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CASE REPORT

An infant with a confirmed diagnosis of pulmonary tuberculosis

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Abstract

Pulmonary tuberculosis is an infection caused by *Mycobacterium tuberculosis*. The diagnosis is made through the association of clinical-radiological data complemented by identification of the bacillus whenever possible. Such procedure becomes a challenge particularly in childhood, because unlike the adult form, childhood disease presents paucibacillary and there is still a sputum limitation to obtain sputum samples, especially in children under five years old. And the gastric lavage used in this age group proves to be ineffective, since most of them are negative in the research of the causative agent. The aim of this study was to describe a case of confirmed pulmonary tuberculosis in a 5-month-old infant and discuss the diagnostic methods available for the pediatric age group.

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INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* (Mtb). Pulmonary TB is the most prevalent form of the disease, which may affect other organs and systems. It is a public health concern on account of the high mortality and morbidity rates seen in developed and developing nations[1].

According to the World Health Organization (WHO), Brazil ranks 20th in the world in terms of burden of disease and 19th in number of cases of TB/HIV coinfection. Data from 2015 reported about one million new cases of TB in children and 210,000 deaths by the disease in this population[1,2].

Infection may occur by inhalation of bacteria produced by individuals carrying TB bacteria (source case). Differently from adults, children with TB usually have paucibacillary disease, i.e., they present with lung injury with low bacterial loads[3].

Diagnosis is further hampered by differences in pathogenesis and clinical symptoms characteristically seen in individuals in this age range. Therefore, the disease is diagnosed in pediatric patients based on clinical, epidemiological, and imaging signs combined with the interpretation of the tuberculin skin test (TST). However, confirmation of the causing pathogen must be sought whenever possible[4].

OBJECTIVES

This article describes a case of pulmonary TB in a previously health 5-month-old infant positive for the disease based on gastric lavage bacilloscopy.

CASE REPORT

A.S.P.R, a previously healthy brown female infant aged five months, was initially hospitalized due to wheezing and dyspnea. She did not experience fever, loss of appetite, or weight loss. The patient was prescribed antibiotics for seven days as she was suspected for pneumonia. Two weeks after discharge, the symptoms still remained and she began having bouts of fever in the early evening accompanied by tachydyspnea. The patient was hospitalized with respiratory distress and subcostal retractions. Auscultation revealed low vesicular breath sounds on the left lower lung and crackles mainly in the left hemithorax. She was placed on oxygen therapy with a nasal cannula. The patient was started on antibiotics again. Initial chest X-rays showed extensive hypotransparency in the left hemithorax (Figure 1). On account of the longstanding pneumonia symptoms unresolved after the administration of conventional antibiotics, chest computed tomography (CT) scans were ordered and showed parenchymal consolidations and a cavity measuring 1.5 cm in diameter on the left lung, alterations consistent with inflammatory infectious pneumonia (Figure 2). The patient was transferred to a referral hospital for children with infectious diseases.

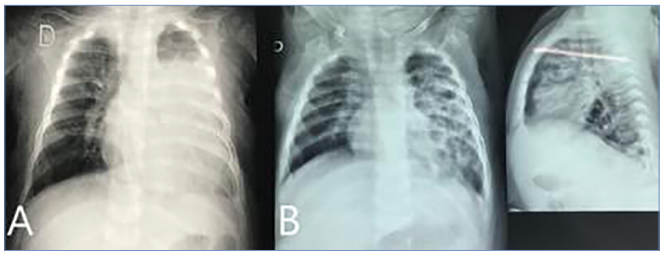


Figure 1. A: Chest X-ray image, anteroposterior view, showing opacities throughout most of the left lung, sparing parts of the upper lobe, obliterating the outline of the heart. B: Chest X-ray images, anteroposterior and profile views taken 15 days later, showing partial resolution of the consolidation and the appearance of small cavities and some air bronchograms.

The infant arrived at the hospital in good general condition in ambient air, weighing 7480 grams (p50), with a length of 62.6 cm (p50-10), and a head circumference of 43 cm (p50). Samples were collected from three consecutive gastric lavages with positive bacilloscopy for acid-alcohol resistant bacilli (AARB). Rapid molecular test for TB (RMT-TB) was positive for rifampicin-sensitive *Mtb.* Antibiotic therapy was suspended and the patient was started on the RIP (rifampicin, isoniazid, pyrazinamide) antituberculous drug scheme with age-adjusted dosage. The infant's immunization record showed that she had taken the BCG vaccine. A test for human immunodeficiency virus (HIV) came back negative. Chest X-ray images of her mother did not show alterations, and her sputum and TST were also negative for tuberculosis. Epidemiologic investigation found that her paternal grandfather had been diagnosed with TB.

