

## Commentary

Mycobacterial infections have long been associated with a paradoxical response to treatment, the reversal reaction in leprosy being the prototype.<sup>[1]</sup> The paradoxical reaction is a clinical or radiological worsening of infectious disease, or the development of new lesions, in a patient that initially responded to treatment.<sup>[2]</sup> This behavior is unusual in the normal course of the disease and hence a paradox.

Paradoxical reaction has been extensively described in HIV-positive patients started on Highly Active Anti-Retroviral Therapy (HAART).<sup>[3]</sup> It is likely to occur when there is a latent, occult, or past infection; many *Mycobacterium* species and other organisms have been implicated. It has been attributed to a sudden, inappropriate, treatment-induced surge in immunity causing an intense reaction to the infective pathogen, and resulting in the immune reconstitution inflammatory syndrome (IRIS).<sup>[4]</sup> Occurring in 10-25% of patients,<sup>[1]</sup> IRIS is usually self-limiting; however, fatal reactions have been described, particularly when the reaction involves the central nervous or respiratory systems.<sup>[4,5]</sup>

Over several years now, reports of paradoxical reactions in HIV-negative patients have been coming in, particularly in extra-pulmonary tuberculosis (2.3% to 24% of all cases).<sup>[2,6,7]</sup> The reaction is attributed to a clash between excessive antigen load from treatment-induced bacteriolysis and a reconstituted immunity.<sup>[2]</sup> Paradoxical reactions may develop within days, but are most commonly seen in the first few months of starting treatment. Their occurrence, when the patient is responding to anti-tubercular treatment, may confuse clinicians as the manifestations may be difficult to differentiate from drug resistance, relapse, or from treatment failure due to poor compliance or poor absorption of the drug.<sup>[2,7]</sup> In this context, the experience of Das *et al*, 2012, is helpful.<sup>[8]</sup> In this issue of the Journal of Neurosciences in Rural Practice, they report that a high index of suspicion is important in the diagnosis of paradoxical reaction. The clue is that these patients demonstrate good initial response to treatment with documented compliance. Their response to corticosteroid treatment clinches the diagnosis.

In order to be able to predict which patient is likely to develop a paradoxical reaction, researchers are attempting to identify risk factors.<sup>[9]</sup> In HIV-positive patients, a lower CD4 count is implicated;<sup>[4]</sup> in HIV-negative patients, younger age, anemia, and lymphopenia at baseline are reported to be independent risk factors.<sup>[9]</sup> More studies on larger samples will help elucidate the role of risk

factors so that patients recently started on anti-tubercular treatment can be monitored for the development of paradoxical response depending on their baseline characteristics. As described by Das *et al*, once treatment compliance is ascertained, patients suspected to have paradoxical reaction should continue on anti-tubercular treatment; corticosteroids may be added or the dose can be enhanced to limit the inflammatory damage.<sup>[8]</sup>

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