59-Year-Old Man With Pelvic Pain and Hypergammaglobulinemia

SHAJI KUMAR, MD,* AND MARTHA Q. LACY, MD†

A 59-year-old man was referred to our institution by his local physician for further evaluation and management of pelvic pain of 3 months’ duration. He had been well until 3 months previously when he developed left testicular pain with fever (temperature, 40°C) and vomiting. Two to 3 days later the fever had subsided, but he experienced severe pelvic pain, described as deep, poorly localized, and worse with weight bearing and hip abduction. Treatment with nonsteroidal anti-inflammatory agents and other analgesics provided little benefit. He denied having persistent fever, anorexia, or weight loss. There were no changes in bowel pattern and no hematochezia, hematuria, or worsening of the pain with micturition or bowel movements. Aside from the pelvic pain, findings on review of systems were normal.

The patient’s medical history was unremarkable except for hyperlipidemia. Physical examination revealed only tenderness over the symphysis pubis. He had normal passive range of motion of his hips but had tenderness on abduction bilaterally. Slight edema of his left lower extremity was evident.

An extensive evaluation before referral showed an elevated sedimentation rate (ESR) of 104/mm in 1 h (reference ranges shown parenthetically) (<10 mm/1 h), elevated IgG of 2680 mg/dL (700-1500 mg/dL), and normal IgM and IgA. Presence of a small monoclonal spike was suspected within a broad polyclonal band. A metastatic bone scan showed no lytic or sclerotic lesions. Magnetic resonance imaging (MRI) of his pelvis, performed to evaluate pelvic pain, showed only a slightly abnormal marrow signal. The possibility of multiple myeloma was raised, and he was referred for further work-up.

1. Which one of the following tests would be least helpful in confirming the diagnosis suspected in this patient?
   a. Bone marrow examination
   b. Plasma cell labeling index (PCLI)
   c. Metastatic skeletal scan
   d. Serum and urinary protein electrophoresis
   e. Marrow cytogenetics

The conspicuous feature of this patient’s presentation is the poorly localized pelvic pain. Patients with multiple myeloma often present with bone pain. Fever and testicular pain are unusual presenting symptoms for multiple myeloma, although such patients are at a higher risk for infections. Multiple myeloma is typically accompanied by (1) an increase in plasma cells in the bone marrow, (2) lytic bone lesions on radiographs, and (3) serum and/or urinary monoclonal immunoglobulins (M component). A minimum of 10% to 15% of plasma cells seen at bone marrow biopsy has traditionally been considered necessary for diagnosing multiple myeloma. However, in a recent large series of patients with confirmed multiple myeloma, 14% had less than 10% plasma cells in the marrow. The plasma cell in multiple myeloma often shows features of immaturity. The PCLI is a measure of the proliferative activity of plasma cells and is expressed as the fraction in S phase, indicated by the capacity of cells to incorporate a DNA precursor like tritiated thymidine or bromodeoxyuridine. Because the PCLI can confirm the clonality of marrow plasma cells, it is useful not only diagnostically but also prognostically.

Plain radiographs, as used in metastatic skeletal scans, reveal bony abnormalities consisting of punched out lytic lesions, osteoporosis, or fractures in about 75% of patients. These abnormalities are usually multiple and are most commonly seen in the skull, ribs, sternum, spine, or proximal long bones. Radionuclide imaging of the bone is less useful in multiple myeloma since it tends to detect areas of new bone formation, which is typically absent in myeloma bone lesions. Computed tomography (CT) and MRI are often helpful in demonstrating vertebral lesions not seen on plain films. In about 0.5% to 3% of patients, osteosclerotic lesions predominate, and this is frequently associated with POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes).

Serum protein electrophoresis may reveal an M protein. The M protein represents the monoclonal immunoglobulin overproduced by the clonal population of plasma cells. A serum M protein of more than 3.0 g/dL has been used as a diagnostic requirement for multiple myeloma, but a clear...
2. Which were normal. The PCLI was 0%.

Various cytogenetic abnormalities have been described in multiple myeloma but are not required for the diagnosis.

