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CLINICAL CASE
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TUBERCULOUS MENINGITIS OF SEVERE EXPRESSION IN PEDIATRICS

TUBERCULOSIS MENÍNGEA DE EXPRESIÓN GRAVE EN PEDIATRÍA

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ABSTRACT

Tuberculosis (TB) remains a global public health problem. The true magnitude of this epidemic is underestimated due to difficulties in diagnosing children and poor reporting. The diagnosis of childhood TB represents a challenge, since in children the infection usually proceeds with nonspecific clinical manifestations and is often asymptomatic, which delays the diagnosis, leading this age group to a high risk of disseminated infection. We then describe the case of a preschool child with meningeal tuberculosis (TM), with subacute clinical presentation of fever, progressive sensory disorder and signs of intracranial hypertension. The epidemiological history allowed the diagnosis and initiation of anti-tuberculosis therapy to be guided. The clinical course of the patient was torpid, developed very serious complications, with a fatal outcome.

Key words: Tuberculosis; Meningitis; Child (source: MeSH NLM).

RESUMEN

La tuberculosis (TB) sigue siendo un problema de salud pública mundial. La magnitud real de esta epidemia está subestimada debido a las dificultades en el diagnóstico en niños y al escaso reporte. El diagnóstico de TB infantil representa un desafío, ya que en el niño la infección suele cursar con manifestaciones clínicas inespecíficas y muchas veces es asintomática, lo que retrasa el diagnóstico, conllevando a este grupo etario a un alto riesgo de infección diseminada. A continuación, describimos el caso de un niño preescolar con tuberculosis meníngea (TM), con presentación clínica subaguda de fiebre, trastorno de sensorio progresivo y signos de hipertensión endocraneana. El antecedente epidemiológico permitió orientar el diagnóstico y el inicio de la terapia antituberculosa. La evolución clínica del paciente fue tórpida, desarrolló complicaciones muy graves, con desenlace fatal.

Palabras clave: Tuberculosis; Meningitis; Niño (fuente: DeCS BIREME).

INTRODUCTION

Tuberculosis (TB) is a public health problem worldwide, despite the health policies implemented for timely diagnosis and treatment. TB in pediatric age is underestimated due to difficulties in diagnosing children and the poor reporting[1,2].

According to the report of the World Health Organization (WHO) in 2019, it estimated that, of the 10 million incident cases of TB calculated in 2018, approximately 1.1 million (11%) occurred in children under the age of 15 years; with similar frequency among boys and girls[1].

Most children become infected at home by being in

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contact with people with TB, particularly parents or other caregivers. Even in circumstances where adult index cases are negative in sputum, transmission to children has been documented in 30-40% of households[3].

Age-related deficiencies in the immune response in children increase the risk of developing disseminated infection[4]. TM represents the most severe form of tuberculosis infection in children. Early diagnosis and management of the disease, although difficult, is essential to avoid death or neurological disability. Therefore, a high degree of suspicion and a combined battery of tests that including clinical, bacteriological, and neuroimaging help in the diagnosis of TM.[5].

In order to contribute to the reinforcement of alertness for the diagnosis of this disease, we present the case of a preschool male with tubercular meningitis, by reviewing the most relevant aspects of the disease.

CASE REPORT

A twenty-six month male patient from Lima, with no relevant personal history, entered the pediatric emergency service with a disease time of twelve days, characterized by the presence of three non projectile vomits associated with progressive drowsiness, and history of unquantified and persistent thermal surge sensation. Three days prior to the patient's admission, he had difficulty walking. On admission to the clinical examination, he was subfebrile, dehydrated, hypoactive, with little response to stimuli and with pupillary mydriasis associated with little reactivity to the light stimulus. Upon admission, a blood test and a cerebral computed tomography (CT) scan were requested due to progressive clinical deterioration of the sensorium with signs of intracranial hypertension and probable neuroinfection.

The results of the blood tests were hemogram with mild anemia without alteration of the leukocytes or platelets, normal biochemical, hepatic and coagulation profiles; result of brain CT without alterations (Figure 1).

Given the suspicion of probable meningoencephalitis, a lumbar puncture was indicated, a procedure that the parents did not accept, so empirical treatment with broad antibiotic coverage, acyclovir and mannitol was started, all of these medications were administered intravenously.

48 hours after admission, while the patient was in the Emergency Intensive Care Unit, he presented greater sensory involvement. Due to the unfavorable evolution, parents authorized the lumbar puncture procedure. They reported the result of cerebrospinal fluid with 10 cells/µL, 100% mononuclear, glucose at 21 mg / dL (serum 102 mg / dL) and protein at 132 mg / dL.

