

NEUROTUBERCULOSIS AND ITS COMPLICATIONS: CASE REPORT

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Abstract: Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. Central nervous system involvement occurs in approximately 1-8% of all patients with active tuberculosis. This is a case report diagnosed by the Pediatrics Service of the Hospital Escola de Valença (HEV), in the city of Valença - RJ from April 2021 to May 2021. The clinical manifestations are varied: in most patients there are persistent evening fever for more than 15 days, radiological image without improvement with the use of antimicrobials for common germs, history of a family member with chronic cough or contact with patients with tuberculosis. This report highlights the importance of recognizing the pattern of complications in TB despite the absence of microbiological confirmation. It also demonstrates the challenge in arriving at diagnosis, given that there is absolute specificity in the gold standard diagnostic tool (TB culture), despite repeated large-volume CSF analysis, and the low sensitivity of CSF TB PCR. The case is special in illustrating the sum of these complications that occur concomitantly.

Keywords: Tuberculosis. Neurotuberculosis. Case report. Pediatrics.

INTRODUCTION

Tuberculosis (TB) is one of the top ten causes of death worldwide. In 2019, about 10 million people developed the disease and 1.4 million died. Globally, the annual number of people reported receiving treatment for the disease has grown in recent years, from about 6 million in 2015 to 7.1 million in 2019. Brazil is among the 20 countries with the highest estimated number of TB cases incidents defined between the period 2016-2020 (WHO, 2020).

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*, an aerobic Gram-positive, alcohol-acid-

resistant bacillus. CNS involvement occurs in approximately 1-8% of all patients with active tuberculosis. Inhaled *Mycobacterium tuberculosis* disseminated hematogenously from the pulmonary alveoli to the subependymal and subpial cerebral and medullary regions. The time and clinical presentation will depend on the age and immune status of the patient.

TB in children has specificities that must be considered during its diagnostic investigation. The pulmonary form differs from the adult form, as it is usually bacilliferous, that is, negative on bacteriological examination, due to the reduced number of bacilli in the lesions. In addition, children, in general, are not able to expectorate. Clinical manifestations can be insidious, with the patient being irritable, with low-grade fever, night sweats, and inappetence. Cough is not always present. The physical examination may be unimpressive (BRAZIL, 2019).

The Brazilian score presents the most validation studies with consistent sensitivities and specificities as a support system for the diagnosis of pulmonary TB in childhood in relation to other existing scores (PEARCE et al., 2012; SANT'ANNA et al., 2006).

Central nervous system (CNS) involvement is the main extrapulmonary form in children under 15 years of age, responsible for high morbidity and mortality. The diagnosis of tuberculosis in the CNS in children is based not only on the identification of the agent by microbiological methods in organic fluids, but particularly on clinical, laboratory and epidemiological data (MOURA-RIBEIRO & FERREIRA, 2010).

In approximately two-thirds of the patient with neurotuberculosis there is evidence of active disease in other organs, usually the lung and occasionally the small intestine, bone and kidney. The lethality of cases of tuberculous meningitis is around 15% to 40%,

despite adequate treatment (RODRIGUES E VILANOVA, 2017).

The diagnosis of Neurotuberculosis is difficult. Thus, in the face of a high degree of suspicion, treatment must be promptly initiated. The performance of neuroimaging studies is essential to demonstrate the extent of the involvement of the central nervous system (RODRIGUES E VILANOVA, 2017).

The symptomatology of meningoencephalitis is composed of a prodromal period of about two weeks that courses with fever, apathy, sleep disorders, abdominal pain and myalgia. Then, the child evolves with more specific neurological manifestations, starting, then, with meningism, nausea, vomiting, sensory and behavioral changes. Approximately 30% of them have focal neurological signs. Cranial nerve involvement occurs in approximately 25% of cases, and hemiplegia, hemiparesis, and seizures may occur in 10% to 15%. The clinical manifestations resulting from tuberculomas depend on their location, infratentorial lesions predominate in children. Seizures and visual field changes occur in hemispheric tuberculomas, ataxia and intracranial hypertension, in those with cerebellar location and cranial nerve syndrome and involvement of long tracts, in tuberculomas located in the brainstem (XAVIER *et al.*, 2003).

The neurological sequelae can be manifested by cognitive, sensory, motor deficits, epileptic syndromes and definitive obstruction of CSF transit in the basal cisterns (MOURA-RIBEIRO & FERREIRA, 2010).

