

## Case Report

## Tuberculous Osteomyelitis Presenting as Shoulder Pain

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**ABSTRACT.** A case of tuberculous osteomyelitis of the proximal humerus is described. The relevant literature is reviewed with attention to epidemiologic data. Issues highlighted include the frequent presentation in a subacute course without systemic illness; the value of plain radiography and especially magnetic resonance imaging; the importance of obtaining a tissue diagnosis; and the high rate of cure with medical therapy. Although rare in Western countries, skeletal tuberculosis is not uncommon in endemic areas and in migrants from such areas. With the growing use of biologic therapies, rheumatologists must be familiar with the diagnosis and treatment of tuberculosis in all its forms. (*J Rheumatol* 2003;30:851–6)

*Key Indexing Terms:*  
OSTEOMYELITIS  
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OSTEOARTICULAR TUBERCULOSIS  
SHOULDER PAIN  
HUMERUS

Shoulder pain is a commonly encountered problem in ambulatory care and prompts many referrals to rheumatologists. Most cases originate with rotator cuff pathology, while others arise from a variety of inflammatory disorders. Because shoulder pain of mechanical origin is so common, the diagnosis of uncommon conditions is likely to be delayed. One such rare condition is musculoskeletal tuberculosis (TB). In this case report of TB osteomyelitis presenting as shoulder pain, we will review the literature in relation to the characteristic and unusual aspects of the case, and discuss when one should have a relatively high index of suspicion for pursuing such a diagnosis.

## CASE REPORT

A 37-year-old woman had epilepsy that was difficult to control despite treatment with phenytoin and valproate; she was a native of Puerto Rico who immigrated to the US in 1988. Four months before admission, she had 8 unwitnessed seizures in one day. It was unclear whether she had had trauma during these seizures, but she began to have pain in the left shoulder and elbow the same day. She sought medical attention 2 weeks later. Examination was notable for pain with abduction of the left shoulder, tenderness worst at the deltoid, and absence of any erythema, swelling, warmth or neurologic compromise. A plain radiograph of the shoulder was

initially interpreted as normal (Figure 1). She was prescribed nonsteroidal antiinflammatory drugs and physical therapy for a presumed soft tissue injury. This treatment provided no relief during the next 2 months.

At a subsequent examination 3 months after onset of pain, point tenderness over the deltoid, pain with abduction, and limited active abduction were noted again. Mild swelling anterior and lateral to the shoulder joint, without erythema or warmth or a sinus tract, was also observed, and she was referred for a rheumatologic evaluation. The limitation in abduction and ill defined swelling were still noted, and no evidence for a systemic rheumatic disease was revealed by history or examination. Empiric injec-



*Figure 1.* Among the earliest radiographic signs are local osteopenia and bone resorption, which are caused by hyperemia and edema within Haversian canals. Initial anteroposterior radiograph of the left shoulder was interpreted as normal. In retrospect, a subtle rounded intramedullary lucency is noted in the superolateral aspect of the humeral head (arrow). No cortical disruption is apparent.

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tion of 40 mg methylprednisolone and 3 ml 1% lidocaine into the subdeltoid space provided some immediate relief of pain but no improvement in range of motion. The swelling and the lack of improvement in range of motion after injection were atypical for subdeltoid bursitis or rotator cuff tendonitis, so a magnetic resonance image (MRI) was ordered.

The MRI, performed one week after the rheumatologic evaluation, showed a large subdeltoid fluid collection communicating with a lesion in the humeral head (Figure 2). An ultrasound guided aspiration was performed, which yielded 80 cc of purulent-appearing fluid; microscopic examination revealed 1533 white blood cells (WBC)/ $\mu$ l (100% neutrophils), 5800 red blood cells/ $\mu$ l, many degenerating cells, negative Gram stain, and negative acid fast bacillus (AFB) stain. Routine bacterial culture was negative. She was admitted for debridement. Laboratory values were notable for mild elevations in AST (44 U/l), alkaline phosphatase (325 U/ml), and globulin (4.9 g/dl), with normal WBC (6700 cells/ $\mu$ l), and modestly decreased hematocrit (34%), and elevated erythrocyte sedimentation rate (ESR) (90 mm/h) and C-reactive protein (8 mg/dl). Human immunodeficiency virus status was not determined. Chest radiograph was normal. In the operating room, purulent material was drained from the subdeltoid bursa, and necrotic bone was debrided from the humeral head near the greater tuberosity. The rotator interval (a triangular space between the supraspinatus and subscapularis tendons) contained purulent material and was debrided. The shoulder joint was opened and found to be free of pus.

