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CASE REPORT

Rare manifestations of tuberculosis in children: a case series

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Abstract

Tuberculosis (TB) is an infectious and contagious disease that poses a challenge in pediatric practice, since children can present rare manifestations, which makes their diagnosis difficult. Five cases of uncommon manifestations of TB are presented in children vaccinated with BCG at birth and with no history of previous contact with bacilliferous adults. The difficulty and importance of the diagnostic suspicion of TB in rare cases of the disease in children is emphasized.

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INTRODUCTION

Tuberculosis (TB) remains a public health problem. In 2019, around 10 million people became ill from TB worldwide, and approximately 12% of cases were in children[1]. Underdiagnosis of pediatric TB is common, especially in countries with a high prevalence of the disease. It is an infection that mainly affects the lungs and it can progress to disease to the lungs or outside the lungs. In contact with a bacilli-positive adult, children under two years of age or who are immunocompromised are at greater risk of developing severe forms of the disease[2]. The frequent non-specificity of signs and symptoms, the paucibacillary characteristic of the disease and the difficulty in expectoration in children (under 10 years of age) make diagnosis a huge challenge in pediatric TB[3,4]. Therefore, the diagnosis is generally based on clinical, radiological, immunological and epidemiological parameters, and less on bacteriological or molecular confirmation of the pathogen[5,6]. On the other hand, TB in adolescents (aged 10 or over), in general, presents in a similar way to adults, often allowing bacteriological confirmation of the patient[2]. In Brazil, the scoring system is recommended for diagnosing pulmonary TB in children and adolescents with negative smear microscopy or the undetected Xpert MTB/RIF7 gene.

Extrapulmonary TB (EPTB) results from the process of hematogenous and lymphatic dissemination of Mycobacterium tuberculosis from the lungs during TB primary infection, which can lead to the implantation of an infection foci in other organs[8]. Of all reported TB cases worldwide in 2018, 15% were EPTB[1]. Despite this, the global impact of EPTB is still little known, due to its underreporting and diagnostic difficulty[9]. It is estimated that around 20% of childhood TB cases are EPTB. Peripheral ganglia, meninges, pleura and bones are the most common locations[7]. It is noted that childhood TBEP can manifest itself in different ways, and its symptoms can be restricted to the affected organ or system, which often delays the diagnosis and, consequently, treatment onset[8].

This case series comprises five patients with pediatric TB of unusual presentation, all vaccinated at birth with the BCG (Bacillus Calmette-Guérin) vaccine, with no history of previous contact with bacilliferous adults, three patients with EPTB, one with pulmonary TB and one case of the intrathoracic pseudotumor form of the disease. In none of the cases there was an initial diagnostic hypothesis of TB.

The present study was approved by the Research Ethics Committee of the Universidade Federal Fluminense (CAAE number 67103117.4.0000.5243).

CASE REPORTS

Table 1 presents the main demographics, clinical characteristics and laboratory results of patients diagnosed with TB.

Case 1: Pseudotumor form of TB

This is a three-month-old male Infant, admitted for diagnostic investigation of an expansive formation in the upper lobe of the right hemithorax, with the initial diagnostic hypothesis of pulmonary neoplasia, after recurrent fever unresponsive to oseltamivir and amoxicillin-clavulanate. His general condition was good, and he was taking oxacillin and vancomycin to treat osteomyelitis in the left fifth finger, noticed on the 5th day of hospitalization, but without improvement in the infectious process. Computed tomography (CT) and angio-CT of the chest showed a mediastinal mass with a hypodense center and a small hole inside, hilar, paratracheal and infracarinal lymph node enlargement, suggestive of pulmonary and lymph node TB. Broncho-alveolar lavage (BAL): smear microscopy and GeneXpert MTB/RIF negative; negative tumor markers (ferritin, lactate dehydrogenase, beta-HCG, alpha-fetoprotein, uric acid and vanillylmandelic acid). Due to the clinical-radiological dissociation, the radiological appearance suggestive of TB and the non-response to osteomyelitis treatment, we started treatment with rifampicin + isoniazid + pyrazinamide (RIP) for 12 months, considering bone TB associated with intrathoracic TB (pseudotumor form). He continues in outpatient follow-up, showing good clinical evolution and radiological improvement. He subsequently had two episodes of pneumonia. During the outpatient investigation, a diagnosis of chronic granulomatous disease was made using DHR (dihydrorhodamine), performed and repeated after 15 days, both with altered results.

Case 2: Recurrent wheezing in the infant

A 5-month-old male infant had two hospitalizations in the first month of life with bronchiolitis, at three months due to pneumonia in the right lung base, and at four months due to persistent wheezing associated with pneumonia in the same location. A chest CT scan showed consolidations with air bronchograms in the right middle and lower lobes, and multiple centrilobular micronodules in the right upper and lower lobes, suggesting airway filling related to an inflammatory and/or infectious disease. Diagnostic bronchoscopy showed widening of the carina angle, reduction in the caliber of the main bronchi and the bronchi of the right bronchial tree, due to extrinsic compression. BAL: bacilloscopy and Gene Xpert MTB/RIF were negative. Due to the clinical-radiological dissociation (radiological changes with little clinical expression), we started he on RIP, with good clinical and radiological response.

Case 3: Panuveitis

This is a six-year-old female student, diagnosed with Weill-Marchesani syndrome (congenital mesodermal dystrophy characterized by subluxation of the lens, short stature, brachydactyly and joint stiffness). He has a history of nonspecific recurrent panuveitis since he was 3 years old and has already undergone 16 procedures for surgical correction of glaucoma. Report of chronic use of corticosteroids (for six months), which was suspended 10 months ago. The tuberculin

Tabela 1. A1 Characteristics of patients with rare manifestations of TB.

