Monostotic Paget's disease of the radius: a case report

Zinon T. Kokkalis[1]
Stefania Kokkineli[1]
Ilias D. Iliopoulos[1]
Panayiotis D. Megaloikonomos[2]
Andreas F. Mavrogenis[2]
Andreas Panagopoulos[1]

[1] Department of Orthopaedics, University of Patras, School of Medicine, Rio-Patras, Greece
[2] First Department of Orthopaedics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

Address for correspondence:
Zinon T. Kokkalis
Department of Orthopaedics, University of Patras,
School of Medicine
Rio-Patras, Greece
E-mail: drkokkalis@gmail.com

Summary

Paget's disease of bone, osteitis deformans or chronic inflammation of bone is a chronic non-metabolic bone disorder that typically begins with excessive bone resorption followed by an increase in bone formation. Isolated monostotic Paget's disease of the radius is extremely rare, often mimicking various entities. A high index of suspicion is required supported with imaging studies for the correct diagnosis. Long-term follow-up is mandatory in these patients in order to identify and treat any subsequent recurrence or secondary malignancy.
This article describes a 56-year-old man who presented with progressive deformity of the right radius previously misdiagnosed as giant cell tumor. Definite diagnosis was obtained with bone biopsy supported by magnetic resonance imaging and bone scan.

KEY WORDS: Paget's disease; bone; monostotic; radius.

Introduction

Paget's disease of bone, also known as osteitis deformans or chronic inflammation of bone is a chronic bone disease first described by Sir James Paget in 1877 (1). It is the second most common bone disorder in the elderly and typically begins with osteoclastic hyperactivity followed by compensatory osteoblastic activity (mixed lytic and blastic phase) (2). This leads to a structurally disorganized mosaic of bone (woven bone-sclerotic phase) that is mechanically weaker, larger, less compact and more susceptible to fracture than the normal adult lamellar bone (3). This woven bone pattern allows the bone marrow to be infiltrated by excessive fibrous connective tissue and blood vessels, leading to a hypervascular bone status that is prone to deformity, bowing and fracture (4). The etiology of Paget's disease of bone remains largely unknown. A recent study suggested that it may be the result of a slow-acting viral infection on a genetically vulnerable bone, while hereditary hypothesis is also supported (5). However, the exact pathogenetic pathway leading to the disease is unclear.
Paget's disease of bone may involve a single bone (monostotic), or more frequently multiple bones (polyostotic) that is characterized by increasing risk for complications (2). The disease has a predilection for the axial skeleton (pelvis, femur, lumbar spine, skull and tibia in descending order of frequency), however, any bone may be affected (6). Isolated Paget's disease of the radius is rare and only scarcely reported in the literature (7, 8). In this article, we present a 56-year-old man with a lesion at the distal radius initially misdiagnosed as a giant cell tumor of bone. Bone biopsy showed Paget's disease of bone. Imaging studies showed isolated, localized, monostotic disease. The purpose of this article is to increase the awareness of the treating physicians for the occurrence of Paget's disease at the radius, and to discuss the role of imaging studies and biopsy for accurate diagnosis.

Case presentation

A 56-year-old man underwent a magnetic resonance (MR) imaging scan of his right forearm due to persistent edema over the past 2 years without a history of trauma. Then, based on the MR imaging findings, the radiologist diagnosed a giant cell tumor of bone at the distal radius; his local orthopaedic surgeon recommended observation. At presentation, 2 years after initial symptoms, physical examination showed swelling and deformity at the right forearm with an obvious anterior bowing deformity. The patient did not experience any local pain or tenderness; range of motion of the wrist and elbow was normal. He did not have any other skeletal deformities; his past medical history was unremarkable.
Radiographs of the forearm and wrist showed an extensive lesion involving the distal radius with mixed lytic-sclerotic appearance, coarse trabeculation and arcuate deformity (Figure 1). MR imaging showed an intramedullary lesion at the distal third of the right radius extending through the metaphysis to the subchondral bone, with broadening of the radial shaft, thinning of the cortex and bone erosion (Figure 2). MR imaging differential diagnosis included giant cell tumor of bone, lymphoma, chondroblastoma and osteosarcoma. Whole-body bone scintigraphy showed marked increased