Although the patient was afebrile after the first day of treatment, she had trouble swallowing the medication, and would often regurgitate and vomit. A gastric lavage performed 15 days after the start of the RIP scheme was still positive for TB (seven AARB per field) and her culture tested positive for *Mtb.*

A month into the introduction of proper therapy, her gastric lavage was still positive for AARB (six per field). A new chest CT was ordered and parenchymal consolidations were seen in her left lung, with oval images suggestive of clustered lymph nodes and a right lung compensating for the left lung (Figure 2). Nevertheless, the patient was clinically stable and afebrile. She gradually accepted the medication. After discharge, the patient was referred to an outpatient clinic specialized in tuberculosis located closer to the town where she lived. She was followed with clinical and imaging examination and was kept on the antituberculous drug scheme.

COMMENTS

The infant described in this article had a history of wheezing, cough, and persistent imaging findings even after the prescription of antibiotics for common pathogens. During diagnostic investigation, chest X-ray images showing parenchymal consolidation and cavitation, both unusual signs in this age

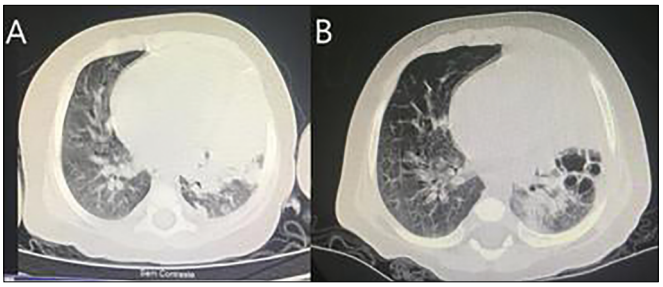


Figure 2. A: Chest CT scan showing parenchymal consolidations in the left lung, notably in the upper lobe, with air bronchograms and a cavity measuring about 1.5 cm in diameter. Parenchymal ground-glass opacities in the apical segment of the lower right lobe. B: Chest CT scan showing parenchymal consolidation in the left lung, with aerated images of bizarre shape communicating with the bronchial tree in the upper love and a decreased lung volume. Minor marginal septated pleural collection to the left. Right lung compensating for the left lung, with some poorly defined opacities in the upper lobe.

range, and gastric lavage with positive results in bacilloscopy, RMT-TB, and Mtb culture led to the introduction of specific therapy for TB.

According to recent data from the Brazilian Ministry of Health (MH), pulmonary TB accounts for 75% of the cases of TB in children and adolescents. TB/HIV coinfection accounted for 9.5% of all cases of the disease reported in 2017. HIV-related immunosuppression is an independent risk factor for TB and negatively affects the clinical progress of individuals with these conditions. Therefore, performing an HIV rapid test is recommended whenever a patient is diagnosed with TB[1,2].

Clinical manifestations vary. Most patients have persistent fever in the afternoon for more than 15 days, show no sign of improvement in X-ray images from the use of antimicrobial agents for common pathogens, have a family history of chronic cough or of have been in contact with individuals with TB[5,6].

Transmission occurs via the inhalation of droplets emitted by individuals infected with Mtb, mainly as they cough and rarely through sneezing, talking or kissing. Disease development varies from individual to individual. Most are partially immune to the bacillus and stay healthy for many years, with what is referred to as latent TB infection. However, five percent of the individuals will suffer from increased bacterial loads after a first infection and develop primary TB[1,7].

Children aged two years or less, malnourished individuals, persons with HIV treated with immunosuppressants, and subjects with diabetes are more likely to contract the disease[1,7]. Cases of the disease must be investigated among individuals that have been in contact with the patient. The infant described in this case had been in close contact with her grandfather, a person with chronic cough and TB as determined in epidemiologic investigation.

A child hospitalized for longstanding pneumonia unable to improve after the introduction of antibiotics must be further investigated for epidemiologic, clinical, and imaging findings. In specific occasions, a more thorough investigation is warranted. The first tests one should order are X-rays and TST. X-ray images play a key role in TB diagnosis and are useful during patient follow-up to monitor for possible complications[8].

The most frequent X-ray findings in children are lymph node enlargement (hilar or mediastinal), miliary tuberculosis (diffuse retinal nodular involvement), parenchymal disease (lung condensation), atelectasis, and pleural effusion (a rare find in subjects aged five years or less). Similarly to the pattern seen in adults, the most common findings in adolescents are infiltrate and condensation in the upper third of the lungs and cavitation[9].