Our patient had no evidence of lytic or sclerotic lesions on his metastatic bone scan. A bone marrow biopsy revealed 5% plasma cells, which appeared normal. Serum electrophoresis revealed a polyclonal IgG band but no monoclonal spike, and findings on urinary electrophoresis were normal. The PCLI was 0%.

2. Which one of the following tests would be least useful for further evaluation of this patient’s pelvic pain?

a. Plain radiograph of the pelvis including hip joints
b. CT of the pelvis
c. MRI of the lumbosacral spine and pelvis
d. Colonoscopy
e. Pelvic ultrasonography

The pattern of pain in our patient is highly suggestive of a musculoskeletal origin, and this dictates our diagnostic approach. Plain radiographs of the pelvis are relatively inexpensive, and they provide valuable information regarding fractures and destructive lesions involving bones and joints as well as other conditions involving the hip joint, like avascular necrosis of the femoral head and degenerative joint disease. Changes seen on a plain film also could raise suspicion of infections and bony tumors. Pelvis CT can help to evaluate the bony structures and visualize adjacent soft tissue. It also has the added advantage of visualizing the visceral organs. In the setting of bone infections, MRI is useful and often helps to identify bone marrow pathology. In the evaluation of bony abnormalities in this patient, MRI of the lumbosacral spine and pelvis might be useful, although radiculopathy seems unlikely. Colonoscopy, a valuable tool in the evaluation of bowel symptoms, is unlikely to be useful because our patient has no bowel symptoms. Ultrasonography provides valuable information on visceral organs and would be helpful in the evaluation of pain originating from these structures.

The plain films of the hip showed separation of the symphysis pubis and slight bony irregularity of the bony borders. Computed tomography confirmed the separation but showed no additional findings. A bone scan revealed slightly increased uptake over the symphysis. Osteomyelitis involving the pubic symphysis was suspected.

3. Which one of the following conditions has a clinical presentation that closely mimics the suspected diagnosis (and may be an alternative diagnosis) in this patient?

a. Pelvic fracture
b. Osteitis pubis
c. Bony malignancies
d. Radiation necrosis
e. Cystitis

Our patient gave no history of trauma, and a fracture is unlikely in the absence of trauma. Stress fracture in the absence of trauma is more likely in the presence of severe osteoporosis. Osteitis pubis is a painful noninfectious, inflammatory condition involving the pubic bone, symphysis, and surrounding structures that closely mimics pubic osteomyelitis in clinical presentation. It often follows pregnancy, direct trauma, athletic exertion, urologic manipulation, and urologic and gynecological surgery, all of which can predispose to pubic osteomyelitis. The white blood cell count (WBC) and ESR may be elevated, and radiological changes similar to osteomyelitis can be seen. Radiographic changes include symmetrical bone resorption at the medial ends of the pubic bones, widening of the pubic symphysis, and rarefaction or sclerosis along the pubic rami. Bone scans can show diffuse uptake in the symphysis even before plain films reveal abnormal findings. The cause of osteitis pubis is unclear, but some experts have suggested that it is analogous to sympathetic dystrophy. Bony tumors are more likely to present with radiologically visualized growths and are unlikely to be mistaken for osteomyelitis. Radiation necrosis can often mimic osteomyelitis, but our patient reported no history of previous radiation therapy. Cystitis can produce pelvic pain but does not cause radiological abnormalities.

4. Which one of the following procedures would be most informative for confirming the suspected diagnosis in this patient?

