Cryoglobulinemic Vasculitis

Cryoglobulinemic vasculitis is a vasculitis of small blood vessels that is caused by deposition of immune complexes: large aggregates of antibodies and the other proteins they are bound to. Some other types of vasculitis are also caused by immune complexes, but cryoglobulinemic vasculitis is defined by a laboratory test that identifies immune complexes that fall out of solution in the cold. The severity of the disease is highly variable. Skin, joints, and nerves are commonly affected. Kidney disease is somewhat less common and with a wide range of severity. The heart, brain, or gastrointestinal tract each are affected in fewer than 10% of cases.

Who gets cryoglobulinemic vasculitis?

Most patients with cryoglobulinemic vasculitis (CV) are chronically infected with hepatitis C virus (HCV). However, fewer than 3% of persons infected with HCV will develop cryoglobulinemic vasculitis, although the number of patients who test positive for cryoglobulins may be as high as 50%. Many of the remaining patients with cryoglobulinemic vasculitis have lupus, Sjogren's syndrome, rheumatoid arthritis, or white blood cell cancers (lymphoma, myeloma, or Waldenstrom's macroglobulinemia) as the underlying cause.

Development of cryoglobulinemic vasculitis is rare among patients with these diseases. Since all of these diseases can affect persons of both sexes and all ages, cryoglobulinemic vasculitis affects a similar diversity of patients.

Symptoms

Most patients have weakness or fatigue, and many have sore joints or muscles. The most common appearance of vasculitis in the skin is purpura (bright red circles, from the size of a pinhead up to half an inch, often painful or itchy), but open sores are also common.

Damage to nerves (neuropathy) causes numbness, tingling, severe burning pain, and or weakness in a hand or foot.

Involvement of the gastrointestinal organs causes abdominal pain.

Heart involvement could cause symptoms of a heart attack (chest pain) or congestive heart failure (difficulty breathing, swelling in the legs).

Brain involvement can cause strokes, including multiple small strokes, and might also cause headaches. Any symptoms that resolve within a few hours are unlikely to be caused by vasculitis. Kidney disease causes no symptoms until severe kidney failure occurs.

Diagnosis

Most patients will have a biopsy of skin or nerve that shows vasculitis, or a kidney biopsy that shows a characteristic type of inflammation called membranoproliferative glomerulonephritis (MPGN).

In those settings, a positive blood test for cryoglobulins establishes the diagnosis of cryoglobulinemic vasculitis.

In patients with syndromes highly suggestive of cryoglobulinemic vasculitis, the blood test may allow diagnosis without biopsy.

The cryoglobulin test is difficult to do properly, since it requires that the tube of blood be transported and processed at body temperature. For this reason, doctors are concerned about the possibility of a "false negative" cryoglobulin test and often order other tests that are usually but not always abnormal in cryoglobulinemic vasculitis: rheumatoid factor (usually positive), complement (usually with low C4 protein), and serum protein electrophoresis (SPEP, often shows evidence of a "monoclonal" antibody). All patients with cryoglobulinemic vasculitis should be tested for HCV infection.

Treatment

For patients with HCV, anti-viral therapy is indicated regardless of the degree of severity. For less severe cases (e.g., purpura, weakness, and joint pain), anti-viral therapy alone is the treatment of choice.

Involvement of vital organs requires addition of immune-suppressive drugs. Prednisone, azathioprine, and cyclophosphamide have been widely used, but recent studies have indicated that rituximab may be superior to these medications. Cryoglobulinemic vasculitis without HCV infection is also treated using these medications or methotrexate (which is not used in HCV-infected patients), but no comparison of treatments has been reported.

Patients with life-threatening or organ-threatening cryoglobulinemic vasculitis often receive plasma-pheresis in addition to immune-suppressive medications.

What is the prognosis of cryoglobulinemic vasculitis?

For cryoglobulinemic vasculitis associated with HCV, effective anti-viral therapy usually prevents recurrence of vasculitis. If permanent damage to nerves or internal organs has not occurred, long-term prognosis is excellent.

Cryoglobulinemic Vasculitis *continued*

For patients in whom anti-viral therapy cannot be used or is ineffective, or in patients without HCV, repeated or long-term therapy with immune-suppressive drugs may be needed. Such treatment is usually effective in preventing further damage but has potentially serious side effects and requires regular monitoring by a doctor familiar with these medications.

Kidney disease in cryoglobulinemic vasculitis is usually not severe enough to lead to dialysis, but since it can be, monitoring of kidney function is also important.

The Vasculitis Foundation gratefully acknowledges Dr. Paul Monach, Boston University Vasculitis Center, for his expertise and contribution in developing this informational brochure.

The Vasculitis Foundation acknowledges an educational grant for support of this brochure from Genentech, Inc., and Biogen, Idec.

VASCULITIS FOUNDATION®
Support | Awareness | Research