Tuberculous Spondylodiscitis and Meningitis

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Tuberculosis is one of the oldest and most widespread diseases, dating back to pre-Columbian times and the Egyptian mummies. It is estimated that 20–43% of the world population is infected with TB and 3 million people will die, mostly from third world countries [1].

Tuberculosis involvement of the central nervous system is an important and serious type of extrapulmonary disease. It has been estimated that approximately 10% of all patients with TB have CNS involvement. We describe a male patient with concomitant spinal spondylodiscitis and meningitis secondary to *Mycobacterium tuberculosis* infection that was associated with tuberculous vasculopathy.

Patient Description

A 76 year old man was admitted to hospital with a high grade fever and low back pain of 1 week duration. His previous medical history was remarkable for pulmonary TB dating 30 years earlier. In addition, he suffered from myasthenia gravis for 18 years, which had originally presented with symptoms of diplopia and was successfully treated by pyridostimgmine. Ten months prior to admission, therapy was stopped due to respiratory failure, and immunosuppressive therapy with glucocorticoids and azothiaprine was started resulting in rapid clinical improvement. His physical examination, which included a neurologic evaluation, was normal except for tenderness over lumbar vertebras L4-L5 upon percussion. His laboratory results included an elevated white blood count of 11,000/ml^3 and elevated erythrocyte sedimentation rate. Chest X-rays showed right pleural thickness; a PPD skin test was negative, and computed tomography and magnetic resonance imaging of the lumbar spine showed evidence of spondylodiscitis with no indications of abscess [Figure 1].

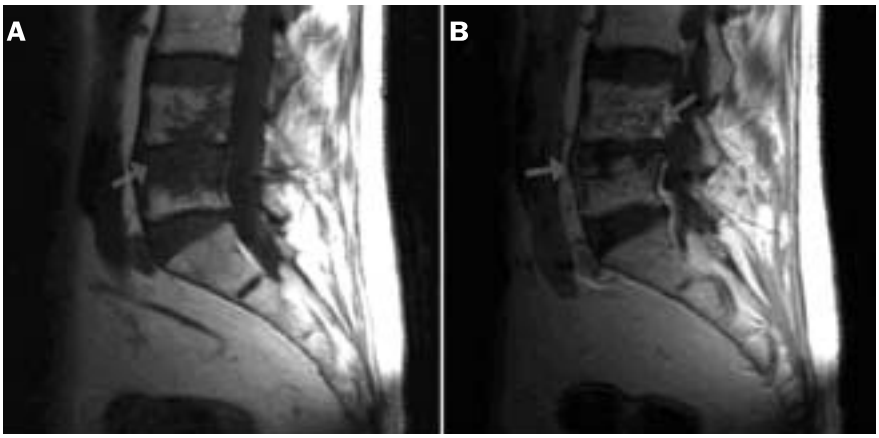

Figure 1. MRI of the lumbar spine showing sagittal T1-weighted image without contrast **[A]**, sagittal T1 **[B]** weighted images after contrast injection. T1-weighted image without contrast shows decreased signal from the affected vertebral marrow, L4-L5. The cortical definition of the endplates of both vertebras is lost and there is partial collapse of L5. After injection of gadolinium [**B]**, there is enhancement of the involved vertebras and the anterior part of the intervertebral disk L4-5.

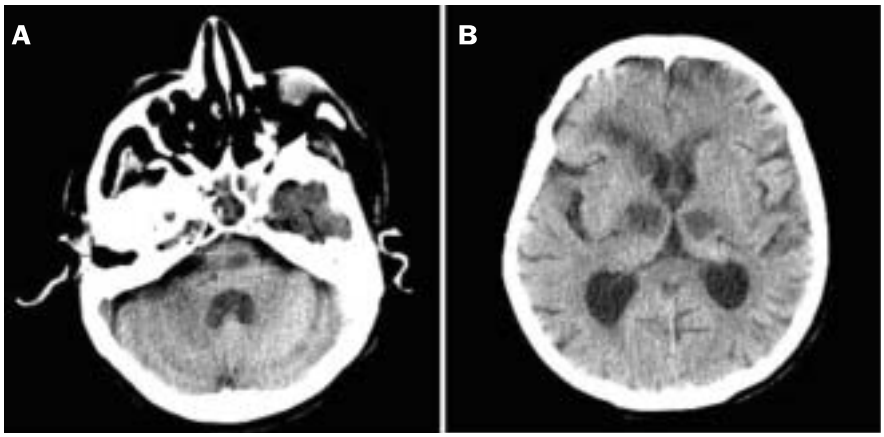

Figure 2. CT of the brain showing axial cuts without contrast injection. **[A]** Image at the fourth ventricle and the level of the pons showing infarct, and **[B]** image at the level of the third ventricle demonstrates bilateral infarcts in the thalami and an infarct in the right frontal lobe. A CT performed 10 days earlier was normal.

