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Resistant Pulmonary TB-HIV Co-Infection in an Infant: About a Case

Mariam Maiga[1*], Pierre Togo[2], Tati Simaga[2], Mariam Traoré[1], Moussa Konaté[1], Mamadou Diallo[1], Alou Samaké[1], Mamadou Keïta[1], Korotoumou Wélé Diallo[3], Djibril Kassogué[4]

[1]Pediatrics Department, Distric VI Reference Health Center, Bamako, Mali
[2]Paediatrics Department, Gabriel Touré Teaching Hospital, Bamako, Mali
[3]Pediatrics Department, Mali Hospital, Bamako, Mali
[4]Paediatrics Department, Timbuktu Regional Hospital, Bamako, Mali
Email: *m_mariam07@yahoo.fr

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Abstract

Diagnosis of childhood tuberculosis (TB) is difficult, especially in resource-limited countries where the number of reported cases of TB-HIV co-infection continues to rise. This co-infection poses a diagnostic and therapeutic problem for caregivers. We report a case of rifampicin-resistant HIV-TB pulmonary coinfection in a 19-month-old infant.

Keywords

Tuberculosis, Rifampicin Resistance, HIV, Infants

1. Introduction

WHO estimates that 8 to 10 million new cases of tuberculosis occur worldwide each year. The disease is responsible for nearly 2 million deaths per year, including 300,000 children. Nearly 60% of cases occur in Africa, where children account for 20% to 25% of cases [1] [2]. Over the last decade, the incidence of tuberculosis has increased, particularly in Africa. This increase is attributed to several factors: the deterioration of the social situation, the mixing of populations linked to armed conflicts, the low capacity of national anti-tuberculosis programs and, above all, the spread of HIV infection [3] [4]. Because of their relative fragility and inescapable contact with adults, children are a prime breeding ground for tuberculosis. However, the diagnosis of childhood tuberculosis, even in its pulmonary form, has been and remains difficult, especially in developing countries, due to the lack of effective means. As if that weren't enough, the HIV pandemic has altered the epidemiological, clinical and paraclinical profile of tu-

berculosis throughout the world, presenting the scientific community with numerous challenges, the main ones being the difficulties of diagnosis, treatment and infection control. In countries with limited resources, the number of reported cases of TB-HIV co-infection is constantly increasing, with HIV prevalence among TB-infected children ranging from 10% to 60% [5]. In Mali the frequency of TB-HIV association was estimated at 13% in 2015 (all ages combined) [2]. No case of rifampin-resistant TB-HIV co-infection has ever been reported in an infant in Mali. We report the first case of HIV-tuberculosis pulmonary coinfection resistant to rifampicin in a 19-month-old infant diagnosed at the Pediatrics Department, distric VI Reference Health Center.

2. Observation

This was a 19-month-old male infant admitted to the department for altered general condition and consciousness. He was the second of two siblings, born of a full-term pregnancy, poorly monitored, vaginal delivery with no notion of resuscitation. Breast-feeding was mixed before 6 months, then supplemented by the family dish from 6 months. His psychomotor development was behind his age (he was not yet walking, and his language was only monosyllabic). The family had a low socioeconomic status, no known medical or surgical history, and no history of tuberculosis. According to the story, the onset of the illness was around 10 months ago, marked by fever, cough, dyspnea, anorexia and progressive weight loss, for which the parents had used conventional and traditional medicine without success. As the symptoms persisted, he was referred to us for better management. On initial physical examination, his temperature was 39.9 degree Celcius, he weighed 5.9 kg for a height of 73 cm and a weight/height ratio < −3 Z score indicating severe acute malnutrition. Heart rate was 124 beats/min. He presented with marked paleness of the mucous membranes and severe oral mycosis. Respiratory symptoms included respiratory pauses, respiratory rate 68 cycles/min, intercostal tugging, nasal flaring, oxygen saturation 81% on room air, and crepitus rales in both lung fields. Neurologically, consciousness was impaired, with a Blantyre score of 3. Faced with this picture of pallor, respiratory distress and altered consciousness against a background of severe malnutrition, further investigations (paid for by the parents) were carried out: the blood count showed severe normocytic hypochromic anaemia at 5 g/dl, hyperleukocytosis (18,700/mm^3) with neutrophil predominance; hepatic transaminases and creatininaemia were normal; thick drop and malaria RDT were negative; the frontal chest X-ray showed unsystematized parenchymal opacities (**Figure 1**); HIV serology was positive for HIV1; GeneXpert® had moderate detection (2+) of Mycobacterium tuberculosis (MTB) with rifampicin resistance (RR). In view of these findings, the diagnosis of HIV1-rifampicin-resistant pulmonary tuberculosis was adopted. Therapeutically, the patient was admitted to the intensive care unit, where he received suctioning, oxygenation and F75 therapeutic milk via nasogastric tube. Antibiotic therapy including Amoxicillin/clavulanic acid 200 mg/kg/day

