



Selective IgA Deficiency

CHAPTER

4

Individuals with Selective IgA Deficiency lack IgA, but usually have normal amounts of the other types of immunoglobulins. Most affected people have no illness as a result. Others may develop a variety of significant clinical problems. Selective IgA Deficiency is relatively common in Caucasians.

Definition of Selective IgA Deficiency

Selective IgA Deficiency is the complete absence of the IgA class of immunoglobulins in the blood serum and secretions. There are five types (classes) of immunoglobulins or antibodies in the blood: IgG, IgA, IgM, IgD, and IgE. The immunoglobulin class present in the largest amount in blood is IgG, followed by IgM and IgA. IgD is much lower, and IgE is present in only minute amounts in the blood.

Of these immunoglobulin classes, it is primarily IgM and IgG that protect us internally from infection. It is also important that the body is protected at surfaces that come into contact with the environment. These sites are the mucosal surfaces, which include: mouth, ears, sinuses and nose, throat, airways within the lung, gastrointestinal tract, eyes, and genitalia. IgA antibodies are transported in secretions to mucosal surfaces and play a major role in protecting these surfaces from infection. Other immunoglobulin classes are also found in secretions at mucosal surfaces, but not in nearly the same amount as IgA. This is why IgA is known as the secretory antibody. If our mucosal surfaces were spread out they would cover an area equal to one and one-half tennis courts, so the importance of IgA in protecting our mucosal surfaces cannot be overstated.

IgA has some special chemical characteristics. It is present in secretions as two antibody molecules attached by a component called the J chain (“J” for “joining”). In order for these antibodies to be secreted, they must also be attached to another molecule called the secretory piece. The IgA unit that protects the mucosal surfaces is actually composed of two IgA molecules joined by the J chain and attached to the secretory piece.

Although individuals with Selective IgA Deficiency do not produce IgA, they do produce all the other immunoglobulin classes. In addition, the function of their T-lymphocytes, phagocytic cells and complement system are normal. Hence, the term *Selective IgA Deficiency*.

The causes of Selective IgA Deficiency are unknown. It is likely that there are a variety of causes for Selective IgA Deficiency and the cause may vary from individual to individual.

Low serum IgA, like *absent serum IgA*, is also relatively common. Similarly, most people with low serum IgA have no apparent illness. Some people with low serum IgA have a clinical course very similar to people with common variable immunodeficiency (see chapter titled *Common Variable Immune Deficiency*).

Clinical Features of Selective IgA Deficiency

Selective IgA Deficiency is one of the most common primary immunodeficiency diseases. Studies have indicated that as many as one in every five hundred people have Selective IgA Deficiency. Many of these individuals appear healthy, or have relatively mild illnesses and are generally not sick enough to be seen by a doctor and may never be discovered to have IgA deficiency. In contrast, there are individuals with Selective IgA Deficiency who have significant illnesses. Currently, it is not understood why some individuals with IgA deficiency have almost no illness while others are very sick. Also, it is not known precisely what percent of individuals with IgA deficiency will eventually develop complications; estimates range from 25% to 50% over 20 years of observation. Studies have suggested that some patients with IgA deficiency may be missing

a fraction of their IgG (the IgG2 and/or IgG4 subclasses), and that may be part of the explanation of why some patients with IgA deficiency are more susceptible to infection than others.

A common problem in IgA deficiency is susceptibility to infections. This is seen in about half of the patients with IgA deficiency that come to medical attention. Recurrent ear infections, sinusitis, bronchitis and pneumonia are the most common infections seen in patients with Selective IgA Deficiency. Some patients also have gastrointestinal infections and chronic diarrhea. The occurrence of these kinds of infections is easy to understand since IgA protects mucosal surfaces. These infections may become chronic. Furthermore, the infection may not completely clear with treatment, and patients may have to remain on antibiotics for longer than usual.

Clinical Features of Selective IgA Deficiency continued

A second major problem in IgA deficiency is the occurrence of autoimmune diseases. These are found in about 25% to 33% of patients who seek medical help. In autoimmune diseases, individuals produce antibodies or T-lymphocytes which react with their own tissues with resulting inflammation and damage. Some of the more frequent autoimmune diseases associated with IgA deficiency are: Rheumatoid Arthritis, Systemic Lupus Erythematosus and Immune Thrombocytopenic Purpura (ITP). These autoimmune diseases may cause sore and swollen joints of the hands or knees, a rash on the face, anemia (a low red blood cell count) or thrombocytopenia (a low platelet count). Other kinds of autoimmune disease may affect the endocrine system and/or the gastrointestinal system.

