Longitudinal analysis of Serum Cytokine Profile among Patients with Tubercular Multifocal Serpiginoid Choroiditis: A Pilot Study

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Background: Serpiginous-like choroiditis (recently termed as multifocal serpiginoid choroiditis; MSC) is a distinct variant of tubercular (TB) posterior uveitis that affects Asian-Indian young adults. In the context of ocular TB, very few studies have shed light on the biochemical basis of the disease (but not on paradoxical worsening). Mediators such as IFN-γ, IL-10, TNF-α and TGF-β may play a central role in the pathogenesis of ocular TB. This study was performed to monitor cytokine levels in patients with TB MSC and determine characteristics of the cytokine signaling that leads to development of paradoxical worsening.

Patients & Methods: This prospective study was performed at PGIMER, Chandigarh, India. The inclusion criteria were presence of active TB MSC lesions, and exclusion of other non-infectious uveitis entities (such as sarcoidosis) by clinical or relevant laboratory tests. For the purpose of serum cytokine analyses, venous blood sample was drawn. A baseline venous blood sample was taken from all the patients before starting the therapy followed by obtaining samples at 1 week, 3 weeks and 6 weeks after initiation of treatment. The cytokines that were measured and analyzed were TNF-α, IFN-γ, IL-10, and TGF-β. The levels of IFN-γ, TNF-α and IL-10 were measured using LEGENDplex™ bead based immunoassay. The data was analyzed using FCAP array software (BD Biosciences USA) to get the levels of TGF-β in serum samples.

Results: Twelve Asian Indian patients with TB MSC were enrolled in the study which included 3 females and 9 males (mean age: 32.58 years). All the patients with active disease in one or both the eyes were started on both ATT and oral steroids (prednisolone acetate 1mg/kg). Four (33.3%) out of twelve patients developed paradoxical worsening after initiation of ATT.

IL-10: Mean IL-10 value at baseline was higher in paradoxical worsening group as compared to the non-paradoxical worsening group. (17.54 ± 22.79 pg/ml versus 7.60 ± 8.4 pg/ml).

IFN-γ: There was sharp rise in levels of IFN-Ɣ between baseline to 1 week in patients who showed paradoxical worsening (p=0.01) but no significant change among those who did not show paradoxical worsening.

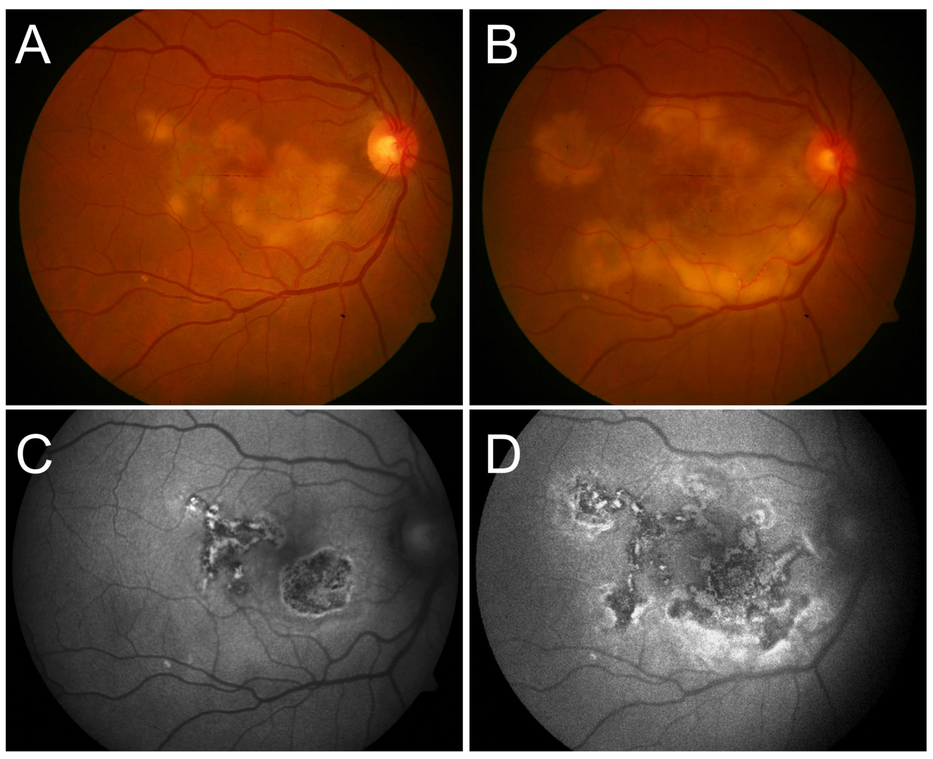
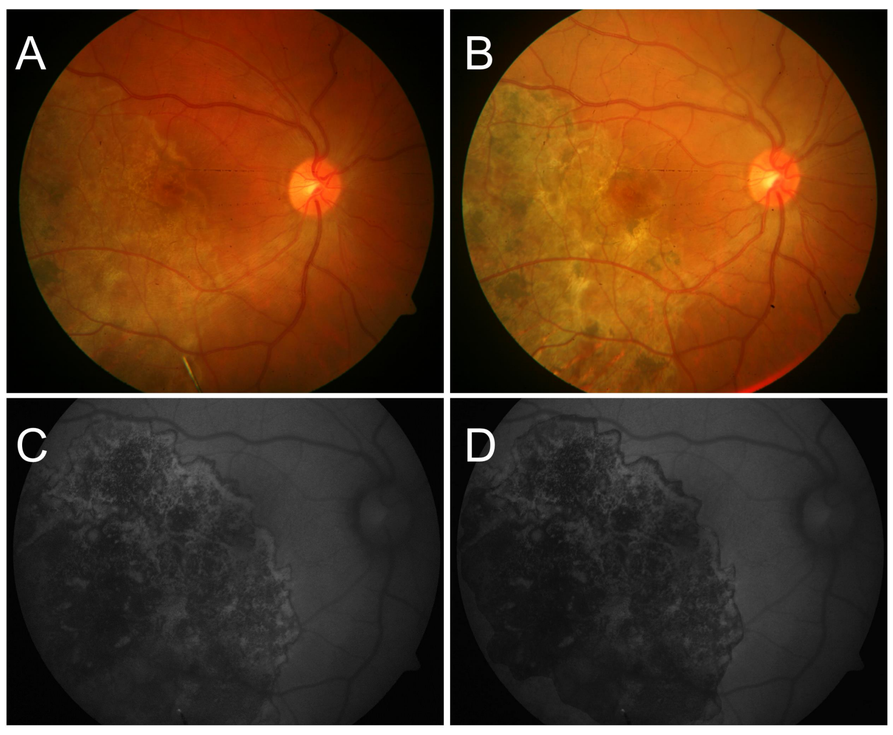


