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Case Report

Early Diagnosis and Treatment Problems with Perinatal Tuberculosis as a Challenge to Health Care Providers

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Abstract: The diagnosis of tuberculosis (TB) in a newborn is often difficult as clinical signs are nonspecific. Neonatal infection is rare but it has a mortality up to 50%. The suspicion of TB in the mother is a powerful tool for diagnosis in the neonate, but physicians need to make mandatory steps to consider maternal TB in countries where the incidence is high. In this report we present two newborns with perinatal TB, the different clinical aspects in their mothers, and the problems that arised during investigation and diagnosis. We emphasize the need for improvement regarding screening of women at risk and sensitization of the medical community about this entity. We need to think in TB.

Keywords: Perinatal Tuberculosis, Mycobacterium Tuberculosis, Tuberculosis Control, Vertical Infection, Maternal-Fetal Infection

1. Introduction

Tuberculosis (TB) remains a major global health problem. It is the second leading cause of death from an infectious disease worldwide after HIV. [1] About one-third of the world's population is infected with Mycobacterium tuberculosis bacillus [2] In our country the incidence of TB is 21.9/100000; a half of new infections are women in reproductive age. [3] Congenital TB is a rare condition but it has a direct relation with the incidence of the disease in the population, with a mortality up to 50%. The term perinatal TB might be better to name tuberculous disease acquired before, during, or immediately after birth. [4] [5] Mycobacterium tuberculosis, the causative agent, may be transmitted from the infected mother to the fetus by the transplacental route or by aspiration of infected amniotic fluid or neonatally by postnatal direct contact. Also endometrial TB usually manifests as infertility; however congenital TB can be identified in the presence of asymptomatic maternal TB endometritis.

Genital TB is an important cause of infertility in Latin America with atypical presentations and misdiagnosis. It results in a low chance of conception, even after successful diagnosis and treatment, causes secondary amenorrhea and oligomenorrhea. [6]

Clinical diagnosis of TB may be difficult among pregnant women, because of similarities of the symptoms related to the physiological response to pregnancy. The majority of TB in pregnancy is diagnosed during the third trimester [7]

When Congenital TB result of haematogenous spread through the umbilical vein a primary focus subsequently develops in the liver, with involvement of the peri-portal lymph nodes and is possible detected whith ultra sound abdominal scan.

To detect and manage TB in the early newborn period a high index of suspicion, detailed maternal history and epidemiological views are requiered, since the proportion of women of child bearing age contracting tuberculosis increase worlwide. [8]

2. Cases Report

Patient 1: An emergency cesarean section was made to a

22-year-old homeless pregnant woman. Uncontrolled, she arrived with severe respiratory failure and stupor. A TB treatment with isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) was initiated after a chest radiograph showed miliary infiltrates and multiple caverns. The CS was made to treat fetal distress and hypoxemia. The surgeon described a miliary peritoneal seeding and ascitic fluid which was negative for acid-fast bacilli (AFB) staining. The following day the patient died, without the possibility of necropsy. In multiple samples of amniotic fluid, placenta and peritoneo there was not AFB, starting the long process of Mycobacterium tuberculosis specimen cultures. There was not pathologic TB findings in the placenta. Serologic testing for HIV was negative.

A 35 weeks premature male infant was born with 1500gr of birth weight, APGAR 7/8 Lubchenko SGA. He presented respiratory distress and required ventilation and surfactant replacement therapy. No AFB was isolated on tracheal aspirate, gastric lavage, blood and CSF which were cultured for mycobacteria and common germs. With suspected sepsis he began treatment with ampicillin and amikacin, associated with H. Only a PCR for Mycobacterium tuberculosis was positive in gastric and tracheal aspirates, after what we incorporated R and P to the treatment. The cerebro-spinal fluid was normal. The newborn developed jaundice and an increase in liver enzymes but ultrasonography did not show liver granulomas or portal system lymph nodes affected. The patient evolved favorably and graduated at 40 days of life with outpatient treatment with H and R. After discharge we received positive culture for Mycobacterium tuberculosis in the neonatal gastric and tracheal aspirates.

Patient 2: A 39 weeks term SGA male newborn baby was transferred from a primary health center to the neonatal reference center, with no health complications, weighing 2,215 grams with his mother, a 22-year-old G3 P2 undocumented and uncontrolled woman. Immediately and exclusively breastfed, with adequate thermal homeostasis, appropriate blood glucose level, respiratory stability and normal vital signs, only presented a mild jaundice with a bilirubin measurement of 9.39mg/dl. The full blood count including haematocrit and platelet count was normal, the same as tests for individual infections: Cytomegalovirus, Toxoplasmosis and Rubella (antibodies IgG, IgM), Chagas disease and Human immunodeficiency virus (ELISA) and Syphilis (VDRL).

A week later we decided it was the optimal time for discharge, with physiological stability, feeding progressing well with steady weight gain, no evidence of clinical illness, social support and an appropriate follow-up plan in the neighborhood health care center.