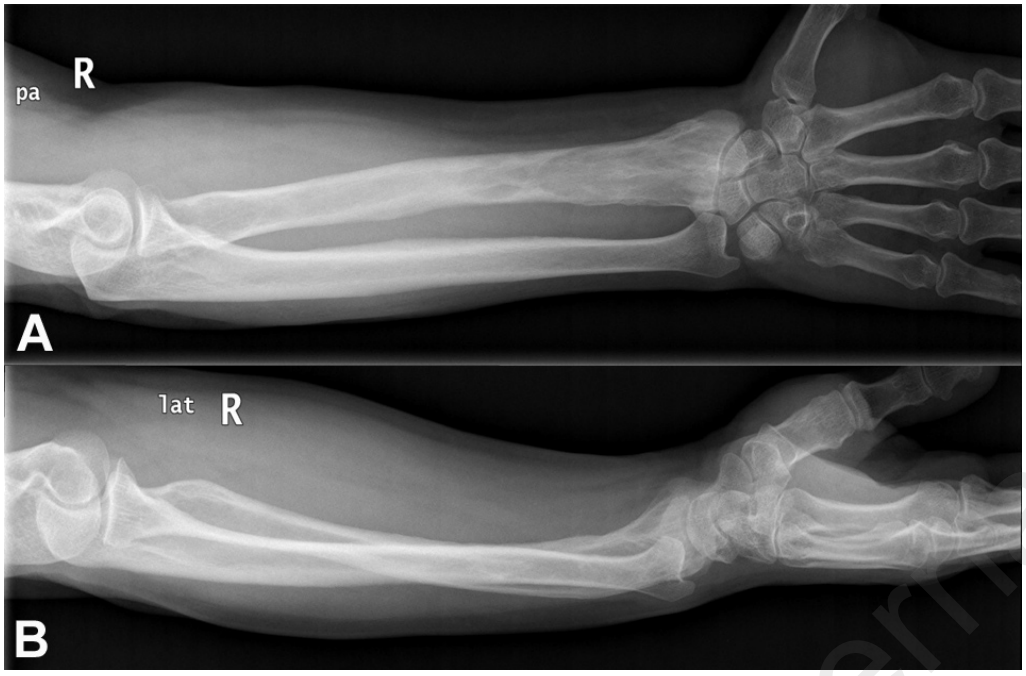

Figure 1 A, B - (A) Anteroposterior and (B) lateral radiographs of the right forearm show a mixed lytic-sclerotic lesion involving the distal radius with coarse trabeculation and arcuate deformity.

