

Case Report

Immune reconstitution inflammatory syndrome in non human immunodeficiency viruses children on anti tubercular treatment

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ABSTRACT

The term IRIS is almost solely used in human immunodeficiency virus seropositive patients who initiated anti-retroviral therapy (ART), the term paradoxical reaction is generally used to describe a clinical worsening of tuberculosis disease after the initiation of antituberculosis treatment. Distinguishing this paradoxical reaction (PR) from disease progression or treatment failure is an important issue in CNS tuberculosis management. Thus, one must keep a watch for neurological deterioration in a child with Central nervous system tuberculosis (CNS TB). We are presenting a case of a non-Human immunodeficiency virus (HIV) child who developed TB-IRIS while on anti-tubercular drugs, who subsequently responded to steroids along with continuation of antitubercular treatment (ATT).

Keywords: Anti retro viral therapy, Antitubercular treatment, Central nervous system tuberculosis Immune reconstitution Inflammatory syndrome, Human immunodeficiency virus, Paradoxical reactions

INTRODUCTION

Tuberculosis-associated IRIS can present as one of two main syndromes: paradoxical reaction after the start of ART in patients receiving tuberculosis treatment ("Paradoxical" tuberculosis-associated IRIS) or a new presentation of tuberculosis that is "unmasked" in the weeks following initiation of ART ("unmasking" tuberculosis associated IRIS).¹

Paradoxical reactions (PR) are defined as transient worsening or appearance of new signs or symptoms or radiographic manifestations of tuberculosis that occur after initiation of treatment and are not the result of treatment failure.²

The time of onset of PR is defined as the number of days from the start of treatment to the commencement of deterioration. The median duration of PR is two-three

months.^{3,4} Paradoxical neurologic TB-IRIS accounts for 12% of paradoxical TB-IRIS cases.⁵ Neurologic TB-IRIS include new or recurrent neurologic symptoms and signs like headache, focal neurologic deficits, nuchal rigidity, confusion, seizures, cerebellar signs, cognitive impairment or psychiatric manifestations.^{5,6} A case of non-HIV child with CNS tuberculosis developing PR after start of ATT has been reported.

CASE REPORT

A 6yrs girl presented with history of fever for 8 days and 1 episode of generalized tonic clonic convulsions on day 8 of fever. The child was initially admitted in a nearby hospital, where she was diagnosed and treated as bacterial meningitis. In view of persisting meningeal signs and fever despite of appropriate treatment, child was re-evaluated, repeat CSF analysis was suggestive of

TB meningitis as seen in (Table 1). CSF showed cobweb formation. CSF culture did not grow any organism.

Table 1: CSF examination.

CSF Examination	Results
Sugar	35mg/dl
Protein	380g
LDH	32U/L
Cells	50, all lymphocytes

CT brain and chest X-ray were normal, Mantoux test was negative, child was put on ATT and steroids. Child improved symptomatically, she was discharged on ATT.

After 21 days of ATT, child again developed neck stiffness and fever. On further evaluation child had signs suggestive of meningitis with left sided facial nerve weakness. MRI brain showed ring enhancing lesions with perilesional oedema scattered over cerebrum, cerebellum as shown in (Figure 1).

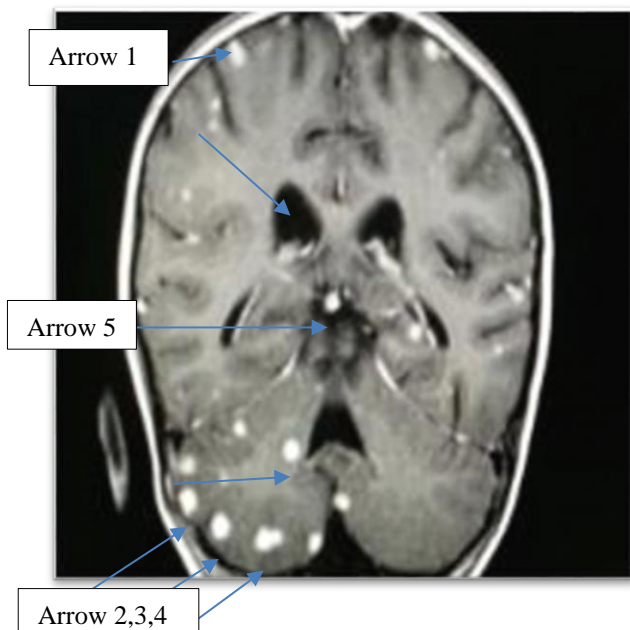


Figure 1: 6 year girl with reactivation of CNS tuberculosis after starting ATT i.e. IRIS. MRI brain of this child shows ring enhancing lesions scattered over cerebrum (arrow 1), cerebellum (arrow 2,3,4), even in ventricles (arrow 5).

