Cryoglobulinemia

March 28, 2016 By Alan Franciscus

Cryoglobulinemia is a blood disorder caused by abnormal proteins in the blood called cryoglobulins. The cryoglobulins precipitate or clump together when blood is chilled then dissolve when rewarmed. The proteins can be deposited in small and medium-sized blood vessels which can lead to restricted blood flow to joints, muscles, and organs. The term frequently used is essential mixed cryoglobulinemia because the exact cause is unknown. There are three types of cryoglobulinemia – type I, type II and type III. Type I does not have rheumatoid factor activity whereas types II and III have rheumatoid factor activity. Rheumatoid factor is an antibody found in the blood of people afflicted with rheumatoid arthritis (a chronic autoimmune disease characterized by inflammation of the joints).

HCV AND CRYOGLOBULINEMIA

The relationship between HCV and cryoglobulinemia is believed to occur by way of the hepatitis C virus attaching itself to B lymphocyte cells, which causes the immune system to produce autoantibodies. The high prevalence of hepatitis C in people with cryoglobulinemia lends credence to the direct link between HCV and cryoglobulinemia. One study found that 90% of patients with type 2 or type 3 cryoglobulinemia had evidence of the hepatitis C antibodies.

Additionally, treating the underlying cause—hepatitis C—improves or resolves cryoglobulinemia further establishing the link. Also, cryoglobulinemia is associated with the hepatitis B virus and other liver disorders but to a much lesser extent.

Additional factors that strongly correlate with an increased risk for HCV-related cryoglobulinemia include the presence of cirrhosis, HCV infection over many years or decades, and female gender. In people with hepatitis C only about 3% of people with cryoglobulinemia show signs or symptoms of this condition. The other 97% of people with HCV and cryoglobulinemia have few symptoms or any of the blood or organ disorders associated with the more severe outcomes. It is important, however, to be monitored on a regular basis to make sure that the symptoms or disease progression does not worsen.

SYMPTOMS

People with symptomatic hepatitis C-related cryoglobulinemia can have ongoing problems that can cause many symptoms and disorders. The most common symptoms and complications associated with the cryoglobulinemia include:

- Vasculitis: inflammation of the small blood vessels of the skin, kidneys, gastrointestinal tract and other organs of the body. It can also cause red or purple blotching skin that usually appears on the lower extremities of the body. Rashes, sores, and ulcers can also occur
- Renal (kidney) disease: caused by deposits of the cryoglobulins in the kidneys. Symptoms include blood and proteins in the urine Arthralgias and arthritis: pain and/or inflammation in the joints
- Pruritus (itching): mild to severe
- Fatigue: mild to severe
- Pain: mild to severe
- Lymph node enlargement: swollen gland-like tissue in the lymphatic vessels containing cells that become lymphocytes (white blood cells)
- Peripheral neuropathy: numbness and tingling in the hands, legs and feet due to decreased blood and/ or inflammation of the peripheral nerves
- Stomach pain
- Bleeding disorders: internal bleeding and abnormal blood clot formations
- Non-Hodgkin's lymphoma: (cancers of the lymphoid system)
- Raynaud's syndrome: a disorder that causes the blood vessels in the fingers, toes, ears, and nose to constrict or narrow causing pain
- Multiple myelomas: cancer of the bone marrow and blood. The more serious consequences of cryoglobulinemia usually occur after many years or decades of infection with the hepatitis C virus.

Note: Everyone with hepatitis C should be evaluated and receive HCV treatment. Current treatment is very expensive, and many insurance companies and Medicaid are restricting HCV treatment to people with the most severe HCV disease progression. One of the conditions that qualify people for HCV treatment is symptomatic cryoglobulinemia. Be sure to discuss any symptoms and conditions with your medical providers and have them included in your medical records. If you do not have insurance, you may qualify for free medications through the pharmaceutical patient assistance programs. If you have insurance, there are co-pay assistance programs.

DIAGNOSIS

A simple blood test is performed to diagnose cryoglobulinemia, but the blood sample has to be handled carefully – drawing the blood sample at room temperature then cooling it to see if the blood precipitates or clumps together.

TREATMENT

The approach to treating HCV-related cryoglobulinemia is to treat the underlying cause – hepatitis C. Cryoglobulin disappearance, improvement in kidney function and complete or partial resolution of cryoglobulinemia syndrome occurs after successfully curing hepatitis C. The study reported in this issue of SnapShots demonstrates that direct acting antiviral medications are safe and effective to treat hepatitis C and cryoglobulinemia. Now that we have interferon- and ribavirin-free therapies the future of treatment for cryoglobulinemia and other HCV-related extrahepatic manifestations is bright.

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