Pott's Disease Associated With Tuberculous Meningitis Causing Blindness

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Citation

Abstract
Although the overall incidence of tuberculosis (TB) appears to be decreasing in the United States, the proportionate rate of extrapulmonary TB continues to rise. Therefore, TB of the spine, also known as Pott's disease, remains a significant health risk. This article presents a case of Pott's disease, undiagnosed until late in the disease process, associated with the subsequent development of tuberculous meningitis (TBM) causing blindness. Pott's disease is diagnostically challenging and misdiagnosis is common, contributing to the development of potentially severe neurologic deficits including this rare complication of a TBM causing blindness. Recently recognized risk factors for extrapulmonary TB, as well as established risk factors, clinical presentation, and treatment modalities are reviewed.

INTRODUCTION
Although the vast majority of the estimated 8 to 10 million new cases of tuberculosis (TB) per year continue to occur in developing countries, there has also been a resurgence of TB in developed countries. In the United States, the incidence of TB had been decreasing for decades and was often limited to the elderly until 1985 when the trend reversed. Children, young adults, racial/ethnic minorities, and immigrants have accounted for the majority of this rise in new cases. Contributing factors for the increased incidence are thought to include an influx of immigrants from developing countries, the human immunodeficiency virus (HIV), deficient infrastructure, homelessness, noncompliance with medication, and drug-resistant strains of Mycobacterium tuberculosis. Spinal TB, also known as Pott's disease, has a reported incidence of less than 1% to 5% of all TB cases, but accounts for a substantial proportion of extrapulmonary cases. Although recent data suggest that new TB cases again are decreasing in the United States, the proportion of extrapulmonary TB has continued to increase. Pott's disease, therefore, will likely remain a significant health problem.

We report a highly unusual case of Pott's disease, undiagnosed until late in the destructive process, that subsequently resulted in the development of tuberculous meningitis (TBM) causing multiple cranial nerve abnormalities including blindness. In our review of the literature, there has not been a previous report of spinal TB associated with blindness, and thus, this case occurring in a native-born, otherwise healthy woman represents a rare occurrence. In this report we discuss the presentation of Pott's disease as well as TBM, which is particularly relevant given that diagnosis of Pott's disease in particular can be challenging, with misdiagnosis a common occurrence. Subsequent delays in appropriate treatment can increase the potential for severe neurologic complications, as occurred in this case. A review, therefore, of the often-varied presenting signs and symptoms, risk factors, diagnostic considerations, potential complications, and treatment of Pott's disease is essential.

CASE REPORT
A 48-year-old native-born African American woman presented to the emergency department (ED) with an approximate 9-month history of low back pain that had worsened over the past month. She reported a recent 50-pound weight loss and had been seen by her primary care physician on several occasions for back pain. She had been treated conservatively, without radiographic imaging. She was known to have had a positive tuberculin skin test, presumably from contact with a brother who developed TB 10 years previously. The patient herself, however, had no history of active TB.

X-rays in the ED showed evidence of an L3 fracture, which was presumed to be pathologic in nature (Fig. 1). The patient
was discharged to home with plans for further diagnostic evaluation, but returned to our facility 2 days later with a primary complaint of headaches as well as visual blurriness, nausea, and vomiting. Mild right lower extremity weakness and intermittent urinary incontinence were also reported. No pulmonary symptoms were present.

**Figure 1**
Figure 1: Lateral lumbar x-ray demonstrating an L3 fracture.

On examination, the patient was alert and oriented but had nuchal rigidity, a right cranial nerve (CN) VI palsy, and mild, diffuse extremity weakness. Pulmonary exam was negative. Chest x-ray and head computed tomography (CT) were negative, but magnetic resonance imaging (MRI) of the lumbar spine showed destruction of the L3 vertebral body with stenosis of the canal, as well as evidence of paraspinal abscesses (Fig. 2). She was admitted for probable Pott’s disease and underwent evaluation for meningitis. Infectious disease and neurology services were consulted. A lumbar CT-guided biopsy was performed, which confirmed infection by Mycobacterium tuberculosis. She also underwent brain imaging by MRI with the finding of a small right cerebellar hemisphere abscess. Combination chemotherapy consisting of isoniazid, rifampin, ethambutol, and pyrazinamide was instituted.

**Figure 2**
Figure 2a: Post-contrast, sagittal lumbar MRI demonstrating destruction of the L3 vertebral body with epidural compression.
Given her systemic symptoms, the degree of kyphosis and canal compromise, and the large bilateral psoas abscesses, surgical decompression and stabilization of the lumbar spine was felt to be indicated. A 2-stage approach involving initial anterior debridement and decompression followed by posterior stabilization was planned. She subsequently underwent a left retroperitoneal approach for drainage of the iliopsoas abscesses, L3 total vertebrectomy, and L2 partial vertebrectomy. The right psoas abscess cavity was continuous with the vertebrectomy defect, allowing drainage of both abscesses from the single approach. Decompression of the dural sac was uneventful and no cerebrospinal fluid leak was noted. An autologous iliac crest strut graft was then placed, and stabilized by instrumentation from L2 to L4.

