(CASE REPORT)

Bacilliferous pulmonary tuberculosis of the infant: Report of 3 cases in the pediatrics department of the hospital of Mali

Bourama Kané 1, *, Korotoumou Wélé Diallo 1, Boubacar Mami Touré 2, Oumou Koné 3, Guédiouma Dembélé 1, Sow Djénéba Sylla 4, Modibo Mariko 4, Alassane Traoré 5, Diallo Baba 6, Aboubacar Sidiki Thissé Kané 6, and Yacouba Toloba 7

1 Department of Pediatrics of the Hospital of Mali
2 Medical Imaging Service
3 National Institute in Public Health
4 Department of medicine and endocrinology of the Hospital of Mali
5 Gyneco-obstetrics service
6 Department of odontology
7 Department of pneumo-phthisiology of CHU Point G

Publication history: Received on 21 September 2020; revised on 06 October 2020; accepted on 12 October 2020

Abstract

Introduction: Tuberculosis is one of the top ten killers worldwide. In 2015, an estimated one million children developed the disease and 170,000 died from it. We report three cases of pulmonary tuberculosis in infants diagnosed and treated in the pediatric ward of the Mali Hospital.

Clinical cases:

Observation 1: He is a 7 month old infant hospitalized for fever and weight loss. He received the BCG. There was no notion of TB contagion. On admission, he had poor nutritional status with a Zscore <- 3 and pallor. He had bronchial groans. Xpert / RIF returned positive to \textit{M. tuberculosis} sensitive to rifampicin. An anti-tuberculosis treatment (2RHZ / 4RH) associated with the transfusion of the globular concentrate at a rate of 20 ml / Kg / 1d over 1 hour and nutritional management have been instituted. After 2 months of treatment, we observed clinical radiological improvement. Xpert control of gastric fluid returned negative.

Observation 2: He was an 8-month-old infant hospitalized for fever and weight loss. He did not receive BCG. There was no notion of family storytelling. On admission, he had a poor nutritional status with a Z score <-3. The respiratory rate was 32 cycles / min. There were crackling groans. Direct gastric fluid examination and Xpert / RIF were positive for \textit{M. tuberculosis} sensitive to rifampicin. He could not be treated because the family requested discharge against all medical advice.

Observation 3: He was a 10 month old infant admitted for cough, fever and weight loss. He received the BCG, there was the notion of family contagion. At the entrance, he had a poor nutritional status with a zscore <- 3. He had a polypnea at 45 / min and crackling groans. Direct examination and culture of gastric fluid were positive for rifampicin-sensitive \textit{M. tuberculosis}. A treatment including oxygen, anti-tuberculosis drugs (2RHZ / 4RH) and nutritional management was initiated. Within 2 months of treatment, we observed clinical and radiological improvement. Direct examination and culture of gastric fluid returned negative.

Conclusion: tuberculosis in infants is poorly documented because of unspecific symptoms and difficulties in obtaining bacteriological confirmation. It should be systematically sought in all malnourished infants in endemic countries.

* Corresponding author: Bourama Kane
Department of Pediatrics of the Hospital of Mali.
Keywords: Tuberculosis; infant; pediatrics; Mali Hospital

1. Introduction

Tuberculosis is a chronic bacterial infection caused by *Mycobacterium tuberculosis* (*M. tuberculosis*). It is a major cause of mortality and morbidity worldwide. Pulmonary tuberculosis is the main form of the infection as well as the mode of transmission [1].

Tuberculosis is one of the 10 leading causes of death in the world. In 2015, 10.4 million people contracted the disease and 1.8 million died from it (of whom 0.4 million also died of HIV). More than 95% of TB deaths occurred in low- and middle-income countries [2].

Tuberculosis in children is always the result of contamination by an adult with the disease [3]. Mortality due to the disease is proportionally higher in children than in adults: although children account for 10% of all tuberculosis cases, they account for 15% of deaths. Delayed diagnosis and the rapidly evolving forms of the disease in young children are the main factors in this high mortality [4]. In 2015, an estimated 1 million children developed tuberculosis and 170,000 died from it (excluding those with HIV) [2]. The form of TB in children depends on age and immunity. Infants and young children are particularly prone to severe, widespread, and often fatal forms of the disease. It presents as tuberculous meningitis or miliary tuberculosis [5].