Postoperatively, a tuberculin (PPD) test was placed, which was negative after > 48 h. Pathology of the debrided bone showed noncaseating granulomas and necrosis (Figure 3). She was started on a 4 drug antituberculosis regimen including isoniazid, rifampin, pyrazinamide, and ethambutol. Several weeks later, the original culture of percutaneously drained abscess fluid grew *Mycobacterium tuberculosis* (mTB), pansensitive; culture of the biopsy specimen was negative.

The shoulder was free of pain within a few weeks of starting treatment and functioning normally within 2 months. The treatment course was complicated by polyarthritis involving the wrists, metacarpophalangeal joints, knees, and ankles, which developed after 5 weeks of treatment. This syndrome resolved over a few weeks after all antituberculosis medications

were held. Isoniazid and ethambutol were restarted without recurrence of arthritis. She has received a total of 12 months of therapy (minus one month during the probable adverse drug reaction) and is expected to complete treatment after 2 more months of isoniazid and ethambutol.

## DISCUSSION

**Epidemiology.** Of the 17,000 to 20,000 cases of tuberculosis reported to the US Centers for Disease Control and Prevention (CDC) yearly between 1997 and 1999, 18–20% were primarily extrapulmonary. Eleven percent of extrapulmonary cases (2% of total TB cases, or about 400 cases annually) have involved bone and/or joint<sup>1-3</sup>. The thoroughness of reporting of cases is thought to exceed 99%<sup>4</sup>. Thus, skeletal TB is a rare disease in the US and in other Western countries, with an incidence that is probably lower than that of rare vasculitides. However, groups at high risk for pulmonary TB are at proportionally increased risk for skeletal TB, so that skeletal TB is relatively common in certain populations, especially natives of and immigrants from endemic areas<sup>5,6</sup>. For example, in England and Wales in 1978-79, the incidence of skeletal TB in immigrants from the Indian subcontinent was 25–35/100,000<sup>6</sup>, or roughly equal to the incidence of new cases of rheumatoid arthritis<sup>7</sup>. The incidence of TB in Puerto Rico is currently the same as in the mainland US<sup>1-3</sup>; 3 decades ago, when this patient was a child, that incidence was 2–3 times higher.

First described by Pott in 1776, TB of the spine accounts for nearly half of skeletal TB cases. In 10 large series comprising several thousand patients, 24–60% of cases of skeletal TB were spinal<sup>16,8-17</sup>. Few series distinguish between TB osteomyelitis and TB arthritis (which often also involves