Due to a high index of suspicion for TB, a drug regimen of four antituberculous antibiotics was begun. Bone biopsy confirmed the tubercular etiology and cultures taken from bone specimens were positive after 2 weeks of incubation. One week later, after bone biopsy, the patient developed respiratory failure and mental confusion and was intubated. Lumbar puncture was performed, revealing a raised opening pressure as well as elevated lactate, lymphocytosis, hypoglycorrhachia and gram-negative bacteria. CT of the head revealed multiple infarcts [Figure 2]. Cerebrospinal fluid was cultured and was

TB = tuberculosis
CNS = central nervous system

positive for TB. The dosage of steroids was increased; nonetheless, the patient died. Our diagnosis was tubercular spondylodiscitis and meningitis.

Comment

Tuberculosis can affect a gamut of CNS functions. The classification of intracranial CNS TB includes tuberculous meningitis, tuberculous meningitis with military TB, encephalopathy and vasculopathy, space-occupying lesions such as tuberculoma or abscess [2]. The mechanism of central nervous system involvement associated with tuberculous meningitis is unknown. According to the hypothesis of Rich et al. [3] the CNS TB develops in two stages. Firstlyl isolated military tubercules form in the parenchyma of the brain or meninges during hematogenous dissemination of tubercle bacilli after primary infection or after endogenous reactivation of latent TB. Most often, the primary source arises from the lungs. Later, rupture of a subependymal tubercle into the subarachnoid space produces development of various types of CNS TB.

Patients with tuberculous meningitis usually have a prodrome of malaise, low grade fever and headache progressing to vomiting, confusion, and neurologic deficits; however, the clinical spectrum is quite broad. Cranial nerve palsies may be a presenting manifestation of the disease, while focal neurologic deficits may occur at the onset or at a later stage of the disease.

Risk factors for the development of tuberculous meningitis include more advanced age, alcoholism, malnutrition, drug abuse, homelessness, and human immunodeficiency virus infection. Other risk factors include exposure to pulmonary TB or travel to countries endemic with TB. Less than 50% of people who have contracted tuberculous meningitis have had a history of pulmonary TB [4].

Diagnosis is made by CSF examination. Lumbar puncture may reveal an elevated opening pressure, lymphocytic pleocytosis (10–500 cell/mm^3), an elevated protein concentration (100–500 mg/dl) and a decreased glucose concentration. Culture of the cerebrospinal fluid for tubercle bacilli is not invariably positive. Rates of positivity for clinically diagnosed cases range from 25 to 70% [2–4]. The best method for diagnosing mycobacterial infection is the polymerase chain reaction that has a specificity of 80–100% and a sensitivity of 25–80%. Nonetheless, when the diagnosis is doubtful, PCR should be performed [4].

Neuroimaging is non-specific. Computed tomography or magnetic resonance imaging may reveal thickening and intense enhancement of meninges, especially in basilar origin, cisternal enhancement, and infarcts. The middle cerebral artery and its branches are often affected, especially the small perforating arteries. The infarcts are usually in the basal ganglionic and thalamic regions, commonly bilateral. CT and MRI may also demonstrate tuberculoma, communicating and/or obstructive hydrocephalus [4].

There is currently no general consensus about the form of chemotherapy or optimal duration of treatment for tuberculous meningitis. The World Health Organization recommended initial pulse therapy with streptomycin, isoniazid, rifampicin and pyrazinamide for 2 months followed by 7 months continuation with isoniazid and rifampicin [1].

One of the controversial aspects of treatment of tuberculous meningitis is the use of corticosteroids. It was recently demonstrated that corticosteroids may improve both survival rate and neurologic outcome, with subsequent resolution of basal exudates by CT scanning [5]. The indications for corticosteroids in tuberculous meningitis according to those observations contain altered sensorium, focal neurologic deficit, significantly increased spinal fluid pressure, basilar exudates, and hydrocephalus [5]. Neurosurgery is used to treat hydrocephalus using ventriculostomy and ventriculo-peritoneal shunt [4].

The mortality from tuberculous meningitis is very high. The single most important determinant of outcome for both survival and sequelae is the stage of tuberculous meningitis at which treatment was initiated [5]. If treatment was begun in the prodromal phase, the mortality and morbidity are very low. In more severe disease with clouding of sensorium, convulsions and focal neurologic deficit, almost 50% of patients die. Other worst prognostic factors for tuberculous meningitis are age older than 60 years, malnutrition, presence of underlying debilitating disease or military disease, hydrocephalus, focal neurologic deficit, low level of CSF glucose or markedly elevated CSF protein [5].

This case is of a particular interest for several reasons. First, it is the first reported case of both TB spondylodiscitis and tuberculous meningitis simultaneously, although there are many concomitant cases of extrapulmonary tuberculosis [2,4]. Possible explanations may be contamination during bone biopsy, rupture of subependymal tubercle due to trauma, or hematogenous dissemination. This patient's mental confusion began 1 week after bone biopsy of the lumbar spine. It is possible that mycobacterium was then introduced into the CSF, resulting in later meningitis. Second, we suspected that the absence of an adequate immune response in a patient with myasthenia gravis who was treated with immunosuppressive therapy may play an important role in the development of concomitant spondylodiscitis and tuberculous meningitis. Despite prompt treatment for TB, the patient nonetheless died of TB meningitis.

References

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CSF = cerebrospinal fluid

PCR = polymerase chain reaction