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CLINICAL CASES

Tuberculous meningitis and septic shock due to miliary tuberculosis in Down syndrome: a case report

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Abstract

Introduction: *Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis. Only 1% of tuberculosis cases present as septic shock.* **Case presentation:** *A 41-year-old male with a history of trisomy 21. The condition began with holocranial headache, paresis of the left upper extremity, and paresis of the ipsilateral pelvic limb. As he did not present perfusing blood pressure, management with norepinephrine was initiated. Sampling showed positivity for M. tuberculosis. Antituberculous therapy planned for 12 months was started and dexamethasone was added.* **Conclusion:** *In patients with Down syndrome, it is necessary to intentionally look for extrapulmonary forms.*

Keywords: *Tuberculosis. Tuberculous meningitis. Tuberculosis septic shock. Miliary tuberculosis. Down syndrome.*

Introduction

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*, listed by the World Health Organization in 2020 as the second cause of death from a single infectious agent, after coronavirus disease-19. That same year, a global incidence rate of 127 cases/100,000 inhabitants was estimated[1].

In Mexico, 22,285 new cases of tuberculosis were reported in 2019; the majority are pulmonary (80%) and then meningeal (2.1%)[2].

Extrapulmonary tuberculosis represents 20% of tuberculosis cases, distributed in order of extrapulmonary involvement in lymph nodes, pleura, bones/joints, genitourinary tract, meninges, and peritoneum[3].

The main risk factors for the development of extrapulmonary disease are infection with the human immunodeficiency virus, living with people with tuberculosis, female sex, chronic alcoholism, smoking, diabetes mellitus, drug use, and desnutrition[3,4].

Only 1% of tuberculosis cases present as septic shock due to tuberculosis, which is a rare entity and may or may not be associated with hematogenous dissemination called Landouzy septicemia[5].

Case report

A 41-year-old male with trisomy 21, of low socioeconomic level. The patient began the condition with upper respiratory tract infection, chills, and non-productive cough predominantly at night, weight loss of 10 kg in 3 months, and use of multiple antibiotics without improvement. After this, he presented intense holocranial headache, paresis of the left upper extremity, and paresis of the ipsilateral pelvic limb that made ambulation difficult. He had a saturation of 89% to room air, tachycardia, tachypnea, and hypotension of 80/50 mmHg with a temperature of 38.4°, so it was decided to admit him to the hospital.

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On physical examination, he presented a body mass index of 17.7 kg/m^2, a tendency to drowsiness, pale integuments, dehydrated oral mucosa, bilateral cervical and axillary lymphadenopathy, bilateral infrascapular crackles, abdomen without visceromegaly, hypotrophic extremities with the presence of transverse palmar groove, bilateral sandal sign and 4-s capillary refill.

In the neurological examination, the patient showed a tendency to inattention, neck rigidity, positive Kerning sign, positive Brudzinski sign, positive Binda sign, hypotonia of the left hemibody, decreased muscle strength in the left upper and lower extremity, and response extensor plantar in the left pelvic limb.

Fluid therapy, supplemental oxygen, and antibiotic therapy were initiated; however, as there was no perfusion arterial pressure, norepinephrine was administered, achieving temporary hemodynamic improvement. Given the refractory septic shock, vasopressin and hydrocortisone were added with suspension of the second vasopressor 2 days after improvement.

The chest X-ray showed a diffuse bilateral micronodular pattern (Fig. 1), and the chest tomography detected multiple bilateral micronodules (Fig. 2), as well as images of a budding tree (Fig. 3) and multiple mediastinal lymphadenopathy.

Fiberoptic bronchoscopy sampling for acid-fast bacilli, mycobacterial culture, and GenExpert *M. tuberculosis* (MTB)/rifampicin (RIF) ULTRA demonstrated positivity for *M. tuberculosis*. The HIV enzyme-linked immunoassay test was negative and no other site of infection or co-infection was identified by blood or urine cultures.

