An Uncommon Cause of Longitudinally Extensive Transverse Myelitis

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ABSTRACT

Considering that currently Romania has the highest tuberculosis incidence in Europe, the recognition of the infection is an acknowledged health issue. Central nervous system tuberculosis accounts for approximately 1% of all cases of tuberculosis. Longitudinally extensive transverse myelitis is a contiguous inflammatory lesion of the spinal cord which involves three or more spinal segments. In tuberculosis, spinal cord involvement is rare and is usually rather due to radiculomyelitis or spinal tuberculoma, and only very rare due to longitudinally extensive transverse myelitis.

We present the case of a 52-year-old man referred to our department for progressive neurological deficits due to a longitudinally extensive transverse myelitis. After a thorough work-up we diagnosed the patient with longitudinally extensive transverse myelitis secondary to infection with Mycobacterium tuberculosis.

Keywords: Central nervous system tuberculosis, longitudinally extensive transverse myelitis

BACKGROUND

Longitudinally extensive transverse myelitis is defined as a contiguous, usually inflammatory lesion that involves three or more spinal segments.

In currently developing countries, such as Romania, tuberculosis is still a very important health issue. In a report published in 2014, World Health Organization (WHO) estimated that there approximately 20 000 of new cases of tuberculosis registered every year in Romania, making the country the first one at TB incidence among countries from the European Economic Area (EEA) and European Union (EU) (1).

Of all cases of tuberculosis, central nervous system is affected in approximately 1%, with spinal cord involvement seen in less than half of these cases, with a higher prevalence for HIV infected individuals (2). Most often, central nervous system tuberculosis pertains to tuberculous meningitis (95%), space-occupying cerebral or medular tuberculoma, and radiculomyelitis, and very rarely to longitudinally extensive transverse myelitis (LETM) (3).

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CASE REPORT

A 52-year-old man, chronic smoker with 32 pack-years of exposure, with a history of alcohol consumption and with a nephew recently diagnosed with tuberculosis was referred to our department for a history of lower limbs ascending paresthesias, shortly followed by urinary retention and muscle weakness 5 days prior to admission. On admission the patient was febrile (37.6 °C) without any other general signs. Muscle power was of 1/5 MRC (medical research council) in both lower limbs and 4/5 MRC in right upper limb. Deep tendon reflexes were brisk in the upper limbs, normal in right lower limb and absent in left lower limb, with no plantar response in right lower limb and a flexor response in left lower limb. All sensation modalities (pain, touch, temperature, joint position and vibration) were impaired below thoracic 8 (T8) spinal level. He also presented with urinary retention. No other additional sign was noted.

Routine blood tests were normal except for liver enzymes which were elevated (GOT 269 U/l, GPT 443U/l) and for a mild hyponatremia (Na 133 mmol/l). Serum vitamin B12 levels were also normal. HIV serology was negative and a chest X-ray was interpreted as normal.

We performed a cerebral MRI which proved normal, but the cervical and thoracic spine MRI showed a contiguous long lesion, extending from cervical vertebral level C2 to thoracic vertebral level T2, which was isointense on T1 and hyperintense on T2-weighted images, without contrast enhancement. Also, the MRI showed a certain extent of cervical vertebral degeneration (C4-C7).

FIGURE 1. Chest X-ray postero-anterior view- no obvious evidence of tuberculosis

FIGURE 2. T2-weighted sagittal cervical and thoracic spinal cord MRI showing a long intramedullary hyperintense lesion without contrast enhancement

FIGURE 3. T2-weighted MRI showing a hyperintense lesion that extends from C2 to T2 spinal segments.
Considering the findings we performed a lumbar puncture. The cerebral spinal fluid analysis showed 39 white blood cells count/mm³ with 15.4% lymphocytes and 84.6% neutrophils, elevated proteins (95 mg/dl), and a CSF glucose of 57 mg/dl (blood glucose 154 mg/dl), with normal opening pressure. Ziehl-Nielsen stains were negative, as well as the Gram stains.

The clinical and MR findings were consistent with longitudinally extensive transverse myelitis, so a thorough work-up was performed for possible causes of LETM, testing for a series of markers of autoimmune disorders. ANA, DNA-ds as well as CSF angiotensin converting enzyme were found to be negative. Considering the patient’s history (his nephew was recently diagnosed with tuberculosis) and the results from the lumbar puncture, we had a polymerase chain reaction (PCR) for Mycobacterium tuberculosis from the CSF which also turned out negative. In order to rule out Neuromyelitis optica (frequently associated with LETM) and multiple sclerosis (associated with transverse myelitis) we tested our patient for Anti-AQP4 antibodies, and for oligoclonal bands respectively, both being negative.