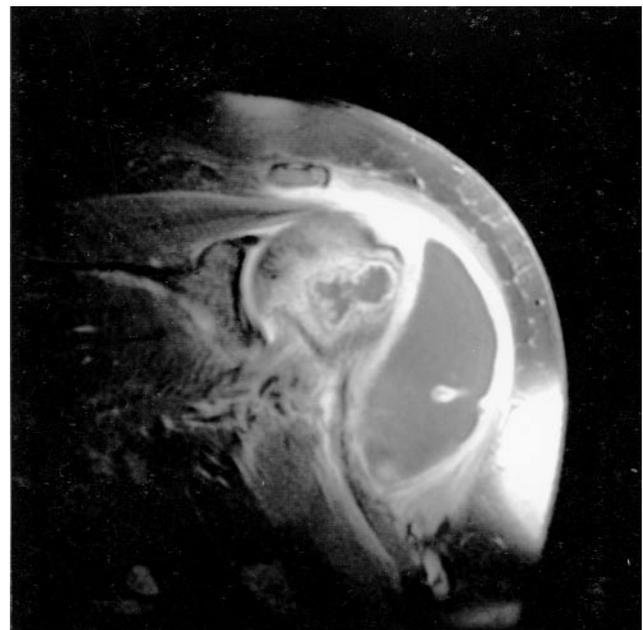
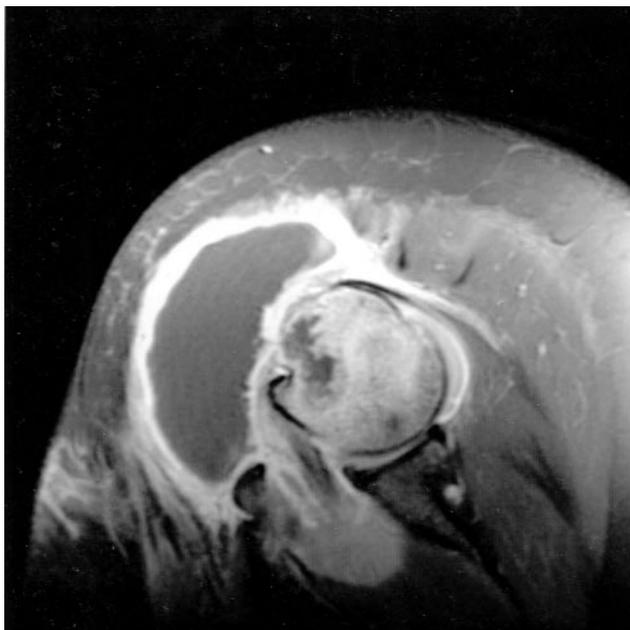
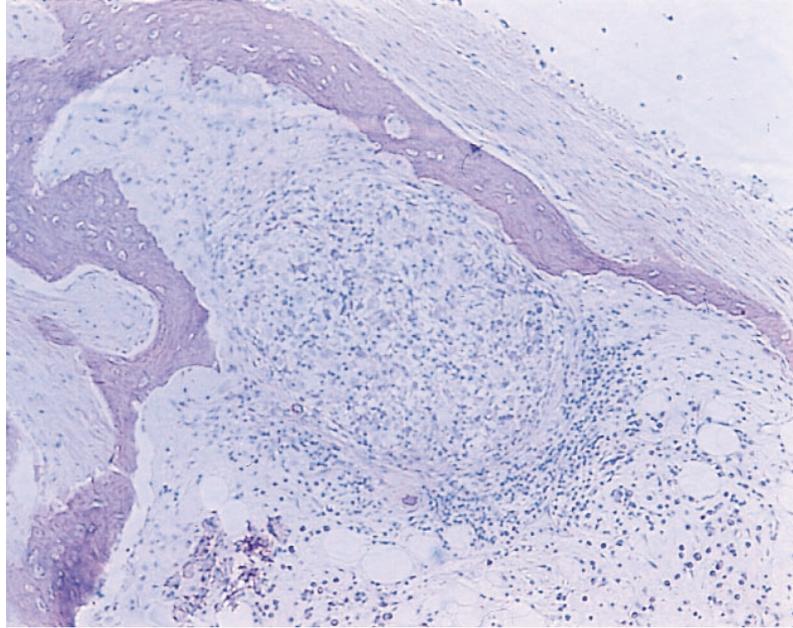


Figure 2. Delayed diagnosis of TB infection in the extraaxial bones may result in joint involvement or formation of a parasosseous mass or collection. Axial (left) and coronal (right) T1 weighted, fat saturated, post-IV and intraarticular gadolinium images of the left shoulder show an intraosseous abscess communicating through a cloaca with the subdeltoid bursa.



*Figure 3.* At medium power, an intraosseous granuloma, with central histiocytes surrounded by a ring of lymphocytes, nearly fills the marrow space. Although central necrosis of granulomas was not seen, larger areas of necrosis were seen in this specimen, from intraoperative curettings (H&E, original magnification  $\times 200$ ).