Another particularity of childhood tuberculosis is the difficulty in obtaining bacteriological confirmation of the disease, either because the disease is extra-pulmonary or collection of material for bacteriological examination is difficult, or because children with pulmonary forms do not produce sputum [5]. These main factors explain why infant tuberculosis is poorly documented in low-income countries with limited diagnostic capacity.

In 2017, according to the World Health Organization (WHO), nearly 69% of infant and young child tuberculosis cases are underreported compared with 40% of children aged 5-14 years [6]. In 2004 a hospital study in Brazzaville showed a frequency of 14.6% in infants under 24 months of age [7]. In Mali in 2016, 738 cases of all forms of tuberculosis were reported, including 79 cases in children under 15 years of age and 12 cases in children under one year of age [8]. We report three cases of pulmonary tuberculosis in infants diagnosed and treated in the pediatric ward of the Mali Hospital.

2. Observation

It was a 7-month-old male infant hospitalized for pallor and weight loss. His mother was a 20-year-old primiparous student with no significant medical-surgical history (TCDA). The infant was born of a pregnancy that was carried to term without major incidents. He was born vaginally with good adaptation to extrauterine life. It was a newborn with low birth weight according to the mother. Vaccinations were in progress and the BCG vaccine scar was visible. There was no notion of tuberculosis contagion in his environment.

The onset of the disease dated back to the neonatal period marked by episodes of rhino-bronchitis associated with a progressive deterioration of the general condition. His mother first opted for traditional treatment and then took him to their local health center without success, hence his referral to our service. On admission, he was pale and had a fever of 38.7°C. He weighed 5.3 kg for a height of 62 cm and a weight/height ratio < -3 Z score.

He had a good chest magnification, hemoglobin oxygen saturation (Spo2) at 96% under air and bronchial rales in both lung fields. Heart sounds were audible and regular, there was tachycardia at 170/min and intense systolic murmur at the mitral site. The abdomen was soft, the liver and spleen were not palpable and transit was normal. The rest of the clinical examination was without major peculiarities. A 7-month-old infant with intrauterine growth retardation TCDT, admitted for undernutrition, fever and bronchial rales, we hypothesized a viral or bacterial respiratory infection on undernutrition.

To support the diagnosis, some additional tests were requested:

- The Blood Count (CBC) Showed A Severe Anemia At 3.6 G / Dl Microcytic Normochrome With A Hyperleukocytosis At 22000 / Mm3 With Lymphocyte Predominance.
- On Blood Culture, HIV Serology Was Negative.
- The Tuberculin Intradermal Reaction (TDR) Was Negative.
The Test For Acid-Fast Bacilli (AFB) In Gastric Fluid Was Negative Three Times. Chest X-Ray Showed An Area Of Right Para-Helicical Frosted Glass Against A Background Of Bilateral Reticulonodular Opacity (Figure 1). The Genexpert MTB/RIF Was Positive. Thus The Diagnosis Of Pulmonary Tuberculosis Under Positive Microscopy Was Retained.

An antituberculosis treatment combining rifampicin 10mg/Kgs/d, isoniazid 10 mg/Kgs/d and pyrazinamide 30 mg/Kgs/d for 2 months followed by rifampicin 10mg/Kgs/d, isoniazid 10 mg/Kgs/d for 4 months was instituted. The globular concentrate was transfused at 10mg/Kg/d over 1 hour. Nutritional management was instituted. After 2 months of treatment, we observed a clinical radiological improvement (figure 2). The Xpert control of gastric fluid returned negative.

**Figure 1** Radiograph of the frontal thorax: right para-hilar frosted glass area against a background of bilateral reticulo-nodular opacity.

**Figure 2** Thoracic scan coronal section parenchymal window: at 2 months the treatment showed the persistence of bilateral peri-hilar frosted glass image with disappearance of the interstitial syndrome.
3. Observation

It was an 8-month-old female infant hospitalized for fever and weight loss. The parents were farmers with no known medical-surgical CDTAs. Our patient had an estimated full-term unattended pregnancy. She screamed at birth and her birth weight was normal according to her mother. She was the third child of a sibling group of three. Her siblings were doing well. The tuberculosis vaccine was not given. There was no notion of tuberculosis contagion in the family. She was in her fourth hospitalization. She was hospitalized twice for severe malaria and once for severe acute malnutrition in their local health center.

The onset of the disease was about 1 month ago, marked by fever, chronic cough, diarrhea, vomiting and weight loss. His parents first treated him with herbal decoctions and then brought him to the health center without success. When her symptoms worsened, she was referred to us for treatment.