a. Plain radiographs
b. Bone scan
c. CT
d. MRI
e. Needle aspiration and culture

Several imaging modalities are available for the evaluation of bone and joint infection. The results of these studies depend on the site and chronicity of infection, degree of inflammation, presence of foreign bodies, vascularity, contiguous vs hematogenous, etc, and the type of comorbidities present, such as neuropathic osteopathy in a patient with neuropathy. None of these modalities can confirm or rule out osteomyelitis with certainty, and findings should be interpreted in the clinical context. The initial study...
should include plain radiographs of the specific bone. Changes due to infection usually take 1 to 2 weeks to become obvious on a plain radiograph and include cortical destruction, periosteal elevation, and new bone formation. Radionuclide imaging exploits the increased osteoblastic activity at sites of infection and the increased vascularity induced by inflammation. The most commonly used radionuclide imaging is the technetium Tc 99m bone scan. Triple phase bone scans use delayed images to separate soft tissue inflammation, which shows early uptake, from bony involvement with persistent uptake. However, these scans are less specific and should be used in conjunction with another radionuclide study like indium-labeled WBC scintigraphy. Bone scans are more sensitive compared to plain films, and they can rule out osteomyelitis with an accuracy of more than 90%. Since radionuclide studies depend on adequate regional blood flow, they may be less helpful in the setting of compromised perfusion. Indium-labeled WBC scintigraphy is more specific for infection but is much less sensitive. Gallium citrate Ga 67 has also been used in the diagnosis of bone infections but is less specific than technetium-labeled scans. Computed tomography is especially useful in the evaluation of the spine, pelvis, and sternum. Early findings on CT include intramedullary gas or increased marrow density. Other changes like sclerosis, demineralization, periosteal reaction, and sequestra are often seen with chronic osteomyelitis. In the evaluation of musculoskeletal pathology, MRI has certain advantages. Marrow abnormalities on MRI appear earlier in the course of disease than lytic changes seen radiographically. Active osteomyelitis shows a low signal on T1-weighted images and a high signal on T2-weighted images, representing increased marrow water due to edema, exudate, and hyperemia. Compared with CT, MRI provides better resolution of abscesses and soft tissue processes and is the modality of choice for suspected spinal infection. The overall sensitivity of MRI has ranged from 92% to 100% in different studies, with specificity between 89% and 100%; however, the image quality can be substantially degraded by orthopedic hardware. The “gold standard” for the diagnosis of osteomyelitis remains microbiologic and histopathologic examinations of the bone. Blood cultures may be of value in acute cases and are positive in about one third of the cases of hematogenous osteomyelitis in children and in 25% of adults. Needle aspiration or needle biopsies of the involved bones and joints usually provide enough material for definitive microbiologic diagnosis of osteomyelitis. Inflammatory markers like C-reactive protein and ESR are elevated in more than 90% of patients with acute osteomyelitis, and C-reactive protein in particular normalizes rapidly after successful treatment and can be used to monitor response.

A needle aspirate was obtained from the pubic symphysis under CT guidance, and cultures from the aspirate were positive for group A β-hemolytic streptococci. Acid-fast stains were negative, and mycobacterial and anaerobic cultures remained negative on prolonged incubation.

5. Which one of the following is the next most appropriate step in the management of this patient?
   a. Parenteral antibiotics
   b. Oral antibiotics
   c. Antibiotic-impregnated polymethylmethacrylate beads
   d. Surgery and débridement
   e. Observation

Antibiotic therapy guided by in vitro susceptibility studies performed on culture remains the cornerstone of therapy and should be administered parenterally, at least initially. Oral antibiotics can be substituted later in the course of treatment. Empirical antibiotic therapy should be avoided unless a microbiologic diagnosis cannot be established. Local instillation of antibiotics is an attractive option in certain selected clinical situations, and various methods have been tried, including closed suction-irrigation and antibiotic-impregnated beads. Presence of sequestra and of foreign body or prosthesis often requires surgery and débridement for cure, as does failure of medical therapy. Patients with osteomyelitis should be carefully followed up, and clinical improvement remains the best measure of response. Osteitis pubis, as mentioned earlier, is often a self-limiting inflammatory condition of the pubic symphysis and can be managed expectantly. However, once an infectious cause is confirmed, observation alone is not a choice, and antimicrobial therapy must be instituted.

Although penicillin G has traditionally been considered the antimicrobial agent of choice for the treatment of serious infections due to β-hemolytic streptococci, once-daily ceftriaxone is a convenient, practical, and attractive choice for outpatient administration. Thus, our patient was given once-daily intramuscular ceftriaxone for 6 weeks, during which he gradually improved. At 1-year follow-up, he was doing well and had no symptoms. His ESR and immunoglobulins had returned to normal.