The anamnesis was expanded, father responds that he had pulmonary TB when the patient was three months old and that his home contacts did not receive prophylaxis. Due to probable TM, specific treatment plus dexamethasone was started and orders for direct smear microscopy were generated. 24 hours after starting specific treatment for TB, the patient presented sudden deterioration in the level of consciousness, score 3 according Glasgow Coma Scale (ECG 3), which is why the patient was intubated and subsequently placed under ventilation invasive mechanics.

New neuroimaging was requested, evidencing the presence of ventricular dilation associated with diffuse cerebral edema with multiple hypodense areas at the bilateral frontoparietotemporal level and the brain stem (Figure 2). The neurosurgery unit programmed the patient for placement of external ventricular drainage (EVD), the procedure being delayed due to the patient's general poor condition.

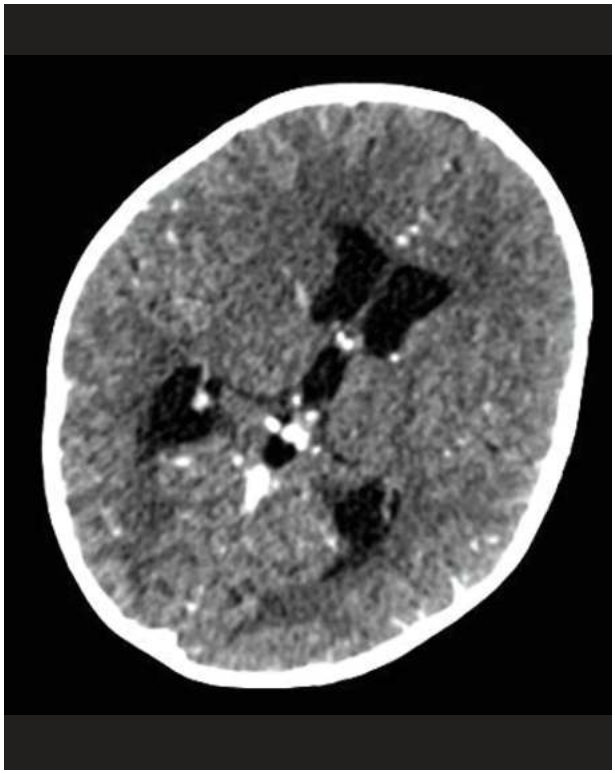

Figure 1. Cerebral computerized axial tomography (CAT) of normal characteristics upon admission to the emergency room.

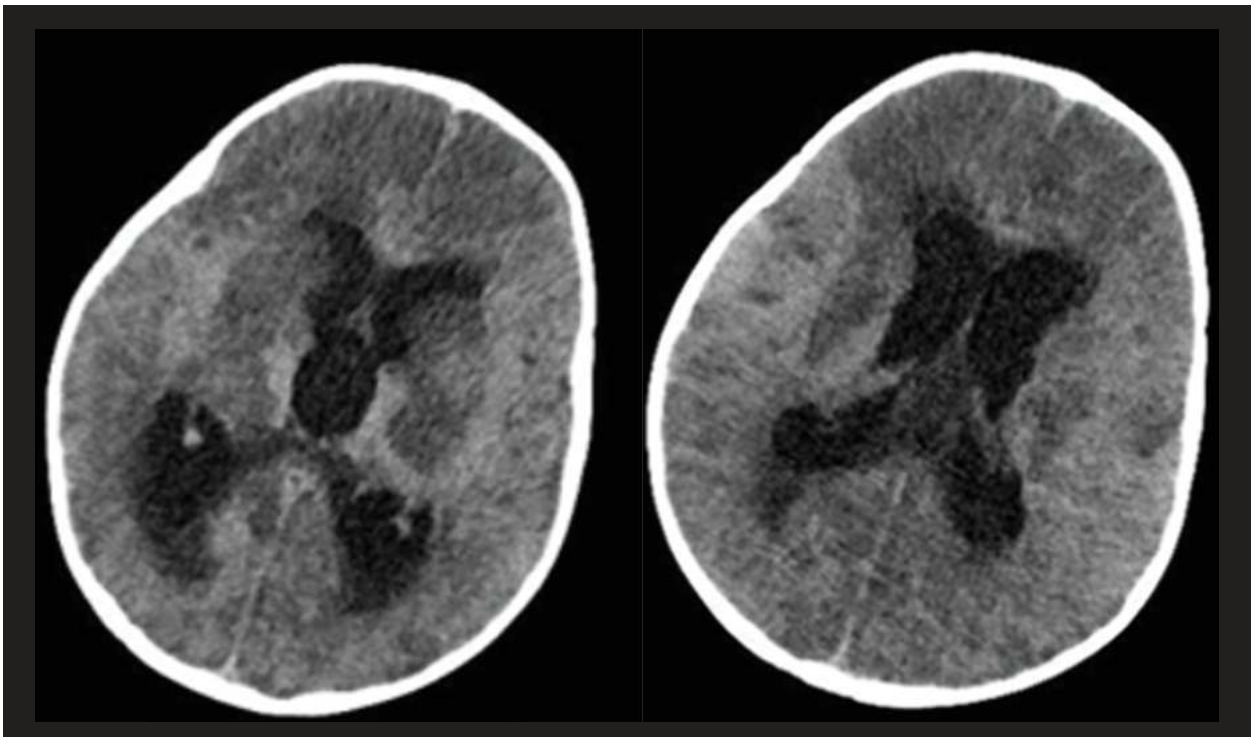

Figure 2. Cross-sectional computed axial tomography (CT) of the brain, with images compatible with multiple cerebral infarcts.