At admission she weighed 5 kg and was 68 cm tall. She had a fever of 40°C and a poor nutritional status with a Z score < -3. Her respiratory rate was 32 cycles/min. Oxygen saturation was 95% in air. Vesicular murmur was well perceived. There were crackling rales in both lung fields and regular tachycardia at 180/min. The rest of the clinical examination was not very peculiar.

In summary, this was an 8 month old infant with TCDT of malaria and severe acute malnutrition who was hospitalized for weight loss, hyperthermia at 40°C, cough, polyphoea and rales on auscultation we raised the hypothesis of pulmonary starting point sepsis on severe acute malnutrition.

The complementary examinations carried out were:

- The blood culture was negative;
- The cbc showed a hypochromic microcytic anemia at 7.6 g/dl;
- The crp was negative;
- Chest x-ray showed confluent alveolar-nodular opacities that were quite diffuse and more pronounced on the right (figure 3).

![Figure 3](image3.png)

**Figure 3** X-ray of the thorax with confluent alveolar-nodular confluent opacities that are quite diffuse and more pronounced on the right.

To explore this radiological image we asked for a tuberculosis assessment. Direct examination of the gastric fluid and GeneXpert MTB/RIF were positive. The diagnosis retained was miliary tuberculosis. It could not be treated because the family requested discharge against medical advice.
4. Observation

This was a 10-month-old female infant admitted for chronic cough, fever and weight loss. His parents were peasants. His mother and older brother were known tuberculosis patients undergoing treatment. She was vaccinated against tuberculosis.

Our patient had no known neonatal CDAD. She had received the tuberculosis vaccine. At 3 months of life, he presented with recurrent fever, chronic emetogenic cough, and progressive deterioration of general condition, prompting a series of consultations in their local health center without success. In view of the persistence of the signs and the notion of familial tuberculosis contagion, the search for BK in the gastric fluid was carried out. It revealed tuberculosis, hence its referral to our department for treatment.

At the entrance, she weighed 5.2 kg for a height of 63 cm. She had a fever of 38°C. Her nutritional status was poor with a zscore < -3. Her thorax was harmonious with polypnea at 45/mn and oxygen saturation at 92%. She had intercostal and subcostal traction. Vesicular murmur was decreased in the right lung field with the presence of crackling rales. The rest of the clinical examination was unremarkable.

The diagnosis retained was pulmonary tuberculosis with positive microscopy. The paraclinical examinations requested on admission were:

- CBC which showed normocytic and normochromic anemia at 8.2g/dl. The white blood cells were 99000/mm3 and platelets 150000/mm3;
- Creatinemia was 18 µmol/l, azotemia was 4.36 mmol/l;
- Alamine aminotransaminase was 17 IU/l and aspartate aminotransferase was 34 IU/l.
- HIV serology was negative;
- Gastric fluid culture isolated rifampcin- and isoniazid-sensitive M. tuberculosis.
- Frontal chest X-ray showed multiple straight pulmonary cavity images with water level. At the apical level there is alveolar filling, associated with homolateral pleural thickening of minimal abundance and compensatory hypervascularization of the contralateral lung (Figure 4).

She was put under oxygen: sufficient quantity for saturation ≥ 95% and an antituberculous treatment including rifampcin 10mg/Kgs/d, isoniazid 10 mg/Kgs/d and pyrazinamide 30 mg/Kgs/d for 2 months then rifampcin 10mg/Kgs/d, isoniazid 10 mg/Kgs/d for 4 months. Nutritional management has been maintained.

At the end of 2 months of treatment (intensive phase), we observed apyrexia, weight gain, improvement of respiratory and radiological signs (figure 5). Direct examination and culture of gastric fluid returned negative.

Figure 4 Frontal chest X-ray showing multiple images of the right lung cavity with water level.
5. Discussion

Tuberculosis is a public health problem particularly in developing countries. According to the WHO, in 2017, 10 million people will have contracted tuberculosis. Children under 5 years of age account for 52% of cases. The number of deaths was 233,000 among children aged 0-14 years. Children under 5 years of age accounted for 80% of these deaths [6].

The essential feature of infant tuberculosis is its rapid spread. The immune immaturity of the infant and the massive contamination, often familial, may partly explain it. This immune immaturity combined with undernutrition explains the tuberculinic anergy so often observed at this age (62-75% of cases) [9].

