Right hip and pelvic pain

Follow-up imaging confirmed a clinical suspicion.

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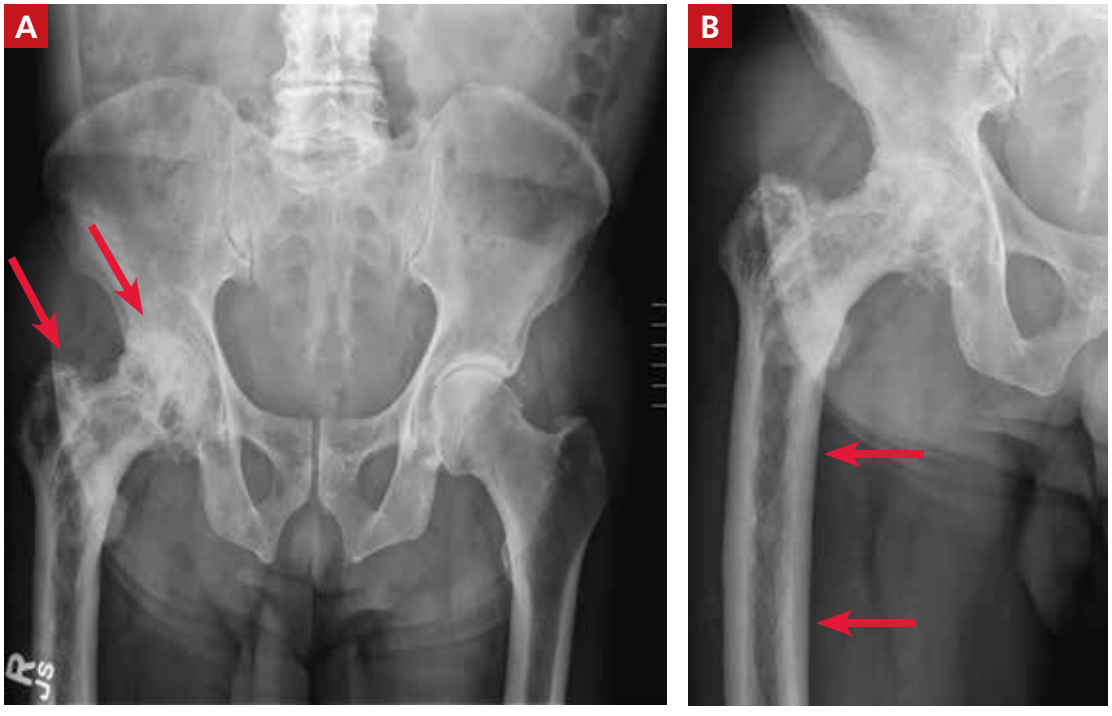
A 65-YEAR-OLD MAN with a history of remote colon cancer, peptic ulcer disease, gastroesophageal reflux disease (GERD), and bilateral knee replacements presented with right groin and hip pain of more than a year's duration. The patient described his hip pain as aching and said that it had worsened over the previous 6 months, interfering with his sleep. He said the pain worsened following activity, and it briefly felt better following an intra-articular corticosteroid injection into his right hip. The patient denied recent trauma or fracture and said he had no scalp pain, hearing loss, or spinal tenderness. Physical examination showed limited range of motion of the right hip and mild tenderness to palpation. Laboratory values were within normal limits. X-rays of the pelvis (**FIGURE 1A**) and right hip (**FIGURE 1B**) were ordered.

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE 1

X-rays reveal a coarsened trabecular pattern and mild bony enlargement of the right femoral head, neck, and diaphysis



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Dx: Paget disease of bone

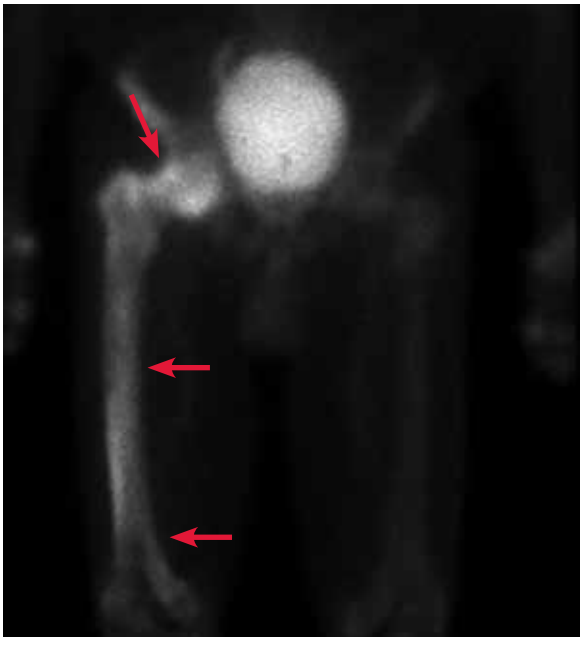
Based on the patient's clinical history and initial imaging studies, which showed characteristic trabecular thickening with bony enlargement of the right femur, we suspected that he had Paget disease of bone. This was confirmed on subsequent whole-body ^{99m}Tc-MDP bone scan (**FIGURE 2**), which revealed corresponding diffuse increased radiotracer uptake of the right femur. There was no scintigraphic evidence of osseous involvement of the skull, spine, or pelvis.

