CASE REPORT

A paradoxical reaction during antituberculosis therapy for congenital tuberculosis

Ji Ae Park, Seong Shik Park, Su Eun Park*

Department of Pediatrics, School of Medicine, Pusan National University, Busan, Korea

Introduction

A ‘paradoxical reaction’ (PR) is defined as the worsening of clinical or radiological findings following the initiation of appropriate antituberculous treatment.1—7 Once treatment starts, there should be no evidence of disease relapse or a second diagnosis. A PR has been reported in 5—35% of patients receiving treatment for tuberculosis (TB), mostly in immunocompromised patients (such as those with HIV infections).2,5,8 There are no known prior reports of a PR in patients with congenital TB. Here, we report an infant diagnosed with congenital TB who developed a PR during TB therapy and improved after the administration of oral prednisolone.

Case report

A 21-day-old female infant presented with fever and dyspnea for four days, and was referred from a local hospital. The history was significant for treatment with antibiotics for five days because of a fever without a focus four days after birth. Although no organisms were identified at that time, the baby was diagnosed with sepsis. On admission to our hospital, the patient had mild subcostal retractions and tachypnea, and chest radiography showed diffuse patchy opacities. Our initial diagnosis was sepsis caused by pneumonia. Despite antibiotic treatment, the tachypnea and fever persisted, and serial chest radiography showed progression of the lung pathology with the presence of bilateral patchy opacities. The patient’s mother had a persistent cough for about one month before delivery, and was diagnosed with TB and pleurisy in a community hospital on the ninth day of her hospital stay. We evaluated the baby for congenital TB. Bacterial cultures of the blood, cerebrospinal fluid and urine were negative. The analysis of the cerebrospinal fluid was
normal. Gastric aspirates contained acid-fast bacilli (AFB) on stain, the AFB cultures, and PCR for *Mycobacterium tuberculosis* were positive. The tuberculin skin test was negative. A chest radiograph showed bilateral multiple nodular opacities, and a computerized tomography (CT) of the lung revealed enlargement of the lymph nodes in the subcarinal and bilateral hilar regions, as well as diffuse multiple nodules in both lung fields (Figure 1). Based on the history and clinical findings, we diagnosed the baby with congenital TB and treatment (rifampicin 10 mg/kg, isoniazid 10 mg/kg, pyrazinamide 25 mg/kg, streptomycin 20 mg/kg) was started. Fourteen days after treatment, the clinical symptoms improved and the patient was discharged. However, she was readmitted to hospital two months later with a fever, cough, wheezing and respiratory difficulties. Direct observed therapy (DOT) is not performed in our country. The patient was reported to be taking the medication at home daily; good compliance was verified by the remaining drug. A follow-up chest CT showed aggravation of the pre-existing TB lesion (Figure 2). Gastric aspirates contained AFB on stain, the AFB culture, and PCR for *M. tuberculosis* were all negative. The

*Discussion*

The development of a PR during the treatment of TB is difficult to distinguish from treatment failure, drug resistance or another secondary infection. A PR is defined as the worsening of clinical or radiological findings, following the initiation of appropriate TB treatment, in the absence of evidence of disease relapse or another diagnosis.1–7 The development of a PR is not uncommon; it is reported in up to 35% of immunocompromised patients with HIV infection and in fewer than 5% of immunocompetent patients.2,5,8 Our case was a neonate with an immature immune system. Most cases of PR have been described in adults, particularly in the setting of recovering host immune function. T-cell responses in neonates are defective. Qualitative and quantitative differences have been observed compared with adult immune responses.9 Cytokine-secreting T cells increase significantly and promote humoral and cellular immune responses during the first six months of life.10 Therefore, the relative immaturity of immune responses in neonates is similar to that of adult patients recovering from deficiencies in cell-mediated immune responses.

The pathogenesis of a PR is unclear, but probably has an immunological basis. There are two hypotheses: the reconstitution of host immune responses after the initiation of antituberculosis therapy and a hypersensitivity reaction to the antigens released from dying tubercle bacilli.2,8,11 Patients identified with a PR generally have a negative tuberculin skin test and decreased lymphocyte blastogenesis at the time of diagnosis, but a positive tuberculin skin test and increased lymphocyte blastogenesis after the initiation of therapy.11–13 These findings might support the hypothesis of reconstitution of the immune response. In our case, the patient had a higher lymphocyte count within four weeks of the start of treatment. This finding might support the hypothesis of hypersensitivity to the dying bacilli; lipoarabinomannan, a protein found in the cell wall of *M. tuberculosis*, induces tumor necrosis factor-α from mononuclear phagocytes.2,3,11,14,15 It was not necessary to change or discontinue the TB treatment because 95% of mycobacteria isolated were susceptible to the initial medication used for therapy.5 Treatment of PRs includes systemic corticosteroid therapy and surgical intervention.2,3,5,16 The effect of steroid treatment is probably the immunological regulation and reduction of intracranial tuberculoma edema. Our patient’s symptoms improved after treatment with oral prednisolone.

In conclusion, congenital TB is rare.17 There have been no previous reports of a PR in a patient with congenital TB during the course of treatment. The possibility of a PR should be considered in TB cases with clinical deterioration. In cases

Figure 1  Chest CT scan showing enlargement of lymph nodes in the subcarinal and bilateral hilar regions, and diffuse multiple nodules in both lung fields.

Figure 2  Follow-up chest CT scan showing progression of the pre-existing TB lesion.
confirmed to be a PR, corticosteroid treatment appears to be effective therapy.

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References