Postoperatively her lower extremity exam was stable; however, the patient became obtunded 2 days after surgery and began having seizures. On transfer to the neurosurgery ICU, a new right CN III palsy and right upper extremity dysmetria were noted. Isoniazid was added to her chemotherapy regimen. She remained partially obtunded, but when aroused complained of decreased vision in the right eye. An ophthalmological examination revealed a right afferent papillary defect. Given the clinical progression of her TBM, intravenous corticosteroids were instituted. Repeat MRI of the brain showed an increase in size of the right cerebellar hemisphere abscess, as well as new leptomeningeal enhancement of the brainstem and optic chiasm (Fig. 3).

**Figure 5**

Figure 3a: Pre-contrast, coronal brain MRI with the arrow pointing to the optic chiasm and arrowheads pointing to the leptomeninges.
Figure 6
Figure 3b: Post-contrast MRI demonstrating extensive enhancement of the optic chiasm (arrow) and leptomeninges (arrowheads).

Over the course of a day, visual symptoms developed in her left eye and then progressed to complete visual loss in conjunction with deterioration in her mental status. Given the severity of her meningitis, the second stage of her surgery was deferred. Combination chemotherapy was continued with eventual improvement in her mental status over the following 3 weeks. The patient's visual loss, however, remained permanent.

One month after her initial operation, the patient underwent a posterior T10 to L5 instrumented fusion. Her subsequent hospital course was unremarkable, and she was discharged to a subacute facility. At her 6-week follow-up visit, the patient reported improvement in her back pain and weakness. Alignment was stable on x-rays. At the 3-month follow-up visit, her extremity examination had returned to normal. Unfortunately, there was no improvement in her vision.

DISCUSSION
TB extending beyond the thorax is classified as extrapulmonary TB. Reported to occur in 8% of all cases of TB in 1964, the proportion has steadily risen to approximately 16% in 1991 and to 20% in 2001.\textsuperscript{1,8} The etiology underlying this increase in extrapulmonary disease remains unclear, although Yang et al. retrospectively evaluated 705 patients to demonstrate that a positive HIV status, female gender, and race (non-Hispanic black) were significant risk factors.\textsuperscript{8} Interestingly, our patient possessed 2 of these risk factors. Common sites of extrapulmonary TB include the musculoskeletal system, genitourinary tract, and lymphatic system.\textsuperscript{10} Pott's disease accounts for approximately 50% of extrapulmonary TB that involves the bones and joints, but has a reported incidence of less than 1% to 5% of all TB cases.\textsuperscript{11}

Diagnosing Pott's disease. Diagnosis of Pott's disease can be challenging, since in the early phases the clinical presentation and radiographic imaging are often nonspecific. Malignancy as well as pyogenic or fungal vertebral infections can have similar presentations and imaging characteristics. Nussbaum et al. reviewed 29 patients with Pott's disease and found that 41% were initially misdiagnosed.\textsuperscript{9} Diagnosis can therefore be delayed for months to years, increasing the potential for neurologic complications.\textsuperscript{12,13} History of a positive tuberculin test, active TB, HIV, immunosuppression, or contact with an individual with TB should raise the index of suspicion for Pott's disease, but these “flags” are often not present.

Clinically, the most common symptom is back pain.\textsuperscript{9,12,13} Pertuiset et al. evaluated 103 patients with Pott's disease and found 97% presented with back pain, which was consistent with previously reported data.\textsuperscript{7} Found to a lesser degree was fever in 31% and weight loss in 48%. Neurologic deficit was noted in 50% of patients, but rates ranging from 22% to 76% have been observed in other studies.\textsuperscript{6,7,9,12,14} Specific deficits resulting from compression of the spinal cord, conus medullaris, cauda equina, or nerve roots consist of bowel/bladder incontinence, sensory disturbance, and weakness including paraplegia.

Although nonspecific, laboratory tests of value include an elevated erythrocyte sedimentation rate (ESR), abnormal liver function tests, and a rise in the white blood cell count. Of these tests, the ESR appears most helpful, with an increase (>20mm/h) reported to occur in 88% to 100% of afflicted patients.\textsuperscript{7,9,14} Similar to the clinical presentation and laboratory testing, imaging can be helpful but is typically not pathognomonic. Chest roentgenograms are often normal in patients with extrapulmonary TB, including those with Pott's disease.\textsuperscript{9,10}
Although changes on spine roentgenograms may be delayed up to 8 weeks, there is, classically, a collapse of 2 adjacent vertebrae anteriorly with destruction of the intervening disc. Malignancy, in particular, can appear similarly but often will have preservation of the intervening disc. CT imaging offers the advantage of earlier and more detailed visualization of bony involvement and detection of paraspinal soft tissue masses. Characteristics suggestive of TB on CT imaging include the combination of a multi-locular, calcified paraspinal abscess with an irregular enhancing rim in conjunction with vertebral body bony fragmentation. Due to its multi-planar capability and high resolution of soft tissue and bone, MRI is now the imaging modality of choice. MRI can show additional sites of infection as well as detect early changes involving the endplate. In particular, T2 hyperintensity, T1 hypointensity, and enhancement with contrast, while not completely specific, are often consistent with TB. The degree of spinal cord or nerve root compression as well as intraosseous, intraspinal, and paraspinal abscesses with characteristic patterns of rim enhancement can also be visualized. Based on suggestive imaging characteristics, CT-guided or open biopsy can then provide definitive diagnosis.

