



# Bone and Joint Tuberculosis

Tuberculosis affects one third of the world's population. While the disease may be adequately treated by chemotherapy, surgery plays an important role in the management of complications of the disease process. Tuberculosis is rare in the Western world, often leading to a delay in diagnosis and treatment. Our goal is to review the diagnosis and management of the musculoskeletal manifestations of tuberculosis, including osteomyelitis, arthritis, and spondylitis.

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Despite extensive efforts to achieve disease control, tuberculosis remains a worldwide public health concern<sup>1-4</sup>. While the first global burden of disease study predicted that tuberculosis would be the seventh leading cause of disability adjusted life years by 2020<sup>1</sup>, revised projections, based on data from 2002, suggest that tuberculosis may fall to the twenty-third leading cause of death and the twenty-fifth leading cause of disability adjusted life years by 2030<sup>2</sup>.

In the United States, the incidence has decreased by 44% between 1993 and 2003, but has increased in foreign born persons, who comprise 24-50% of reported cases<sup>5-7</sup>. While these findings are encouraging, establishing the diagnosis of tuberculosis, particularly in the small subset of patients presenting with extrapulmonary disease, is difficult and often delayed. The disease is most common in urban areas, in individuals of lower socioeconomic status, and in adults (especially older than 65 years)<sup>7</sup>. An increased risk of tuberculosis may also be associated with lower socioeconomic status (crowding, lower educational status, poverty, public assistance, and unemployment), HIV infected persons, the homeless, injection drug users, and detainees in correctional facilities<sup>7</sup>.

From 1993 to 2006, while the absolute number of cases decreased in the United States, the relative percentage of extrapulmonary TB increased from 15.7% to 21% (2006)<sup>8</sup>. Approximately ten to thirty percent of patients will exhibit extrapulmonary manifestations of the disease, and a smaller percentage of cases will involve the musculoskeletal system. The initial focus of infection is visceral, and musculoskeletal involvement occurs via hematogenous or lymphatic seeding. Tissue damage occurs through a vigorous host inflammatory response. While medical treatment is curative in the majority of cases of both pulmonary and extrapulmonary disease, surgery plays an important role in establishing a diagnosis and in treating complications of the musculoskeletal manifestations of tuberculosis, namely osteomyelitis, arthritis, and spondylitis<sup>9-11</sup>. In less than 1% of cases, bursitis or tenosynovitis may be observed. A high index of suspicion is required to make the diagnosis in nonendemic regions, and microscopic examination remains the cornerstone of diagnosis. While cultures

have traditionally been grown on both solid and liquid media (for example Lowenstein-Jensen), concerns regarding the length of time required for identification have led to the development of a variety of commercial systems for rapid detection, such as automated liquid culture systems<sup>12</sup>. Other techniques for rapid detection are under investigation, such as probe detection methods, polymerase chain reaction (PCR) followed by reverse hybridization, PCR restriction enzyme analysis, and direct nucleic acid amplification methods<sup>12</sup>.

## Osteomyelitis

Osteomyelitis is the least common musculoskeletal manifestation of tuberculosis, representing less than five percent of cases. Clinical findings such as localized pain and soft tissue swelling are usually mild, have been present from days to months, and may be accompanied by low grade fevers, weight loss, and malaise. Regional lymphadenopathy is common, and sinuses may be observed. The Mantoux skin test is positive in the vast majority of cases, and the erythrocyte sedimentation rate is usually elevated but may be normal.

Tuberculous osteomyelitis may mimic a variety of conditions on plain radiographs, and the most common finding is a solitary cystic lesion with a sclerotic rim. Lesions may cross the physis (Figure 1). Sequestrae are uncommon and are described as "feathery," and subperiosteal new bone formation may be observed as well<sup>10,13-16</sup>. As the differential diagnosis includes neoplasm, Brodie's abscess, chronic osteomyelitis, and other granulomatous lesions, a biopsy is required to establish the diagnosis<sup>13-15</sup>. When performing the biopsy, diagnostic material is most commonly obtained within the granulomatous focus or in the synovium adjacent to a cyst<sup>17</sup>. If the diagnosis can be established on frozen section, then curettage without bone grafting is sufficient, followed by medical therapy<sup>10,15,18,19</sup>. Rare forms of tuberculous osteomyelitis include multiple cystic tuberculosis, disseminated skeletal tuberculosis (compromised host), closed multiple diaphysitis, and tuberculous dactylitis<sup>14,20-25</sup>. The multiple cystic form usually is diagnosed in children, and involves multiple cystic areas of rarefaction in the metaphysis and