**DISCUSSION**

Osteomyelitis of the symphysis pubis occurs infrequently, constituting less than 1% of hematogenous osteomyelitis and less than 10% of infections involving pelvic bones. Fewer than 100 cases have been reported in the English literature since its initial description. Although primarily seen after gynecological and urological procedures, osteomyelitis of the symphysis pubis has also been reported after vaginal hysterectomy and even normal vaginal delivery. In men, it has usually occurred after penile prosthesis place-
ment or prostatectomy. It has also been reported after other procedures, like inguinal hernia repair, cardiac catheterization, renal transplantation, and suprapubic catheterization, and after trauma in athletes. Radiation therapy to the pelvis has been associated with onset of pubic osteomyelitis years later. More recently, osteomyelitis of the pubic symphysis has been noted with increasing frequency in intravenous drug users. In some patients, such as our patient, no predisposing factor is identified, even after a thorough search.

Several hypotheses have been suggested to explain the pathogenesis of this unusual infection. In vesicourethral suspension procedures, the bladder neck and urethra are often sutured directly to the ligaments overlaying the symphysis pubis, allowing direct spread of infection from the urinary stream. Hematogenous spread has also been incriminated in the cause of pubic osteomyelitis, and our patient most likely had a transient bacteremia leading to eventual osteomyelitis. Hematogenous osteomyelitis is seen more often in children and involving the metaphyseal ends of long bones; however, the pubic symphysis has been described as a metaphyseal equivalent. Metaphyseal ends are defined as portions of flat and irregular bones adjacent to cartilage. The metaphyseal type of vascular anatomy with large sinuses and sluggish flow predisposes them to hematogenous seeding. The most commonly encountered organisms are *Pseudomonas* (especially in intravenous drug users), staphylococci, and Enterobacteriaceae. Eleven patients with tuberculous osteomyelitis involving the pubis were described in one series.10

The typical presentation is anterior pelvic pain, often radiating to the groin, hips, and even thighs and made worse by weight bearing.11 The pain is often poorly localized and described as deep-seated pelvic or low back pain. Patients frequently have a waddling gait attributed to adductor and rectus abdominis muscle spasm. A painful hip can be the sole presenting symptom in children. Findings on physical examination often reveal point tenderness over the pubic symphysis but can also be normal.

Laboratory investigations usually demonstrate an elevated ESR and WBC. Plain films of the pelvis may show the typical changes of irregular bony borders, rarefaction, superficial bony destruction, and symphyseal widening. Progressive changes in the appropriate clinical setting are particularly helpful in establishing the diagnosis. Presence of a sequestrum on an x-ray film is highly suggestive of osteomyelitis,11 and CT can help identify this. Radionuclide bone scans often show abnormalities, but care in the interpretation of such findings is necessary because bladder activity overlaying the pubic symphysis can be misleading. Early postmicturition or oblique views can overcome this problem. For detecting associated soft tissue masses and sequestra, CT and MRI can be helpful. A microbiologic diagnosis is required for confirming the diagnosis, in distinguishing this condition from osteitis pubis (as discussed previously), and in guiding appropriate antimicrobial therapy. Needle aspiration of the joint or open biopsy is usually successful in obtaining material for culture. Blood cultures are occasionally positive and may eliminate the need for joint aspiration.

Many authors have believed that surgical débridement, particularly in the setting of chronic osteomyelitis, is crucial in the eradication of infection,1,12 but studies have shown complete healing with antibiotics alone, as in our patient. Although 4 to 6 weeks of antimicrobial therapy is optimal, clinical, laboratory, and radiographic factors can help determine the duration of therapy. Initially, the radiographic appearance may actually worsen despite clinical improvement. However, if the patient’s condition does not improve, surgical intervention for abscess drainage or débridement may be necessary. After initial medical or surgical therapy, osteomyelitis can relapse after several years, and hence an extended close follow-up is recommended.

The diagnosis of pubic osteomyelitis is often delayed because of its rarity and the nonspecific signs and symptoms. Awareness of this condition may lead to an earlier diagnosis.

We thank Dr Randall S. Edson for reviewing this manuscript.

REFERENCES


Correct answers: 1. e, 2. d, 3. b, 4. e, 5. a