Immunodeficiency Evaluation in Adults

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Although primary immunodeficiency (PI) diseases have typically been associated with the world of pediatrics, there is a growing appreciation that adults can also be affected by the PI disease. The advances in diagnosis and treatment of the childhood immunodeficiency diseases have allowed many children born with the PI disease to survive into adulthood. Additionally, several common PI diseases often present “de novo” in adulthood, causing significant morbidity. Furthermore, the advent of immunosuppressive treatments in autoimmune conditions and organ transplantation has opened the doors for acquired immunodeficiency conditions that can potentially mimic the clinical presentation of PI conditions.

Definition
The immunodeficiency diseases represent a group of disorders in which there is an impairment of the immune system causing an increased susceptibility to infections and noninfectious comorbidities that span many organ systems. These diseases are caused by hereditary or new genetic or acquired defects and can present at birth, early childhood, or adulthood. Traditionally, the type of infection is determined by whether the defect is located in cellular (lymphocytes, phagocytes, and neutrophils) or humoral (antibodies) immunity. Of note, many patients will have combined cellular and humoral immunity defects, making it harder to diagnose the type of immune deficiency based on their clinical presentation.

Clinical presentation
The clinical suspicion for primary immunodeficiency should arise if one encounters a patient with any of the following features: severe infections requiring a hospitalization, persistent infections or an infection caused by an uncommon organism, recurrent infections, or a family history of recurrent infections. For example, in our practice we diagnosed PI in a number of patients whose initial presentation was a life-threatening pneumonia or acute bacterial meningitis. Additionally, in many patients we had found chronic sinusitis symptoms or recurrent bronchial infections and bronchiectasis before diagnosing PI.

The type of infection seen in PI can vary based on underlying disease. For example, the patients with IgA deficiency or common variable immunodeficiency (CVID) often present with recurrent sinopulmonary infections with encapsulated organisms, while the patients with chronic granulomatous disease commonly present with the infections caused by Staphylococcus aureus, Serratia marcescens, Burkholderia cepacia and Nocardia.

We have also learned that many patients with PI may not present with infections. Noninfectious phenotypes of CVID, including autoimmune disease (idiopathic thrombocytopenic purpura, hemolytic anemia, etc.), granulomatous inflammation, lymphoid hyperplasia, or gastrointestinal disease may be presenting, coexistent, or sole manifestations of this immunodeficiency. Moreover, these noninfectious presentations of CVID can mimic other conditions, such as sarcoidosis, inflammatory bowel disease, or interstitial lung disease, leading to a significant impediment in diagnosis of CVID. Because these conditions mimicked by CVID often require immunosuppressive treatments, any delay in diagnosis and appropriate treatment of CVID may cause significant complications and increase the risk of an infection.

Diagnosis
The standard screening test for antibody deficiency starts with measurement of IgG, IgA, and IgM immunoglobulin levels in the blood serum. Occasionally, an IgE level will be checked if clinical features suggest the diagnosis of hyper-IgE syndrome. If clinically indicated, one can measure specific antibody production (also known as amnestic vaccine response) to better evaluate antibody function. The patient might need to be immunized with common vaccines, including those with protein antigens (such as tetanus toxoid, diphtheria toxoid) and carbohydrate antigens (such as Pneumovax®), and repeat serologic studies should be obtained approximately four to six weeks after the immunization.

Laboratory testing to diagnose chronic granulomatous disease relies on the evaluation of oxidative burst in neutrophils and macrophages. This can be measured by using a number of different methods including the nitroblue tetrazolium (NBT) test. Many immune deficiencies are associated with specific genetic defects, and additional genetic studies might be needed to confirm the diagnosis of PI disease. Occasionally, complement studies will be ordered to rule out complement defects. Finally, the secondary causes of abnormal immune studies should be ruled out before making a diagnosis of PI disease.

Treatment
The patient with confirmed PI disease will often require prophylactic treatments to prevent infections or complications of infections (such as bronchiectasis) and immunosuppressive therapy to manage noninfectious manifestations. Some patients with an isolated decrease in IgG level and infrequent infections may not require treatment. The most common prophylactic treatments include immunoglobulin replacement therapy in humoral immunodeficiency conditions, interferon gamma in CGD, and/or prophylactic antibiotics in patients with humoral or cellular immunodeficiency. Once a diagnosis has been made, therapy will likely be lifelong. In some instances, reevaluation of the diagnosis may be undertaken by discontinuing therapy and retesting immune function.