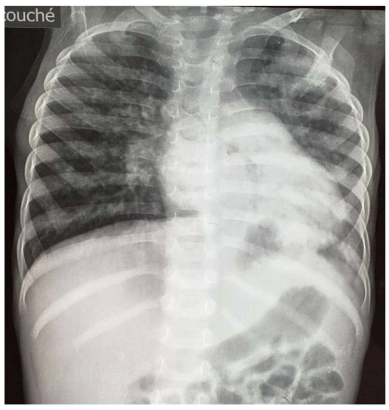

Figure 1. Frontal chest X-ray shows various parenchymal lesions (excavations, heterogeneous opacities, air bronchogram) bilaterally.

in 3 intravenous doses and cotrimoxazole 30 mg/kg/day orally was initiated for 10 days without success. Following the diagnosis of tuberculosis and a multidisciplinary consultation between pediatricians and infectiologists, an anti-tuberculosis treatment including 2nd-line drugs was initiated. It combined Bedaquiline (50 mg/d), Moxicillin (10 - 15 mg/kg/d), Linezolide (15 mg/kg/d) + Clofazimine (2 - 5 mg/kg/d), Cycloserine (15 - 20 mh/kg/d) per os through the nasogastric tube. HIV treatment was deferred.

The evolution was marked by persistent fever and worsening respiratory distress. After 30 days of hospitalization and 7 days of anti-tuberculosis treatment, the infant died in respiratory distress.

3. Discussion

3.1. Frequency

TB-HIV co-infection is most frequently encountered in severely immunosuppressed adults with very low CD4 counts. However, TB-HIV co-infection is very rare in children in Mali. Some African studies have described the frequency of TB-HIV co-infection, notably in Cameroon (55%) [6], Morocco (40%) [7], Burkina Faso (5.5%) [8] and South Africa (46.6%) [9]. The differences observed seem to be linked to diagnostic difficulties that depend on countries' level of development.

3.2. Age

Our case concerns a 19-month-old infant (<2 years). The greatest impact of HIV infection in African children is in the under-5s, where the risk is greatest in the under-2s, with a proportion of severe and/or disseminated infections in the first year of life, but confirmation of pulmonary tuberculosis cases is very rare in this age group. This is consistent with the studies by IKHOUBA in Morocco [7] and Mabiala-Babela in Congo [10], who report a predominance of TB-HIV coinfection in the 0 - 2 age group, but contrary to that of Koueta in Burkina Faso [8], where the 5 - 9 age group was the most represented.

3.3. Clinical Features

As in our infant, prolonged fever, chronic cough, weight loss and peripheral adenopathy were the clinical signs most frequently encountered during TB-HIV co-infection. These signs are found at variable frequencies in most studies [7] [8] [9]. Most of these signs are constant in HIV infection alone. In our infant, the location of the tuberculosis was pulmonary, which is common in all regions of the world [8].