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**Figure 1.** The radiographic manifestations of tuberculous osteomyelitis vary considerably, and the most common presentation is a lytic lesion with a sclerotic rim. Tuberculosis can cross the physis, as seen in this example. These lesions may occasionally have an aggressive appearance, with a prominent perisoteal reaction, and a biopsy is usually necessary to establish the diagnosis.

diaphysis<sup>14,20,21</sup>. Disseminated disease may involve both osseous and articular structures<sup>22-25</sup>. Closed multiple diaphysitis is very rare, occurs in children, and involves swelling in the forearms and the legs<sup>25</sup>. Plain radiographs show a thickening in sclerosis in the diaphyseal region. Tuberculous dactylitis is most common in children, and four radiographic forms have been described, the most common of which involves a spindle-shape expansion of a phalanx (spina ventosa)<sup>25</sup>.

## Arthritis

Tubercle bacilli are deposited in the synovium via a hematogenous route, but may also gain access through direct penetration from a metaphyseal focus of osteomyelitis. A monoarticular presentation is most common, and the literature has focused on involvement of the hip and knee<sup>26-34</sup>. The first clinical finding may be an effusion associated with a synovial hypertrophy (Figure 2), and the differential diagnosis includes a host of other conditions including septic arthritis, Lyme disease, hemophilia, pigmented villonodular synovitis, and juvenile rheumatoid arthritis. Synovial hypertrophy/thickening may be appreciated clinically, and discomfort with palpation or range of motion is usually mild.

Both the treatment and the outcome depend upon the stage at which the disease is diagnosed. The natural history evolves over two to four years, and begins with proliferation of granulation tissue at the joint periphery<sup>10</sup>. This manifests clinically as a joint effusion with or without thickening



**A**



**B**

**C**

**Figure 2.** The natural history of tuberculous arthritis progresses over several years from synovitis to joint destruction. The process typically involves both sides of the joint, and in this case the morphology is consistent with the “mortar and pestle” subtype described by Shanmugasundaram (A). (A) and (B) illustrate early stage knee involvement with significant soft tissue swelling and no bony involvement. (C) demonstrates multiple joint involvement in the midfoot with bony involvement of the navicular and cuneiforms.

of synovial tissue. Radiographically, there is soft tissue swelling and diffuse osteopenia, without a focal abnormality. Granulation tissue spreads across the joint, and the first bony changes are marginal erosions, which are evident radiographically. Over time, there is erosion of the articular cartilage and of the underlying bone, resulting in loss of joint space on plain radiographs. Ultimately, degeneration of the joint is observed. The early findings on magnetic resonance imaging are nonspecific, and include a joint effusion, marrow edema, and during the stage of arthritis there may be abnormalities within the articular cartilage and subchondral bone<sup>35,36</sup>. While chemotherapy can effectively treat the disease at any stage, the ultimate functional result depends upon the degree of tissue damage that has occurred when treatment is started. If the diagnosis is made during the stage of synovitis, treatment focuses on gaining or maintaining motion, relief of weight bearing, and splinting to prevent deformity (especially flexion)<sup>31,32</sup>. In the presence of a fixed deformity, serial casting or traction may help to improve motion. Full return

of function is possible with an early diagnosis and prompt treatment. The role of synovectomy in the early stages of disease remains controversial<sup>10, 26,27,31-33</sup>. For the hip, while some authors have recommended chemotherapy alone<sup>26</sup>, others have recommended synovectomy with or without joint debridement in addition to medical management<sup>10,27,28,34</sup>.

