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Immune Reconstitution Inflammatory Syndrome in CNS Tuberculosis

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Background: Immune Reconstitution Inflammatory Syndrome (IRIS), an exaggerated inflammatory response with clinical worsening due to immune recovery during treatment, is rare in the immune-competent population. **Case characteristics:** A 5½-year old immune-competent girl with CNS tuberculosis without HIV who developed paradoxical IRIS. **Outcome:** Response to supportive care along with Anti-tuberculosis treatment. **Message:** IRIS can occur in tuberculosis, even in the immuno-competent.

Keywords: *Hypersensitivity, Immunity, Tuberculosis.*

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. It is mostly described in HIV-infected patients initiated on highly active antiretroviral therapy (HAART). It can also occur in patients with solid organ transplant, bone marrow transplant, cytoreductive chemotherapy, and rarely, in tuberculosis [1,2]. IRIS

includes increased lymphoproliferative response to mycobacterium antigens, restoration of cutaneous response to tuberculin, and increased activation markers like CD38, TNFA-308*1 and IL6-174*G [3]. We report a girl who developed IRIS after initiating Anti Tuberculosis Treatment (ATT).

CASE REPORT

A 5½-year-old girl was admitted with low grade fever of 1 week duration, drowsiness of two days, signs of

meningeal irritation and papilledema. CSF study showed pleocytosis; 150 cells/cumm³, 70% lymphocytes, with protein 88 mg/dL and sugar 32 mg/dL. Bacterial and AFB cultures of CSF were negative. CSF was also negative for TB PCR, HSV PCR and Cryptococcus. Her HIV ELISA was negative. Chest X-Ray showed right sided pneumonia, Mantoux test and gastric aspirate for AFB were negative. Initial completed tomography (CT) of brain revealed no abnormality. She was initially started on ceftriaxone and acyclovir. She had a history of contact with tuberculosis in grandfather. She had been started on INH chemoprophylaxis 1 year ago, but stopped after 1 month. Repeat CT brain after 1 week showed hydrocephalus. After 1 week, in view of poor improvement and history of contact with tuberculosis, X-ray chest findings and compatible neuroimaging findings, a diagnosis of CNS tuberculosis was made and ATT (SHRZ) was started along with oral steroids. She improved slowly and was discharged after 1 month of daily ATT; streptomycin was changed to ethambutol at discharge.

Six weeks after initial presentation (one week after discharge), she was re-admitted with worsening of the condition. She had fever, vomiting, frontal headache of three days duration, papilledema and anisocoria. Repeat CT scan with contrast revealed, moderate hydrocephalus, diffuse cerebral edema, abnormal nodular enhancement in right temporal region suggestive of tuberculoma, and diffuse exudates around the Circle of Willis (**Fig. 1**). In

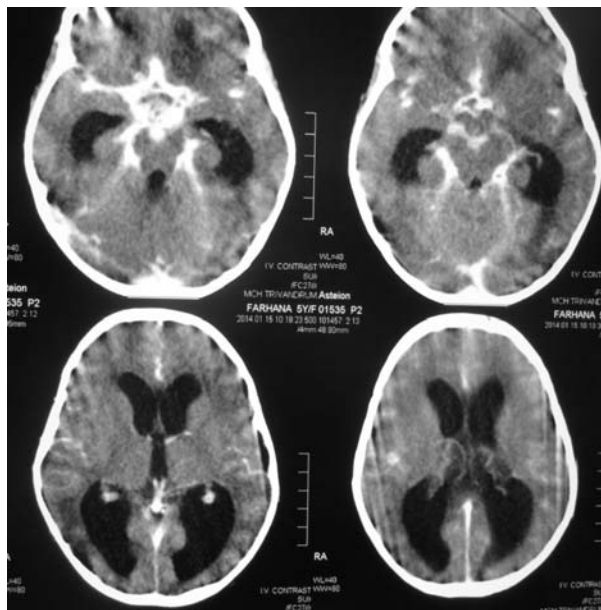


Fig. 1 CT Scan showing hydrocephalus, brain edema, tuberculoma in right temporal region and exudates around circle of Willis.

addition to tuberculoma, there was also gyral enhancement (**Fig. 2**). Repeat CSF study showed 570 cells: 60% polymorphs, protein 102 mg/dL, sugar 45 mg/dL and sterile cultures. Repeat Mantoux test was strongly positive (25 mm).

In view of the clinical worsening and restoration of Mantoux positivity, the possibility of IRIS was considered. She was restarted on decongestive measures along with parenteral dexamethasone; ATT was continued. She stabilized over the next week and was discharged on ATT and oral prednisolone after 10 days of hospitalization. Prednisolone was tapered after 12 weeks and 0.5 mg/day was continued for total of 6 months, till the papilledema disappeared. She is now stable after follow-up of 6 months.

DISCUSSION

Diagnosis of CNS tuberculosis in this child was in accordance with the Modified Ahuja Criteria [4]. IRIS was diagnosed on the basis of clinical and CT findings, and restoration of Mantoux test positivity [5].

IRIS is common in HIV patients with or without tuberculosis, but rare in immuno-competent HIV-negative patients. Among the two types – paradoxical and unmasking – the diagnosis of paradoxical IRIS (worsening of symptoms/new manifestations of a known condition) was considered in this child. Unmasking IRIS (appearance of diseases not previously suspected that become apparent shortly after initiation of treatment) was unlikely in this case [6-8]. Apart from tuberculosis, IRIS can occur in herpes infections, hepatitis, fungal infections, human papilloma virus infections, malignancies and sarcoidosis.

IRIS is the result of a disordered immune recovery leading to dysregulated immune response to an antigen

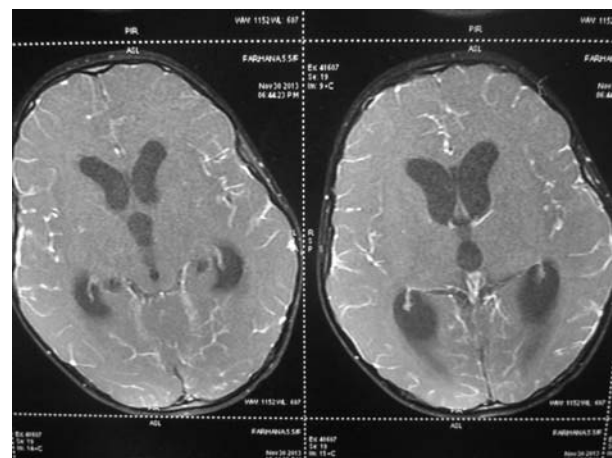


Fig. 2 CT Scan showing gyral enhancement.

and resultant exaggerated inflammatory features within a milieu of pro-inflammatory cytokines [3]. In the diagnosis of IRIS, it should be ensured that deterioration is not due to non-adherence to treatment, insufficient therapy and development of resistance to specific therapy. If symptoms are not severe, watchful approach is recommended with anti-inflammatory agents and specific therapy [9]. In unmasking IRIS, specific antimicrobial therapy for the unmasked disease is also warranted with or without additional anti-inflammatory agents.

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