The most frequent complications of meningoencephalitis/tuberculoma include ischemic infarctions that can occur in up to 40% of patients, hydrocephalus in 50% to 70%, in addition to hemiparesis/hemiplegia, visual alterations, epilepsy and delay in neuropsychomotor development (XAVIER *et al.*, 2003).

Empirical treatment must not be delayed, given the high mortality and complication rate of untreated infection. Initiation of empirical treatment is warranted for patients with relevant epidemiological factors (history of previous TB infection or illness, known or possible TB exposure, and/or past or present residence or travel to an area where TB is endemic), clinical manifestations (subacute presentation of stiff neck, headache, fever, and vomiting), pertinent radiographic findings (such as hydrocephalus, basilar meningeal thickening, edema, and/or tuberculomas), and typical cerebrospinal fluid (CSF) findings (pleocytoselymphocytic, elevated protein concentration) and low glucose concentration). The likelihood of a favorable clinical outcome increases with early initiation of therapy. Delaying treatment (even for a few days) may be associated with an increased likelihood of an unfavorable outcome (GARG, 2021).

The therapy instituted corresponds to that recommended by the World Health Organization: in the first two months, an association of Rifampicin, Isoniazid, Pyrazinamide associated with Prednisolone is used with the aim of preventing meningeal fibrosis and vasculitis. In the following ten months, the association of Rifampicin and Isoniazid is maintained. The regression of lesions is quite slow and does not necessarily mean drug resistance or lack of adherence to treatment. (XAVIER, 2017).

The scientific literature lacks publications to diagnose and treat cases of Neurotuberculosis early, since the symptoms are very variable, to verify the evolution of complications and the effectiveness of the treatment performed, since few cases reported in the pediatric age group are found in the literature and the topic in question is very prevalent in Brazil, which has high rates of tuberculosis cases. Thus, a retrospective study was carried

out with a clinical case to be reported. The present study was submitted to the Ethics and Research Committee of the Valença Medicine Course in accordance with Resolution 466/2012. The objective is to report a case of pulmonary tuberculosis that evolved with Neurotuberculosis associated with complications such as Ischemia and Hydrocephalus.

CASE REPORT

The work in question refers to a case of a 9-month-old infant. This is a female child, born on 07/08/2020 at the Maternity Hospital of the Hospital Escola de Valença, hospitalized in April 2021 for 14 days, being readmitted in May 2021, staying for another 22 days in an in-hospital environment. diagnosed with pulmonary tuberculosis that evolved with Neurotuberculosis associated with complications such as Ischemia and Hydrocephalus.

The 9-month-old infant had been in contact since the neonatal period with an adult with tuberculosis, without performing prescribed isoniazid prophylaxis. He later returned for a second hospitalization due to the persistence of fever even in outpatient antibiotic use for 4 days, due to a Urinary Tract Infection and cough for more than 20 days, associated with inappetence and adynamia. In-hospital investigation, PPD reactor and 40 points on the diagnostic score proposed by the Ministry of Health were performed, and treatment for pulmonary tuberculosis was initiated with a regimen of Rifampicin, Isoniazid and Pyrazinamide. In an outpatient consultation after hospital discharge, the infant had ptosis on the right, regression of developmental milestones, paresthesia of the right upper limb and paresis of the right lower limb, in addition to a return of fever. He was admitted to the hospital again, where a Computerized Tomography of the Skull (CT) was performed,

which showed ischemic vascular insult in the subacute phase and moderate hydrocephalus with areas of hypodensity in the left thalamus/internal capsule measuring 1.1 and 1.5 cm and in the left occipital lobe. Lumbar puncture was performed for CSF analysis with BAAR (Alcohol Acid Resistant Bacillus) and ADA (Adenosine Deaminase), non-reactive. Due to the infant's clinical condition, previous diagnosis of TB and in order not to postpone treatment, a diagnosis of Neurotuberculosis was made, treatment with a RIP regimen (Rifampicin, Isoniazid and Pyrazinamide) was restarted for 2 months associated with Prednisone for 4 weeks, followed by Rifampicin and Isoniazid for another 10 months. The lactating woman showed good evolution to the proposed treatment.

DISCUSSION

Of all systemic TB cases, 2-5% experience CNS TB complications. This number increases to 10% in patients with HIV coinfection. The spectrum of CNS TB varies widely, commonly manifesting in the brain as tuberculous meningitis (the most severe and common form of neurotuberculosis), tuberculous abscess, tuberculoma, or rarely as hypertrophic pachymeningitis. And in the spinal cord it manifests as tuberculous myelitis, spinal tuberculoma, Pott's column with epidural abscess and arachnoiditis (THWAITES et al. 2000).