If the diagnosis is made after the disease has progressed beyond the stage of arthritis, several alternatives for salvage are available. Splinting of the joint in a functional position can be maintained until ankylosis occurs. If a symptomatic fibrous ankylosis ensues, arthrodesis can be performed, depending upon the joint involved. While arthrodesis may be well tolerated at the knee or foot/ankle, loss of hip mobility is poorly tolerated in cultures where the majority of daily activities are performed close to the floor. Either an excisional arthroplasty<sup>10,34</sup> or a pelvic support osteotomy<sup>37,38</sup> are reasonable options when motion is desirable and a prosthetic reconstruction is unavailable. For joints which have become ankylosed in a nonfunctional position, an osteotomy will reposition the limb in space. When the technology is available, total joint arthroplasty may be advisable<sup>39-45</sup>. While early information suggested that a ten-year disease free survival was optimal, recent evidence suggests that arthroplasty can be performed as long as adequate perioperative chemotherapy is maintained.

While the literature contains a host of articles on tuberculous arthritis in other joints such as the shoulder, elbow, sternoclavicular, sacroiliac, and the foot/ankle, the general principles of diagnosis and treatment remain the same<sup>46-52</sup>. In the foot and ankle, while involvement of the calcaneus is most common, any of the tarsal or metatarsal bones may be affected, and multiple sites are commonly observed due to local spread of disease<sup>10,52,53</sup>. Radiographic findings may include osteopenia, loss of joint space, and subperiosteal scalloping on both sides of the joint. Symptoms or findings associated with sacroiliac involvement include gait disturbance, radicular pain, an abscess (gluteal or inguinal), and an associated spondylitis<sup>49</sup>.

## Spondylitis

Spinal disease is seen in approximately fifty percent of patient with bone and joint tuberculosis, and challenges include establishing the diagnosis early in the disease process, and preventing or treating kyphotic deformities. The disease typically involves the thoracic and thoracolumbar spine, although any region may be affected, and "skip lesions" occur rarely. Medical treatment is effective, and while the duration of therapy has traditionally been 12-18 months, there is data to suggest that 6-9 months may be efficacious<sup>10,53,54</sup>.

The most common presentation is "paradiscal," involving bony destruction adjacent to the endplates or two or more vertebral bodies<sup>10</sup>. There may be some loss of disc space height. Isolated involvement of the central portion of a single vertebra is less common and may result in collapse (vertebra plana), and subligamentous spread anteriorly may be associated with scalloping of multiple vertebrae (aneurysmal phenomenon)<sup>10</sup>. Isolated involvement of the posterior elements is rare, and other atypical features include lateral vertebral translation,

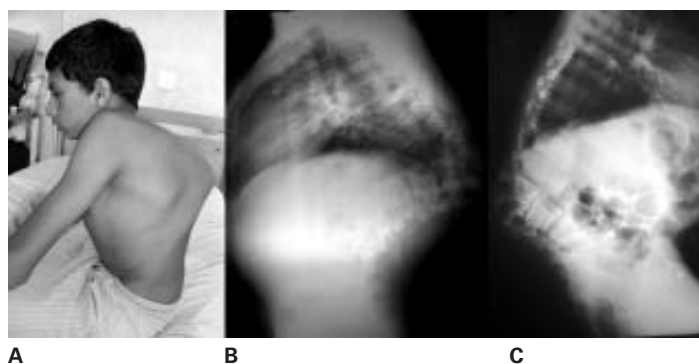
circumferential involvement, and the spinal tumor syndrome (neurologic deficit without plain radiographic abnormality)<sup>25</sup>.

Abscess formation is common, and disease progression may result in collapse of one or more vertebrae. Loss of anterior column support results in kyphotic deformities, which may occur in both the active and healed phases of the disease, with or without surgical arthrodesis<sup>55-59</sup>. Progression of kyphosis is most common in children with multiple levels of involvement in the thoracic spine (Figure 3)<sup>55,56</sup>. Radiographic factors suggestive of an increased risk of progressive kyphosis include dislocation of the facets, bony retropulsion, lateral vertebral translation, and toppling of one vertebra over the next<sup>57</sup>. When all three columns of the spine are involved, spinal instability (translational or rotational deformity) may develop. Abscesses may migrate posteriorly into the spinal canal, anteriorly underneath the anterior longitudinal ligament, as well as into neighboring visceral structures. Below the diaphragm, abscesses typically migrate along the psoas sheath and exit via sinuses in the groin or buttock region.

