Clinical Presentation

EB, an individual in their 20s, who was positive for human immunodeficiency virus (HIV), presented to the neurologic department of the University Teaching Hospital in Lusaka, Zambia, with a burning sensation in all extremities, progressive tetraparesis, and urinary and bowel retention. The symptoms had started 3 months previously with neck pain and paresthesias of the hands and were progressive since then. At that time, EB had presented to the neurologic outpatient clinic, but was lost to follow-up before additional workup could be done.

EB had been diagnosed with tuberculous myelitis 2 years previously and prescribed antituberculous treatment with isoniazid, rifamycin, ethambutol, and pyrazinamide for 12 months. EB had improved after treatment and was ambulating without walking aids, with only mild weakness in the legs (4/5 muscle strength distally, bilateral) and no sensory deficits. EB was considered cured and the antituberculous treatment had been discontinued 1 year ago. There was no history of headaches, fevers, or weight loss. EB denied any exposure to toxins or radiation or substance abuse.

At admission, EB had an unremarkable general examination except for crackles in the right lower lung. EB was awake, alert, and fully oriented, with intact memory and attention. EB did not have any speech or language impairment, denied headaches, and did not have signs of meningeal irritation.

There was increased muscle tone in both legs with weakness in the left arm (4/5 muscle strength proximally and distally) and the legs (4/5 muscle strength proximally, 3/5 muscle strength distally). Deep tendon reflexes were reduced to 1+ in both upper limbs. Patella and adductor reflexes were increased with spreading to 3+ bilaterally; ankle jerk was 3+ on the right and absent on the left. EB’s toe was upgoing on the left. In the sensory examination, no clear sensory level could be determined. EB had reduced sensation to pain and temperature from the toes up to the middle of the thighs. EB was unable to walk without substantial support. Coordination was normal. At the time of presentation, EB complained about a burning sensation, spreading in a stocking-glove fashion in all extremities.

A chest radiograph was unremarkable except for mild lymphadenopathy. Blood examination results were within normal ranges except for a mild increase in white blood cell count. Venereal disease research laboratory and cryptococcal antigen testing were negative. Immunoglobulin G for cytomegalovirus was reactive, whereas immunoglobulin M was nonreactive. Viral load was undetectable, but CD4 count was low, with 108 cells/mm3. A urine lipoarabinomannan bedside antigen test resulted positive. In repetitive lumbar punctures, cerebrospinal fluid (CSF) revealed a normal white cell count, slightly elevated protein level, normal glucose level, negative gram stain, negative acid-fast bacilli test, and negative India ink test. Toxoplasmosis antigen test was positive initially, but repeat examinations did not confirm this result.
A noncontrast MRI of the spine was obtained, showing T2 hyperintensity in most of the cord, representing generalized edema of the spinal cord. Cystic cavity/syrinx formation was seen in the lower thoracic spine (T9 through T11 levels, as well as T12). Furthermore, dorsal mildly T1 hyperintense, T2 dark and enhancing nodules were seen at the T7 level, appearing intradural and extramedullary in location (Figure 1).

No imaging from the initial tuberculous myelitis diagnosis could be retrieved. The costs of MRI have to be covered by patients or relatives, making its use limited in Zambia. Some hospitals store imaging data centrally, but most centers give the imaging results to the patient. An MRI of the lumbar spine had been performed during the initial tuberculous diagnosis, 2 years previously, at an external hospital. The patient could not provide these images, and the images were not stored centrally.

**Case Resolution**

EB was started on empiric quadruple antituberculosis treatment as well as adjacent pyridoxine and dexamethasone therapy. A urinary catheter was placed, considering the urinary retention. EB was discharged on antituberculous treatment, pyridoxine, and oral prednisolone. At follow-up 3 months later, EB was able to ambulate without walking aids. The antituberculous treatment was continued with a gradual tapering of the prednisolone therapy.

**Discussion**

Spinal tuberculous radiculomyelitis (TBRM) is a rare complication of central nervous system (CNS) tuberculosis. It usually develops through the breakdown of granulomatous foci into the subarachnoid space. The gelatinous exudate in the subarachnoid space leads to encasement and compression of the spinal cord and impingement of the spinal nerve roots. Involvement at any level of the spinal cord is possible.