Two weeks after was readmitted with diagnosis of pneumonia, poor weight gain and emetic cough. On physical examination, his body temperature was 38.2°C, and heart rate 140 beats/min. He had a respiratory distress with a respiratory rate of 58 breaths/min. Arterial blood gas analysis showed pH, 7.35; PCO_2, 38.0 mmHg; PO_2, 98 mmHg; HCO_3, 20.5 mmol/L; base excess, − 4 mmol/L. The complete blood count showed hemoglobin, 10.6 g/dL; white blood cells, 18,500/mm^3 with segmented neutrophils of 63%; and platelets, 450,000/mm^3. C-reactive protein (CRP) level was 10.2 mg/L. Liver function tests showed normal levels of aspartate aminotransferase (15 IU/L) and alanine aminotransferase (18 IU/L). Chest X-ray revealed diffuse fine miliary infiltration in both lung fields.

Blood, urine, and cerebrospinal fluid cultures were negative for bacteria and fungi. No virus was detected in the polymerase chain reaction (PCR) of nasopharyngeal aspirates for respiratory virus and Bordetella Pertussis. Despite broad-spectrum antibiotic therapy and supportive care, respiratory distress continued to worsen over the next 48 hours, and chest X-ray infiltration did not improve with negative blood cultures. As her mother had productive cough, we performed a thoracic Rx that reveals the presence of bilateral pulmonary infiltrate, and “caving formation” present in both lungs. The diagnosis is far-advanced tuberculosis. The Mantoux test was 16 mm but she receive bacillus Calmette-Guerin vaccination at birth.

A new interrogatory was made and the mother confirmed TB diagnosis during pregnancy, an improper treatment regimens and failure to complete the whole course of treatment. Thereafter we stopped intravenous antibiotic therapy and started a therapy with four antituberculosis drugs isoniazid (7mg/kg/d), rifampicin (10mg/Kg/d), pyrazinamide (20mg/Kg/d), and ethambutol (15mg/kg/d) as empiric treatment with very good response.

3. Discussion

In 1994 Cantwell defined diagnostic criteria for congenital TB, following those first described by Beitzke in 1935, and still remains as the accepted standard in diagnosing congenital TB worldwide. According to Cantwell`s criteria, it is necessary at least one of the following: a) tuberculous lesions in the first week of life; b) primary hepatic complex; c) Confirmation of TB in the placenta, and d) exclusion of postnatal transmission. [4] Patient 1 didn´t fulfil Cantwell's criteria but had congenital TB. His mother had clinical features compatible with miliary gastrointestinal TB with a fatal outcome, which involves a high risk of congenital transmission of the disease. Maternal history and positive PCR made us start immediate treatment for TB. As a late sepsis we included antibiotics active against TB such as amikacin instead of gentamicin.

This is why it requires a high index of suspicion and should be valued with maternal clinical and epidemiological aspects, since mortality increases to 50% without adequate treatment and is imposible wait four or six weeks to obtain results in the traditional Lowenstein-Jensen's culture medium. Congenital TB is a rare condition but is associated with high neonatal and perinatal mortality.

Maternal TB diagnosis is difficult due to the non-specific symptoms, the increased frequency of extrapulmonary disease, the delay in radiological examinations, and the high rate of tuberculin anergy. Maternal history of tuberculosis is often

forgotten by obstetricians, neonatologists and midwives.

In patient 2, suspicion and interrogatory allowed a late diagnosis through a mother with few symptoms. Transmission is believed to be either in utero by haematogenous spread through the umbilical vein or ingestion of infected amniotic fluid; intrapartum aspiration or ingestion of amniotic fluid or direct contact with infected cervix/endometrium; or postpartum by inhalation or ingestion from an infectious source.

TB can mimic other common diseases in a newborn and, therefore, can be a difficult diagnosis to make. It is necessary to consider maternal TB in countries where incidence is high. When TB is suspected around delivery, the mother should be screening using tuberculin skin test, assessed by chest x-ray and sputum smear; separation of mother and offspring is indicated only if the mother is non-adherent to medical treatment, needs to be hospitalized, has close contact with relatives with infectious TB, or high risk of developing active disease or when drug-resistant TB is involved. [9]

The new interferon gamma release assay (IGRA) tests are recommended in BCG-vaccinated pregnant women with positive TST and no known risk factors for TB; or immunocompromised woman with clinical suspicion of TB but negative TST. [10]

Congenital TB is extremely rare and may be evident at birth but it usually presents after the second week of life. In newborns with no family history of TB, the disease should be considered in cases of miliary pneumonia, hepatosplenomegaly with focal lesions, or lymphocytic meningitis with hypoglycorrhachia, especially in our high TB-burden countries. TST is usually negative, IGRAs have lower sensitivity than in older children and positive amniotic fluid or gastric or tracheal aspitate smear especially in congenital TB, the best available marker fot TB for individual patient monitoring and for drug treatment.

4. Conclusion

Pregnant women should be screened regularly for the early detection, prevention, and TB treatment and for reduce perinatal TB. Newborn survival needs that health services, community, and family works with key interventions at all stages of pregnancy, delivery, postpartum, and postnatal care, particularly in TB hight prevalence settings, whith tuberculosis care recommended by WHO, United Nations Children's Fund, and the Global Fund to Fight AIDS, Tuberculosis, and Malaria.

We believe that the anamnesis is the parameter that allows a valid early diagnosis and a rapid initiation of treatment in cases with potential diagnosis of TB. Early diagnosis is a very important factor that affects prognosis.

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