Vasculitis Syndromes of the Central and Peripheral Nervous Systems

U.S. DEPARTMENT OF HEALTH
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What is vasculitis?

Vasculitis is inflammation of blood vessels (which includes the veins, arteries, and capillaries) that carry blood throughout the body. Vasculitis can affect blood vessels of any type, size, or location. The inflammation can cause the walls of blood vessels to weaken, stretch, thicken, and develop swelling or scarring, which can narrow the vessel and slow or completely stop the normal flow of blood. This reduced blood flow can permanently damage organs and tissues, including the brain and spinal cord (the central nervous system, or CNS), and peripheral nervous system (PNS, which transmits information from the brain and central nervous system to other parts of the body). In some cases, the weakened vessel can burst, causing bleeding into surrounding tissues. In the brain, the inflammation can cause headaches and stroke-like symptoms, or even death.

Vasculitis (also called angiitis) can affect anyone, although some types occur more often in people who have autoimmune disorders (disorders that occur when the immune system attacks healthy body cells) such as lupus and rheumatoid arthritis, or infectious disorders such as hepatitis B or C. Some forms of vasculitis affect a particular organ, while others may affect

many organs at the same time. Vasculitis affecting only the brain and spinal cord that is not the result of another systemic disorder is called primary angiitis of the central nervous system. In some instances, the vasculitis may improve without treatment, while other times, it requires medications.

What causes vasculitis?

Vasculitis occurs when the immune system attacks blood vessels in the body by mistake. In most instances, the cause of the attack isn't known. In others instances, an ongoing or recent infection, other disease of the immune system, an allergic reaction to medications or toxins, and certain blood cancers (such as lymphoma and leukemia) can trigger an immune system reaction and cause the damaging inflammation.

How does vasculitis affect the nervous system?

Vasculitis can cause problems in the central and peripheral nervous systems, where it affects the blood vessels that nourish the brain, spinal cord, and peripheral nerves. Nervous system complications from vasculitis include:

- headaches, especially a headache that doesn't go away
- cerebral aneurysms (a weak spot on a blood vessel in the brain that balloons out) can burst and spill blood into surrounding tissue (called hemorrhagic stroke)
- blood in the inflamed blood vessel can clot (thrombosis), blocking blood flow and causing ischemic stroke

- confusion or forgetfulness leading to dementia
- abnormal sensations or a loss of sensations
- muscle weakness and paralysis, usually in the arms and legs
- pain
- swelling of the brain
- vision problems
- seizures and convulsions
- trouble speaking or understanding.

Symptoms of vasculitis generally include fever, a sick feeling, weight loss, unusual rashes or skin discoloration, and damage to virtually any organ system.

How are these syndromes diagnosed in the nervous system?

Diagnosing vasculitis can be difficult, as some diseases have similar symptoms of vasculitis. It is especially difficult to distinguish from non-inflammatory causes of vasoconstriction (a decrease in the diameter of a blood vessel due to a muscle contraction in the vessel wall). The diagnosis of a CNS or PNS vasculitis disorder will depend upon the number of blood vessels involved, their size, and their location as well as the types of other organs involved. A doctor who suspects CNS or PNS vasculitis will review the person's medical history, perform a physical exam to confirm signs and symptoms, and order diagnostic tests and procedures, including:

- blood and urine tests to look for signs of inflammation (such as abnormal levels of certain proteins, antibodies, and blood cells)

- analysis of the fluid that surrounds the brain and spinal cord (cerebrospinal fluid) to check for infection and signs of inflammation
- biopsy of brain or nerve tissue (involving removal of a small piece of tissue that is studied under a microscope)
- diagnostic imaging using computed tomography (CT) and magnetic resonance imaging (MRI) scans that produce two- and three-dimensional images of the nerves, brain and other organs, and tissues. Scans are performed before and after injection of a contrast agent to determine if the contrast agent leaks from the weakened vessels.
- Angiogram (x-ray imaging using a special dye that is released into the bloodstream) to detect the degree of narrowing of the blood vessel in the brain, head, or neck
- ultrasound to produce high-resolution images of the blood vessel walls and to measure blood flow velocity.

How is vasculitis treated?

Treatment for vasculitis typically depends on the organ(s) affected and involves drugs aimed at suppressing the abnormal immune system activity and reducing inflammation. Duration of treatment depends on the type of vasculitis but usually long-term treatment is needed. Medications used to treat vasculitis include:

- Glucocorticoid drugs ("steroids") such as prednisone. These drugs, which are often the primary treatment for

vasculitis, have anti-inflammatory effects and are generally quick-acting. They may be given in combination with other immunosuppressive drugs.

