Congenital Tuberculosis: A Case Report

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Congenital tubercolosis is an unusual and severe clinical pattern of tuberculosis presentation of *Mycobacterium tuberculosis* infection. Furthermore, it usually has a difficult treatment. We report a two-month-old male infant who presented with fever, dyspnea and a diffuse micronodular pattern at x-ray; mother with severe tuberculosis. Treatment with the triple drug regimen was initiated, but the child developed jaundice and an increase in liver enzymes on various occasions during treatment. A regimen specifically developed for cases of intolerance was initiated but there was no improvement in hyperthermia. Finally, the dose of INH and RMP was increased, the fever receded and the child was cured. This case remarks difficulties on diagnosis and therapeutic management about this important severe disease in public health, and alert for development of protocols that foresee these difficulties.

Key Words: tuberculosis, congenital, antituberculosis medication, mycobacterium.

A two-month-old male infant, mulatto, born in Salvador, Bahia, Brazil, was admitted to the hospital. According to his medical history, the patient was healthy at birth but at fifteen days after birth developed a progressively worsening state of dyspnea, fever, anorexia, abdominal distension, anemia, papular erythematous lesions on the trunk and upper limbs and low weight gain. When the child was two months of age, x-ray showed a miliary pattern (Figure 1), and he was admitted to hospital. He had been vaccinated with BCG and Engerix-B in his first month of life. His mother developed tuberculosis (TB) at the third month of pregnancy when she was accompanying a patient receiving care at the same hospital; however, following diagnosis she failed to use the prescribed medication. After giving birth, she was kept apart from the child and admitted to hospital for treatment in a critical state of health. The placenta was not examined maybe because of lack of resources. Treatment with the triple drug regimen (INH, RMP and PZA) was initiated in the child; however, intolerance developed, followed by clinical jaundice and a further increase in the child's already high liver enzymes. Treatment was interrupted, after which various treatment regimens were attempted with drugs specifically chosen to avoid intolerance(STM, and after ETH), and liver enzymes were monitored. Tests carried out consisted of: PPD, gastric lavages with culture for *M. tuberculosis*, VDRL, serological investigations for HIV, toxoplasmosis, CMV, herpes virus 1 and 2, rubeola, HBsAg, blood culture for pyogenes, myelogram and bone marrow cultures. All tests were negative. Abdominal ultrasonography revealed hepatosplenomegaly with increased echotexture of the liver. No granulomas were seen. HRCT of the thorax showed a diffuse micronodular pattern (Figure 2). A right cervical lymph node was seen but biopsy was not done. In view of the epidemiology and the toxemia, it was decided to continue monitored use of antituberculosis drugs and to manage the fever. In the third month of hospitalization, after careful reintroduction of INH, RMP and PZA, one after another and the maintenance of fever, we decided to increase the dose of INH and RMP to 20mg/kg/day. Within seven days, complete remission of fever was achieved. The child was released from hospital and followed up as an outpatient for one year. At the age 2, he begun to feel fever, was admitted in a infectious disease hospital and was diagnosed as meningitis with a negative cytology and high protein level. Culture was negative, but tuberculosis reactivation was raised as possibility. He started using triple drug regimen but died at the fourth day of treatment.

Discussion

Of all the clinical manifestations of tuberculosis, congenital tuberculosis is rare [1,2]. Despite the high incidence of tuberculosis in women of reproductive age, of subclinical forms of the disease during pregnancy, and the lack of adequate prenatal care in countries with a low development rate, this incidence is estimated at only 2%. Some authors believe that under-notification of cases could explain this phenomenon [3]. The appearance of AIDS has contributed towards an increase in the incidence of the disease, thereby increasing the risk of congenital tuberculosis. Although the incidence is low, congenital TB is generally a serious manifestation with a mortality rate of 22% among patients receiving chemotherapy [4].

Fetal contamination by mycobacteria may occur hematogenously or by pulmonary aspiration of contaminated amniotic liquid.