The infant is more often symptomatic than the older child. In children under one year of age the frequency of symptoms is as follows: cough (79%), fever (64%), anorexia (43%), rales localized at auscultation or wheezing (38%), diarrhea and/or vomiting (17%), weight loss (15%), convulsions (11%) [9,10]. The risk of developing a severe form (disseminated form or meningitis) is greater. Infants with disseminated forms often have hepatosplenomegaly [9,10].

In forms with pulmonary localization, tracheobronchial complications are more frequent. Node fistulization must be feared in case of febrile attack, cough, sudden decrease in node volume. It can produce an asphyxic picture by flooding the airways in case of fistulization of laterotracheal adenopathy. Even under treatment, lymphadenopathies can increase in volume, cause ventilation problems, and fistulize [10].

Diagnosis is based on three elements: X-ray data, the detection of \textit{M. tuberculosis} and finally the search for a contaminant [9]. Radiological images are often evocative: mediastinal adenopathies associated with segmental or non-segmental opacity in the upper lobes or the middle lobe, miliary is frequent [9].

The discovery of \textit{M. tuberculosis} in gastric tubing is more frequent than in older children (20 cases out of 26 for Rosenfelt, 75% of cases for Vallejo. Lumbar (LP) puncture should be systematic because central nervous system (CNS) damage has been reported in 20-35% of cases [9].

Cerebral CT scan is required in cases of tubercular meningitis, miliary meningitis, or when there is a minor cerebrospinal fluid anomaly. Some authors have highlighted cerebral tuberculomas in the latter case. The prognosis is bleak in cases of associated CNS involvement; neurological sequelae are frequent [9].

The standard treatment recommended in children not infected with HIV and with a low probability of resistance to isoniazid is daily treatment in 2 phases, including during the first phase of 2 months the combination of 3 antibiotics: isoniazid (H), rifampicin (R) and pyrazinamide (Z), then during the second phase of 4 months the combination of isoniazid and rifampicin [11]. The use of ethambutol is therefore not systematic in children but is reserved for children co-infected with HIV, with extensive and/or bacillus-rich forms or suspected isoniazid-resistant bacilli [11].
For miliary and disseminated disease, the duration of treatment required for miliary aspects is not perfectly codified. In the absence of associated neuromeningeal damage, a classical scheme of initial quadritherapy for 2 months, followed by dual therapy for the following 4 months seems sufficient [11]. Since this duration is not sufficient in the case of neuromeningeal damage, it is essential to eliminate all neuromeningeal damage in miliary forms by cerebral imaging or by lumbar puncture in order to best determine the correct duration of treatment. If a neuromeningeal localization is associated, a 12-month treatment is necessary [11].

Treatment of contact infants: the frequency of disseminated forms leads to treating any change in TRI with at least two therapies and to instituting the same treatment in case of family contact with negative TRI. This treatment can be discontinued after three months if the TST remains negative and the chest X-ray remains normal [10].

We have reported 3 observations of pulmonary tuberculosis in infants. These were infants at 7, 8 and 10 months of age. The parents of 2 of our patients were farmers. The notion of familial contagion was found in one patient. Young age, poor socioeconomic conditions, and the notion of familial contagion are the main risk factors for developing the tuberculosis disease described by Christophe Delacourt [12]. One of our patients did not receive the tuberculosis vaccine and did not receive any treatment after his diagnosis at the request of his peasant parents. This can be explained by.

6. Conclusion

Tuberculosis often goes unnoticed in infants because of non-specific symptoms (e.g., fever, altered general condition, etc.) and because of difficulties in obtaining bacteriological confirmation. However, they are prone to severe and often fatal forms, hence the interest in systematically gastric tubing for tuberculosis in all infants suffering from severe acute malnutrition in countries with high tuberculosis endemicy.

Compliance with ethical standards

Acknowledgments
- Dr. Bréhima Traoré: microbiologist at the tuberculosis research unit at the Charles Mérieux Infectiology Center in Bamako, Mali.
- Doctor Ibrahim Guindo: microbiologist at the Department of Laboratory and Biomedical Research at the National Institute of Public Health in Bamako, Mali.
- Mr. Albert Bosco Mallé: translator at the Mali Hospital, Bamako, Mali.
- Director of the Mali Hospital, Bamako.

Disclosure of conflict of interest
The authors do not declare any conflict of interest.

Statement of informed consent
Informed consent was obtained from all individual participants included in the study.

References