3.4. Paraclinical Aspects

Tuberculin Skin Test (TST): We did not perform a tuberculin TST in our infant. The low contribution of the TST is usual in HIV-infected children, due to the tuberculin anergy generated by acquired immunodepression. A TST is not mandatory for the diagnosis of tuberculosis in children [11].

3.5. Chest X-Ray

In our infant, the X-ray showed various parenchymal lesions (excavations, heterogeneous opacities, air bronchogram). The same observation had been made by other authors [5] [9] [12]. This supports the notion that BK is frequently disseminated in lung tissue during HIV infection.

Bacteriology The availability of the Xpert® MTB/RIF test helped us diagnose rifampin-resistant tuberculosis in our infant. According to Burundi guidelines, whenever possible, bacteriological confirmation of tuberculosis should be sought, even if this is difficult in children [11]. The WHO recommends the use of nucleic acid-based molecular tests (Xpert® MTB/RIF) to improve yield, speed of diagnosis and drug sensitivity testing, especially in HIV-positive patients [5]. In children, no "test treatment" should be used to diagnose tuberculosis [13].

3.6. Treatment

Given the concomitance of rifampicin-resistant tuberculosis with HIV, malnutrition and severe anemia, we prioritized nutritional rehabilitation followed by antituberculosis treatment in collaboration with the specialized TB/MR center, with second-line molecules including: Bedaquiline + Moxicillin + Linezolide + Clofazimine + Cycloserine. According to the specialist center's guidelines, cases of multidrug-resistant tuberculosis are treated with second-line drugs. Rifampicin monoresistance should be treated with isoniazid, ethambutol and a fluoroquinolone for at least 12 to 18 months, with the addition of pyrazinamide for at least the first two months. Very few second-line drugs are produced in paediatric formulations, and tablets have to be split, with the attendant risks of inaccuracy in terms of dosage and blood concentration levels. With regard to nutritional treatment, our infant had spent 4 weeks in the acute phase without being able to stabilize his complications, which was in line with the WHO publication suggesting 50% - 100% energy supplementation to the usual nutritional treatment [13]. In cases of severe acute malnutrition, antiretroviral (ARV) treatment is in-

itiated in the rehabilitation phase or phase 2, to improve tolerance and absorption of ARVs. HIV-positive children with drug-resistant tuberculosis should also receive:

- pyridoxine (5 - 10 mg/kg per day);
- cotrimoxazole preventive treatment [13].

Preventive cotrimoxazole treatment increases survival rates in co-infected patients.

3.7. Evolution-Prognosis

Our infant had a fatal outcome. HIV infection exposes children with tuberculosis to an unfavorable or even fatal course [14].

The outcome of tuberculosis treatment in HIV-infected children is poorer than in the absence of HIV infection, with a high case-fatality rate, particularly during the first two months of treatment; and because of the frequency and severity of opportunistic infections, particularly tuberculosis. The risk of mortality is higher in cases of severe malnutrition in HIV-infected children than in uninfected children [5]. Kouetta F. *et al.* found a case-fatality rate of 18.2% for TB-HIV co-infections in children. The poor prognostic factors in their series were young age, severe immunodeficiency and maternal orphan status. Younger age and immunodeficiency favor more severe disease, while orphan status predisposes to poor quality of care for the child [8].

4. Conclusion

TB-HIV co-infection is common in children, but remains under-diagnosed. Diagnosis by molecular biology not only provides a diagnosis of certainty, but also looks for antibiotic resistance. Rifampicin-resistant TB-HIV co-infection is rare in children in our context, and especially in infants. Early management before nutritional complications allows simultaneous treatment of tuberculosis and HIV, and is the only survival gas. Efforts are still needed to achieve earlier diagnosis, and the implementation of Prevention of Mother-to-Child Transmission (PMTCT) would be the best strategy for avoiding HIV infection in children.

Ethical Considerations

The information gathered from this patient's medical record for the writing of this article has been kept confidential.

Conflicts of Interest

The authors declare that they have no conflict of interest in relation to this publication.

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