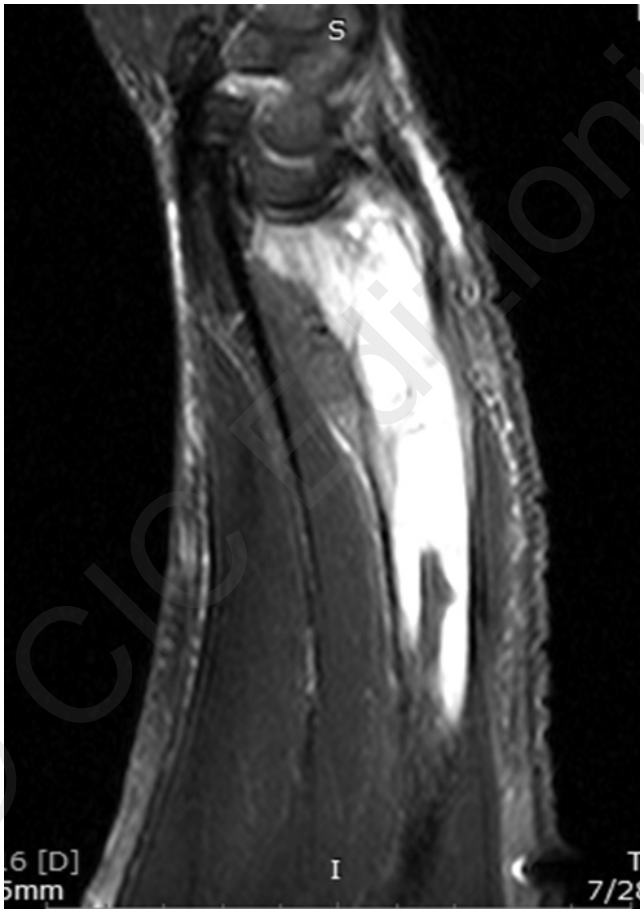

Figure 2 - Contrast-enhanced T2-weighted MR imaging shows broadening and erosion of bone, cortical thinning and bowing deformity of the radius.

uptake at the shaft and distal end of the right radius; no other skeletal lesion was observed (Figure 3). Routine blood tests were within normal values; total serum alkaline phosphatase value was three times higher than normal, serum homocysteine and folate acid were normal, and vitamin B was deficient. Based on the radiographic, MR imaging, bone scan and laboratory findings, the diagnosis of isolated monostotic Paget's disease of the right radius was assumed.

For histological confirmation of the diagnosis, biopsy of the lesion was done; histological section of tissue samples showed cancellous bone with mild osteoclastic and intense osteoblastic activity, and marrow spaces filled with loose, highly vascularized connective tissue. The ossification lines within the trabecular bone indicated a mosaic, jigsaw-puzzle like pattern (Figure 4) that is typical of Paget's disease of the bone (6). After histological confirmation of the diagnosis, the patient was offered surgical treatment with curettage and bone grafting of the lesion or medical treatment with bisphosphonates. However, he did not consent to any further treatment except than periodical clinical and radiographic follow-up.

Discussion

Paget's disease of bone isolated to the radius is extremely rare with very few cases previously reported in the related literature (7, 8). It can affect both men and women, most commonly above the age of 50 years, with a slight predominance for men in some series (9). It is rarely reported in Scandinavian countries and Asia and most commonly occurs in people of British decent as well as in France, Germany, Spain or Italy; a familial aggregation has been reported (10). In 30% of cases, disease incidence involves more than one member of the family and it is inherited in an autosomal dominant fashion (3).