Epidemiology/incidence. Paget disease, also known as *osteitis deformans*, is fairly common in the aging population, with a prevalence ranging from 2% to almost 10%.[1,2] Although onset before age 40 is rare, the diagnosis should be considered in younger patients, given the high prevalence. There is a slight male predominance, and the disease is more common in the United Kingdom and Western Europe, as well as in countries settled by European immigrants.[3]

Both genetic and environmental causes are believed to contribute to the pathogenesis of Paget disease. Mutations in the gene encoding sequestosome 1 (SQSTM1) can be seen in the autosomal dominant familial type (25%-50% of these cases), as well as in sporadic cases.[4] Environmental influence has also been postulated as a possible cause, with a viral etiology (eg, chronic measles infection) being the most cited.[5]

FIGURE 2

Bone scan confirms suspected Dx



A ^{99m}Tc-MDP bone scan shows abnormal increased radiotracer uptake with near whole bone involvement of the asymmetrically enlarged right femur.

Most patients will be asymptomatic

Paget disease can affect any bone in the body, although the skull, spine, pelvis, and long bones of the lower extremity are the most commonly affected sites.[2] Most patients with Paget disease are asymptomatic. When symptoms are present, they either result from direct involvement of the bone or are secondary to bone overgrowth and deformity.

Direct involvement manifests as deep, constant bone pain that is worse at night. Symptoms related to bone overgrowth and deformity include spinal stenosis and related neurologic abnormalities, increased skull size, hearing loss (impingement of cranial nerve VIII), pathologic fracture (most commonly of the femur), and deformity such as protrusio acetabuli or femoral or tibial bowing.[6] High-output heart failure and abnormalities in calcium and phosphate balance are uncommon but do occur.

Degeneration into osteosarcoma is a rare but almost invariably fatal complication of Paget disease, with an incidence of 0.2% to 1%.[7] It clinically manifests as increased bone pain that is poorly responsive to medical therapy, local swelling, and pathologic fracture.[8]

Radiography is key to the work-up

The diagnosis of Paget disease is primarily radiographic. Early in the disease process, lytic lesions with thinning of the cortex will be noted. Later in the disease, there will be a mixed lytic/sclerotic phase, in which enlargement of the bone, a thickened cortex, and coarsened trabeculae are observed.

Characteristic radiographic findings. Focal lytic lesions in the skull are known as *osteoporosis circumscripta*. In the sclerotic phase, there is a thickening of the calvaria (termed "cotton wool"). Lesions involving the long bones will begin at the proximal or distal subchondral region and progress toward the diaphysis, with a sharp oblique delineation

between involved bone and normal bone; this is described as "blade of grass" or "flame-shaped."[9]

Within the pelvis, there will be cortical thickening and sclerosis with enlargement of the iliac wing. Within the spine, there will be enlarged vertebrae with a thickened sclerotic border, resulting in a "picture frame" appearance. Later in the disease, the sclerosis will involve the entire vertebrae (termed "ivory vertebra").[10]

Additional testing options include magnetic resonance imaging (MRI), bone scintigraphy, laboratory testing, and biopsy.

MRI is recommended when degeneration into osteosarcoma is present—indicated by permeative lesions with cortical breakthrough and a soft-tissue mass. MRI is helpful to further characterize the lesion. Absence of the normal fatty marrow on T1-weighted images would be concerning for tumor involvement.

Bone scintigraphy is used to determine the extent of disease. It will show increased uptake when the lesions are active.

Laboratory testing. Serum alkaline phosphatase (sAP) is frequently elevated in patients with Paget disease (normal range, 20-140 IU/L) and reflects the extent and activity of disease. However, this correlation is not always reliable; it depends on monostotic vs polyostotic involvement, as well as which bones are involved. For example, sAP levels may be markedly elevated when the skull is involved but normal when other bones are involved.[11] In patients with elevated sAP, serum calcium and 25-hydroxyvitamin D measurements should be obtained in anticipation of bisphosphonate treatment.

Biopsy. If the radiographic findings are typical for Paget disease, bone biopsy is not indicated. However, the main competing diagnosis to consider is malignancy; in atypical cases when imaging is unable to elucidate an underlying tumor, biopsy would be warranted.

Differentiating Paget disease from sclerotic metastasis is important. In metastasis, there will be no trabecular coarsening or enlargement of the bone.

Bisphosphonates are a Tx mainstay

Indications for treatment include symptomatic or asymptomatic disease with any of the following: elevated sAP with pagetic changes at sites where complications could occur; sAP more than 2 to 4 times the upper limit of normal; normal sAP with abnormal bone scintigraphy at a site where complications could occur; planned surgery at an active pagetic site; and hypercalcemia in association with immobilization in patients with polyostotic disease.

Newer generation nitrogen-containing bisphosphonates are the mainstay of treatment; they ease pain, slow bone turnover, and promote deposition of normal lamellar bone, which over time will normalize sAP levels.[12] The most frequently used and studied bisphosphonates include oral alendronate, oral risedronate, and intravenous zoledronic acid.[13]

Prior to treatment initiation, the patient should have documented normal serum levels of calcium, phosphorus, and 25-hydroxyvitamin D, and these levels should be monitored throughout the first year of treatment. All patients should receive supplemental vitamin D and calcium to avoid hypocalcemia. sAP should be measured at 3 to 6 months to assess the initial response to therapy. Once the levels equilibrate, sAP can be measured once or twice a year to asses bone activity.[14]

Our patient was referred to Endocrinology for management of Paget disease of his right hip and femur. Lab values, including sAP and liver function test results, were normal. The patient was prescribed a zoledronic acid infusion (Reclast). At 4-week follow-up, the patient reported moderate relief of bone pain and improved sleep. JFP

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If the radiographic findings are typical for Paget disease, bone biopsy is not indicated.

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death. The decision to undergo PSA screening should be made by both the provider and the patient, after a discussion of the limited benefits and associated harms. The interval of follow-up screening may vary from 2 to 4 years depending on patient age, level of PSA, and whether a patient is taking medications such as 5-alpha-reductase inhibitors. JFP

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