The skull tomography showed a hypodense lesion with a digitiform appearance in the right frontoparietal lobe related to vasogenic edema and associated leptomeningeal enhancement (Fig. 4). Magnetic resonance imaging of the skull showed an area of right frontal encephalomalacia and leptomeningeal enhancement (Fig. 5).

Lumbar puncture showed pleocytosis with a predominance of neutrophils, hypoglycorrhachia, and hyperproteinorrhachia. Cerebrospinal fluid culture for mycobacteria and GenExpert MTB/RIF ULTRA was positive for *M. tuberculosis*, with elevated adenosine deaminase.

Tomography of the abdomen and pelvis showed regional lymph node dissemination with evidence of multiple retrocavoaortic, paracaval, and bilateral inguinal lymphadenopathy. Antituberculosis therapy was started with RIF, isoniazid, pyrazinamide, and ethambutol for 12 months and dexamethasone was added. Bone marrow aspirate and urine mycobacterial culture were negative.

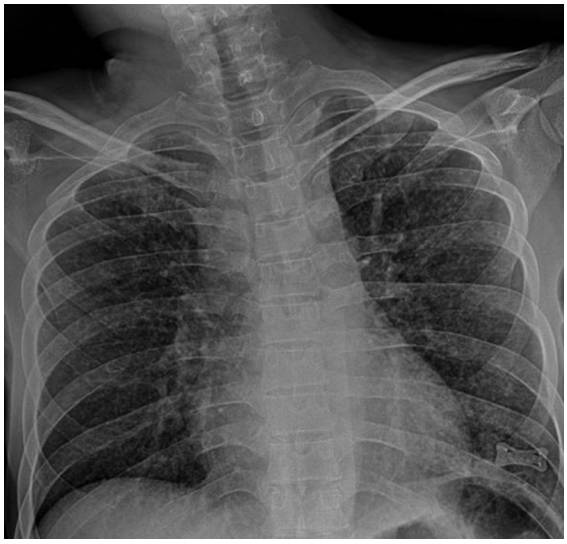

Figure 1. Chest X-ray with diffuse micronodular infiltrate in both hemithorax.

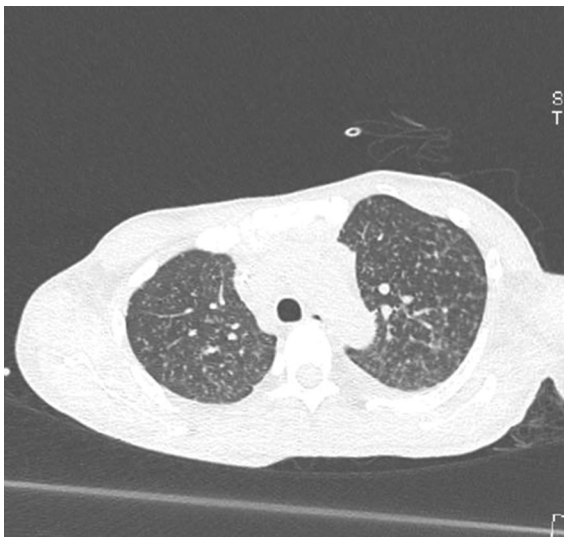

Figure 2. Chest tomography with bilateral micronodular pattern.

The diagnoses of septic shock due to *M. tuberculosis*, miliary tuberculosis, and tuberculous meningitis were integrated. There was remission of septic shock 5 days after starting vasopressor support and fluid therapy, adding neurological improvement 7 days after starting glucocorticoid therapy, and completing a 15-day hospital stay. As part of the follow-up, chest X-rays were

