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Abstract: RATIONALE: Congenital tuberculosis (TB) is described as a rare, but severe disease. In contrast to the cases with severe symptoms reported so far, we describe a child with asymptomatic congenital TB. PATIENT CONCERNS: An 8-week-old girl was investigated because of newly diagnosed TB in her mother, which complained about cough since 21 weeks gestation. Lung biopsy tissue specimens of the mother revealed necrotizing granuloma with a single acid-fast bacillus (AFB) and Mycobacterium tuberculosis (MTB) was detected by polymerase chain reaction. Bronchoalveolar lavage was negative for AFB smear and culture, arguing against postnatal transmission of MTB. TB contact investigations were negative. The child, at the age of 8 weeks at first assessment, was in an excellent general condition and diagnosed with congenital TB by culture-positive lung TB and exclusion of postnatal transmission. DIAGNOSES: The child fulfilled Cantwell criteria to diagnose congenital TB. INTERVENTIONS: Ambulatory anti-tuberculosis treatment was initiated for 6 months. OUTCOMES: The 18 months follow-up was uneventful. LESSONS: This case of asymptomatic congenital TB in a young child illustrates the diagnostic difficulties in congenital TB and raises the question whether congenital TB is underestimated.

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Asymptomatic congenital tuberculosis

A case report

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Abstract

Rationale: Congenital tuberculosis (TB) is described as a rare, but severe disease. In contrast to the cases with severe symptoms reported so far, we describe a child with asymptomatic congenital TB.

Patient concerns: An 8-week-old girl was investigated because of newly diagnosed TB in her mother, which complained about cough since 21 weeks gestation. Lung biopsy tissue specimens of the mother revealed necrotizing granuloma with a single acid-fast bacillus (AFB) and *Mycobacterium tuberculosis* (MTB) was detected by polymerase chain reaction. Bronchoalveolar lavage was negative for AFB smear and culture, arguing against postnatal transmission of MTB. TB contact investigations were negative. The child, at the age of 8 weeks at first assessment, was in an excellent general condition and diagnosed with congenital TB by culture-positive lung TB and exclusion of postnatal transmission.

Diagnoses: The child fulfilled Cantwell criteria to diagnose congenital TB.

Interventions: Ambulatory anti-tuberculosis treatment was initiated for 6 months.

Outcomes: The 18 months follow-up was uneventful.

Lessons: This case of asymptomatic congenital TB in a young child illustrates the diagnostic difficulties in congenital TB and raises the question whether congenital TB is underestimated.

Abbreviations: AFB = acid-fast bacillus, BAL = bronchoalveolar lavage, CT = computed tomography, IGRA = interferon-gamma release assay, IVF = in vitro fertilization, MTB = *Mycobacterium tuberculosis*, PCR = polymerase chain reaction, TB = tuberculosis, TNF = tumor necrosis factor, TST = tuberculin skin test.

Keywords: asymptomatic, congenital, miliary, tree-in-bud opacities, tuberculosis

1. Introduction

Congenital tuberculosis (TB) is difficult to diagnose.[1] We were recently challenged by a child with culture-proven lung TB acquired by vertical transmission illustrating these diagnostic difficulties in clinical practice. Interestingly, in contrast to the cases of congenital TB with severe symptoms reported so far,[2] this child did not manifest any symptoms.

2. Case report

An 8-week-old girl was investigated because of newly diagnosed TB in her mother, which presented the first time 4 weeks after birth with a cough that emerged at 21 weeks gestation, during treatment of indeterminate colitis with the anti-tumor necrosis factor (TNF)-α antibody adalimumab (Fig. 1A). She was HIV negative. No radiographic studies were conducted so far. The interferon-gamma release assay (IGRA), performed before pregnancy under treatment with prednisolone because of colitis, was negative. Her computed tomography (CT) scan 4 weeks after delivery showed numerous nodules and tree-in-bud opacities (Fig. 1A1), a pattern characteristic for miliary TB.[3] Lung biopsy tissue specimens revealed necrotizing granuloma (Fig. 1A2) with a single acid-fast bacillus (AFB) (Fig. 1A3), and *Mycobacterium tuberculosis* (MTB) was detected by polymerase chain reaction (PCR). Bronchoalveolar lavage (BAL) was negative for MTB, arguing against postnatal transmission of MTB. TB contact investigations led to the investigation of this child and were otherwise negative.

The child, at the age of 8 weeks at first assessment, was in an excellent general condition (Fig. 1B). Pregnancy induced by in vitro fertilization (IVF), birth, and neonatal period were unremarkable. Physical examination, laboratory evaluation, abdominal ultrasound, and chest x-ray were normal (Fig. 1B1). Surprisingly, the tuberculin skin test (TST) was positive with an induration of 9×6 mm at 8 weeks of age, and 20×10 mm at 10 weeks of age. Three gastric aspirates did not show AFB by microscopy, but 1 grew MTB in culture after