bone and is, therefore, referred to as osteoarticular TB). These studies report that about 16% (8–20% in 5 large series) of skeletal TB presents as osteomyelitis not involving the spine<sup>6,8,9,12,18</sup>. Thus, only about 60 cases of peripheral TB osteomyelitis are reported in the US each year. Even in large series of TB osteomyelitis from endemic areas, TB of the humerus, as in this report, is rare: 4 of 218 patients (1.8%) in the reports we reviewed<sup>6,8,12,18,19</sup>, with osteoarticular disease of the shoulder being somewhat more common. Osteoarticular disease in the lower extremities outnumbers disease in the upper extremities, by a factor of 1.5 to 9.9 in large series<sup>6,8-10,12-14,16-19</sup>, and case series of TB limited to the upper extremity appear infrequently<sup>20,21</sup>. Individual studies vary widely on the relative prevalence of disease in the wrist, elbow, and shoulder, and the number of reported cases of isolated osteomyelitis in these areas is too small to allow general conclusions to be drawn about prevalence in particular bones. Large series have shown multifocal disease in 3–12% of cases<sup>9,12,18,22,23</sup>; such a presentation is more common in endemic areas and in immigrants from those areas.

Skeletal TB presents in both sexes and all ages. Series from areas endemic for TB have larger numbers of children and young adults, and within Western countries, the age of patients with skeletal TB has risen over time<sup>15,16</sup>. The age of presentation is lower among immigrants from endemic areas<sup>6,14,17,24</sup>. This last finding, however, may be due to the lower average age of immigrants generally<sup>6,14</sup>. Immuno-

suppressed patients exposed to mTB, either recently or remotely, are more likely to develop significant disease. Patients treated with the tumor necrosis factor-binding antibody infliximab appear to be at increased risk for developing TB; the cases reported to date include an unusually high percentage of extrapulmonary and disseminated cases, but not an unusual number of skeletal cases<sup>25</sup>.

As with all forms of TB, the lung is thought to be the primary focus of infection in the majority of skeletal TB cases. Although the mechanism by which the mycobacterium reaches bone is unknown, it is presumed to do so hematogenously, and grows in the richly supplied marrow cavities (hence its predilection for vertebral bodies, the ends of long bones, and smaller bones in children). However, cases suspicious for local spread from other organs are not uncommon<sup>26</sup>, and it has been proposed, with experimental support from anatomic studies in animals<sup>27</sup>, that lymphatic spread from the pleura to the paraaortic lymph nodes could be a major cause of spinal disease<sup>26,27</sup>.

Several features of this case are worthy of discussion relative to the typical features of skeletal TB: the presence of a soft tissue “cold” abscess, the lack of constitutional symptoms, the possible association with previous trauma, the negative PPD test, the elevated ESR, the apparently normal plain radiograph of the shoulder early in the disease course, the normal chest radiograph, the successful diagnosis by culture and histology, and the treatment with surgical debridement and antimicrobial therapy. Most

studies on these topics involve data pooled from patients with spinal disease, osteoarticular disease, sacroiliitis, and peripheral osteomyelitis; the consistency and strength of data for patients with only osteomyelitis will be noted.

*History and clinical findings.* A presentation dominated by chronic local pain and swelling is typical of skeletal tuberculosis of any variety<sup>8,9,18,24,28-30</sup>, with the prevalence of a clinically evident abscess or draining sinus varying widely. Spinal TB is well characterized with regard to the formation of associated soft tissue abscesses; the prevalence is about 60% in large series<sup>31,32</sup>. The prevalence of extension into soft tissue from other bones is less clear: 7% of patients had an abscess or sinus tract in a series from Canada<sup>8</sup>, 32% in another from India<sup>30</sup>, and 44% and 92% in 2 series from Algeria<sup>9,18</sup>. One can speculate either that disease progresses more rapidly in endemic areas<sup>14,17,24</sup>, or that patients in such areas seek medical attention later. The series from Algeria are notable for the recovery of pyogenic organisms from > 40% of draining sinuses<sup>9,18</sup>, a finding that could easily delay the successful diagnosis of the underlying skeletal TB if one did not have a high suspicion for it. Authors generally agree that purely tuberculous abscesses are typically “cold” (without erythema or warmth), as in our case.

