Polymyalgia Rheumatica: The Great Imitator

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Polymyalgia rheumatica (PMR) is an inflammatory condition with an annual incidence rate varying between 12.8 and 18.7 per 100,000 individuals aged 50 years or older. The condition primarily affects the shoulders or proximal regions of the arms and hips or proximal aspects of the thighs with increased levels of serum acute-phase reactants and with swift response to corticosteroid therapy. Various medical conditions can initially present like PMR, including inflammatory arthritides such as seronegative rheumatoid arthritis presenting in older adults, remitting seronegative symmetrical synovitis with pitting edema (RS3PE syndrome), or spondyloarthropathies; inflammatory myopathies such as polymyositis; vasculitidies primarily giant cell arteritis; malignancies such as myelodysplastic syndrome and multiple myeloma; endocrine/metabolic disorders such as hypothyroidism; and infections, especially infectious endocarditis. In this article, we present the case of a patient initially diagnosed with PMR who was eventually diagnosed with brucellosis-induced sacroiliitis.

PATIENT DESCRIPTION

An 81-year-old patient with past medical history notable for hyperlipidemia and osteoporosis initially presented to the rheumatology clinic complaining of worsening bilateral shoulder, knee, hip, and low back pain over the past year with considerable morning stiffness and difficulty walking. Her joint pain had progressed to the point where it lingered during most hours of the day, and even woke her up from sleep. She recalled having a self-limited 2-week febrile illness prior to the initial onset of symptoms, but denied any recent rashes, fevers, or night sweats. She noted chronic headaches without recent change in intensity or character and denied any jaw claudication or changes in her vision. Laboratory testing was notable for elevated inflammatory markers with erythrocyte sedimentation rate (ESR) of 70 mm/hr (normal range for women 0 to 29 mm/hr) and C-reactive protein (CRP) of 3.6 mg/dl (normal range 0–0.5 mg/dl). Rheumatoid factor (RF), anti-neutrophil antibody (ANA), hepatitis B and C serologic tests, as well as complement and immunoglobulin levels were all within normal ranges.

Based on her report of bilateral shoulder and hip pain and elevated inflammatory markers, she was diagnosed with PMR. She began prednisone tapering at a prednisone dose of 20 mg/day with a decrease in dosage to 15 mg/day over a 2-month period noting only mild improvement in her shoulder pain but worsening low back, hip, and knee pain.

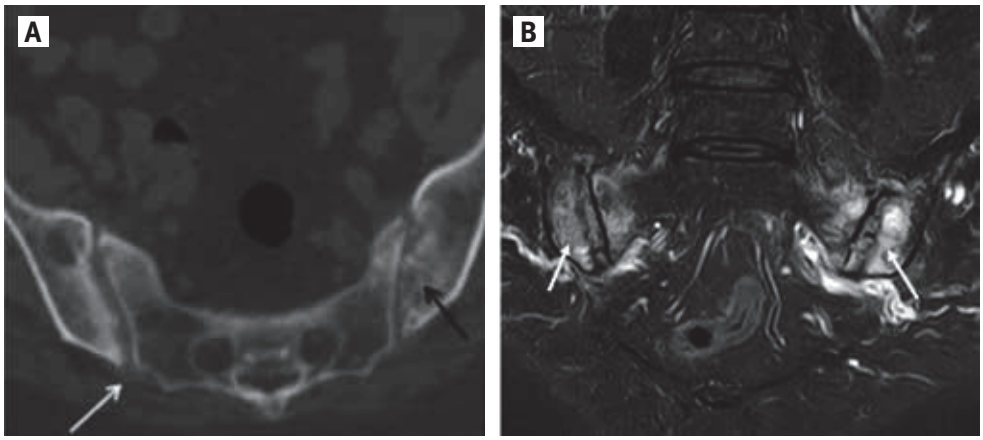
She subsequently underwent further workup including a computed tomography (CT) of her chest, abdomen, and pelvis demonstrating only mild facet arthropathy without concerns such as abdominal mass or lymphadenopathy. Due to the lack of improvement in her back pain and further elevation in CRP levels, she was subsequently admitted to the hospital for further evaluation.

On admission, the patient was afebrile, with physical exam notable for considerable bilateral knee joint effusion, which she reported as recent, as well as considerable bilateral shoulder, hip, and sacroiliac joint tenderness accompanied by considerable limitation in range of motion of these joints. The results from a flexion abduction external rotation (FABER) test were flagrantly positive, eliciting severe bilateral sacroiliac joint pain. Laboratory tests revealed normal complete blood cell count and differential, normal electrolyte, kidney, and liver function tests; elevated ferritin level of 594 ng/ml (normal range 15–150 ng/ml); CRP of 3.8 mg/dl; and ESR of 44 mm/hr. Anti-cyclic citrullinated peptide (anti-CCP) was normal, as were HLA-B27 and HLA-B5 testing. Review of her previous CT scan showed severe, bilateral erosive changes of both sides of the sacroiliac joints [Figure 1A] consistent with bilateral sacroiliitis of unknown chronicity.

