

Lupus

America's Least Known Major Disease

VASCULAR DISEASE

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THE VASCULAR SYSTEM

WHAT IS LUPUS?

The vascular system of the body is composed of a complex network of blood vessels (arteries and veins). A protein, known as hemoglobin, resides in red blood cells and is responsible for supplying oxygen to the various tissues around the body. Red blood cells, along with other types of cells and proteins, are propelled by the heart through the arteries until they reach their final destination. Oxygen is extracted by the tissues (muscles and skin for example), and blood is then returned through veins to the lungs for replenishment. Although the vascular system may be viewed as an intricate plumbing system for the transport of oxygen and nutrients, its function is vital for the survival of the tissues and organs of the body.

Interruption of arterial or venous blood flow may result in serious problems. When deprived of oxygen, a particular organ may be damaged or fail. For example, a heart attack is the result of a blockage in the coronary arteries (arteries that supply blood and oxygen to the heart). Although the disruption of normal blood flow is caused by a blockage within a blood vessel, there are several different reasons for an obstruction to occur. Arteries may become obstructed because of cholesterol build-up (atherosclerotic plaque) or blood clots (thrombosis), whereas obstruction to venous flow is generally caused by a blood clot within the vessel. To make matters even more complicated, blood clots can occur for a variety of reasons. Blood clots may occur because of inflammation in the vessel wall (vasculitis), or they may occur because of certain characteristics that render the blood more likely to clot, or coagulate (a hypercoagulable state). Each of these mechanisms is very relevant to SLE.

ATHEROSCLEROSIS

Over the last 20 years, much attention has been paid to cholesterol. High blood cholesterol may promote the formation of atherosclerotic plaque in the arteries of the heart as well as in other arteries. This may lead to cardiovascular disease and increase one's risk of a heart attack or stroke. Everyone of us needs to contend with this health issue, but patients with lupus should be particularly aware as those patients who have had the disease for at least 5 to 10 years appear to be at increased risk for cardiovascular disease, particularly for myocardial infarction. Traditional risk factors, such as age, high cholesterol levels, hypertension, diabetes, and obesity, contribute to atherosclerosis, but these factors alone cannot explain the extent of risk. Investigators have pointed out that patients with SLE are more prone to develop atherosclerotic disease because of inflammation, steroids, or kidney disease.

It is critically important to identify the presence of traditional and treatable cardiovascular risk factors such as smoking, high cholesterol, hypertension, or diabetes. Scientists are working to understand why lupus patients are more prone to develop vascular disease.

THROMBOSIS

Thrombosis is the medical term for a blood clot. Thrombosis may occur in large or small arteries or veins. If it occurs in an artery, the tissues or organ supplied by that artery are deprived of blood and oxygen. The end result is damage to that particular area of the body. If the occlusion occurs in a large vein, blood cannot return to the heart, and the area below the obstruction becomes swollen and painful. An example of such an event would be phlebitis of a leg vein (deep vein thrombosis). Although clots in the venous system cause less local damage than arterial clots, an additional concern relates to the ability of the clot to dislodge and travel to the lungs where it may interrupt blood flow (pulmonary embolus).

There are two main reasons why a thrombosis may occur. The blood vessel may be abnormal and promote the formation of a clot. Such is the case in vasculitis, an inflammation of the blood vessel. Alternatively, the blood cells or blood proteins flowing through the blood vessels may trigger clot formation. This latter scenario is referred to as a hypercoagulable state.

VASCULITIS

Vasculitis refers to inflammation of blood vessels; either arteries or veins may be involved. The culprit in lupus vasculitis is an overactive immune system, which generates antibodies and white blood cells that attack the blood vessel. An inflammatory reaction occurs within the blood vessel wall, and this process



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results in a damaged artery or vein. The clinical consequence of the damage depends on the type of vessel that is involved. If a very small vessel in the skin is damaged, the only manifestation may be a tiny red spot (purpura) in the skin. This is a reflection of the blood vessel becoming leaky, and red blood cells inappropriately escaping into the skin. If vasculitis affects a large thick-walled artery, the vessel does not typically become leaky. Rather, the outcome relates to an interruption of blood flow as a thrombus may develop at the site of inflammation and occlude the artery. If blood can no longer flow to the area of the body supplied by the inflamed artery, one could develop an infarction. Infarction refers to a state when tissues die because they are deprived of oxygen. Infarctions may occur anywhere in the body, e.g. heart (myocardial infarction), brain (stroke), intestines (bowel infarction), fingers and toes.

Diagnosing vasculitis can sometimes present a challenge to the physician. Manifestations of vasculitis are quite variable. They can include rash (purpura or ulcerations), persistent discoloration of a finger or toe, numbness or tingling, chest pain, stomach pain, or visual disturbances. Most of these symptoms, however, are not specific to vasculitis! Therefore, you should consult your physician, and let your doctor determine how to handle the situation. When vasculitis is present in the skin, rheumatologists and dermatologists can rapidly identify the process. On occasion, a relatively painless skin biopsy might be performed. When vasculitis affects internal blood vessels and organs, the diagnosis is more difficult to make. Depending on the area of suspected involvement, biopsies (nerve biopsy) are sometimes performed, and in other situations, imaging tests of the blood vessels (angiograms) are performed. Because of the urgency of the situation and the need to acutely treat a patient, doctors often make a clinical diagnosis without invasive testing.

Vasculitis can vary tremendously in its severity. Some patients with mild skin vasculitis, consisting of a few purpura, may not require any treatment, whereas others with more severe skin involvement, consisting of ulcerations, may require aggressive therapy with steroids or immunosuppressives. When vasculitis involves internal organs, aggressive therapy is a must. This may take the form of high dose steroids and often an immunosuppressive therapy such as cyclophosphamide. Vasculitis is fortunately a rare complication of SLE. Nevertheless, it can be very serious, and patients need to contact their doctors if they are not feeling well.

THE HYPERCOAGUABLE STATE

Hypercoaguability refers to the tendency for certain patients to form blood clots. These clots may develop in medium to large arteries or the large veins of the body. The consequences of arterial occlusions in the hypercoaguable state are essentially similar to those of vasculitic occlusions. The consequences of venous occlusion are local pain and swelling as well as the additional concern of an embolus.

Patients may form clots as a result of having overactive platelets, cells that normally assist in forming a blood clot. Alternatively, patients may be at increased risk if they have an abnormality of any of the numerous proteins in the body that are involved in maintaining the balance between clotting and bleeding. One of the most common hypercoaguable conditions in SLE is the antiphospholipid (aPL) syndrome. Patients with this syndrome make autoantibodies to phospholipids and/or a protein known as b2-glycoprotein I. The result of such antibody formation can be the development of blood clots in the: 1) large veins of the legs or arms (deep vein thrombosis), 2) arteries of the lung (pulmonary embolus), 3) arteries of the brain, heart, or abdomen (stroke, heart attack, bowel infarction, respectively), or 4) vessels of the placenta (miscarriage). Patients with lupus kidney disease (lupus nephritis) who lose a lot of protein in their urine may also be hypercoaguable. Patients who have had blood clots are typically treated with anticoagulants (medicines that prevent clot formation) such as heparin and coumadin.

THE FUTURE

Vascular biology is an exciting field, and it is assured that a greater understanding of the vascular system in SLE will arise from current and future research efforts. This will no doubt eventually result in safer and more effective therapies to deal with autoimmune diseases like SLE.