Diagnosing TBM. TBM occurs less frequently than Pott’s disease, comprising just 15% of extrapulmonary TB cases and only 0.7% of all TB cases. In adults, TBM can develop in isolation or with another form of the disease, particularly miliary or pulmonary. Typically, TBM develops in 2 stages. There is an initial hematogenous dissemination with the primary infection, or alternatively, dissemination during the course of a chronic infection resulting in caseous foci of bacilli deposited within the brain. Subsequent rupture of a focus into the subarachnoid space results in meningitis. More rarely, the meninges can be infected from a site of tuberculous spondylitis, presumably from direct extension of the infection through the adjacent dura. Either route, hematogenous dissemination from chronic infection or direct extension, may have contributed to the development of TBM in our patient.

The clinical manifestations of TBM are varied and result from multiple factors including the development of a thick basilar exudate, vasculitis, vascular occlusion, allergic reaction to tuberculoprotein, cerebral edema, and formation of tuberculomas. Symptoms typically are gradual in onset with malaise, low-grade fever, intermittent headache, and change in personality. Subsequently, a more pronounced meningitic phase develops within 2 to 3 weeks involving persistent headache, meningismus, vomiting, confusion, cranial nerve palsies, or long-tract signs. Symptoms can progress to stupor or coma followed by seizures, hemiparesis, and hemiplegia. Death typically occurs within 5 to 8 weeks if left untreated. Cranial nerve palsies from basilar exudates occur in 20% to 30% of patients and most commonly involve CN VI and less frequently CN III followed by CN IV and VII. Other cranial nerves are rarely affected, but involvement of CN II can cause optic atrophy and blindness. Similar to Pott’s disease, the tuberculous etiology of the meningitis, when it occurs in isolation, can be diagnostically challenging. A high index of suspicion in the patient with a history of TB or evidence of extrapulmonary TB is essential. Laboratory testing is typically not helpful, although an elevated ESR and positive tuberculin test may be present. Lumbar puncture for cerebrospinal fluid analysis should be performed but can also be nondiagnostic. Prognosis is highly dependent on the timing of treatment. Early initiation of treatment, prior to focal neurologic deficit or mental status changes, will lead to the best outcomes. Even short delays involving several days to a week can result in significantly increased risk for permanent neurologic deficit and mortality. Empiric therapy is therefore recommended based on clinical suspicion and suggestive laboratory data.

Treatment. The cornerstone of treatment for Pott’s disease and TBM involves combination chemotherapy. The standard has been a triple drug regimen of isoniazid, rifampin, and pyrazinamide for 12 months. However, recent increases in drug-resistant organisms have led to the addition of a fourth or even a fifth anti-TB drug consisting of ethambutol and/or streptomycin. While controversial, several clinical studies have also shown corticosteroids (12 mg/day in adults, 8 mg/day in children weighing less than 25 kg) to improve the morbidity and mortality associated with TBM. Our patient received a 4-drug regimen as well as corticosteroids. While the role of surgery in Pott’s disease is controversial, some have advocated surgery for every infected site. However, given the effectiveness of chemotherapy in even those patients with mild neurologic deficit, surgery is now predominantly reserved for significant or progressive neurologic deficit and deformity correction. On presentation, our patient had a significant kyphotic deformity as well as large abscesses involving the iliopsoas muscles. Surgical drainage of the abscess as well as debridement and stabilization was therefore felt to be indicated, even though her spine-related neurologic deficits were relatively mild. The need for aggressive supportive
care, chemotherapy, multiple surgical procedures, and prolonged hospitalization, along with the major impact of her permanent blindness, highlight the importance of early identification of extrapulmonary TB and instituting chemotherapy in a timely fashion.

CONCLUSION
Although recent evidence shows a decreasing incidence of TB in the United States, the rate of extrapulmonary TB continues to rise. Pott's disease, therefore, will remain a significant health risk. Diagnosis of Pott's disease is challenging and misdiagnosis is common, contributing to the development of potentially severe neurologic deficits including this rare complication of a TBM causing blindness. Knowledge of recently recognized risk factors for extrapulmonary TB, including female sex, race (non-Hispanic black), and positive HIV status, in addition to the well known clinical signs for TB including weight loss, fatigue, and persistent and progressive back pain, may be of benefit in early diagnosis. Regardless of risk factors, however, it is crucial to maintain a high index of suspicion in such cases.

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