Clinical trait		Case 1	Case 2	Case 3	Case 4	Case 5
Age		3 months	5 months	6 years	9 years	11 years
Initial clinical diagnosis		Osteomyelitis and mediastinal tumor	Recurrent infant Wheezes	Panuveitis	Erythema nodosum	Rheumatic fever
Ultimate diagnosis		Intrathoracic tuberculosis (pseudotumoral and osseous types)	Pulmonary tuberculosis	Ocular tuberculosis	Ganglionic tuberculosis	Pulmonary and osseous tuberculosis
Clinical manifestation of tuberculosis?		Yes	Yes	No	No	Yes
Chest X-Ray findings		Hypotransparency in the right and left lung apices and mediastinal shift	Right lung apex hypotransparency	Normal	Normal	Hilar and paratracheal lymphadenopathy
Chest CT scan		Mediastinal mass associated with hilar, paratracheal and infracarinal lymphadenopathy	Consolidation with air bronchogram in the right middle and lower lobes with air bronchogram in the right upper and lower lobes	Not done	Not done	Smooth and sparse-density small nodules in both lungs and multiple mediastinal and hilar lymphadenopathy
Tuberculosis contact at home		No	No	No	No	No
Tuberculin test		4mm	8mm	15mm	18mm	18mm
Nutritional status (Z score/ Percentile)	Weight/ Age	Mild malnutrition	Eutrophic	Eutrophic	Eutrophic	Does not apply here (patient older than 10 years of age)
	BMI X Height	Mild malnutrition	Eutrophic	Eutrophic	Eutrophic	Eutrophic
Ministry of health Scoring system (version 2019)		35 points	45 points	Does not apply here (exptrapulmonary tuberculosis)	Does not apply here (exptrapulmonary tuberculosis)	40 points

skin test was reactive, the Interferon Gamma Release Assay (IGRA – Quantiferon) was negative, and the chest X-ray was unremarkable. We decided to start him on the RIP scheme, which was prescribed for six months, considering the diagnostic hypothesis of ocular TB. He presented good clinical evolution, with uveitis improvement.

Case 4: Erythema nodosum

Schoolboy, 9 years old, male, admitted for diagnostic investigation of nodular lesions in the upper and lower limbs, fever and bilateral inguinal lymph node enlargement. We ran a biopsy of the skin and lymph node lesions, which revealed a granulomatous inflammatory process with caseous necrosis and positive smear microscopy. We started him on the RIP regimen, and the patient evolved clinically well, with resolution of the skin lesions.

Case 5: Poncet polyarthritis

This is an 11-year-old female adolescent with arthritis, hospitalized for diagnostic investigation of fever and oligoarthritis, with initial hypothesis of rheumatic fever, being treated with benzathine penicillin. His Erythrocyte Sedimentation Rate (ESR) was 56 mm/h (Upper Limit up to 15 mm/h); his transthoracic echocardiogram was unremarkable. She was referred to the pediatric rheumatology outpatient clinic, where his constitutional symptoms were associated with oligoarthritis onset, such as high afternoon fever (not measured) and night sweats, in addition to repeated use of azithromycin and amoxicillin to treat his tonsillitis. Upon clinical examination, his ankle involvement was highlighted, with bilateral tenosynovitis, characterized by morning stiffness, pain on movement and phlogistic signs. We considered the diagnoses of juvenile idiopathic arthritis, Chikungunya and reactive TB (Poncet's rheumatism). We started here on nonsteroidal anti-inflammatory drugs (NSAIDs) during hospitalization. Her blood count showed chronic iron deficiency anemia; and her ankles MRI revealed extensive and diffuse tendon sheath synovitis, with an inflammatory appearance. Although she did not have a hard cough during the investigation of the joint condition, CT and chest radiography demonstrated mediastinal enlargement

- hilar and right paratracheal. A biopsy and culture of the ankle synovial sheath were performed, both of which were negative for Mycobacterium tuberculosis. Due to symptoms suggestive of pulmonary TB and osteoarticular TB (fever, night sweats and oligoarthritis), treatment with rifampicin + isoniazid + pyrazinamide + ethambutol (RIPE) was initiated for 2 months followed by a rifampicin + isoniazid regimen for 10 months, with good clinical evolution and symptoms resolution.

DISCUSSION

The main finding of this study was the fact that all the patients presented unusual manifestations of TB and had no positive contact identified. The absence of a typical presentation and recognized source case led to long diagnostic investigation processes, which delayed the diagnosis and initiation of treatment. The TB diagnosis still presents itself as a challenge in daily clinical practice, even in countries like Brazil, where there is a high burden of the disease[1].

The active search and identification of the source case, especially infected infants, must mainly cover their family members[8]. In this way, the importance of actively searching all contacts for the source case should there be a new case of pediatric TB is reinforced, aiming to reduce the disease transmission chain3.

It is estimated that children infected with HIV are at greater risk of developing TB and its disseminated form due to acquired cellular deficiency[10]. Although they had rare forms of TB, all the patients in this case series were HIV-uninfected. The child in case 1 was later diagnosed with immunodeficiency and the child in case 3 had a prolonged use of corticosteroids; and two other children, younger than two years of age, behaved as physiologically immunosuppressed, and thus are more likely to developing severe forms in the natural course of TB, if not addressed promptly. In children under one year of age, the probability of developing the disseminated form is around 10-20%, falling to 2-5% at ages between one and two years[8].

In developing countries, and in TB endemic areas where resources are limited, it is essential that cases of the disease are recognized early, in order to provide better targeting of resources, treatment and prevention policies. In this sense, it is essential that the TB diagnosis is considered more frequently, even in uncharacteristic cases, such as those presented in this series of cases.

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