Paradoxical Deterioration During Anti-Tuberculous Therapy in Non-HIV-Infected Patients with Pleural Tuberculosis: A Pragmatic Approach

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ABSTRACT
We report a case of paradoxical deterioration. A male patient diagnosed with pleural tuberculosis, but who was not infected with human immunodeficiency virus (HIV), experienced clinical deterioration 3 weeks after the initiation of anti-tuberculous treatment. After other diagnoses were ruled out, a paradoxical response to treatment was established and the patient was started on systemic corticosteroids. Paradoxical response to treatment should be considered in patients with clinical deterioration after they start on anti-tuberculous treatment.

LEARNING POINTS
• The deterioration of patients with pleural tuberculosis during anti-tuberculous treatment should raise the suspicion of paradoxical response to treatment.
• Despite the clinical deterioration, patients should be kept on anti-tuberculous treatment.
• There is no clear evidence concerning the benefits and harms of systemic corticosteroids or pleural drainage as additional treatment to control the patient’s symptoms in this scenario.

KEYWORDS
Pleural tuberculosis, antitubercular agents, paradoxical response

INTRODUCTION
Clinical or radiological worsening of pre-existing tuberculous in a patient after they have start on specific treatment is defined as paradoxical response to treatment. Although paradoxical reactions are more common in human immunodeficiency virus (HIV)-infected patients, they can also be diagnosed in HIV-uninfected patients.[1] Paradoxical worsening of tuberculous pleural effusion is a rare condition with only a few cases published.[2]
Immunopathological damage as a consequence of an exaggerated and dysregulated host’s inflammatory response or the excessive antigen load resulting from rapid mycobacterial lysis after initiation of treatment have been suggested as explanations for paradoxical worsening. It has not been established how clinicians should deal with such patients. In this paper we describe the case of a patient with a paradoxical response. In the discussion, we highlight the rationale for his differential diagnosis and the approach proposed for managing the patient’s deterioration.
CASE REPORT
A 44-year-old man was referred to our clinic because of fever, arthralgia and myalgia. Clinical assessment, blood tests and chest x-ray were uninformative. The patient was prescribed symptomatic treatment and scheduled for another appointment 4 weeks later. On the second visit, patient reported shortness of breath and pleuritic chest pain on the left side where he had developed pleural effusion (Fig. 1). C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were raised (23 mg/l and 49 mm/h). A thoracentesis showed a lymphocytic exudate with an adenosine deaminase (ADA) level of 50 IU/l. A QuantiFERON-TB test was positive, while an HIV test was negative. The patient was diagnosed as likely having tuberculosis and started on isoniazid, rifampicin and pyrazinamide.

The patient still remained in poor health 4 weeks after starting treatment. He reported a slight clinical improvement during the first 3 weeks, but then began to feel even worse than before treatment initiation. On analysis his CRP and ESR were raised (106 mg/l and 67 mm/h), while his blood count, liver enzymes, urea, creatinine and electrolytes were normal. Pleural effusion remained similar on x-ray (Fig. 2). Pleural aspiration was repeated showing non-complicated lymphocytic exudates. Due to his poor health, the patient was started on a short course of corticosteroids, with clinical improvement noted after the first week. The patient completed the 6-month treatment schedule for tuberculosis with complete clinical resolution of disease except for slight residual pleural thickening on chest x-ray (Fig. 3).

Figure 1. Chest x-ray before the patient started on anti-tuberculous treatment
Figure 2. Chest x-ray after 4 weeks of anti-tuberculous treatment
Figure 3. Chest x-ray 3 months after completion of anti-tuberculous treatment
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