HIV status was negative. A diagnosis of TB-IRIS was considered, and Dexamethasone was started then changed to prednisolone given for 4 weeks along with continuation of ATT. she showed improvement and was discharged.

DISCUSSION

Paradoxical worsening of TB after initiation of antitubercular treatment has been reported in about 2-

23% of treated TB patients without HIV infection. It occurs more frequently in patients with extrapulmonary dissemination.

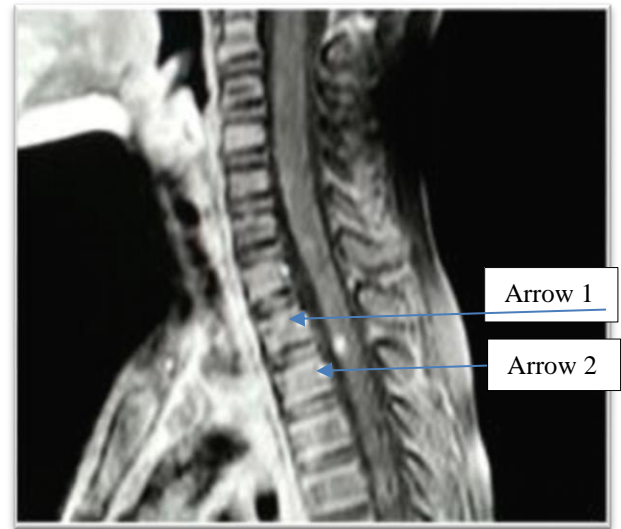


Figure 2: The same child with ring enhancing lesions scattered over brain stem, spinal cord vertebra C7, D2 with extensive leptomeningeal enhancement as shown by the arrow 1 and 2 respectively. These findings are as a part of IRIS.

Immune Reconstitution Inflammatory Syndrome (IRIS) is a heightened inflammatory response to a pathogen in the setting of immunologic recovery after immunosuppression. It occurs in those who have undergone a reconstitution of the immune responses against an antigen.⁷ It is an exuberant and dysregulated inflammatory response to invading microorganisms. It manifest when an abrupt shift of host immunity from an anti-inflammatory and immunocompromised status towards a pathogenic proinflammatory state occurs as a result of rapid decrease or removal of factors promoting immunosuppression or initiating inflammation.⁸

The cause of the PR in immunocompetent person can be attributable to several factors like persistence of lipid rich insoluble cell wall antigen, exposure and release of new antigen targets during mycobacterial killing, hypersensitivity to tuberculo-protein and exaggerated immune restoration following TB induced immunosuppression.⁹ An acute exacerbation of Th1 responses against mycobacterial antigens appear to cause IRIS in patients co-infected with HIV and TB.¹⁰

In addition to HIV, IRIS has also been observed in solid organ transplant recipients, women during post-partum period, neutropenic patients, tumour necrosis factor antagonist recipient.⁹

Antitubercular drug resistance should be excluded in all cases of suspected TB-IRIS and corticosteroids should be

used with caution for patients with presumed TB-IRIS until the results of drug susceptibility testing is known.¹¹

Though it is important to distinguish TB-IRIS from other causes like inadequate drug regime and multidrug resistant TB, distinguishing IRIS from clinical deterioration due to ongoing immunodeficiency is ill defined and controversial in paediatric population.¹² Majority of patients with IRIS have a self-limiting disease course. Mortality associated with IRIS is relatively uncommon.¹³ In the present study the child with CNS tuberculosis was immunocompetent, developed PR between 14 to 45 days after commencement of ATT. This child had spinal intramedullary tuberculoma, cerebellar, pontine tuberculoma with facial nerve palsy, which is rare.¹⁴ These reactions can be effectively managed with continuation of ATT along with systemic corticosteroids.

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