

Clotting Disorders

Some patients with lupus can be predisposed to the formation of abnormal blood clots in the veins or arteries.

Frequently, the reason for this is the presence of abnormal antibodies called antiphospholipid (anticardiolipin) antibodies, and the lupus anticoagulant antibody.

The presence of the antiphospholipid antibodies can be detected using specific lab tests. A test called the partial thromboplastin time (PTT) is one of the tests of coagulation, and when prolonged, it may indicate the presence of the lupus anticoagulant antibody. Contrary to its name, this antibody acts as a promoter for clotting. Other blood tests that may be ordered in this condition include the Dilute Russel Viper Venom Time (DRVVT) which can be prolonged, and the syphilis test (VDRL) which can be false positive.

As briefly mentioned above, the antiphospholipid syndrome is a constellation of clinical findings which includes predisposition to blood clotting, frequent miscarriages, and reduced platelet counts. Antiphospholipid syndrome can exist in patients with lupus, but also separately in those without lupus. Sometimes, the initial presentation of this syndrome is the formation of a blood clot in a vein, called deep venous thrombosis (DVT). This most commonly occurs in the lower extremity, but can occur elsewhere. Blood clots can also occur in the arteries, which can lead to stroke, heart attack, visual loss, and other problems depending on the area affected.

Patients with these antibodies sometimes have an unusual appearance of the skin called 'livedo reticularis', where the skin appears mottled. It is important to think about looking for these abnormal antibodies if a patient develops blood clots for unclear reasons, in unusual sites, or at an unusually young age.

The treatment of this problem involves starting anticoagulant drugs, which reduce the body's ability to form a blood clot. These drugs come in injectable form (heparin) and in oral form (coumadin). The treatment is usually with life-long coumadin, such that catastrophic clotting can be prevented. The mere presence of the antiphospholipid antibodies or lupus anticoagulant does not predicate starting anticoagulation therapy. This therapy is usually reserved for those who have developed evidence of clotting.

Frequent miscarriages are a commonly encountered problem in patients with this syndrome. The pregnancy loss usually occurs in the second trimester, and is thought to be due to inadequate blood supply through the placenta, possibly because of blood clotting. Pregnancies have been successfully carried to full term by using aspirin and heparin. The use of warfarin is contraindicated in pregnancy because of teratogenic effects on the fetus.

There are other factors that may predispose a patient to easy clotting in lupus. The urinary loss of a protein called anti-thrombin III in patients with nephrotic syndrome, a subtype of lupus nephritis where large amounts of protein are lost in the urine, may be a cause of easy clotting.

There are various hereditary causes of easy clotting which are not specific to lupus.



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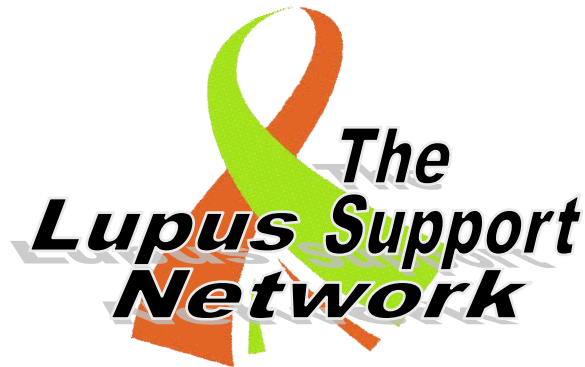
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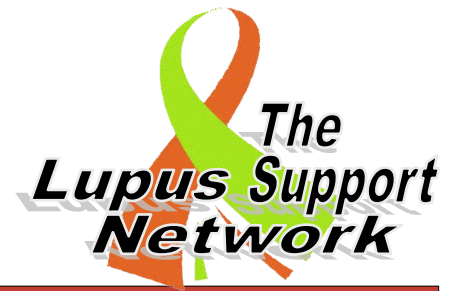
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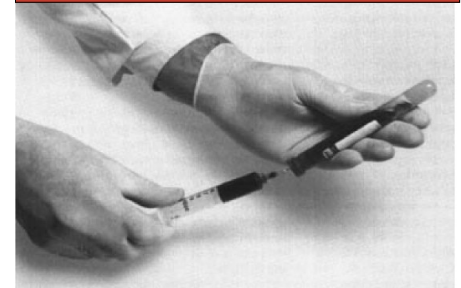
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Blood Disorders



