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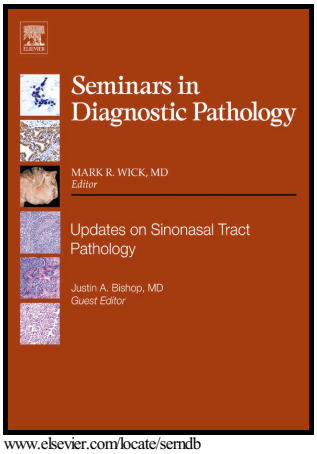

www.elsevier.com/locate/semdb

PII: S0740-2570(17)30055-2
DOI: http://dx.doi.org/10.1053/j.semdp.2017.04.010
Reference: YSDIA50512

To appear in: *Seminars in Diagnostic Pathology*

Cite this article as: Ann Marie Nelson, Yukari C. Manabe and Sebastian B Lucas Immune Reconstitution Inflammatory Syndrome (IRIS): What pathologist should know, *Seminars in Diagnostic Pathology* http://dx.doi.org/10.1053/j.semdp.2017.04.010

Immune Reconstitution Inflammatory Syndrome (IRIS): What pathologists should know

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Summary:
Antiretroviral therapy has significantly improved the quality and length of life for those patients able to access effective and sustained treatment. The resulting restoration of the immune response is associated with a change in the clinical presentation of opportunistic infections, and the histologic reaction to pathogens. A complex combination of alterations in host response across the stages of HIV infection has been documented over the past 3 decades. The defects are seen in both acute and chronic phases of inflammation and involve innate and adaptive immunity. In advanced stages of HIV infection, the marked disruption of lymphoid tissue and loss of follicular dendritic cells limits the host's ability to process antigen and mount specific responses to pathogens. There are qualitative and quantitative defects in CD4 T cells due to HIV infection. The resulting indirect effects include loss of cytokine production, dysregulation of B-cell function, loss of cellular mediated immunity and "holes" in the immunologic repertoire that may not be restored with the use of antiretroviral therapy. Immune reconstitution allows the host to respond to and control infection, but a significant number of patients will have atypical inflammatory syndromes during the recovery period. We briefly discuss the impact of HIV infection on the immune system and give an overview of the spectrum of conditions attributed to the Immune Reconstitution Inflammatory syndrome (IRIS).

Introduction

Medicine and diagnostic pathology were presented with unexpected challenges from the late 1970s on, when increasing numbers of people presented to hospitals with signs of advanced immunodeficiency, of unknown cause, and died. They had opportunistic infections (OI) that hitherto were uncommon (e.g. pneumocystosis and mycobacteriosis avium) and unusual tumors such as Kaposi sarcoma and primary cerebral lymphoma. All had profound cell-mediated immune deficiency with reduced CD4+ T-cell numbers, as measured in tissues and (more conveniently) in peripheral blood counts. Within a few years of the first publications announcing this 'new' disease (1,2), the viral cause had been identified: initially