Neurologic deterioration may occur in both the active and healed stages of the disease. In the former (good prognosis), spinal cord dysfunction results from local inflammation and extradural compression (pus, caseous material, granulation tissue, bony debris)<sup>10,60,61</sup>. In the latter (poor prognosis), the spinal cord may be compressed at the apex of the deformity (internal gibbus), or by circumferential bands of fibrotic tissue<sup>10,60,62-64</sup>. In some cases, dysfunction may be observed in the absence of bony abnormalities; a "spinal tumor syndrome" results from tubercular granulomas in an intradural, extradural, or intramedullary location.

The differential diagnosis includes both infectious (pyogenic vertebral osteomyelitis, fungal infection, brucellosis, syphilis), chronic granulomatous (sarcoid), and neoplastic (benign, malignant, metastatic) diseases. Establishing the diagnosis may be a challenge even when a biopsy is performed, as the smear is positive in only 15-68%, and a histologic diagnosis is made in approximately 60-70% of cases<sup>65,66</sup>.

While plain radiographs are sufficient to establish the diagnosis in endemic areas once the disease is established (patients usually are delayed in presentation), more advanced imaging studies are helpful in nonendemic areas when



**Figure 3.** Tuberculous spondylitis usually involves the anterior column of the spine. Children with involvement of multiple level in the thoracic spine are predisposed to a progressive kyphosis (A) even after appropriate medical treatment. (B) and (C) illustrate severe, sharp kyphotic deformities in patients with "healed disease."

patients present early in their course of symptoms. General imaging features suggestive of tuberculosis include more than two levels of involvement, involvement of the vertebral body (or bodies) with relative preservation of the disc space, subligamentous spread, posterior element involvement, rim enhancement around abscesses, and larger sized abscesses (often with calcifications)<sup>66-70</sup>. While computed tomography is best for evaluating the degree of bony involvement, magnetic resonance imaging (with gadolinium enhancement) provides more comprehensive information, including the extent of involvement/degree of destruction, the location and size of paravertebral and/or epidural abscesses, and the presence of spinal cord pathology (impingement or compression, intradural/intramedullary disease, myelomalacia)<sup>66-70</sup>. While the majority of abnormal findings on MRI are common to both pyogenic and nonpyogenic infections, including hypointensity on T1 images and hyperintensity on T2 images, Chang et al suggested that found significant differences in several parameters, including vertebral destruction (82% TB vs. 30% pyogenic), intraosseous abscess with rim enhancement (79% TB vs. 0% pyogenic), disc abscess with rim enhancement (9% TB vs. 64% pyogenic), and a well defined paraspinal abnormal signal intensity (82% TB vs. 18% pyogenic)<sup>67</sup>.

The indications for surgery in tuberculous spondylitis remain debated, and to an extent depend upon the resources available locally. From a conservative perspective, surgery is directed towards complications of the disease process. In economically developed countries, the disease may present at an earlier stage, and surgery is commonly required to establish the diagnosis and to prevent deformities in patients who are at a high risk or who have demonstrated progression. In economically less developed countries, patients often present later in the disease course, and surgery is more commonly required to treat neurologic dysfunction and/or to prevent/treat kyphotic deformities. Multiple publications from the Medical Research Council studies (Great Britain) revealed that uncomplicated spinal tuberculosis is adequately treated by outpatient chemotherapy, and there was no additional benefit from bedrest, bracing, or surgical debridement, although surgical debridement and bone grafting resulted in faster healing and less kyphosis<sup>71,72</sup>. It should be noted that children treated medically must be followed through skeletal maturity, as both progression and improvement in the degree of kyphosis may be observed<sup>58</sup>.