Chest CT is indicated in situations where X-ray scans look normal or suspicious and lung injuries from TB require better visualization and differentiation from other thoracic conditions, particularly in immunosuppressed patients. Lobar consolidation and hypodense areas are seen in more than 80% of the CT scans, while cavitation is seen in less than 25% of the cases[9]. The patient described in this article had typical pulmonary TB injuries in her X-ray and CT scans. Nevertheless, CT scans were taken at her hospital of origin. Additional CT scans were ordered to check how well the patient was progressing one month into the start of proper therapy, since she still tested positive for Mtb infection.

TST helps identify individuals with *Mtb*, regardless of how long ago they took the BCG vaccine. Immune response 48-72 hours to the Mantoux test is considered positive when indurations are ≥ 5mm and negative for indurations < 5mm[1]. TST was unavailable in the town where the patient was first hospitalized.

Children usually develop paucibacillary primary TB, and only 20% of the cases have tests confirming presence of Mtb. Microscopy is quick, but not very sensitive. The remaining 80% of individuals with disease are diagnosed without laboratory testing for Mtb on account of the limitations inherent to the pediatric age range. Children under five and six years of age are generally unable to spontaneously eliminate mucus, which makes sputum bacilloscopy difficult to perform[10,11].

Invasive methods are employed to collect samples for bacteriology tests in infants and preschoolers, such as sputum induction, gastric lavage, and aspirates (bronchial or bronchoalveolar) with bronchoscopy. From this age onwards, sputum bacilloscopy and culture may be attempted. In adolescents, diagnosis can be confirmed via bacteriology tests, since most individuals in this age range have bacterial loads similar to those of adults[10,11].

Although rare, the formation of cavities in children with pulmonary TB has been associated with severe forms of the disease and higher bacterial loads, which may be picked up in laboratory tests as in the case of the infant described in this article[9].

Cultures can be used to identify *Mtb* in 40-50% of the cases. In solid medium (Löwenstein-Jensen), however, the test takes 6-8 weeks to yield a result and does not allow early diagnosis. A fluid medium (Middlebrook 7H9) currently

available allows for faster growth of Mtb and is more sensitive to paucibacillary samples[11,12].

Whenever available, the RMT-TB can be used in children aged 10 years and under to supplement the diagnosis. The RMT-TB is a polymerase chain reaction (PCR) test that uses the Gene Xpert platform to detect sequences of nucleic acids from the Mtb genome and screen between drug-resistant strains. The test takes about two hours to yield a result, but is not very sensitive in children (66%) due to difficulty obtaining sputum samples[11,13].

Immune tests include the TST and the IGRA (interferon-gamma release assays), a category of in vitro test kits that detects the production of interferon gamma (IFN-γ) in the T cells of hosts infected specifically with Mtb. The two tests have similar levels of sensitivity at detecting the bacillus, but IGRA is less affordable and its results less reliable in individuals below the age of five years. The Xpert MTB/RIF Ultra test kit is more sensitive than the traditional Xpert MTB/RIF kit for paucibacillary samples[11]. None of these tests was performed in our patient on account of cost, since they are not available in the Brazilian public healthcare system, and due to the fact that their results are still embedded with significant levels of uncertainty for the age range in question.

The MH stipulates that children and adolescents with negative bacilloscopy or undetected levels of bacteria in the Xpert MTB- Rif system (RMT-TB) should be diagnosed with pulmonary TB based on the MH scoring system, i.e., without the confirmation of a bacterial load test[11,12].

The MH scoring system uses epidemiologic, clinical, and imaging data to rate pulmonary TB as very likely (≥ 40 points), possible (30-35 points), or unlikely (≤ 25 points). Patients attaining the latter score are tested with other methods based on availability[11,12]. Our patient was diagnosed based on tests confirming the presence of bacterial load. As mentioned above, we were unable to perform a TST, which hindered the use of the MH scoring system (the only findings were imaging alterations and contact with an adult with tuberculosis within the last two years).

Pulmonary TB is a significant cause of morbimortality globally. In order to decrease the incidence ratio and the number of deaths by TB, effective strategies must be developed to reduce the number of underreported cases in children; develop new, more sensitive, less invasive diagnostic methods; engender strategies to expand HIV screening efforts; and invest in the development of vaccines and drugs suitable for children, while seeking prevention and higher levels of compliance to treatment, so that we can live in a world free from tuberculosis, without deaths, new cases, or the pain caused by the disease[1,7,14].

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