IgA was most prevalent (96%). Only half of the patients had achieved normalization of Ig levels at the end of the observation period. Of these, 84% had become normal by 5 years of age. Of the patients who had not yet normalized at the end of the study, 54% were >5 years old. Two met criteria for selective IgA deficiency. Higher levels of IgGs at presentation were associated with shorter times to normalization. Boys who presented at younger ages normalized more quickly than those who presented later. The opposite was true for girls. On average, the time to normalization for girls was 10-fold longer than the time for boys. Serious infections or death were not observed.

CONCLUSIONS. Most patients with this phenotype are boys with recurrent otitis media, wheezing episodes, and atopy. Girls with this presentation may be at greater risk for prolonged immunodeficiency. A “definitive” diagnosis of transient hypogammaglobulinemia can only be conferred retrospectively (ie, after Ig levels have normalized).

REVIEWER COMMENTS. There were several interesting new observations in this group of patients. In particular, the gender differences in time to normalization stand out; the immunologic significance of this finding is not known. The authors correctly pointed out that patients must be followed at least until clinical resolution, if not actual normalization, of Ig values. Only half of the patients normalized during the observation period. It is possible that other specific immunodeficiency diagnoses may be conferred on some of the patients who are still hypogammaglobulinemic. The authors did not comment on whether some patients who initially presented in this way subsequently developed additional clinical and/or laboratory features leading to the diagnosis of other immunodeficiencies. Without knowing this, it is impossible to estimate the predictive value of intact vaccine responses in this setting (ie, how often do we "miss" a different specific immunodeficiency diagnosis if we stop after this initial evaluation). However, these and other reports suggest that the majority of these patients follow a relatively benign course.

Clinical and Laboratory Characteristics of 75 Patients With Specific Polysaccharide Antibody Deficiency Syndrome

PURPOSE OF THE STUDY. To study the clinical and laboratory characteristics of patients with specific polysaccharide antibody deficiency syndrome.

STUDY POPULATION. This was a retrospective review of records obtained over 8 years of patients from the Mayo Clinic (Rochester, MN) who were found to have recurrent infection defined as ≥4 infections per year and an immunoglobulin G (IgG) level of >500 mg/mL.

METHODS. Serious infections were defined as pneumococcal sepsis, meningitis, pneumonia, or deep-seated abscess. Specific polysaccharide antibody deficiency syndrome (SPADS) is empirically defined as <9 of 12 serotype responses to vaccination with Pneumovax (titers checked preimmunization and 2–4 weeks postimmunization ×2), and no other documented, established primary or secondary immunodeficiency syndrome. An adequate response to pneumococcal serotypes contained in the vaccine was defined as reaching the protective level defined by the laboratory assay. Loss of immune response 6 months after vaccination was also assessed in patients with recurrent infection. In such patients, vaccination was repeated and serologies were remeasured.

RESULTS. Seventy-five patients met the inclusion criteria. The median age at presentation was 42 years (range: 0–76 years), and the median age at diagnosis was 48 years (range: 4–81 years). The median interval between onset of symptoms and diagnosis of SPADS was 4 years. Sixty-nine percent of the patients were female, and 83% were white. The most common documented infections (in order of occurrence) were sinus infection, pneumonia, bronchitis, and ear infections; only 7% of the patients had documented sepsis, meningitis, or deep-tissue abscesses. Eight percent had autoimmune disorder or rheumatic disease. Sixteen percent of the patients had 0 of 12 responses to Pneumovax; 72% had 1 to 6 of 12 responses; and 12% had 7 to 8 of 12 responses. Patients under 18 years of age tended to have less response. The median IgG2 level (150 mg/dL) for patients with 0 responses to Pneumovax tended to be lower compared with patients with >1 response (193 mg/dL; P = .06). When measured, the majority (31 of 35) of the patients had protective levels of antibody to tetanus and diphtheria (18 of 19). In vitro lymphocyte-stimulation test results were normal in the vast majority of patients when measured. Thirty patients were treated with a standard intravenous Ig (IV Ig) therapy, 400 mg/kg per month for an undetermined time period. Patients with a higher number of infections (P = .003) and fewer responses to Pneumovax (P = .01) were more likely to receive IVIg. Of the patients receiving IVIg, the number of infections after treatment was significantly lower (median: 1 vs 8; P < .001).

CONCLUSIONS. SPADS is a disorder of humoral immunity that is seen in patients with recurrent infections. Response to unconjugated pneumococcal vaccine is abnormal despite normal total IgG levels. Other immune abnormalities are not typically seen. Patients with more frequent infections have less responses to Pneumovax and may clinically respond to IVIg therapy.
HUMAN IMMUNODEFICIENCY VIRUS

Immune Reconstitution Syndrome After Highly Active Antiretroviral Therapy in Human Immunodeficiency Virus-Infected Thai Children


PURPOSE OF THE STUDY. Immune reconstitution inflammatory syndrome (IRIS) is a clinical phenomenon characterized by paradoxical worsening of the clinical status of patients with HIV who receive highly active antiretroviral therapy. It is presumed that this is a result of improvement in cellular immune functions and secondary immunopathology in response to organisms that had not been recognized previously. This syndrome has been well described in adult patients. The purpose of this study was to describe IRIS after initiation of highly active antiretroviral therapy in HIV-infected children.

STUDY POPULATION AND METHODS. There were 153 HIV-infected children enrolled at initiation of antiretroviral therapy and then followed prospectively.

RESULTS. Of the 153 children, 29 (19%) experienced 32 episodes of IRIS. The median time of onset was 4 weeks after initiation of antiretroviral therapy. Fourteen episodes were caused by mycobacterial organisms, 7 by varicella-zoster virus, 7 by herpes simplex virus, 3 by Cryptococcus neoformans, and 1 by Guillian-Barré syndrome. In general, treatment was not interrupted, and only 2 patients were treated with short courses of corticosteroids. However, 3 patients died as a result of IRIS or its complications. It is important to note that patients who reactivated mycobacterial disease had substantially lower CD4+ T-cell counts at the time that their antiretroviral therapy was started, compared with patients who reactivated herpes viruses.

CONCLUSIONS. IRIS is common among HIV-infected children who initiated antiretroviral therapy in an advanced stage of HIV disease.

PD-1 Expression on HIV-Specific T Cells Is Associated With T-Cell Exhaustion and Disease Progression


Upregulation of PD-1 Expression on HIV-Specific CD8+ T Cells Leads to Reversible Immune Dysfunction


PURPOSE OF THE STUDIES. Recent evidence from a mouse model of chronic viral infection suggests a crucial role for the programmed death 1 (PD-1)/programmed death 1 ligand (PD-L1) signaling pathway in downregulating the functions of virus-specific CD8+ T cells. PD-1 is an inhibitory receptor that negatively regulates activated T cells, and it is markedly upregulated on the surface of “exhausted” virus-specific CD8+ T cells in mice. HIV similarly induces a virus-specific impairment of T-cell functions. The purpose of these 2 studies was to investigate the expression of PD-1 on HIV-specific T cell in patients infected with the virus.

STUDY POPULATION AND METHODS. Both studies evaluated subjects with HIV and healthy controls and compared PD-1
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