Acute Encephalomyelitis due to Treatment for Tuberculous Meningitis

Michel Ferreira Machado*; Karen Andrade Norremose; Renan Barros Domingues
Neurology Service, Hospital Cruz Azul, São Paulo – Brazil.

Abstract
Tuberculous meningitis develops when granulomas formed by bacillus release their content in the subarachnoid space, triggering an inflammatory activity. After beginning treatment with anti-tuberculosis drugs, some patients may have a paradoxical reaction which has different clinical manifestations. Here we present a case of a severe acute encephalomyelitis. A 38-years-old female presented with refractory headache. CSF analysis of admission showed 235 cel/mm³ (85% lymphocytes) and glucose 5 mg/dl. Two days after beginning anti-tuberculosis treatment, she developed mental confusion, bradypsychism, paraparesis and bilateral Babinsk sing. Electroencephalogram showed a slow base rhythm and MRI demonstrate a pattern suggestive of myelitis. Endotracheal intubation was necessary due to decreased level of consciousness secondary to hydrocephalus. Despite external ventricular shunt and clinical measures, intracranial pressure remained high. After two weeks of treatment, patient died. The paradoxical reaction is not so rare and should not be confused with failure of anti-tuberculosis treatment.

Introduction
World Health Organization (WHO) estimated that in 2016 there were 6.3 million new cases of active Tuberculosis (TB) in the world and, in immunocompetent adults, the Mycobacterium tuberculosis is the second most common cause of death due to infectious disease (in HIV patients, it is the first) [1].

TB can affect any organ, including the nervous system. The most common form of neurologic involvement is tuberculous meningitis, followed by granuloma (tuberculous) in the central nervous system and spinalcord [2]. When the diagnosis is made early, before irreversible neurological deficits have been established, the clinical response to anti-tuberculosis therapy in all forms of nervous system tuberculosis is excellent [3].

It’s important to recognize the paradoxical reaction that can arise after the beginning of treatment, since it can be assigned to diagnostic error and/or therapeutic failure.

Here we present a case of a severe acute encephalomyelitis after beginning treatment for tuberculous meningitis.

Case report
A 38-years-old female, physical education teacher, no known comorbidities, began fever, headache, which worsened in the supine position, and episodes of disorientation and mental confusion, with spontaneous reversal after a few minutes. She went to medical appointments more than once and always re-
The patient died.

It was started empirically ampicillin and acyclovir for treatment of meningitis caused by *L. monocytogenes* and herpes, respectively. After seven days, the results of the CSF revealed a positive PCR for *M. tuberculosis* and ampicillin and acyclovir were suspended. It was also started treatment with anti-tuberculosis drugs (rifampicin, isoniazid, pyrazinamide and ethambutol), maintained dexamethasone, which was in use since admission for headache control. HIV serology was non-reactive.

After two days of the onset of the anti-tuberculosis treatment, the patient complained of low back pain, paresthesias, reduced muscle strength in the lower limbs and urinary retention. In addition, a family member witnessed a short episode of loss of awareness, after which the patient became bradypsychic. She was then transferred to intensive care unit for closer neurological monitoring.

On the next day, it was evidenced paraparesis with sensory level in the T2 and bilateral Babinski sign. The magnetic resonance imaging (MRI) of the thoracic spine was performed (Figure 1).

Anti-tuberculosis treatment was maintained and after a week the patient presented with sudden decrease in level of consciousness, was submitted to endotracheal intubation and the patient was referred for emergency CT that showed important supratentorial lesion, the patient complained of low back pain, paresthesias, and she developed bilateral late ischemic myelomalacia resulting from vasculitis or post-thrombotic stasis due to the pressure associated with meningitis; 2) Ischemia of the basal ganglia.

Emergency external ventricular shunt was performed. Despite the procedure and the clinical strategies adopted to normalize intracranial pressure, its levels remained varying between 30-36 mmHg. The transcranial Doppler showed hemodynamic signs of vasospasm and she developed bilateral late ischemic signs of the basal ganglia.

Fifteen days after beginning of anti-tuberculosis treatment, the patient died.
There are a variety of clinical and radiological manifestations of PR, mainly known from reports and/or small case series. In general, according to Garcia-Monco et al. [11], these manifestations are interpreted as a clinical deterioration that appears a few weeks after the beginning of treatment. Expansion of brain tuberculomas or emerging of new tuberculomas, hydrocephalus and spinal arachnoiditis are common manifestations [10], as it happened in the patient of this report.

The time to start PR involving the central nervous system seems to be longer when compared to other sites. This can be explained by the lower penetration of anti-tuberculosis drugs on the blood-brain barrier of non-inflamed meninges [12]. Our patient, however, had clinical and radiological signs of encephalomyelitis due to PR, less than five days after the beginning of treatment.

Usually, the PR does not affect the clinical outcome of TM, but it was not what happened to our patient. She evolved to death 15 days after the beginning of the anti-tuberculosis treatment, despite the use of high-dose corticosteroids, considered the most suitable approach for the treatment of PR [10].

**Conclusion**

PR is not such a rare phenomenon. The present report demonstrates that this reaction requires significant attention from the attending physician, given its variety of clinical presentations and uncertain time for the onset of symptoms in the central nervous system, thus avoiding the precipitated diagnosis of failure of anti-tuberculosis treatment.

**Authors’ contributions:** All authors have read, revised, and approved the manuscript.

**Compliance with ethical standards**

**Conflict of interest:** On behalf of all authors, the corresponding author states that there is no conflict of interest.

**Consent for publication:** We took a written informed consent from the patient’s guardian to publish his case.

**Ethical Approval:** Approval from an institutional board review is not required for a case report.

**References**