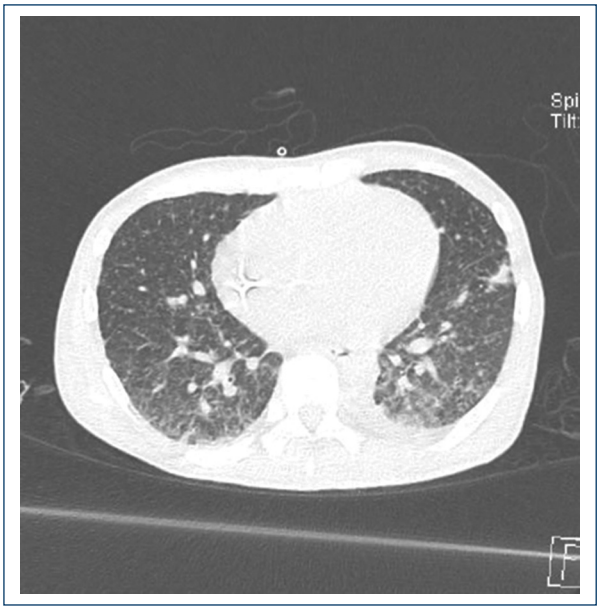

Figure 3. Chest tomography with budding tree images.

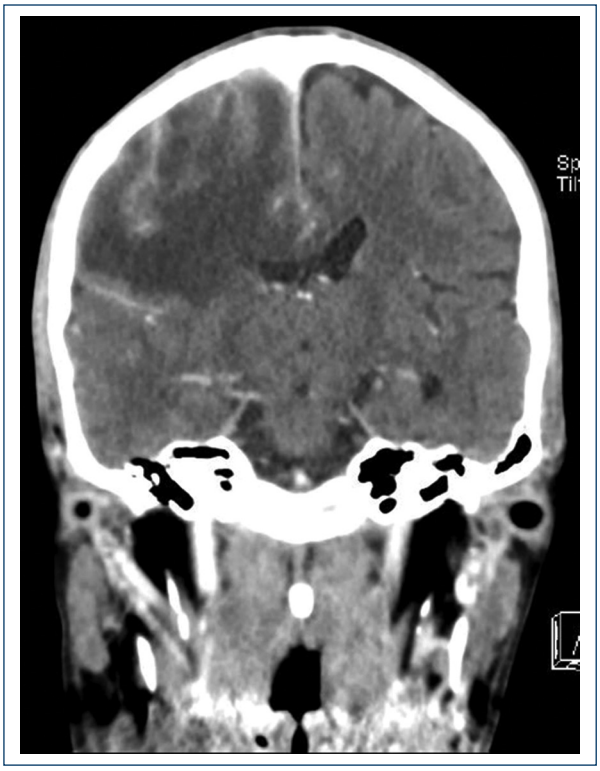

Figure 4. Contrast-enhanced tomography of the skull with hypodense digitiform lesion and right frontoparietal meningeal enhancement.

taken at 4 and 8 months, which showed a bilateral decrease in the micronodular pattern. At present, the patient shows no evidence of neurological sequelae.

