NEUTROPHIL ACTIVATION AND ENHANCED RELEASE OF GRANULE PRODUCTS IN HIV-TB IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME

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Background
Tuberculosis Immune Reconstitution Inflammatory Syndrome (TB-IRIS) remains incompletely understood.

Aim
Neutrophils are implicated in tuberculosis pathology but detailed investigations in TB-IRIS are lacking.

Methods
Unbiased nCounter gene expression analysis was performed in TB-IRIS patients (n=17) versus antiretroviral-treated HIV/TB co-infected controls without IRIS (n=17) in Kampala, Uganda. Flow cytometry was performed in TB-IRIS patients (n=18) and controls (n=11) in Cape Town, South Africa to determine expression of neutrophil surface activation markers, intracellular cytokines and Human Neutrophil Peptides (HNP). Plasma neutrophil Elastase and HNP1-3 were quantified using ELISA. Lymph node immunohistochemistry was performed on three TB-IRIS cases.

Results
There was significant increase in gene expression of S100A9 (p=0.002), NLRP12 (p=0.018), COX-1 (p=0.025) and IL-10 (p=0.045) two weeks after ART initiation in Ugandan TB-IRIS patients versus controls. IRIS patients in both cohorts demonstrated increases in blood neutrophil count, plasma HNP and elastase concentrations from ART initiation to week two. CD62L (L-selectin) expression increased over 4 weeks in South African controls while IRIS patients demonstrated the opposite. Intense staining for the neutrophil marker CD15 and IL-10 was seen in necrotic areas of TB-IRIS patients' lymph nodes.

Conclusion
Neutrophils in TB-IRIS are activated, recruited to sites of disease and release granule contents.