Allergies may also be more common among individuals with Selective IgA Deficiency than among the general population. These occur in about 10-15% of these patients. The types of allergies vary. Asthma is one of the common allergic diseases that occurs with Selective IgA Deficiency. It has been suggested that asthma may be more severe, and less responsive to

therapy, in individuals with IgA deficiency than it is in normal individuals. Another type of allergy associated with IgA deficiency is food allergy, in which patients have reactions to certain foods. Symptoms associated with food allergies are diarrhea or abdominal cramping. It is not certain whether there is an increased incidence of allergic rhinitis (hay fever) or eczema in Selective IgA Deficiency.

Patients with IgA Deficiency are often considered to be at increased risk of anaphylactic reactions when they receive blood products (including IVIG) that contain some IgA. This is thought to be due to IgG (or possibly IgE) anti-IgA antibodies which may be found in some of these people. However, it has been observed that many patients with IgA deficiency do not have adverse reactions to blood products or IVIG. There is no agreement among experts in this field regarding the magnitude of the risk of these types of reactions in IgA deficiency, or the need for caution or measurement of anti-IgA antibodies before administration of blood or IVIG to these individuals.

Diagnosis of Selective IgA Deficiency

The diagnosis of Selective IgA Deficiency is usually suspected because of either chronic or recurrent infections, allergies, autoimmune diseases, chronic diarrhea, or some combination of these problems. The diagnosis is established when tests of the patient's blood serum demonstrate absence of IgA with normal levels of the other major classes of immunoglobulins (IgG and IgM). Most patients make antibodies normally. An occasional patient may also have IgG2 and/or IgG4 subclass deficiency and associated antibody deficiency

(see chapter titled *IgG Subclass Deficiency and Specific Antibody Deficiency*). The numbers and functions of T-lymphocytes are normal. Several other tests that may be important include a complete blood count, measurement of lung function, and urinalysis. Other tests that may be obtained in specific patients include measurement of thyroid function, measurement of kidney function, measurements of absorption of nutrients by the GI tract, and the test for antibodies directed against the body's own tissues (autoantibodies).

Treatment of Selective IgA Deficiency

It is not currently possible to replace IgA in IgA deficient patients, although research toward purification of human IgA is ongoing. However, it remains to be seen if replacement of IgA by any route (IV, oral, or topical) will be beneficial for humans with IgA deficiency. Treatment of the problems associated with Selective IgA Deficiency should be directed toward the particular problem. For example, patients with chronic or recurrent infections need appropriate antibiotics. Ideally, antibiotic therapy should be directed at the specific organism causing the infection. Unfortunately, it is not always possible to identify these organisms, and the use of broad-spectrum antibiotics may be necessary. Certain patients who have chronic sinusitis or chronic bronchitis may need to stay on long term preventive antibiotic therapy. It is important that the doctor and the patient communicate closely so that appropriate decisions can be reached for therapy.

As mentioned above, some patients with IgA deficiency also have IgG2 and/or IgG4 subclass deficiency and/or a deficiency of antibody production. However, these laboratory findings do not always predict a greater frequency or severity of

infections. For patients with IgA and IgG2 deficiency who do not respond adequately to antibiotics, the use of replacement gamma globulin may be helpful in diminishing the frequency of infections (see chapter titled *Specific Medical Therapy*).

There are a variety of therapies for the treatment of autoimmune diseases. Anti-inflammatory drugs, such as aspirin or ibuprofen, are used in diseases that cause joint inflammation. Steroids may be helpful in a variety of autoimmune diseases. If autoimmune disease results in an abnormality of the endocrine system, replacement therapy with hormones may be necessary. Treatment of the allergies associated with IgA deficiency is similar to treatment of allergies in general. It is not known whether immunotherapy (allergy shots) is helpful in the allergies associated with Selective IgA Deficiency, although there is no evidence of any increased risk associated with this therapy in these patients.

The most important aspect of therapy in IgA deficiency is close communication between the patient (and/or the patient's family) and the physician so that problems can be recognized and treated as soon as they arise.

Expectations for Selective IgA Deficiency Patients

Although Selective IgA Deficiency is usually one of the milder forms of immunodeficiency, it may result in severe disease in some people. Therefore, it is difficult to predict the long-term outcome in a given patient with Selective IgA Deficiency. In general, the prognosis in Selective IgA Deficiency depends on the prognosis of the associated diseases. It is important for physicians to continually assess and reevaluate patients with Selective IgA Deficiency for the existence of

associated diseases and the development of more extensive immunodeficiency. For example, rarely, IgA deficiency will progress to become Common Variable Immunodeficiency with its deficiencies of IgG and/or IgM. The physician should be notified of anything unusual, especially fever, productive cough, skin rash or sore joints. The key to a good prognosis is adequate communication with the physician and the initiation of therapy as soon as disease processes are recognized.