Because the patient was an elderly woman, rather than the typical young man presenting with ankylosing spondylitis, and had very severe erosive changes in her sacroiliac joints despite only having recent onset low back pain, her presentation was considered unusual for spondyloarthropathy. At admission to the hospital, she underwent bilateral knee joint aspiration and magnetic resonance imaging (MRI) of her sacroiliac joints for further evaluation. The synovial fluid obtained in joint arthrocentesis was neutrophil-predominant, with a white cell count of 16,030 cells/ul with 43% polymorphonuclear cells and 57% mononuclear cells with a negative Gram stain, consistent with inflammatory arthritis. Her MRI of the sacroiliac joints showed further and active progression of erosive changes noted in her CT scan obtained only 4 months prior [Figure 1B]. Surprisingly, *Brucella melitensis* grew in synovial fluid cultures from both knees. While blood cultures remained negative,

Written informed consent was obtained from the patient whose imaging appears in this report

Figure 1. [A] Computed tomography scan showing bilateral erosive changes of the sacroiliac joints characterized by subchondral bone destruction of both sides of the joints (black arrow), with joint space widening and joint effusion (white arrow). **[B]** Coronal magnetic resonance imaging showing bilateral bone marrow edema, enhancing osteitis, and synovial enhancement on both sides of the sacroiliac joints (white arrows), indicating ongoing joint damage



serology for both *Brucella melitensis* and *Brucella abortus* was positive at high titers (> 1:640). On further questioning, the patient reported routinely drinking unpasteurized camel's milk as she was told by the vendor that it was particularly healthy. A 3-month course of antibiotic therapy with doxycycline, gentamycin, and rifampin was initiated while steroids were tapered off rapidly with disappearance of low back pain and with rapid decline of inflammatory markers with CRP and ESR levels both decreasing to normal limits (0.15 mg/dl and 22 mm/hr, respectively) 2 months after initiating antibiotic therapy, as well as prompt decline in Brucella antibody titers.

COMMENT

In our case, the patient's lack of response to steroid treatment with increasing CRP levels placed her initial diagnosis of PMR in question. A thorough review of her previous CT scan revealed severe erosive changes in her sacroiliac joints, which were overlooked by the radiologist.

Her atypical presentation with regard to age and gender, as well as the rapid rate of progression of sacroiliitis, were clues that she was experiencing a septic, rather than an inflammatory, condition. While *Brucella*-induced sacroiliitis may present as a form of reactive arthritis [1], the rapid joint destruction seen in this case indicates that it was a septic, rather than a reactive process. Indeed, septic arthritis should be suspected in any case of rapidly progressive joint destruction.

Brucellosis is a zoonotic infection caused by an intracellular Gram negative coccobacillus transmitted to humans by contact with fluids or derived food products from infected animals. Most human disease is caused by *Brucella abortus* and *Brucella melitensis*, and while most cases of Brucellosis reported worldwide are attributed to unpasteurized sheep or goat products, unpasteurized camel milk can also lead to infection [2]. Chronic brucellosis typically occurs following an acute episode of febrile illness, such as in this case. Importantly, not all patients with Brucellosis present with daily fevers despite chronic infection. Focal infection occurs in about 30% of cases and can affect any organ system with a vast array of disease presentations. Osteoarticular involvement is the most common involvement, with spondylitis/vertebral osteomyelitis or bilateral sacroiliitis reported most often, followed by large joint septic arthritis [3]. Spondylitis with risk of developing paravertebral, epidural or psoas abscesses is a serious complication of brucellosis, and is more prevalent in older patients and patients with prolonged illness prior to treatment. Chronic brucellosis, as in this case, is characterized by clinical manifestations of infection for more than one year, typically occurring as localized infection and supported by laboratory findings showing evidence of active infection (elevated *Brucella* antibody titers and/or recovery of *Brucella* from the blood or tissues). It was fortunate that in this case, arthrocentesis eventually yielded the diagnosis, as in general, synovial fluid analysis is of rather low yield in brucellosis and is also atypical of septic arthritis in that the synovial fluid white blood cell count does not generally exceed 15,000 cells/microliter [4]. Accordingly, serologic testing is most commonly used for diagnosis. In addition to arthrocentesis, critical in eventually revealing the correct diagnosis in this case, was a thorough review of the entire CT scan. Because septic sacroiliitis is a relatively rare condition accompanied by common signs and symptoms of low back, gluteal, or posterior thigh pain, findings consistent with sacroiliitis are often overlooked by radiologists focusing on lumbar disc lesions, or when detected, are erroneously attributed to axial spondyloarthropathy [5].

CONCLUSIONS

A high index of suspicion for an unusual course of PMR not responding to prednisone therapy pointed to the need to widen the differential diagnosis in this case. Joint arthrocentesis and a thorough review of imaging studies were the key to the eventual diagnosis of Brucella septic arthritis.

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