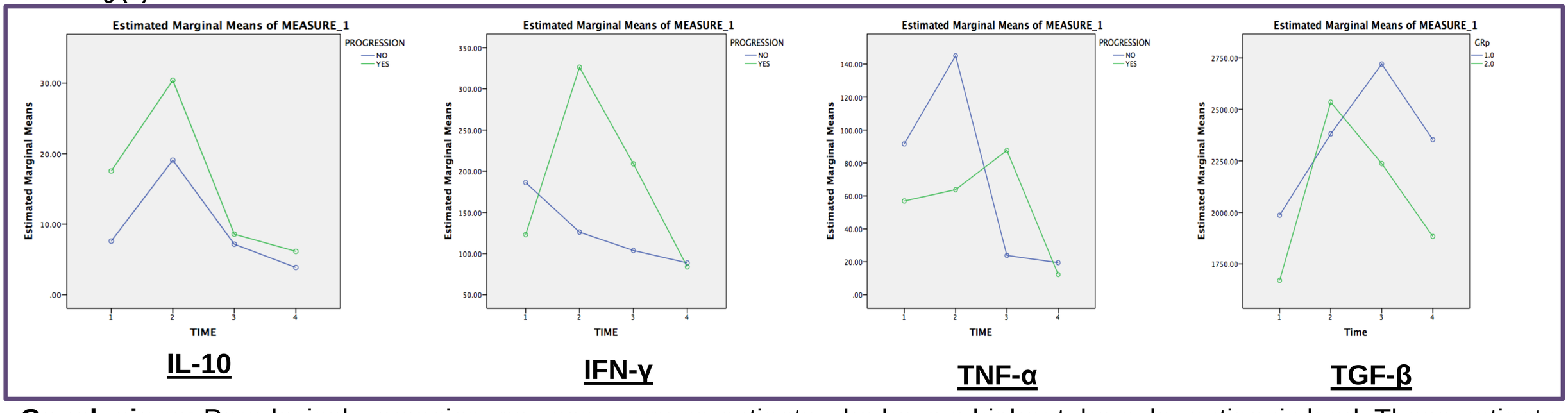
Figure 1: **The figure shows a patient who developed paradoxical worsening (A). Three weeks after initiation of ATT, he developed worsening (B). Autofluorescence shows increase in the hyper-autofluorescent areas compared to baseline (C and D).**



TNF-α: Among patients with paradoxical worsening, the levels of TNF-α showed an increase at 3 weeks. The levels of TNF-α in the paradoxical worsening group at baseline was 56.9 ± 76.97 pg/ml and at 3 weeks was 87.62 ± 56.98 pg/ml (p<0.05).

TGF-β: The levels of TGF-β were highest at 3 weeks after initiation of therapy in the group of patients who showed paradoxical worsening. At 6 weeks after initiation of therapy, there was no significant difference in the levels of TGF-β compared to the baseline values in either group.

Figure 2: **A patient diagnosed with tubercular choroiditis showed presence of a large lesion (A) at baseline. At 3-month follow-up visit, the patient shows healing response (B). Autofluorescence at baseline shows hyper-autofluorescent areas (C) and predominantly hypo-autofluorescent areasat 3 months suggestive of healing (D).**



Conclusions: Paradoxical worsening may occur among patients who have a higher tubercular antigenic load. These patients may show a heightened immune response with higher baseline IL- 10 values, early rising levels of IFN-Ɣ, progressive increase in TGF-β, and rising levels of TNF- α after initiation of ATT and corticosteroids.