By: Zuzana Uhrin, MD

Blood disorders in lupus include anemia, platelet disorders, white blood cell disorders, and clotting disorders. The most common types of anemia are anemia of chronic disease, iron deficiency anemia, and hemolytic anemia. Commonly encountered platelet disorders include ITP and antiphospholipid syndrome. White blood cell abnormalities include reduced lymphocyte and granulocyte counts, and may be due to lupus activity or to medications. An important cause of blood clotting in lupus is the presence of antiphospholipid antibodies or the lupus anticoagulant.

These disorders are important to be aware of because they are commonly encountered in patients with lupus. In fact, they may even be the presenting features of the disease.

Patients with systemic lupus erythematosus may develop disorders of the blood components, also called hematologic disorders. The blood components which can be affected in lupus include red blood cells, platelets, and white blood cells. In addition, patients with lupus may develop antibodies which predispose them to easy blood clotting. In this article I will discuss the various causes of anemia, platelet disorders, white blood cell abnormalities, and clotting abnormalities seen in lupus.



Anemia

Anemia is defined as abnormally low hemoglobin concentration in blood. Red blood cells contain hemoglobin which contains iron and is responsible for carrying oxygen to the tissues of the body. Some symptoms of anemia include fatigue, weakness, palpitations, and shortness of breath. Symptom severity depends on the severity of the

anemia. There are many different causes of anemia. In lupus, the three most common types are anemia of chronic disease are; iron deficiency anemia, and hemolytic anemia. A patient with lupus can have more than one of these types of anemia concurrently. Each of these will be discussed separately.

Anemia of chronic disease can develop in many chronic conditions including lupus and other autoimmune and inflammatory diseases. This form of anemia is perhaps the most common type seen in patients with lupus, occurring in 60-40%. The anemia results from abnormal handling of iron in the bone marrow, reduced life span of red blood cells, and inadequate erythropoietin (a molecule which promotes formation of red blood cells) response to the anemia. The treatment of this form of anemia involves treating the underlying inflammatory process. Anemia of chronic disease is very commonly seen in lupus patients with kidney failure or uremia.

Injectable erythro-poietin is useful in correcting the anemia in this setting. Iron supplementation is not effective in the treatment of anemia of chronic disease. Iron deficiency anemia is also frequently encountered in lupus, and may result from chronic blood loss or inadequate dietary iron intake. Chronic blood loss can often be due to menstruation in women, or to disease in the gastrointestinal tract such as a peptic ulcer or other inflammatory lesions. Non-steroidal anti-inflammatory

drugs (NSAIDs), which are often taken by patients with lupus, can result in irritation of the stomach lining, leading to slow chronic blood loss. A blood test can be done to look for iron deficiency. The stool can also be tested for the presence of small amounts of blood (guaiac test).

When iron deficiency anemia is diagnosed, a source of blood loss should be looked for. Often, it is necessary to perform endoscopy of the gastrointestinal tract looking for abnormalities such as ulcers. The treatment is oral iron replacement therapy and treating any underlying problems causing blood loss.

Another class of anemia seen in lupus is hemolytic anemia. Hemolysis is defined as premature breakdown or destruction of red blood cells. The normal life span of a red blood cell is 120 days, but this can be greatly reduced in hemolytic anemia. In lupus, hemolysis is usually due to autoimmune hemolytic anemia, which results when abnormal antibodies attach to red blood cells in the blood stream. These attached antibodies then act as triggers for red cell destruction, which occurs primarily in the spleen. A test for this type of anemia includes the Coombs' test, which looks for the presence of antibodies on the red blood cells. The cells also have a characteristic microscopic appearance on a blood smear. Treatment of this anemia is aimed at suppressing the abnormal antibody production and usually starts with high doses of corticosteroids such as prednisone. If this is not effective, the patient may need to undergo surgical removal of the spleen, or splenectomy. Other immunosuppressive medications used in this anemia include azathioprine, danazol, cyclophosphamide, and others. Folic acid supplements are useful to promote formation of new red blood cells.

