

Other Antibody Deficiency Disorders



Chapter 8

In addition to the more common immunodeficiencies described in other chapters, there are several other rare, but nevertheless well-described, antibody deficiency disorders. Similar to the patients described in the chapters on X-Linked Agammaglobulinemia (XLA), Hyper IgM Syndrome, Selective IgA Deficiency, Common Variable Immune Deficiency (CVID) and Specific Antibody Deficiency (SAD), individuals with less common antibody deficiencies usually present with upper respiratory infections or infections of the sinuses or lungs, typically with organisms like streptococcus pneumonia and hemophilus influenzae. Laboratory studies show low immunoglobulins and/or deficient specific antibody production. Many of these disorders also include abnormalities in the cells responsible for generating or maintaining an antibody response. The patients often improve with antibiotics but get sick again when these are discontinued. The cornerstone of therapy for antibody deficiency disorders is immunoglobulin (Ig) replacement.

Antibody Deficiency with Normal or Elevated Immunoglobulins

These patients have severe infections similar to patients with CVID, but their immunoglobulin levels are normal or elevated. They have decreased antibody levels to most vaccine antigens, both protein and polysaccharide, which differentiates them from patients with selective antibody deficiency.

Selective IgM Deficiency

These patients have low IgM (less than 30 mg/dl in adults, less than 20 mg/dl in children) with recurrent infections that are often severe. There are variable antibody responses. Some patients are asymptomatic. This disease may be clinically similar to CVID though it should not be referred to by that name. It is important to note that IgM deficiency is also seen commonly in DOCK8 deficiency, typically in association with normal IgG and elevated IgE.

Immunodeficiency with Thymoma (Good's Syndrome)

This primary immunodeficiency is characterized by low immunoglobulins together with a thymic tumor (thymoma). Good's Syndrome is usually first suspected when a thymic tumor is seen on a chest X-ray although in about half the cases the history of recurrent infections precedes the detection of the thymoma. Most patients are adults. Removal of the thymoma does not cure the immunodeficiency although it may help other symptoms. Eosinophils may be very low or undetectable in these patients.

Transcobalamin II Deficiency

Transcobalamin 2 is a protein that transports vitamin B12 to the tissues from the gastrointestinal tract. A hereditary deficiency is associated with anemia, failure to thrive, low white cell counts and hypogammaglobulinemia. It can be treated with B12 injections.

(Other Antibody Deficiency Disorders continued)

Warts, Hypogammaglobulinemia, Infection, Myelokathexis (WHIM) Syndrome

WHIM is an autosomal recessive disorder with severe warts, recurrent bacterial and viral infections, low but not absent immunoglobulins and neutropenia (low granulocytes). (See chapter titled “Inheritance.”) The neutropenia is due to failure of the bone marrow to release granulocytes into the blood stream (myelokathexis). WHIM is caused by a defective gene for CXCR4, a chemokine receptor protein that regulates leukocyte movement. In addition to Ig replacement, treatment includes granulocyte growth factor (G-CSF).

Drug-Induced Antibody Deficiency

Technically this is not considered a primary immunodeficiency disease but must be ruled-out as a cause for antibody deficiency during the evaluation of any patient presenting with defective antibody production. Several medications may depress immunoglobulin and antibody levels, and this may result in recurrent infections. The chief drugs implicated include high-dose steroids (particularly when given intravenously), anticonvulsant drugs (Dilantin and others), anti-inflammatory drugs used for arthritis, and the monoclonal antibody, Rituximab (Rituxan). Rituximab specifically targets B cells, the precursors of the antibody-producing plasma cells. In some instances, severe and permanent agammaglobulinemia can occur with drug therapy, but usually the hypogammaglobulinemia reverses when the drug is discontinued. If antibody deficiency and insufficient response to vaccine challenge persists when the drug is stopped, Ig replacement may be needed.

Kappa Chain Deficiency

This Ig light chain deficiency is inherited from both parents (autosomal recessive). Susceptibility to infection may be due to reduced activation of B-cells to make antibody and to a reduced variety of antibodies. However, some patients may be asymptomatic.

Heavy Chain Deficiencies

In rare individuals, multiple genes that code for different immunoglobulins (IgA, IgG1, IgG2, etc.) may be missing (deleted). These people can only make one or a few types of immunoglobulin (for example, only IgM and IgG3). These individuals may exhibit susceptibility to respiratory and other infections, but they are also often asymptomatic.

Post-Meiotic Segregation (PMS2) Disorder

PMS2 gene mutation leads to defective Ig class switching from IgM to IgG and IgA. It is a very rare primary immunodeficiency resulting in low serum IgG and IgA with elevated serum IgM. This disorder results in café-au-lait spots on the skin, and patients have a predisposition to several types of malignancies.

Unspecified Hypogammaglobulinemia

This diagnosis applies to all forms of low concentrations of serum immunoglobulins, like IgG, IgA, IgM deficiency. In general, these patients are not found to have impaired ability to produce adequate levels of vaccine antibody. It is somewhat of an older term to describe a patient with one or more deficiencies of these serum immunoglobulins. In some patients, unspecified hypogammaglobulinemia may simply be a physiologic variant without any clinical significance. However, it may indicate a developing immunodeficiency and should be monitored, particularly if the patient begins to develop frequent and/or severe infections.