It is difficult to reach an etiological diagnosis according to severity or using the available means, since PPD is negative in the first four weeks of the disease, and sputum microscopy

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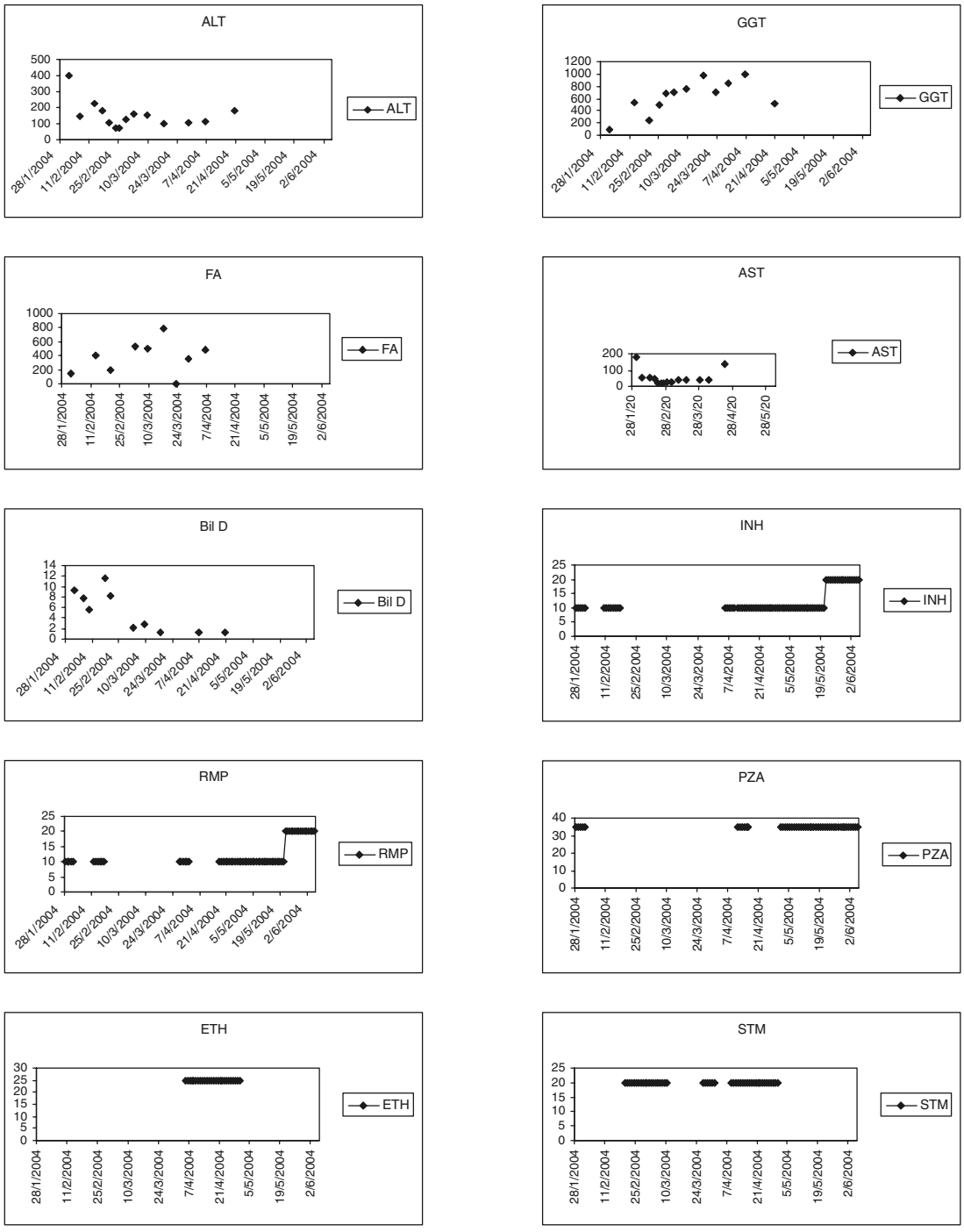
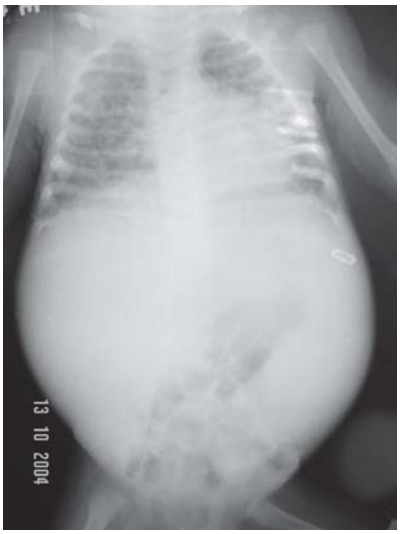
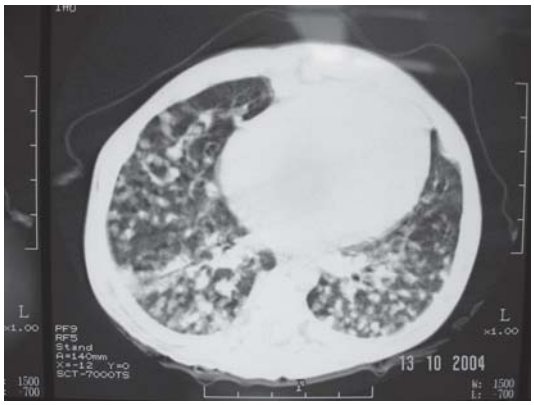
Figure 1. Evolution of the laboratorial exams, and correlation with the use of drugs during treatment in a case of congenital tuberculosis.