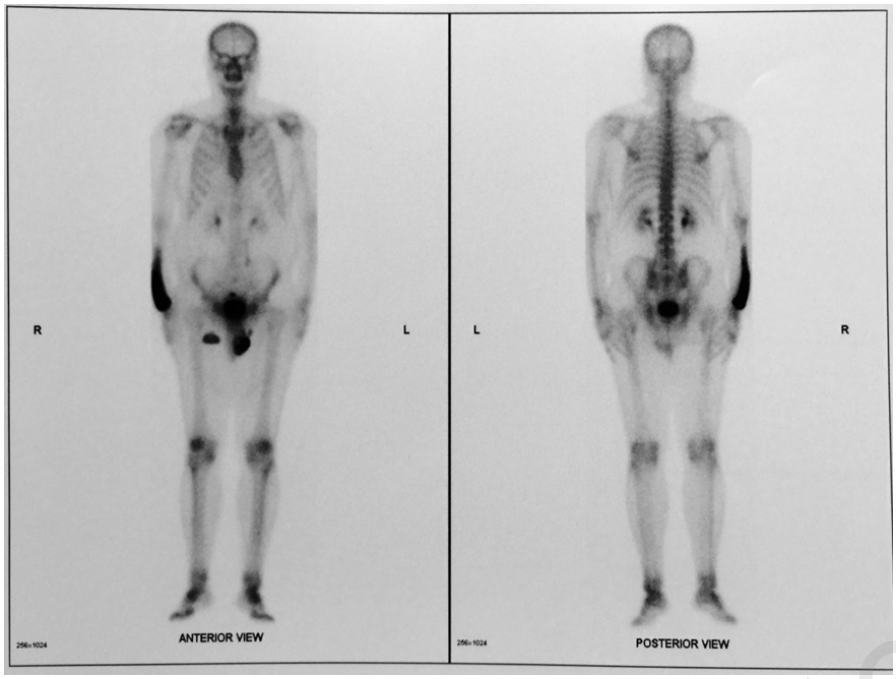

Figure 3 - Bone scintigraphy shows isolated increased radioisotope uptake at the distal radius.

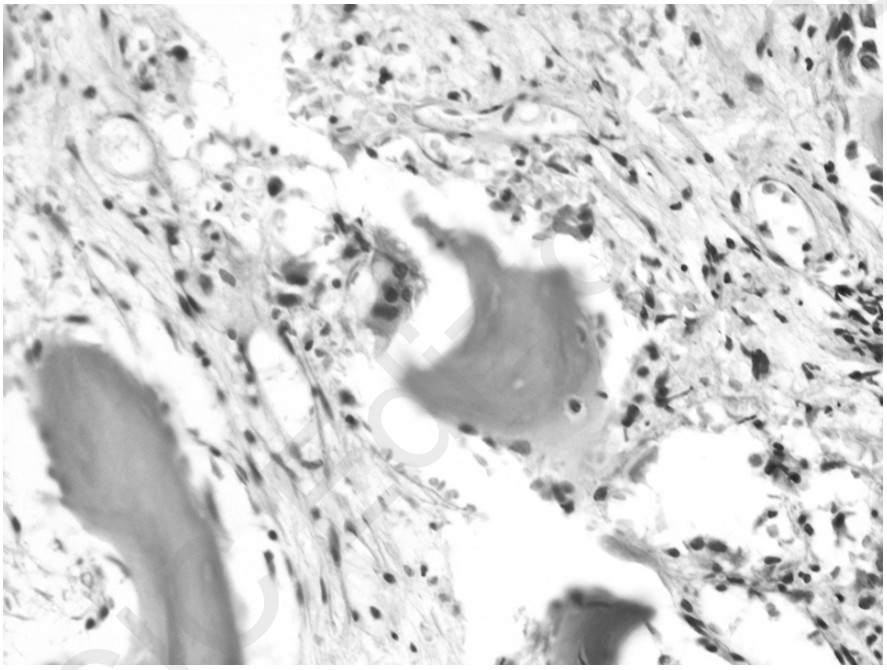

Figure 4 - Histological section of biopsy bone tissue shows abundant osteoblastic and lesser osteoclastic activity producing the characteristic mosaic (jigsaw puzzle) pattern of prominent reversal (cement) lines, thick irregular trabecular bone, osteoclast-like giant multinucleated cells, disorganized osteoblastic activity and new osteoid formation (stain, eosin and hematoxylin; magnification, 100x).

Clinically, most patients are asymptomatic (3). Clinical presentation is often non-specific. Poorly localized bone pain is the most common symptom bringing the patient to a physician followed by bone deformity (5). Pain can mimic arthritic conditions as well as various types of tumors. The differential diagnoses include osteopenia, osteopetrosis, osteomalacia, osteoarthritis, osteoporosis and bone tumors such as giant cell tumor of bone, lymphoma, chondroblastoma and osteosarcoma (7). Potential sources of pain in patients with Paget's disease of bone include disease activity, osteoarthritis, impending or actual stress fracture, radiculopathy caused by spinal involvement and malignant transformation (11).