The results of the positive bacilloscopy (+++) were obtained in gastric aspirate, as well as in tracheal secretion collected through the endotracheal tube, and the Tuberculin Purified Protein Derivative (PPD) skin test was positive. 48 hours after removing sedoanalgesia, the patient's clinical diagnosis was brain death.

The patient evolved with hypotensive shock, multiple organ dysfunction, and a requirement for greater ventilatory parameters. Despite inotropic treatment with adrenaline, the patient remained hypotensive. During cardiopulmonary resuscitation, the patient presented oxygen desaturation, absence of peripheral pulses, progressive bradycardia and asystole. The monitor screen also recorded cardiac asystole, and finally declaring the patient deceased.

Informed consent was obtained from the family member (parent) who authorized the use of their child's disease data for scientific or academic purposes.

DISCUSSION

Globally, almost half a million children become ill with TB each year, and 20-30% are affected by extrapulmonary tuberculosis. The peak of incidence occurs between two and four years of age[5].

In Peru, about 27 thousand new cases of active tuberculosis disease are registered annually and that, according to information from the Pan American Health Organization (PAHO), Peru has 14% of the estimated cases of tuberculosis in the region of the Americas; Lima Metropolitana and Callao are the cities that report the highest number of TB cases in the country (64%)[6,7].

The incidence of TB in children under 15 years of age in Peru is an average of 30 children affected by TB for every 100,000 children under the age of 15. Mortality from TB is higher, in children between the ages of zero to four years of age compared to any other age group, since TB frequently progresses rapidly from latent to active infection, being at high risk of a disseminated disease[4,7].

Mycobacterium Tuberculosisis transmitted to the airway by air when small droplets (1–5 µm) are aerosolized from people with pulmonary or laryngeal TB and enter the alveoli of close contacts[4].

Initially, biological events initiated by alveolar macrophages and dendritic cells are triggered, later activation of the cascade of innate immunological events occurs for the production of proinflammatory cytokines and increases opsonization and phagocytosis to eliminate or control infection. Subsequently, the adaptive immunity response occurs, with the response of T lymphocytes to the presented antigens, responsible for the formation of granulomas[4,8].

The inadequate immune response causes continuous replication of the pathogen, with progression to lung disease and possible spread to extrapulmonary sites. Therefore, it is deduced that infants and young children have a higher risk of disseminated infection[4].

We present the case of TM in a two-year-old boy, who according to what was indicated by the study by Marais et al., The risk of disseminated infection is reported in 2-5% of patients within the age group of one to two years with primary tuberculosis infection. Above that age range, the risk rate of disseminated infection drops to 0.5%[3].

TM represents the most serious form of tuberculosis infection in pediatric age, being the main cause of morbidity and mortality, with a lethality of about 25% of cases. Furthermore, 50% of survivors develop severe neurological sequelae, even receiving adequate treatment[9].

The demonstration of a case of childhood TB represents a sentinel event within a community, since it suggests a recent transmission by a bacilliferous adult, who at the younger age of the patient is generally intra-household[9].

The WHO recommends that all countries have in their TB control programs (PCT), well-defined strategies for studying the contacts of people diagnosed with TB and the administration of isoniazid preventive treatment (IPT), in order to treat latent infection in asymptomatic contact children, under 5 years of age, since the risk of progression in this population is really high[10].

The epidemiological contact that was obtained in the described case was the diagnosis of tuberculosis in one of the caregivers and the patient had not received IPT as stipulated in the TNorma Técnica del Ministerio de Salud[11]. This data allowed guiding the diagnosis of TM.

Infection towards the central nervous system occurs hematogenously and when the mycobacterium crosses the blood-brain barrier, it produces the granulomas formation (Rich focus), within which the microorganism remains inactive. When a condition favoring the growth and rupture of these focus arises, the bacilli and their antigenic products are released into the subarachnoid space and severe inflammation develops at the base of the brain, with the formation of thick gelatinous exudate containing erythrocytes, neutrophils, macrophages and lymphocytes, around the brain stem, Silvio's fissures, and basal cisterns, causing obstruction to the flow of cerebrospinal fluid (CSF) from the cerebral aqueduct or the fourth ventricle. CSF absorption is also interfered with, leading to elevated intracranial pressure (ICP) and hydrocephalus. The basal exudates spread to the arteries of the Willis polygon and its branches, which transport the bacillus to the brain parenchyma, causing vasculitis and subsequent development of a stroke, and frequently involving the basal ganglia, the cerebral cortex, the protuberance and the cerebellum[9,12].