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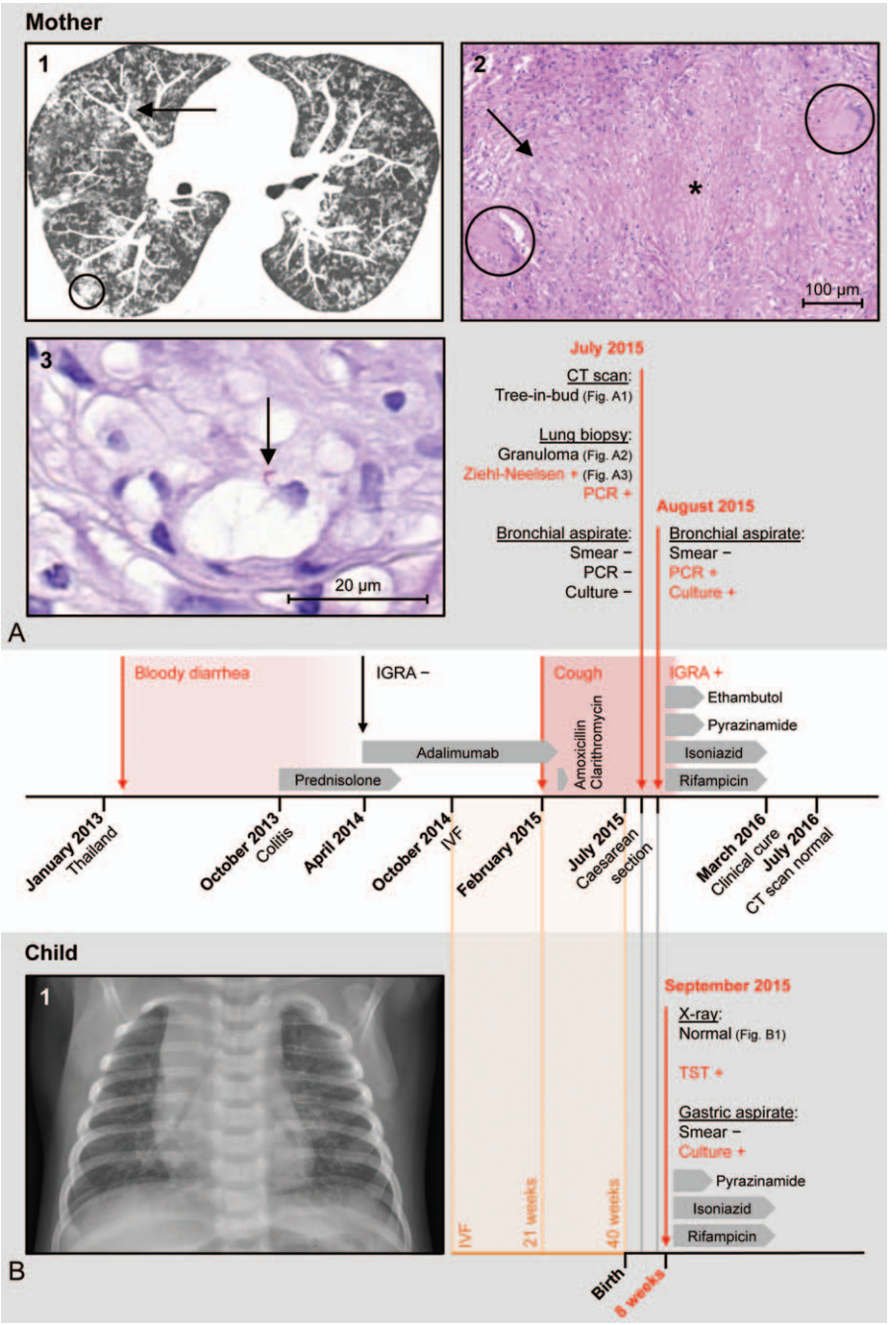

Figure 1. The course of TB in the mother (A) and the child (B). There are 2 *x* axes: the *x* axis above is the timeline of the medical history of the mother (panel A: January 2013–December 2016), and below the timeline of the medical history of the child (panel B: October 2014–December 2016). Symptoms of the mother are indicated as red areas (*x* axis above), and pregnancy is shown as orange area (*x* axis below). Investigations positive for TB are indicated in red (both cultured strains from the mother and the child were identical in sequence and fully susceptible). Treatment regimens are shown as grey arrows. A1: CT scan (axial view) with miliary nodules (circle) and tree-in-bud opacities (arrow). A2: Histopathology of miliary nodules (hematoxylin and eosin stain) showing granuloma characterized by necrotic caseating granuloma center (asterix), epitheloid histiocytes (arrow), and Langhans giant cells (circle). A3: Single acid-fast curvilinear bacillus in lung biopsy tissue specimen (Ziehl-Neelsen stain). B1: Chest x-ray of the child at diagnosis of congenital TB. The TST was performed with 0.1 mL (2 units) PPD RT23 SSI, Statens Serum Institute, Denmark. The placenta was not available for further investigations at diagnosis. Informed consent was given by the mother of the patient. CT = computed tomography; IGRA = interferon-gamma release assay; IVF = in vitro fertilization; PCR = polymerase chain reaction; TST = tuberculin skin test.

3 weeks. Ambulatory anti-tuberculosis treatment was initiated for 6 months (Fig. 1B). The 18 months follow-up was uneventful.

3. Discussion

Both anti-TNF-α treatment and pregnancy are associated with an increased risk of miliary TB.[3] Infertility (requiring IVF)[1,4] and colitis[3] as present in the mother have been associated with genital and intestinal TB, respectively. In fact, cough and colitis completely resolved after initiation of anti-tuberculosis treatment. Disseminated miliary TB in the immunocompromised mother may be in line with hematogenous spread of MTB to the child in utero.[3]

Congenital infection is further supported by the strongly positive TST of the child already at 8 weeks of age. TST conversion occurs

within 6 to 8 weeks after infection, and again in congenital TB the TST is reported to convert months after birth.[5] Together with the negative BAL of the mother 4 weeks after delivery it seems less likely that TB was acquired after birth. We lack the examination of the placenta to eventually proof vertical transmission. Nevertheless, the child indeed fulfilled Cantwell criteria[5] to diagnose congenital TB, that is, culture-positive lung TB and exclusion of postnatal transmission by thorough contact investigation.

In conclusion, this case illustrates the challenges in diagnosing congenital TB and raises the question whether congenital TB can present as asymptomatic infection.

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