In the case presented, attention is drawn to an infant with a history of persistent fever and cough, despite the use of antibiotic therapy for the treatment of urinary site infection. During the collection of anamnesis, household contact with a case of pulmonary tuberculosis was reported. The investigation was started with a chest x-ray and a 10 mm tuberculin skin test (PPD), which, in association with the clinic, led to the diagnosis of pulmonary TB.

According to the latest data from the Ministry of Health (MS), the involvement of PTB in children and adolescents is around 75% of all cases. And of all cases reported in 2017, 9.5% had TB/HIV co-infection. HIV-related immunosuppression is an independent risk factor for the occurrence of TB, causing a negative impact on the clinical course of both diseases. Therefore, the importance of offering rapid HIV testing at the time of diagnosis of lung disease (WORLD HEALTH ORGANIZATION, 2018).

In a similar process, exudates that interfere with the cerebrospinal fluid flow in the basal cisterns can result in hydrocephalus, which can be communicating or obstructive at a later stage, the former being more common. Comparatively, the presence of exudates in HIV-negative individuals is particularly robust and attests to “excess inflammation” with resultant hydrocephalus that occurs preferentially in children in 70% of cases, acting as an indicator of poor prognosis, as opposed to only 12% in adults.

The clinical manifestations are varied: in most patients there is an evening fever that persists for more than 15 days, radiological image without improvement with the use of antimicrobials for common germs, history of a family member with chronic cough or contact with patients with TB (SANT’ANNA *et al.*, 2015).

Transmission occurs by inhaling droplets contaminated with the Mtb bacillus from a sick person, mainly by coughing and rarely by sneeze, speak or kiss. The chance of developing a disease depends on each individual’s organism. Most will have partial immunity to the bacillus, remaining healthy for many years, called latent infection (LTBI). However, in 5% of cases, the bacillus will multiply after the primary infection, developing the disease (primary TB) (WORLD HEALTH ORGANIZATION, 2018).

During the hospitalization of a child with prolonged pneumonia, without improvement with adequate antibiotic therapy, epidemiological, clinical and radiological findings must be considered. Sometimes a more detailed investigation is necessary. The first exams to be requested are x-ray and PT. Radiography is highly relevant in the diagnosis of TB, in addition to being useful in monitoring during treatment and in the emergence of possible complications (Epidemiological Bulletin Department of Health Surveillance. Ministry of Health, 2018).

Chest CT is indicated in situations where the x-ray is normal or doubtful, in an attempt to better visualize TB lesions or to differentiate them from other chest diseases, especially in immunosuppressed patients. Among the changes on CT, lobar consolidations and hypodense areas are found in more than 80% of cases, and in less than 25%, cavitations. (CARVALHO *et al.*, 2018).

PT makes it possible to identify the individual infected by Mtb, regardless of the time of vaccination by BCG. Evaluating the immune response after 48-72 hours of intradermal application of Mantoux, considering it positive when ≥ 5 mm and negative when < 5 mm. (1) During the period of the patient’s hospitalization, there was PT in the municipality, so it was possible to perform (CARVALHO *et al.*, 2018).

In order to collect specimen samples for bacteriological examination in infants, invasive methods are used, such as induced sputum, gastric lavage and aspirates (bronchial and bronchoalveolar) by bronchoscopy. From that age onwards, sputum smear and sputum culture can be attempted. In adolescents, the diagnosis can be confirmed bacteriologically because they are bacilliferous like adults, most of them (CARVALHO *et al.*, 2018).

The culture identifies the Mtb bacillus in 40 to 50% of the cases, in solid medium (Löwenstein-Jensen), however it needs 6 - 8 weeks to complete, making early diagnosis difficult. Currently, there is a liquid medium (Middlebrook 7H9) with faster Mtb growth and greater sensitivity for paucibacillary samples. (CARVALHO *et al.*, 2018).

tool (TB culture), despite repeated large volume CSF analysis, and the low sensitivity of CSF TB PCR. The case is special in illustrating the sum of these complications that occur concomitantly. The presence of multiple complications correlates with the severity of the infection, despite a negative microbiological investigation.

FINAL CONSIDERATIONS

This report highlights the importance of recognizing the pattern of complications in TB despite the absence of microbiological confirmation. It also demonstrates the challenge in arriving at diagnosis given the low sensitivity of the gold standard diagnostic

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