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CASE REPORT

Perinatal Tuberculosis: a diagnosis to be considered

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Abstract

Background: Perinatal Tuberculosis (TB) is a rare disease, transmitted during pregnancy or postnatal. Its clinical presentation is similar to congenital infections and neonatal sepsis, thus, remains underestimated and underdiagnosed. **Case presentation:** A 34 week female child, born vaginally, with no prenatal intercurrences. Was admitted in neonatal Intensive Care Unit (ICU) in need of ventilatory support and antibiotic therapy for presumed neonatal sepsis. During the case evolution, a treatment for suspected fungical sepsis was initiated, and after 48h, the newborn showed bilateral otitis media and otomastoiditis. Meanwhile, the newborns mother was hospitalized with miliar TB. Thereby, the newborn was treated for latent TB with Rifampicin, and a lymph node exeresis was made for tuberculosis quick testing (TRM-Ultra) and culture. Since the TRM-Ultra was positive, the treatment was switched to Rifampicin, Isoniazid and Pyrazinamide in order to treat presumed Perinatal TB. The newborn has evolved well and the culture demonstrated *Mycobacterium tuberculosis.* **Discussion:** The congenital form of Perinatal TB is transmitted intrauterus by mothers with severe and/or genital TB, while postnatal occurs due to newborns contact with bacilliferous individual after birth. The diagnosis, as the differentiation between the two forms, are hampered by non-specific clinical manifestations. **Conclusion:** This case demonstrates the importance of considering perinatal TB in unspecified symptomatology cases that are not responsive to conventional antibiotic therapy. Despite the uncertainty regarding the time of infection, besides late diagnosis and treatment, the patient obtained a satisfactory clinical outcome.

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INTRODUCTION

Tuberculosis (TB), even though it is treatable and preventable, remains a serious public health problem[1]. In 2015, there were about 10.4 million cases of TB in the world, 3% of which were registered in the Americas - Brazil accounted for 30% of this[1].

The seven species that make up the Mycobacterium complex can cause it, with Mycobacterium tuberculosis being the most important[1]. The increase in number of cases may be allied to factors such as social inequality, poverty, lack of structure in health services and increasing HIV infection[1].

Despite the increase in incidence, its perinatal form, which includes congenital and postnatal TB, remains rare, even in endemic countries[2,3]. It presents a wide variety of nonspecific signs and symptoms that can mimic congenital infection or bacterial sepsis and go unnoticed[4,5].

Consequently, a delay in diagnosis and treatment leads to rapid evolution to more severe forms, such as meningitis and miliary TB[5].

Thus, this article aims to include Perinatal TB in the differential diagnosis of nonspecific neonatal symptoms, in addition to explaining clinical and epidemiological criteria that favors its suspicion.

Its rarity and the importance of early recognition and the severity of Perinatal TB justify the presentation of this case.

CASE REPORT

Preterm newborn (NB) (34 weeks), female, born by vaginal delivery in our clinic; presented APGAR 9 and 10 (1st and 5th min, respectively), 1850 grams, 42 cm long. Shortly after birth, she was referred to the Neonatal Intensive Care Unit (ICU) due to respiratory distress and prematurity.

29-year-old mother, G3P1A1, negative usual serology, history of depressive disorder and smoker (10 cigarettes/day). She reported alcoholism during the 1st trimester of pregnancy, but denied the use of illicit drugs and other comorbidities. She reported prenatal care without complications.

Upon admission to the Neonatal ICU, the NB required ventilatory support and was initially stable on oxygen therapy in the Hood. Antibiotic therapy (Ampicillin and Gentamicin) was prescribed for presumed early neonatal sepsis based on risk factors in the NB history: premature rupture of membranes 5 days ago and intrapartum fever. Hepatosplenomegaly was not found, blood cultures and urine cultures were negative and the transfontanellar ultrasonography (USG) showed no alterations. After 6 days of treatment, she was transferred to the intermediate care nursery, asymptomatic and without ventilatory support, for weight gain.

On the 18th day of life (DL), she presented an episode of apnea and cyanosis, being readmitted to the Neonatal ICU. She required non-invasive ventilatory assistance with Continuous Positive Airway Pressure (CPAP) and a new course of antibiotic treatment (Meropenem and Vancomycin for 20 days). A chest X-ray showed extensive atelectasis in the right lung, justifying maintenance on CPAP. She maintained mild tachypnea, negative blood cultures and urine cultures, in addition to considerable clinical and radiological improvement.

On the 47th DL, there was a worsening of the respiratory condition associated with thrombocytopenia and it was then decided to start therapy for presumed fungal sepsis. Doppler echocardiogram and abdominal USG showed no alterations and the blood culture was negative. At the same time, she developed purulent otorrhea and bilateral cervical lymph node enlargement (right: 3 cm; left: 5 cm). A treatment regimen with topical ciprofloxacin and intravenous clindamycin were instituted following guidance from the otorhinolaryngology department. After 7 days of treatment, there was partial regression of lymph node enlargement. Ear secretion culture was positive for Pseudomonas aeruginosa and skull computed tomography (CT) showed signs of otomastoiditis with bilateral otitis media.

On this occasion, the mother was hospitalized for miliary TB, dying after 10 days. The patient's father had been treated for Pulmonary TB and had a negative bacilloscopy (three samples), information not reported at any time until then. Thus, the NB underwent treatment of alleged latent TB infection with Rifampicin.

