The Combined Peripheral and Central Demyelinating Disease Associated with Pulmonary Tuberculosis

Sang Ahm Lee, M.D., Il Soo Choi, M.D.

Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine

Although there are some reports of neuromyelitis optica or Guillain-Barre syndrome in patients with tuberculosis, the combined peripheral and central demyelination associated with tuberculosis has not yet been reported. We report a 43 year-old man with active pulmonary tuberculosis presenting with Guillain-Barre syndrome, bilateral optic neuritis, and multiple central nervous system white matter lesions on MRI. Our case suggests that tuberculosis may be associated with the combined peripheral and central demyelination.


Key Words: Guillain-Barre syndrome, Optic neuritis, Demyelination, Pulmonary tuberculosis

Central or peripheral demyelinating disorders including neuromyelitis optica, isolated optic neuritis or myelitis, and Guillain-Barre syndrome (GBS) in patients with tuberculosis have been well documented in the literature. It has been suggested that they are most likely due to an immune reaction to tuberculosis rather than due to direct invasion of tuberculosis or the adverse effect of antituberculosis medication. However, the combined peripheral and central demyelination associated with tuberculosis has never been reported yet. We report a patient with active pulmonary tuberculosis presenting Guillain-Barre syndrome, bilateral optic neuritis, multiple central nervous system (CNS) white matter lesions on MRI, and cerebrospinal fluid (CSF) oligoclonal bands.

Case report

A 43 year-old man was admitted due to rapidly progressive quadripareisis and bilateral visual loss. He had been well until 8 days before admission, when he noticed distal paresthesia in all extremities. The next day, muscle weakness of bilateral legs and urinary retention developed and were gradually aggravated. Three days later, muscle weakness ascended to bilateral upper extremities. One day prior to admission, bilateral visual loss developed. He was referred to our hospital for further evaluation and treatment.

He was afebrile, with blood pressure of 110/80 mmHg and pulse of 118/min. Physical examination was remarkable only for coarse breath sound and crackle in right upper lung field on auscultation. Mental status was normal. Bilateral visual acuity was completely lost. He could not perceive light. Bilateral optic discs were blurred. Bilateral pupils were modestly dilated and just merely reactive to light. The range of eye movements was preserved. Facial diplegia and tongue weakness were noted along with weakness of neck flexor muscles. He was quadriparitic, predominantly distal and somewhat asymmetric in degree ranging from 4/5 in
shoulder to 1/5 in distal leg. Sensory function including pain, temperature, position, and vibration was markedly decreased below the nipples. There was mild distal diminution of vibration and position sense in both upper extremities. Deep tendon reflexes were absent in legs but preserved in arms. Toe signs were not present.

CSF was under normal opening pressure, with total protein of 439 mg/dl, glucose 72 mg/dl, 110 WBC/mm$^3$ (94% of which were lymphocytes), and positive oligoclonal bands. CSF adenosine deaminase was 0.2 U/L. CSF polymerase chain reaction for Mycobacterium tuberculosis, herpes simplex virus (type I and II), cytomegalovirus, and Epstein-Barr virus were negative. CSF smear and culture for Mycobacterium tuberculosis were negative. The following studies were normal or negative: CBC, erythrocyte sedimentation rate, routine blood chemistry, electrolytes, serum protein electrophoresis, serum complement (C3, C4), rheumatoid factor, antinuclear antibody, and serum VDRL. Chest X-ray revealed patchy increased opacity in right posterior and left apicoposterior segments. The sputum smear for acid fast bacilli was positive and M. tuberculosis was isolated in sputum culture medium after 46 days. Brain and cervical MRI showed multiple T2-weighted high signal intensity lesions in right frontoparietal white matter and cervical spinal cord (C4-7) with cord swelling and mild enhancement (Fig. 1). Nerve conduction study revealed the typical finding of demyelinating polyneuropathy (Fig. 2), which included absent F responses, slowing of nerve conduction velocities, absent or

Figure 1. T2-weighted MRI findings. MRI shows a high signal intensity lesion in the subcortical white matter of the right frontoparietal area (A) and in the cervical spinal cord (B).