Paraneoplastic disease might also be responsible for LETM, so we tested the patient for onconeural antibodies which also proved to be negative.

Considering that even if all the tests for tuberculosis were negative but the patient have been exposed to Mycobacterium tuberculosis and lacking an obvious cause for LETM we performed a CT scan of the lungs which showed a pulmonary nodule in the lower right lobe and a smaller one in the superior right lobe. We referred the patient for a thoracic surgery consult and a biopsy. The histopathologic analysis of the specimen eventually revealed an epithelioid granuloma with caseous necrosis in the center confirming the diagnosis of Mycobacterium tuberculosis infection.

Before making the final diagnosis and starting the appropriate treatment, the patient was started on iv dexamethasone, 16 mg daily and ciprofloxacin daily for urinary tract infection. He gradually improved with corticotherapy, the muscle power of both lower limbs being of 2/5 MRC. The patient was referred to a tuberculosis specialized center and never returned for a follow-up.

**DISCUSSION**

*Mycobacterium tuberculosis* is an acid fast pathogenic bacterium that primarily involves the lungs giving rise to tuberculosis. In developed countries the incidence of tuberculosis decreased in the past decades, but in countries with a lower standard of life, the disease is still a very serious health problem, being one of the front rank causes of infection related mortality and morbidity (4). An important prospective epidemiological study performed in Canada between 1970 and 2001 showed that the chance of developing CNS tuberculosis was 1.0% among 82,764 tuberculosis cases (5). The meninges is the most frequent site of CNS allocation, but amid patients with spinal TB 7% have intramedullary lesions (6).

The etiologies for longitudinally extensive transverse myelitis are fairly broad, but classically it is associated with inflammatory demyelinating disorders of central nervous system, such as Neuromyelitis optica, but many other causes are known, a rare one of them being the Mycobacterium tuberculosis infection (7). LETM due to mycobacterium tuberculosis is very rare.

One of the most important information about spinal cord involvement in tuberculosis...
comes from an article published by Gupta back in 1994, which describes the lesions of myelopathy as being usually hypointense in T1-weighted images, rarely as isointense, with iso-, hypo- or hyperintense lesions on T2 weighted images, with or without gadolinium enhancement according to the type of lesion they identified (11 of there 20 patients had leptomeningitis and intramedullary lesions, 5 of them only intramedullary lesions, 2 leptomeningitis lesions and 2 of them only extradural tuberculosis) (8). Considering this MRI findings we reckoned with the diagnosis of possible tuberculous LETM, even if our patient didn’t have any past medical history of any kind of immunosuppression to which spinal cord involvement is more related to in patients with tuberculosis (9). In case reports described in literature it seems that in more than 80% of tuberculous myelitis the most afflicted regions are the thoracic and cervical ones (10).

Back in 1969, in an extensive report, Dastur and Wadia described in India the most important mechanisms by which M. Tuberculosis infection leads to spinal cord involvement: edema of the spinal cord vascular border zone probably as a result of venous high pressure due to meningitis, myelomalacia secondary to ischemia from the occlusion of the meningeal vessels, even spinal cord infarct because of vascular occlusion and the classical form of caseous intramedullary tuberculomas (11).

Whereas our patients’ CSF PCR for Mycobacterium tuberculosis came negative and that PCR is a very specific test for M. Tuberculosis (with sensitivity that varies from 56% to 90% and a specificity from 88% to 100%) we considered that the mechanism leading to meningitis wasn’t due to meningitis per se, but rather to due to an immune-mediated inflammatory lesion of the spinal cord because of infectious cross-reactivity (12). The CT of the thorax raised the suspicion for this etiology and confirmed the diagnosis. Nevertheless, in 2011 it was published a study that described the association between NMO (with longitudinally extensive transverse myelitis) and pulmonary tuberculosis, citing an immune-mediated inflammatory mechanism as responsible for myelitis (13). NMO diagnosis criteria were revisited in 2015, defining Anti-AQ4 seronegative NMO and NMO spectrum disorder which we considered that might also be a possible diagnosis.

CONCLUSION

Tuberculosis is an important health issue worldwide, especially in countries currently developing. While CNS tuberculosis accounts for only 1% of all cases of tuberculosis, it carries a great burden because of its high morbidity and mortality, and also because it is difficult to recognize. LETM is a rare but remarkable presentation of Mycobacterium tuberculosis infection that should be acknowledged by clinicians. Approaching the diagnosis as fast as possible has an important impact on the prognosis of the disease, especially in terms of disability.

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REFERENCES

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