Only 10–58% of patients with skeletal TB present with fever, and a similar number with other constitutional symptoms, such as anorexia, weight loss, or night sweats<sup>28,29,33</sup>; the percentages specifically for patients with peripheral osteomyelitis are unknown. We assumed, initially, that the association of disease with previous trauma was a coincidence. However, there has long been suspicion regarding an association between trauma and later development of skeletal TB<sup>22,26</sup>. Several studies support that notion, with incidences ranging from the unremarkable 4%<sup>24</sup> to the more suggestive 16–35%<sup>19,29,32</sup>, without, however, control groups for comparison. The time course between trauma and diagnosis of TB in these studies was not reported. Several patients in the latter 2 studies had received intraarticular steroids. Our patient also received a local injection (not into the joint space but possibly into the abscess), which might have accelerated her disease had the diagnosis been further delayed. However, the physical findings consistent, in retrospect, with abscess were present at the time of injection and unchanged at the time of diagnosis by MRI. Associations with trauma and local steroids are interesting to consider, but subject to problems with reporting bias and difficulty in establishing control groups. The possibility of spreading infection to other sites during needle aspiration is also worthy of consideration, but also of uncertain frequency and significance.

*Skin testing and laboratory testing.* The sensitivity of tuberculin skin testing in this population is good but not perfect. In 6 series, skin testing was positive in 79–97% of cases<sup>9,13,18,28,29,33,34</sup> and similar (93%) when only osteomyelitis was considered<sup>18</sup>. It is uncertain, however,

what the baseline rates of positivity were in the tested populations. Even in studies from nonendemic countries, a substantial percentage of the patients were immigrants from endemic areas, and there also may have been confounding by previous exposure to Bacillus Calmette-Guerin vaccine. Laboratory values are usually suggestive of infection, with the ESR elevated in the majority of, but not all, cases<sup>9,13,14,24,30</sup>. In only one of these studies was osteomyelitis considered separately, and the ESR was > 30 mm/h in 22 of 25 (88%) cases<sup>30</sup>.

*Imaging.* Few cases of TB osteomyelitis present with normal plain radiographs; a review of several series suggests that a maximum of 3–6% of bone, joint, or spinal TB have normal plain radiographs<sup>8,9,19,28-30</sup>. Even in nontuberculous osteomyelitis, a more rapidly-developing disease, plain radiographs are likely to be normal for 10–21 days after inoculation, since a 30–50% loss of bone density must occur before radiolucency is apparent<sup>35</sup>. The plain radiograph in this case was done 2 weeks after the onset of symptoms, so it is not surprising that the findings were subtle (Figure 1). TB osteomyelitis can appear in a variety of nonspecific ways by plain radiograph, including focal osteopenia or osteolysis, erosion, cystic lesions, or more widespread destruction of bone and joint (reviewed in<sup>36-38</sup>). Disease of the spine has a particularly broad and well characterized range of radiographic appearance<sup>12,31,39</sup>. Smaller and softer bones (i.e., in children) are more likely to develop periosteal elevation and cystic lesions<sup>38</sup>. Pyogenic osteomyelitis is usually described as having a greater propensity for producing sclerosis, periosteal reaction, or bone sequestration<sup>12,18,36,37</sup>, but these differences are not sufficiently specific to avert the need for a tissue diagnosis. The MRI findings of extraaxial TB osteomyelitis are variable, and appear to be indistinguishable from those of pyogenic osteomyelitis. A focus of infection shows low signal intensity on T1 weighted images and high signal intensity on T2 weighted, short tau inversion recovery (STIR), or fat saturated sequences. The STIR pulse sequence is highly sensitive for bone edema, with a negative predictive value for acute osteomyelitis approaching 100%<sup>35</sup>.

Although plain radiographs of affected bones are seldom normal, chest radiographs often are unremarkable. The percentages reported as normal in studies of more than 20 patients have varied from 10% to 84%, averaging 59%<sup>8,10,12,19,28,29,33,34,40</sup>. Most studies reporting fewer than 50% normal chest radiographs were conducted before 1950<sup>10</sup>, and no studies specifically address chest radiography in patients with TB osteomyelitis. It is unclear whether chest computerized tomography would provide increased sensitivity for active or latent TB.

