COOMBS NEGATIVE AUTOIMMUNE HEMOLYTIC ANEMIA (AIHA)

Autoimmune Hemolytic Anemia in the Absence of a Positive DAT Test

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Nearly all cases of autoimmune hemolytic anemia are associated with a positive DAT. In some cases of AIHA, including hepatitis B, the Coombs test may be negative.

Understanding AIHA

Autoimmune hemolytic anemia (AIHA) is an autoimmune condition in which the immune system produces antibodies that target and destroy red blood cells. In AIHA, the red blood cell’s outer surface membrane is destroyed or lysed, causing the protein hemoglobin to spill out into the plasma. This causes a condition known as hemolysis and a type of anemia called autoimmune hemolytic anemia.

Direct Coombs Test

Up to 98 percent of patients with AIHA have a positive direct Coombs test (also known as the direct antiglobulin test or DAT). The direct Coombs test is used to help diagnose AIHA. A positive DAT means that the patient’s red blood cells are coated with the red blood cell autoantibodies that lead to their destruction.

Autoimmune hemolytic anemia may be classified as cold or warm depending on whether the antibodies are cold IgM antibodies, which react at room temperature or warm IgG antibodies, which react at 37 degrees. Some patients may have mixed AIHA, which means that they have both cold and warm reacting antibodies. In general warm autoantibodies are associated with more severe conditions of AIHA. Patients with AIHA may also have different types of autoantibodies at different times and they may only have a positive direct Coombs test during disease flares.

A positive direct Coombs test is seen in other conditions besides AIHA. A positive direct Coombs may be seen in autoimmune hemolytic anemia, as a result of blood transfusion reactions, transiently in hemolytic disease of the newborn, paroxysmal cold hemoglobinuria, systemic lupus erythematosus (SLE), cold agglutinin disease, Evans syndrome, and infectious mononucleosis. Medications that cause a positive direct Coombs test include high doses of penicillin, methyldopa and quinidine.

Coombs Negative AIHA

In recent years, there has been an increasing number of isolated reports of Coombs negative AIHA occurring as a result of vaccinations or other medical conditions. In these conditions of AIHA in which the direct Coombs test is negative, patients may be
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gnosed as having other types of anemia or non-immune hemolytic anemia. This can lead to inappropriate treatment.

Some of the conditions in which Coombs negative AIHA has been reported include autoimmune hepatitis, diffuse livedo reticularis, renal cancer, drug therapies including piperacillin and rituximab, hepatitis B, hepatitis C, following kidney transplants, myelodysplastic syndrome, and hepatic lymphoma. Coombs negative AIHA has also been reported in a child following two vaccinations for influenza.

**Resources:**


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