The axial skeleton is more often involved[1], but proximal long bones may also be committed in 25 to 35% of cases[10]. Appendicular involvement is usually unilateral[10]. Polyostotic disease is found in 65 to 90% of patients, representing the most common form at diagnosis[10,11].

Disease's etiology remains uncertain[8], but genetic, environmental [9,12] and viral factors[13] are considered. Typical manifestations of Paget's disease are related to its complications[2], which may be classified according to the body system affected: skeletal (bone pain, bone deformities, osteoarthrosis, fractures and spinal channel stenosis), neural (deafness, cranial nerves dysfunction, high intracranial pressure), cardiovascular (ischemic heart disease, aortic valve stenosis, intracavitary calcifications, widespread atherosclerosis, high output congestive heart failure), metabolic (hypercalciuria, hypercalcemia, hyperuricemia, nephrolitiasis), and neoplasia (osteosarcoma, condrosarcoma, fibrosarcoma, giant cell tumor)[14]. At the time of diagnosis, the patient already had several complications of the disease, such as fractures, bone deformities, deafness, and congestive cardiac failure, which reflects the delay in diagnostic.

Diagnosis is ultimately made through image and laboratory findings. Radioisotope bone scanning is the most sensible method to detect early lesions.

Most patients with Paget's disease are identified by an elevation on the levels of alkaline phosphatase which cannot be explained by hepatobiliary pathology or another osteometabolic disorder. Altogether, image findings rely on disease progression to be classified in three distinct stages: lytic phase, with initial reabsorption characterized by osteolysis,established by osteoclast activity; mixed phase, with vascular and osteoblastic repair, leading to thickening and distortion of cortical and trabecular bone; and a blastic phase, which curses with appositional new bone, with an sclerosing scaring aspect[5]. The patient's diagnostic was suspected by the elevated levels of alkaline phosphatase and by radiological imaging characteristics.

Drug treatment is made with bisphosphonates, which are shown to diminish bone pain and biochemical markers of bone remodeling in randomized clinical trials, achieving restoration of histological and radiographic patterns[15]. The first bisphosphonate to be used was etidronate. However, more potent biphosphonates have proved to be more effective, leading to more prolonged periods of remission[16]. Oral alendronate, in a dose of 40 mg/day, for 6 months, leads to a 77% decrease in alkaline phosphatase, compared with the 44% decrease produced by etidronate[17]. Zoledronic acid is 10.000 times more potent than etidronate in reducing the biochemical markers of bone remodeling[18] and patients with resistance to other bisphosphonates usually respond to this drug[19]. As the only bisphosphonate available in public services, the patient has been treated with alendronate sodium 40 mg/d, improving complaints of pain and reducing gradually alkaline phosphatase levels. The apparent slow response to treatment may have been by the major bone involvement at diagnosis, and the fact that the drug considered more potent for the treatment of Paget's disease (zolendronic acid) was not performed, due to financial reasons.

Paget's disease diagnosis is rather difficult to be made, as long as the disease runs a large and variable clinical spectrum, involves many topographies in the body with different degrees of metabolic intensity, a difficulty most marked in asymptomatic patients. Nevertheless, in cases such as the one reported herein, with bone pain and deformities, the possibility of Paget's disease should always be concerned, considering the high impact of the complications brought forward by a delay in disease diagnosis and treatment.

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