The clinical picture of TM can be described in three stages: prodromal, non-specific phase, with symptoms such as general malaise, low fever, headache, vomiting and irritability, meningeal phase where children with more advanced disease may have signs of irritation meningeal and elevation of the ICP and finally, the paralytic phase with development of paralysis of the cranial nerves, with the sixth nerve being the most common; neurological deficit, altered sensory, and movement disorders are also observed[5,13].

The clinical presentation of our case describes a subacute course of fever and nonspecific manifestations in the patient, with signs of endocranial hypertension and progressive alteration of the sensorium evidenced by a decrease in the Glasgow Coma Scale score. The presence of hydrocephalus and multiple cerebral infarcts were part of the complications described in our patient.

Examination of samples obtained from cerebrospinal fluid is an important test for the early diagnosis of TM. Typically, CSF cytochemical evaluation shows elevated protein and glucose low concentrations with predominantly mononuclear pleocytosis. In the Solomons study[14], which described the CSF cytochemical characteristics, in a cohort of 615 patients with suspected TM, during the years 1985 and 2014 in a South African hospital, it was determined that glucose values <2, 2 mmol / L and proteinorachie > 1 g / L, difference between TM and non-bacterial meningitis with good specificity, although with poor sensitivity. In agreement with this study, the presence of these two criteria in the characteristics of the CSF of our patient guides us towards the tuberculous aetiology.

More recent tests, such as nucleic acid amplification tests (NAATs), line probe tests (LPA), mycobacterial growth indicator tube (MGIT), antigen detection, and biomarkers, have recently been described in the CSF to aid diagnosis and provide early treatment and prevent complications, but which in our reality are not yet available[13].

CT of the brain is an accepted instrument and used frequently in diagnosis, with hydrocephalus and basilar reinforcement being the most common characteristics, although infarction involving basal ganglia and internal capsule or solitary or multiple tuberculomas may be present[8,13].

The difficulty of diagnosing TM and the use of different criteria in clinical studies, due to the low number of microbiologically confirmed TB cases, make the search for a universal definition essential. In this sense, the research by Marais et al. provides a definition of TM for studies based on clinical criteria and diagnostic aid according to the score presented in Table 1[15]. The application of the score in our case is 18 points, with the presence of clinical signs, CSF cytochemistry, neuroimaging compatible with TM, and evidence of positive direct bacilloscopy in aspirates of the trachea and stomach, for which the highly probable infection of TM.

Table 1. Diagnostic criteria in the definition of meningeal tuberculosis cases[15].

Clinical criteria (maximum 6 points)	Score
Duration of symptoms> 5 days	4
Symptoms suggestive of TB: weight loss, cough> 2 weeks	2
History of recent close contact with an individual with pulmonary TB.	2
Focal neurological deficit (excluding cranial nerve palsy)	1
Cranial nerve palsy	1
CSF criteria (maximum category score = 4)	
Clear appearance	1
Cells: 10–500 per µl	1
Lymphocytic dominance (> 50%)	1
Protein concentration greater than 1 g / L	1
CSF with a plasma glucose ratio of less than 50% or an absolute CSF glucose concentration less than 2.2 mmol / L	1
Brain imaging criteria (category maximum score = 6)	
Hydrocephalus	1
Reinforcement basal meningeal	2
Tuberculoma	2
Cerebral infarction	1
Precontrast basal Hyperdensity	2
Evidence of tuberculosis elsewhere (maximum rating category = 4)	
Radiography suggesting active pulmonary disease	2
Radiography suggesting Miliary Tuberculosis	4
CT / MRI / US with evidence of TB outside the CNS	2
Positive smear or M. tuberculosis cultures from other places, Sputum, blood culture, gastric aspirate, etc.	4
Confirmed TM: BK observed on CSF microscopy, culture of M. tuberculosis positive CSF against the background of symptoms/ signs suggestive of meningitis. BK seen against the background of histological changes consistent with TB brain or spinal cord along with suggestive symptoms/signs and changes in CSF, or visible meningitis (at autopsy). **Probable TM =** total score of ≥12 when neuroimaging available = total score ≥10 when neuroimaging is not available **Posible TM =** total score of 6-11 when neuroimaging is available = total score of 6-9 when neuroimaging is not available	

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In a country like ours where tuberculosis is a public health problem with high annual prevalence rate, the diagnosis of tubercular meningitis represents a real diagnostic challenge, where clinical suspicion and epidemiological criteria are essential for the timely diagnosis and treatment of these patients.

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