

## Commentary

Paradoxical reactions are defined as transient worsening or appearance of new signs, symptoms, or radiographic manifestations of tuberculosis (TB) that occurs after initiation of treatment and not as a result of treatment failure or other second process. These are usually seen as enlargement of old lesions or unexpected new ones during apparently adequate anti-tuberculosis therapy.<sup>[1]</sup>

Paradoxical response has been classically described in patients with intracranial tuberculoma and lymph node tuberculosis, although it may occur at pulmonary as well as at extra pulmonary sites.<sup>[2]</sup> In this issue, Das *et al.*<sup>[3]</sup> have reported 5 cases of pulmonary and extra-pulmonary TB who developed paradoxical response as symptomatic cerebral tuberculomas during course of their illnesses. Paradoxical response generally occurs 3 to 12 weeks after beginning of anti-tuberculosis therapy; however, it may be observed even later i.e. after 4 months of successful chemotherapy for abdominal TB<sup>[4]</sup> and as late as 6 to 7 months in intracranial tuberculomas.<sup>[5]</sup>

The exact mechanism of this unusual event remains unclear. It has been suggested that active TB can result in immune suppression through an altered cell-mediated response. Once active TB is under control after an appropriate therapy, enhanced focal immune responses (immunological rebound) will recruit lymphocytes and macrophages at the site of these lesions, which then enlarge and become evident.<sup>[6]</sup> Hypersensitivity to tuberculo-proteins released by dying mycobacteria may be other factor as well.<sup>[7]</sup> These events are more frequent among HIV-infected persons receiving anti-retroviral therapy (ART) and are probably related to re-constitution of T cell proliferation and function leading to increased interferon- $\gamma$  secretion after starting ART.<sup>[8]</sup>

The diagnosis of paradoxical response is often by the exclusion of treatment failure due to drug resistance, drug hypersensitivity, and other infections common among immune-compromised patients. It is also important to consider other causes of inadequate response such as wrong diagnosis, inadequate drug regimen, poor treatment compliance, poor drug absorption, atypical mycobacterial disease etc. before attributing their signs and symptoms to paradoxical response.<sup>[9]</sup>

The management of mild to moderate reactions is

conservative including reassurance and perhaps non-steroidal anti-inflammatory agents. Most of the reactions subside by itself in about a month without a change in the anti-tuberculosis drug regimen. Severe reactions such as those causing pressure symptoms and expanding tuberculomas requires systemic corticosteroid therapy. Clinicians must be aware of these frustrating otherwise benign events that may be observed during TB treatment.

Ramakant Dixit, Jacob George P, Smita Sharma

Department of Tuberculosis & Respiratory Medicine,  
J L N Medical College, Ajmer, India

**Address for correspondence:**

Dr. Ramakant Dixit,  
Consultant Pulmonologist,  
A-60, Chandravardai Nagar,  
Ajmer Rajasthan, India.  
E-mail: dr.ramakantdixit@gmail.com

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