The terms arachnoiditis and radiculomyelitis often are used interchangeably. The clinical symptoms vary according to the level of spinal and radicular involvement. The symptoms usually are a mixture of myelitic and radicular symptoms in varying amounts.

The disease often presents as subacute paraparesis or tetraparesis that progresses over time. Additional symptoms may include paresthesias and dysesthesias, bladder disturbances, and muscle wasting. In untreated cases, complete paraplegia usually occurs within a few weeks.

Reflexes usually are decreased to absent, but depending on the spinal cord involvement, brisk reflexes also have been described. Symptoms can be aggravated by thrombosis of the anterior spinal artery, leading to spinal cord infarction.

TBRM can occur many decades after the diagnosis of tuberculous myelitis and can occur even in adequately treated patients after complete sterilization of the CSF.

The formation of a syringomyelic cavity, as in our case, is a long-term complication of TBRM. Patients may first manifest with complications of syringomyelia, although this is rare.

Peripheral neuropathies are the most common neurologic manifestations occurring in individuals with HIV infection.
Distal symmetric sensory polyneuropathies are the most frequently encountered form and can occur as a result of HIV infection or the use of antiretroviral medication. Early differentiation between TBRM and HIV-associated polyneuropathy is of utmost importance, because treatments differ and delay in the treatment of TBRM is associated with substantial morbidity and mortality. Especially in resource-limited settings, where MRI is not readily available, the simultaneous occurrence of peripheral and CNS abnormalities should prompt for additional imaging of the spine to rule out TBRM. The diagnosis usually is made through imaging and CSF examination in suspected cases.

CSF evaluation usually shows lymphocytic pleocytosis in varying degrees as well as very high CSF protein levels. As in our case, a normal CSF examination does not rule out TBRM. Especially in children and immunocompromised people, normal CSF examination results have been reported, albeit rarely. Although the exact pathophysiology remains unknown, T-cell activation seems to play a pivotal role in host response. In immunocompromised individuals, this response may be lacking or delayed. Although normal CSF does not rule out TBRM, it is extremely rare. Furthermore, resource-constrained countries face multiple challenges in CSF examination and interpretation. In our case, the CSF had to be transported for many hours in high ambient temperatures for analysis, which may have influenced the results.

MRI is important in early diagnosis of TBRM. The earliest abnormalities seen on MRI include leptomeningeal and nerve root enhancement. Because the pathophysiology of TBRM involves the entrance of viscous exudate into the subarachnoid space, encasing the spinal cord and leading to adhesions of the nerve roots, T2/fluid-attenuated inversion recovery hyperintensity of the spinal cord accompanied by contrast enhancement of the fibrin-coated nerve roots is a common neuroradiologic finding. The nerve roots may appear fixed peripherally in the thecal sac, which has been described as the empty thecal sac sign. T2/fluid-attenuated inversion recovery hyperintensity can be localized but more frequently spreads over multiple spinal segments. Although more than 80% of cases involve the thoracic spine, involvement of the cervical spine, lumbar spine, and conus medularis have been reported.

During the course of the disease, CSF loculations and blocks may appear because of progressive organization of the tenacious exudate. Neuroradiologic changes may improve, but usually remain unchanged, despite effective treatment. Later findings include cavitation of the spinal cord and syrinx formation, which usually are associated with a worse prognosis.

TBRM must be differentiated not only from other forms of meningoencephalitis, such as partially treated meningitis, but also from immune reconstitution inflammatory syndrome, especially in regions with a high rate of HIV infection, such as sub-Saharan Africa.

The most important aspect of treatment in TBRM is the initiation of antituberculous treatment. Although early treatment plays a pivotal role in preventing morbidity and mortality, clinical deterioration after treatment initiation has been described. Although the reasons for this deterioration in rare cases remain unknown, a delayed hypersensitivity response to mycobacterial antigens seems to be a plausible explanation. Hence, treatment with steroids may play an important role in these cases.

Our patient improved after combined antituberculous and steroid treatment. After 6 months, EB was able to ambulate with aids, and urinary and bowel retention was restored, but the severe dysesthesias, especially in the legs, persisted.

Figure 2. Zoomed image of the sagittal T2-weighted sequences showing thickened nerve roots in the lumbar spinal canal (arrows).

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Disclosures
The authors report no disclosures.