Figure 2. Conduction block is noted on a nerve conduction study at the right ulnar nerve (Stimulation site, A1: wrist, A2: below elbow, A3: above elbow, A4: axilla).
reduced compound nerve action potentials, reduced amplitude of compound muscle action potentials, and conduction block and temporal dispersion in bilateral upper and lower extremities. Sural nerve biopsy showed the degeneration of both axon and myelin with the perivascular lymphocytic infiltration. There was no evidence of vasculitis.

He was treated with high-dose intravenous methylprednisolone, plasma exchange, and antituberculous medication. He started to show improvement in muscle power, somatic sensation, and vision after the fourth day of treatment. Seven months later he was near normal except some visual impairment in right eye and mild paresthesia in distal extremities. At that time, nerve conduction study findings were also much improved but not normal. Conduction block and temporal dispersion disappeared but nerve conduction velocities in all the tested nerves were slow (30~40 m/sec).

**DISCUSSION**

Korea is an endemic area for tuberculosis. We could not exclude the possibility that this demyelinating disease and pulmonary tuberculosis in our case may be coincidental. Recently Silber et al. investigated these interrelated conditions in an area endemic for tuberculosis and then suggested that the close temporal relationship of several neurologic syndromes to pulmonary tuberculosis is not coincidental.

The combined peripheral and central demyelinating disease, so called ‘encephalomyeloneuritis’ (EMN), is a rare disorder in which the unusual combination of encephalitis, myelitis, and polyneuropathy concurrently occurs.\(^1\)\(^2\) It has been sporadically reported in patients with central or peripheral demyelinating disease,\(^5\)\(^6\) systemic cancer,\(^11\)\(^12\) vaccination,\(^13\) and Mycoplasma pneumoniae infection.\(^14\)

The diagnosis of EMN may be difficult because polyneuropathy is often so severe that may mask the features of encephalitis and/or myelitis.\(^4\)\(^12\) In our patient, clinical manifestations including acute onset of distal paresthesia, facial diplegia, ascending quadriparesis, and areflexia in lower extremities were compatible with GBS. Electrodiagnostic study was also indicative of demyelinating polyneuropathy. Bilateral visual loss, sensory level at T4 dermatome, and severe bladder dysfunction, however, suggested the additional involvement of central nervous system, which was confirmed by MRI.

Active pulmonary tuberculosis itself and antituberculous medications are often complicated with various nervous system dysfunctions.\(^2\) Direct CNS invasion of microorganism may cause meningoencephalitis, vasculitis, spinal arachnoiditis, or myeloradiculitis. Optic neuropathy may occur due to ethambutol, and peripheral neuropathy due to isoniazid. CSF pleocytosis in our case may lead one to consider the possibility of direct invasion of microorganism as a cause of CNS lesions. However, negative smear and culture from repeated CSF samples, low levels of CSF adenosine deaminase, and positive CSF oligoclonal bands could all implicate the low possibility of CNS tuberculosis.

In addition, it seems unlikely that the demyelinating polyneuropathy of this patient was caused by direct invasion of mycobacterium.

The most likely pathogenesis may be an immune response of the nervous tissue to pulmonary mycobacterial infection.\(^15\) However, whether this acts via a shared antigen between myelin and the M. tuberculosis bacillus or via another mechanism has not been established. Support for the concept of immune-mediated disease in tuberculosis is provided by several case reports\(^1\)\(^2\)\(^16\) including a patient with pulmonary and peritoneal tuberculosis who was found, following a subacute encephalitic illness, to have the pathologic features of acute disseminated encephalomyelitis.\(^16\) The reports of neuromyelitis optica or GBS in patients with active pulmonary tuberculosis suggested that immune reaction to M. tuberculosis may be complicated with inflammatory demyelinating disorder.\(^1\)\(^2\)

The presence of the CSF oligoclonal bands in this patient could reflect an immune-mediated pathological process in the CNS.\(^17\) It has also been suggested that EMN is an immunologic disorder on the analogy of acute disseminated encephalomyelitis (ADEM) and/or GBS.\(^15\) Recently Nadkarni and Lisak\(^14\) reported the case with GBS, bilateral optic neuritis, and central white matter disease after Mycoplasma pneumoniae infection. They suggested a possibility of a shared pathogenic CNS and PNS epitope.
REFERENCES