In the global context, strategies have varied from chemotherapy alone (no capability for spinal surgery), to the "middle path" (surgery for specific indications), to routine decompression/debridement and bone grafting. A detailed review of the existing literature found insufficient scientific evidence to support routine surgical intervention<sup>73</sup>. The "middle path," popularized by Tuli in India, recommends surgery for specific indications, including an uncertain diagnosis, failure to respond to chemotherapy, increase in size of an abscess, involvement of the posterior elements or circumferential disease, recurrence, and lack of neurologic recovery or progressive neurologic symptoms<sup>74</sup>. With this protocol, surgery was required in only 5% of uncomplicated

cases and 60% of those with neurologic dysfunction. In summarizing the available information, indications must be individualized and include establishing a diagnosis, stabilizing or correcting the spine in cases of progressive or established deformity (or when a deformity is likely), decompressing the spinal cord in the event of neurologic compromise (progressive or severe), and treating incapacitating pain/spasm or nerve root compression<sup>74,75</sup>. Of note, the presence of neurological dysfunction does not mandate surgical intervention. While neurologic symptoms may resolve with successful medical treatment<sup>76</sup>, surgical decompression is indicated for progressive or profound neurological dysfunction. MRI findings which suggest a poor prognosis include myelomalacia, syringomyelia, and thinning of the spinal cord<sup>75</sup>.

A variety of surgical procedures have been described for decompression, stabilization, and deformity correction; recommendations are based upon the location of involvement (anterior, posterior, circumferential), the risk or presence of kyphotic deformity, the neurologic status, the status of the disease (active or healed), the experience of the surgeon, and the resources available locally.

A decompression may be performed anteriorly (open<sup>60,61</sup> or thoracoscopic<sup>77</sup>), posteriorly (transpedicular<sup>78</sup>, or posterolaterally (costotransversectomy or the lateral extrapleural approach)<sup>79</sup>. The anterior approach for decompression (and bone grafting) was popularized in Hong Kong in the 1960's, and provides the most direct access to the pathology<sup>60,61</sup>. Achieving an adequate decompression may be difficult in the presence of a severe, sharp angular kyphosis. A costotransversectomy, in which the rib head and transverse process are removed at one or more levels posteriorly, facilitates drainage of a liquid abscess. However, debridement and grafting cannot be performed. The lateral extrapleural approach, which is an extension of the costotransversectomy procedure, facilitates both decompression and bone grafting while avoiding entry into the chest cavity<sup>79</sup>. The procedure involves removal of two or more rib heads and the adjacent transverse processes, and the intercostal nerves are used to identify each foramen (and pedicles). A complete decompression of the spinal cord is accomplished by removing the pedicles and diseased portions of one or more vertebral bodies. A laminectomy is appropriate for the rare case in which there is isolated involvement of the posterior elements.

Approaches to bone grafting/stabilization include anterior, posterior, anterior and posterior, and the lateral extrapleural<sup>60,61,79-89</sup>. Anterior column defects may be reconstructed using autogenous bone (rib, iliac crest or fibula), structural allografts<sup>80,81</sup>, or a titanium cage<sup>82</sup>. Experience with anterior decompression and grafting without supplementary instrumentation has revealed that graft complications (dislodgement, resorption, fracture, subsidence) are common when more than two disc spaces are spanned<sup>59,89</sup>. In such cases, anterior or posterior instrumentation (2-3 levels above and below the apex) provides mechanical stability and protects the graft<sup>55</sup>. An instrumented posterior spinal fusion (with or without a second stage anterior decompression and fusion) may be considered for neurologically normal (or

stable/improving) patients without a significant deformity, in whom there is a high risk for future progression of deformity or graft related complications<sup>55,86-89</sup>. In addition to preventing a deformity, preservation of anterior growth centers may result in some gradual correction of kyphosis. In the presence of circumferential disease, both an anterior and a posterior fusion (with instrumentation) should be considered. Both basic science and clinical studies have determined that there is no contraindication to the placement of spinal implants during either the active or the healed phases of disease<sup>90</sup>.

The management of patients with severe kyphosis remains challenging and fraught with complications, especially in patients with neurologic dysfunction and those with rigid deformities associated with healed disease. While significant correction may be possible following decompression in patients with active disease, patients with rigid deformities require spinal osteotomies (anterior and posterior, with or without a period in halo traction) followed by an instrumented fusion, or a posterior only approach in which pedicle subtraction osteotomies are followed by an instrumented posterior spinal fusion<sup>91</sup>.

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