Often, the physician may be alerted by an elevated level of bone turnover markers (5). Although a normal alkaline phosphatase level does not exclude the disease in patients with monostotic disease, a total serum alkaline phosphatase value that is higher greater than twice the normal value strongly suggests Paget's disease of bone, especially if the serum calcium and phosphorus and renal function are normal (4). Elevated serum uric acid values have also been reported in patients with Paget's disease of bone (12). Vitamin B deficiency, as in the current patient, increased serum homocys-

teine (HCY) and deficiency of folate acid seem to stimulate bone resorption and adversely affect collagen cross-linking in patients with Paget's disease of bone (13).

The relationship between Paget's disease of the bone and secondary malignant transformation remains uncertain. Sarcomatous degeneration of the pagetic bone is an uncommon but unfortunate complication with dismal prognosis; pagetic bone sarcomas are usually osteosarcoma, fibrosarcoma or chondrosarcoma. Approximately 0.5 to 1% of the patients with Paget's disease of bone may experience secondary osteosarcoma; approximately 20% of the patients with osteosarcoma above the age of 60 years has Paget's disease of bone as a predisposing condition (5, 14). For this reason, after the diagnosis of Paget's disease of bone, closed follow-up is recommended.

The goal of treatment for Paget's disease of bone is to relieve bone pain and prevent progression of the disease. Since the increased activity of osteoclasts is the primary feature of the disease leading to increased bone resorption, first line treatment remains the administration of antiresorptive agents such as bisphosphonates and calcitonin. Antiresorptive agents reduce bone pain, and may also have a positive effect in the setting of surgical treatment preventing postoperative bone resorption, intraoperative bleeding, and heterotopic bone formation (15). In general, patients with Paget's disease of bone should be administered 1000-1500 mg of calcium, adequate sunshine and at least 400 units of vitamin D daily (4, 16). This is especially important for patients being treated with bisphosphonates since hypocalcemia and hyperparathyroidism are common after suppression of bone turnover. Patients with a history of nephrolithiasis should discuss calcium and vitamin D intake with their treating physicians. Moreover, exercise is very important in maintaining skeletal health and joint mobility as well as to avoid gain weight and undue stress on the affected bones. Urine tests may be used for assessing activity and monitoring treatment efficacy. In these tests, a sample of a person's urine is analyzed for the presence of bone markers such as N-telopeptide of type I collagen and alpha-alpha type I C-telopeptide fragments which are sensitive markers of bone resorption. Upon successful treatment of Paget's disease of bone, the levels of these bone markers are expected to decrease (4). An abnormally high alpha-CTx/beta-CTx ratio is present in patients with active Paget's disease of bone. This ratio returns to the reference range after treatment with bisphosphonates.

Indications for surgical treatment in patients with Paget's disease of bone include joint replacement if evidence of arthritis, fracture fixation, osteotomy to correct bone deformity, surgery to correct spinal stenosis, and prophylactic surgery in patients with painful pseudofractures (11). Aggressive operative treatment is also indicated in patients who develop secondary osteosarcoma; in these cases, prognosis is poor with an estimated 5-year survival of approximately 6% (17). Treatment of fractures in patients with Paget's disease of bone is challenging because of bony enlargement, deformity, sclerotic bone, and increased vascularity; a 40% rate of nonunion has been reported in Paget's disease patients with femoral neck fractures treated with internal fixation (18). Arthoplasty seems to be the optimal option in these patients even though technical difficulties related to bone deformity and inability to use conventional prosthesis may be encountered (19). Corrective osteotomy may be necessary to proceed to arthroplasty reconstruction, and may also be indicated in symptomatic patients with disabling deformity without degenerative joint disease.

In conclusion, monostotic Paget's disease of the radius is rare. A high index of suspicion combined with appropriate imaging and laboratory studies is essential for accurate diagnosis. Documentation of the diagnosis is obtained with bone biopsy. Medical therapy is the mainstay of treatment to obtain relief of pain and avoid disease progression. Surgical treatment is indicated when complications of the disease occur. Long-term follow-up is mandatory in order to identify and treat early any disease relapse of secondary sarcoma.

Financial disclosure

All Authors declare that they have no conflicts of interest.

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