Blood transfusion is sometimes required and can be life-saving in cases of severe anemia. Compatibility between the donor's red blood cells and the recipient's plasma must be ensured, otherwise potentially fatal reactions may occur. Other complications of blood transfusions include fever during the transfusion, which is often due to white blood cell antibodies, and is usually transient and mild. The spread of various infections, especially HIV and hepatitis C, has been of great concern over the last several years. Donor blood is screened for these and other viruses and currently the risk of infection is believed to be extremely low.

Platelet Disorders

Platelets are small components of blood which are produced in the bone marrow by fragmentation of large cells called megakaryocytes. Platelets are important in the initial formation of a blood clot and if they are abnormal in function or in number, the patient is at risk for bleeding. A

reduction in the number of platelets in the blood stream is called thrombocytopenia. Thrombocytopenia is not an uncommon finding in patients with lupus, present in about 30-50%. The two most frequent settings in which a low platelet count may be encountered include immune thrombocytopenic purpura (ITP) and the antiphospholipid syndrome. These will be discussed separately.

ITP usually results when abnormal antibodies attack the platelets and lead to their premature destruction. The normal 7-10 day life span of the platelet is reduced to a few hours in this condition. In addition, the total number of platelets can become severely reduced.

The antibody coated platelets are destroyed in the spleen and liver. Clinically, a patient with ITP often develops easy

bruising, easy bleeding of the gums and skin, small red spots (petechiae) due to bleeding into the skin, and other manifestations of easy bleeding. Sometimes, ITP can co-exist with autoimmune hemolytic anemia (Evans syndrome). The treatment of ITP is aimed at stopping the production of the abnormal antibody that attacks the platelets. Again, this is usually accomplished with immunosuppressive drugs. The initial agent used is high dose prednisone. If prednisone fails, the patient may need to undergo splenectomy as in autoimmune hemolytic anemia. Sometimes, even these approaches are not successful in controlling the thrombocytopenia, and additional immunosuppressive drugs such as azathioprine, cyclophosphamide, and others may be used. In addition,

intravenous immunoglobulin (IVIG) is sometimes helpful in treating this condition. IVIG is a mixture of human antibodies, or immunoglobulins, and its exact mechanism of action is not clear. Its effect on improving platelet counts tends to be more short-term than the other agents mentioned.

Another cause of thrombocytopenia in lupus is due to the presence of specific antibodies called antiphospholipid (also called anticardiolipin) antibodies. Sometimes, 'antiphospholipid syndrome' can exist, in which patients can develop thrombocytopenia, frequent miscarriages, and a predisposition to blood clotting. The thrombocytopenia in this condition is usually quite mild and does not predispose the patient to bruising or bleeding. In contrast, patients with this condition tend to be easy clotters. This abnormality will be discussed in greater detail in the clotting disorders section.

Other less common causes of a reduced platelet count in the setting of lupus include reactions to drugs, TTP (thrombotic thrombocytopenic purpura), various bone marrow disorders, and others.

White Blood Cell Disorders

White blood cells are involved in helping fight infection, and are divided into various subtypes. A reduction in the white blood cell count is called leukopenia. The white blood cell subtypes that can be reduced in lupus are lymphocytes and granulocytes. Antibodies can be directed at either of these cell types and cause a reduction in their number. Lymphopenia (reduced lymphocyte count) is more common, and usually does not cause clinical problems. It can sometimes reflect the degree of lupus activity. Granulocytopenia (reduced granulocyte count) can predispose the patient to severe bacterial infections.

Low white blood cell counts can also be encountered as a side effect to the various immunosuppressive drugs used to treat lupus. Usually, stopping the drug or reducing its dose leads to improvements in the white blood cell count.