Excision of enlarged lymph nodes was performed according to ultrasound control and the Rapid Molecular Ultra Test (TRM-Ultra) with detectable Mycobacterium tuberculosis was requested. As TRM-Ultra showed positivity, treatment for presumed Perinatal TB was started with Rifampicin, Isoniazid and Pyrazinamide and since then there has been progressive improvement of the clinical situation. After discharge, she was referred for follow-up at a TB reference service.

The patient evolved asymptomatically and her diagnosis was confirmed with a positive culture for Mycobacterium tuberculosis from the cervical lymph nodes.

DISCUSSION

Perinatal TB is divided into two forms, depending on the time of transmission of the bacillus. When it occurs in utero or during childbirth, it is called congenital TB and, if it occurs after birth, we have postnatal TB[6].

Congenital TB can be transmitted via transplacental hematogenous transmission, by aspiration or ingestion of contaminated amniotic fluid or by direct contact with an infected cervix or endometrium during delivery[7,8]. The criteria for its diagnosis, proposed by Beitzke and revised by Cantwell (1994)[9], include: presence of confirmed tuberculous lesion in the child, in addition to at least one of the following: (1) lesions that occur in the first week of life; (2) caseating granulomas or primary complex in the liver; (3) tuberculous infection in the placenta or in the maternal genitalia; (4) investigation of the NB's contacts to rule out postnatal transmission, including hospital healthcare professionals[7,9].

On the other hand, postnatal transmission can occur through intradomicile contact of the NB with people who have bacilliferous pulmonary TB or through the ingestion of breast milk in the case of breast TB[2].

Due to the difficulty in establishing the moment of infection, the term Perinatal TB is preferable. Moreover, the differentiation between the two forms does not change the diagnostic or therapeutic approach, and the prognosis is similar[8].

The clinical presentation of Perinatal TB usually starts in the first two weeks of life[6]. Manifestations are often nonspecific and are very similar to bacterial sepsis or congenital infection[2]. Among them, the following stand out: respiratory distress (70%), fever (50-100%), hepatosplenomegaly (65-100%), lymphadenopathy (38%), thrombocytopenia (22%), irritability, lethargy, otorrhea, vomiting, diarrhea, low weight and height gain, skin lesions, among others[2,6,7]. Consequently, a late diagnosis is often made, which makes the mortality rate greater than 50%, even with adequate treatment[5].

Furthermore, in congenital TB, in approximately half of the cases, premature delivery occurs[2]. With the exception of hepatosplenomegaly, several of these nonspecific manifestations were observed in the NB in this case.

As for the radiological patterns found in Perinatal TB, a miliary pattern is frequently observed (38-50%), consolidations (76%), nodules (43%), pleural effusion (9.5%) and cavitations[6,7]. Interestingly, in this case, the patient had extensive atelectasis on the right, which could have been caused by an endobronchial tuberculous lesion.

Perinatal TB should be suspected in NBs with nonspecific clinical manifestations and poor response to conventional antibiotic therapy aimed at neonatal sepsis, especially when excluding the possibility of fungal infection6,10. The hypothesis is further reinforced if the mother has had severe TB during pregnancy or if, after delivery, the NB has had contact with bacilliferous individuals[2]. In our case, the mother had no previous diagnosis and information on the father's treatment for TB had not been previously reported.

With regards to the diagnosis of this disease, the triad of negative cultures, certain abnormalities on the chest X-ray (not seen in the case described) and poor response to the usual antibiotic therapy is highly suggestive of Perinatal TB[5]. As soon as it is suspected, the diagnostic investigation must be initiated considering the clinical signs, the radiographic findings and the investigation of the bacillus through possible specimens such as bronchial/gastric aspirate, bronchoalveolar lavage, cerebrospinal fluid or lymph nodes. The culture of the gastric aspirate is the best method to establish the definitive diagnosis, with high yield in NBs[6].

The TRM-Ultra is also used in the diagnosis of the pulmonary form of Perinatal TB with a sensitivity of 46% and specificity of 98% in nasopharyngeal aspirate samples; and 74.3% and 96.9%, respectively, in induced sputum[11]. On the other hand, TRM-TB, when used for diagnosing the extrapulmonary form through aspirates and lymph node biopsies, Xpert, sensitivity and specificity approach 80 and 94%, respectively. For these results, culture was used as the gold standard[12].

The presented case does not fulfill the diagnostic criteria proposed by Cantwell et al, since the NB did not present a tuberculous lesion in the first week of life and it was not possible to evaluate the placenta, since the morbidity in question was not raised during the follow-up of the pregnant woman. The ruling out of postnatal infection could not be ascertained, considering that the mother had contact with the patient before her death. However, clinical findings and culture of the affected cervical lymph node, positive for Mycobacterium tuberculosis – the gold standard – confirm Perinatal TB and reinforce the challenge of diagnosing TB in the mother-NB binomial.

Due to the high lethality of Perinatal TB, healthcare professionals need to be more aware of this suspicion, even if the symptomatology is nonspecific[7], being It is essential to carry out thorough screening for TB throughout pregnancy[13].

CONCLUSION

Perinatal TB is a rare and serious infection that must be considered in the differential diagnosis of neonates, with neonatal sepsis unresponsive to conventional antibiotic therapy, especially if combined with radiographic changes and negative cultures. Suspicion is reinforced if there is a strong epidemiological correlation, especially in countries with high rates of M. tuberculosis infection, such as Brazil. Timely diagnosis and treatment of this condition are essential to reduce mortality from Perinatal TB, as well as meticulous prenatal care and treatment of maternal TB.

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