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Letter to the Editor

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Congenital tuberculosis in a premature newborn

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Sir,

According to the World Health Organization, tuberculosis (TB) is among the ten leading causes of mortality and the first etiology of infectious diseases globally [1,2]. The congenital form is an infrequent presentation of TB (only 300 cases have been reported in the English literature [3]), and it occurs in newborns of mothers who develop active disease during pregnancy or have silent genital TB [3].

The most frequent TB clinical form in pregnant women is extrapulmonary, and it is very difficult to diagnose due to the high variability of symptoms [3]. In newborns, it may present nonspecific clinical manifestations such as irritability, fever, cough, respiratory distress, hepatosplenomegaly, lymphadenopathy, and abdominal distension [3].

We present a congenital TB case in a female newborn to a dichorionic diamniotic twin gestation, who was admitted to the pediatric ICU due to severe respiratory distress and prematurity. Bronchopneumonia of possible fungal etiology was suspected to be the cause of the distress, as chest X-rays (Figure 1) showed bilateral infiltrates. Chest computerized tomography (CT) scans (Figure 2) reported areas of pulmonary consolidation and hepatosplenomegaly.

Treatment started with ceftazidime (33 mg/kg/8h) and vancomycin (15 mg/kg/6h). As there was no clinical improvement, treatment was changed to meropenem (20 mg/kg/8h), azithromycin (20 mg/kg/day), cotrimoxazole (10/50 mg/8h), and fluconazole (12 mg/day). Persistent polypnea continued, so fluconazole was substituted for amphotericin B (5 mg/kg/day) and caspofungin (2 mg/day). Despite respiratory support and empiric broad-spectrum antimicrobial therapy, she did not respond adequately.

After that, hemophagocytic syndrome (HPS) was suspected as it met six of the eight criteria described by the Spanish Association of Pediatrics (AEPED) [4] for its diagnosis, namely: prolonged fever, hepatosplenomegaly, cytopenias (anemia, thrombocytopenia, and leukopenia), hyperferritinemia (2,129-3,212 ng/mL), hypofibrinogenemia (83 mg/dL) and elevated soluble CD25 (470 µL).

The first bronchoalveolar lavage's auramine stain was negative, but at 14 incubation days, MGIT culture and the confirmatory Ziehl-Neelsen stain were positive for *Mycobacterium tuberculosis*. IGRA was not performed as the patient was a newborn. Neonatal anti-tuberculous treatment was started (according to the 2016 SEIP consensus [5]) with isoniazid (15 mg/kg/day), rifampicin (20 mg/kg/day), pyrazinamide (35 mg/kg/day) and amikacin (15 mg/kg/day). She developed hepatotoxicity, so pyrazinamide was changed to levofloxacin (7.5 mg/kg/day), as it is a second-line anti-tuberculous drug and because of its good diffusion to the central nervous system [6]. The patient had complicated hepatosplenomegaly with hepatic and splenic microabscesses, which evolved into calcified granulomas [evidenced by abdominal ultrasound (Figure 2)]. On the other hand, HPS resolved spontaneously when TB was treated.

The patient's twin sister was born healthy. The mother, a 37-year-old Moroccan woman, was asymptomatic and apparently without any clinical background of interest. IGRA was not performed beforehand as the parents reported that it was done in a private clinic, and it was negative. No abnormalities were seen in the chest X-ray, and the sputum's Ziehl-Neelsen stain and cultures were negative. The endometrial aspirate culture was positive for *M. tuberculosis*, so she also started treatment with isoniazid, rifampicin, pyrazinamide, and ethambutol.

The patient completed 1-year oral maintenance anti-tuberculous treatment with isoniazid (90 mg/day), rifampicin (90 mg/day), and pyridoxine (12.5 mg/day) with good response. A contact study was not performed as the parents were asymptomatic, and it was suspected that the mother had a disseminated TB years before.

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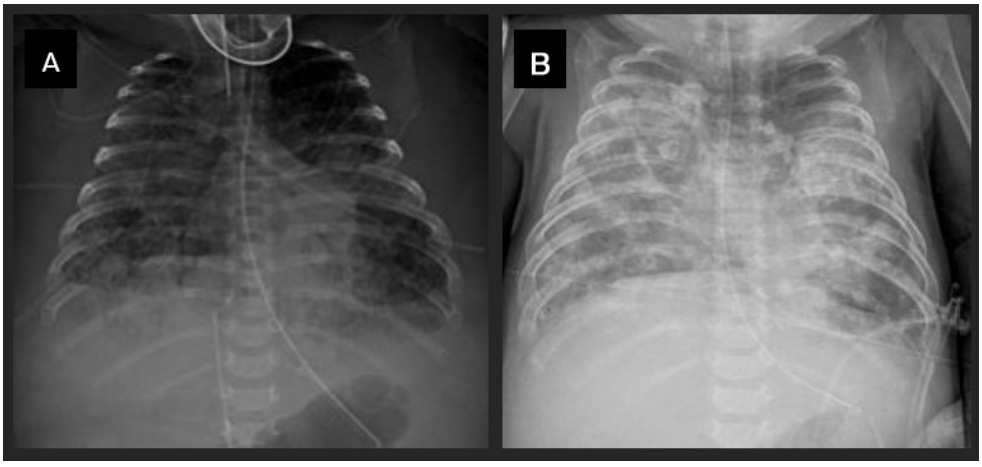

Figure 1 | **Chest X-ray at birth (A): Bilateral infiltrates, predominantly in the right lung. Chest X-ray at 60 days (B): Pulmonary nodules consistent with miliary tuberculosis.**

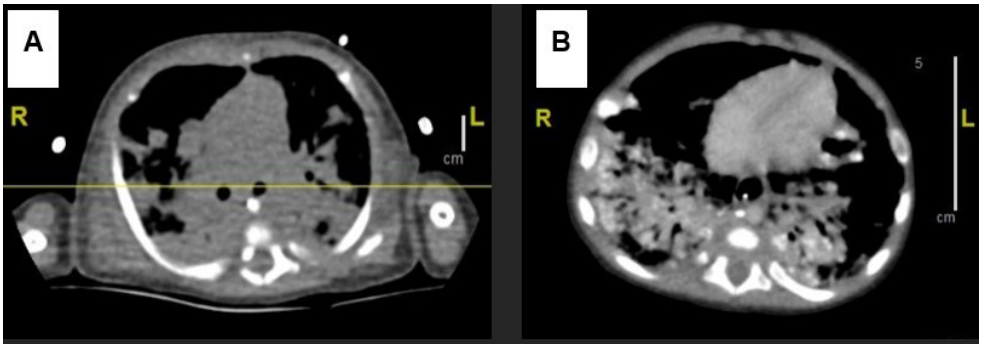

Figure 2 | **Chest CT at birth (A): Diffuse patchy nodular images of consolidation in both lung fields that coalesce to form larger areas of consolidation with air bronchogram. In LIL there is a zone in the area of greatest consolidation that could suggest the beginning of pulmonary cavitation; and 60 days later (B): Pulmonary granulomas, cavitations in the left lung and hilar and mediastinal adenopathies.**

TB continues to be a global public health problem and approaching its diagnosis to pregnant women and their newborns represents a daunting challenge for clinicians. An exhaustive epidemiological background study is crucial to firstly establish a high level of suspicion, and secondly integrate this pathology into the differential diagnoses of multiple clinical conditions that are observed in pregnant women and newborns.

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None to declare

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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