and cultures are frequently negative. However, the possibility of the presence of this disease should always be considered. In the case described above, M. tuberculosis was not detected; however, the history of the mother and the clinical status of the patient suggested empirical therapy. Cantwell et al proposed criteria for the diagnosis of congenital TB. 1) Clinical manifestation of the disease in the first two weeks of life; 2) Rigorous exclusion of contact with the mother or any other affected persons; 3) Primary focus or granulomas in the liver; 4) Contamination of the placenta or extensive contamination

Figure 2. Image exams made during treatment of a two-three month-old congenital tuberculosis patient.





of the genital area. These criteria increase diagnostic sensitivity, leading to earlier initiation of therapy. However, this diagnosis is often difficult since confirmation of the primary complex or detection of granulomas in the liver has to be carried out by biopsy, which is not always available in some healthcare centers, or at autopsy. Reduced positivity following initiation of treatment should also be shown [5].

The most important point that should be emphasized in the management of this case is the difficulty in treatment. In children with congenital TB, the liver is usually affected first, which adds to the hepatoxicity of the therapeutic regimens currently available. Alternative regimens had to be found to reverse clinical state. As all the strategies were tried and the patient continued presenting persisted with fever, when the liver enzymes were stabilized, albeit not yet at normal values, the decision was taken to increase the dose of INH and RMP to 20 mg/kg/day and it was only in response to this change in therapeutic regimen that fever ceased and the patient improved. This may be occurred because liver tolerance to the medications raised at this time and patient could be correctly treated.The reasons why he did not responded to the first lower doses of the medications must be because of the bacilli amounts, or even because treatment time was not long enough, as he developed liver disease. Another possibility is that meninges was involved, and dose had to be increased.

This case illustrates some important obstacles that exist in the management of this disease, such as inadequate epidemiological surveillance for the management of pregnant women with tuberculosis; negligence with respect to early diagnosis (examination of the placenta and amniotic fluid, lack of referral of the newborn to a specialized healthcare service) and the consequent delay in diagnosing the disease; and difficulty in treatment due to intolerance to the medication, leading to the implementation of strategies to cope with the child's hepatic lesion. Therefore, these are important issues that have to be taken into consideration to improve the efficacy of diagnosis and therapy of this serious disease.

Conclusion

This case illustrates the difficulties in diagnostic and therapeutic conduct of this disease, which are of great interest to public health, and points to the need to develop specific protocols to deal with these situations.

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