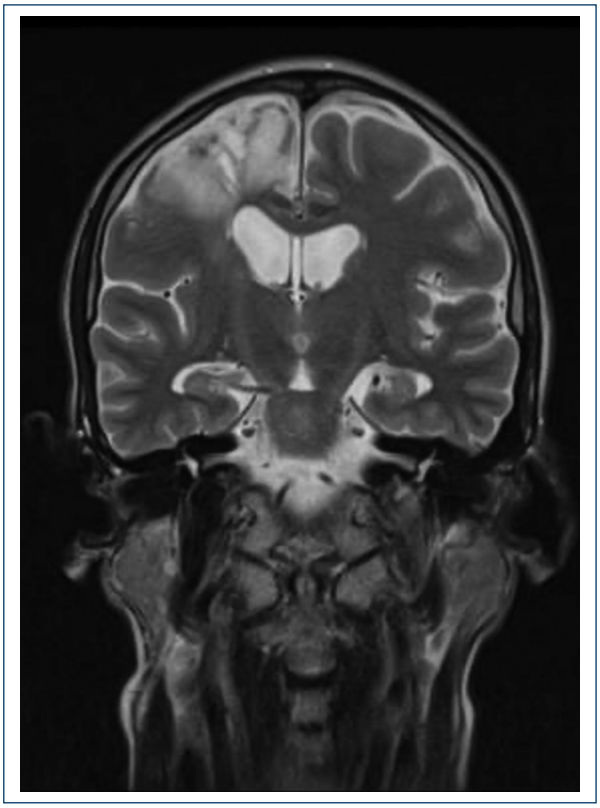

Figure 5. Magnetic resonance imaging shows right frontal leptomeningeal enhancement associated with encephalomalacia.

Discussion

Septic shock occurs in 1% of tuberculosis cases, of which 90% are associated with concomitant lung disease as in our patient, and with mortality of 79%, which improves with the timely administration of anti-tuberculosis treatment[6].

Admission to the intensive care unit for septic shock due to tuberculosis occurs in 12.3% of cases with critical illness due to respiratory failure, hemodynamic instability, or tuberculous meningitis. Vasopressor support and associated lung disease are the main indicators of mortality in the intensive care unit[7]. In turn, the hospital stay in patients with tuberculous meningitis is an average of 15 days, the same length of hospitalization observed[8].

Our patient had a low body mass index (17.7 kg/m^2) that doubles the risk of developing tuberculosis compared to the general population and is associated with higher mortality in patients with septic shock due to *M. tuberculosis*[6,9].

Meningeal infection begins with hematogenous dissemination by *M. tuberculosis* in the subarachnoid

space, forming a caseous lesion called Rich's focus. Later it suffers a rupture, which can cause meningitis and other types of tuberculous neuroinfection[10].

Tuberculous meningitis presents as headache, weight loss, fever, altered level of consciousness, neck stiffness, and only 17% present neurological focal data, consistent with the clinical findings of our patient who presented left hemiparesis[8].

The findings in the cerebrospinal fluid in tuberculous meningitis are hypoglycorrhachia, hyperproteinorrachia, and lymphocytic pleocytosis; however, it is possible to identify a predominance of neutrophils in the early stages of the disease, a situation observed in our patient[11]. Likewise, the determination of adenosine deaminase has a sensitivity and specificity of 79% and 91% for the diagnosis of TM[12]. In tuberculous meningitis, dexamethasone is indicated together with anti-tuberculosis treatment since it reduces mortality by 22%[13].

Down syndrome causes an immunological dysfunction that affects innate immunity and adaptive immunity with decreased cytokine production, low expression of T cell receptors, decreased chemotaxis, alterations in opsonization and phagocytosis, as well as T and natural killer cell dysfunction[14]. Furthermore, the anatomical alterations inherent to the disease and the presence of gastroesophageal reflux, together with immunological dysfunction, cause a higher incidence of respiratory infections regardless of the infectious agent, being predominant in childhood, including tuberculosis[15]. In our patient, multiple risk factors such as malnutrition, low socioeconomic level, and his underlying genetic pathology favored the presence of disseminated tuberculosis.

In the population with Down syndrome, there are only reported cases of neurological involvement due to tuberculosis in pediatric patients. A first case presented due to tuberculous radiculomyelitis manifested with urinary retention and lung involvement[16], and another case presented multiple tuberculomas without lung involvement[17]. There is only one reported case of septic shock due to tuberculosis in a pediatric patient with the presence of active lung disease without central nervous system involvement[18]. Therefore, this is the first reported case of tuberculous meningitis and septic shock due to miliary tuberculosis in an adult population with Down syndrome.

Conclusion

Tuberculosis is an entity that affects global public health. In patients with Down syndrome who have risk factors for tuberculosis, it is necessary to intentionally search for extrapulmonary forms. It is essential to highlight the need to maintain a high suspicion of extrapulmonary disease to expedite the initiation of the diagnostic protocol and positively impact the long-term prognosis.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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