*Tissue diagnosis.* The chance of obtaining a diagnosis by either successful culture or characteristic histology is quite high if at least some tissue is obtained. Authors generally

caution against relying on joint fluid, although the reported rate of positive culture is a respectable 49–80% (reviewed in<sup>41</sup>). The reported rates of positive attempts at culture of nonspinal osseous lesions are 88–92%<sup>6,29</sup>, of diagnostic histology 50–100%<sup>6,29,30</sup>, of obtaining one or the other 84–100%<sup>6,13,18,29,30</sup>. The chance of visualizing AFB in tissue samples is infrequently reported in detail and not specifically for peripheral osteomyelitis<sup>28,33</sup>, but seems to be considerably lower (33% in reference<sup>28</sup>). The technical details in these large series were generally not reported, but other reports show that image guided fine-needle aspiration is a good alternative to open biopsy. Mondal<sup>40</sup> obtained positive cultures in 34/38 (89%) spinal cases; AFB were seen in only 29%. Masood<sup>42</sup> obtained positive cultures in 8/11 (83%), caseating granulomas in 73%, and positive AFB stain in 64% of a combination of osseous and soft tissue cases. Because the chance of seeing AFB is relatively low, one is usually faced with considering a differential for granulomatous disease, especially in a nonendemic area, and with waiting several weeks for culture results. If granulomas are found and there is no alternative diagnosis, the initiation of antimycobacterial therapy with observation of the clinical response, pending the final culture result, is a reasonable strategy. Polymerase chain reaction based techniques may improve the sensitivity (without loss of specificity, one hopes) and significantly reduce the time until diagnosis.

**Treatment.** Since the development of antituberculosis medications, treatment of skeletal TB has become primarily medical, with surgery reserved for complications such as formation of a large abscess, joint deformity, or neurologic compromise. In the spine, such complications are quite common, and authorities differ on whether operative debridement and stabilization should be done routinely (reviewed in<sup>28,43</sup>). In other bones, Martini and colleagues have had good results with antimicrobials alone, and patients rarely required surgery even when they presented with sinus tracts<sup>9,18</sup>. Although the same drugs are used as in pulmonary TB, the proper length of such treatment is debated. In most large series, patients were treated for longer than the contemporary recommendations for pulmonary TB. Dutt, *et al* reported a 96% success rate with a 9 month regimen for all varieties of extrapulmonary TB, comparable to historic rates with longer treatment<sup>44</sup>. However, all of the treatment failures were in bone and joint disease, so that this subgroup's success rate was only 87%. Whether that percentage would have improved at all with longer treatment is unclear; the authors suggested that such treatment failure served as a good indication for surgical intervention<sup>44</sup>. Nevertheless, the most recent recommendations from the CDC and American Thoracic Society recommend standard courses (i.e., as for pulmonary disease) for most sites of extrapulmonary disease, but 12 months for TB of bone and/or joint<sup>45</sup>. Choice of drugs is further directed by

any drug resistance in the pathogen; in Massachusetts, the rate of resistance of mTB to isoniazid was 10–15% from 1992 to 2000<sup>46</sup>, and was 4% in Puerto Rico in 2000.

The authors of the large series cited above emphasize that early recognition and treatment of this uncommon disease can prevent tragic consequences. Even though we had little or no suspicion for TB osteomyelitis before the suggestive MRI (Figure 2) in this case, we did arrive at the correct diagnosis considerably faster, in terms of time between onset of symptoms and diagnosis, than is generally reported. The reason was simply that a collection of features atypical for the common causes of shoulder pain (presence of visible swelling, and lack of help with NSAID, physical therapy, or lidocaine injection) led us to pursue an aggressive diagnostic course earlier than we would have otherwise. The availability of MRI made it possible to address a wide range of rare diagnoses simultaneously. Even if we had not had MRI readily available, however, a repeat series of plain films and an ESR would likely have provided initial, nonspecific clues pointing toward osteomyelitis that would have led rapidly to attempts at a tissue diagnosis. Whether such findings suggest TB depends primarily on whether the patient is from an endemic area or has known prior exposure to mTB. Even though our literature review revealed that TB osteomyelitis of the humerus is very rare, the value of pursuing the tissue diagnosis rather than treating empirically for conventional bacterial pathogens — especially in the setting of such features as a subacute course, a cold abscess, and a likely history of exposure to mTB — is still the best lesson of this case.

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