- Immunosuppressant or cytotoxic drugs. These medications include methotrexate, azathioprine, and cyclophosphamide. These agents stop or decrease the function of immune system cells.
- Rituximab, a type of medication called "monoclonal antibody," works by attaching to certain abnormally functioning immune cells (B cells) and killing them. It has been shown not only to be effective in stopping inflammation, but also for maintenance therapy to prevent flare-ups.

Aneurysms involved with vasculitis may need to be treated surgically, involving procedures that block the flow of blood to an aneurysm.

What are some of the nervous system vasculitis syndromes?

There are many forms of vasculitis that can affect the brain, spinal cord, and nerves, including:

Giant cell arteritis (also called temporal arteritis or cranial arteritis)

Giant cell arteritis is a type of vasculitis that affects the aorta and its primary branches. The temporal artery (found on both sides of the head and running across the temple) and the ophthalmic artery that supplies the eyes are often affected. A biopsy of the temporal artery is often performed to confirm the diagnosis.

Giant cell arteritis typically occurs in people age 50 and older. Symptoms of giant cell arteritis are:

- new, severe headache
- visual problems, including blurred or double vision, or sudden vision loss
- pain in the jaw or tongue when chewing or swallowing
- tenderness in the temporal arteries or the scalp.

Fever, weight loss, and neck or muscle pain can occur, usually in the early phase of the disease. Individuals may also have joint pain, fatigue, and discomfort in the neck/shoulders/hip regions known as polymyalgia rheumatica. Vision loss is a feared complication of giant cell arteritis. Untreated temporal arteritis can cause strokes and even death. Although giant cell arteritis was traditionally thought to affect the arteries of the head and neck region, many individuals with giant cell arteritis can have inflammation in the large arteries within the chest, abdomen, and pelvis.

Primary angiitis of the CNS (or granulomatous angiitis)

The symptoms of this rare disorder typically develop slowly and include headache, dementia, behavioral changes, pain, sensory abnormalities, and tremor. Stroke, transient ischemic attack, multiple mini-strokes, and seizures can occur. Definitive diagnosis may require brain biopsy. The disorder can affect anyone of any age but peaks about age 50, and is most often seen in males. It is fatal if left untreated.

Takayasu's arteritis

This disease affects large arteries such as the aorta, which brings blood to the arms, legs and head. Takayasu's arteritis usually first occurs in women under the age of 40. The main symptoms are headaches, dizziness, a feeling of cold or numbness in the limbs, problems with memory and thinking, and visual disturbances. It may also cause strokes, heart attacks, and damage to the intestines. The disorder can cause partial to complete disability, and can be fatal if left untreated. Imaging studies to evaluate the arteries for signs of narrowing, blockage, or swelling are often required to establish the diagnosis and to monitor disease activity over time.

Polyarteritis nodosa

The onset of this rare disease can occur at any age but most often appears between the ages of 40 and 60 years. Men are affected more often than women. Symptoms can mimic those of many other diseases, but the most common initial complaints are fever, abdominal pain, numbness or pain in the legs and limbs, muscle aches, weakness, abnormal sensations, and unexplained weight loss. As the disease progresses, the kidneys may fail and high blood pressure may develop rapidly. Damage to the PNS with neuropathy is more common than damage to the CNS, but if the disease does involve the CNS, damage to brain and spinal cord tissue can occur. In some instances the disease can recur after a few years. If untreated, the disorder is often fatal, ending in failure of vital organs.

Deficiency of adenosine deaminase 2 (DADA2)

DADA2 is a rare, genetic form of vasculitis caused by a mutation in the *CECR1* gene. Although most forms of vasculitis typically do not run in a family, DADA2 can occur in more than one family member. Symptoms of DADA2 overlap with symptoms of polyarteritis nodosa, including fever, skin nodules, a lace-like rash of the trunk and limbs (livedo reticularis), and joint pain. Most individuals with DADA2 experience strokes in infancy or early childhood. DADA2 was discovered by researchers at the NIH and first reported in the medical literature in 2014.

In addition, other forms of vasculitis can cause neurological complications. Among these disorders is **Kawasaki disease**, a rare form of vasculitis that can cause stroke or brain damage in children. It primarily affects children age 5 or younger. Inflammation of the walls of blood vessels in the coronary arteries may cause aneurysms. Symptoms include high fever lasting at least five days, swollen hands and feet, red eyes and lips, and swollen lymph nodes. Most children can fully recover if treated early. Among other systemic vasculitis syndromes that can affect the nervous system are Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome, cryoglobulinemia, system lupus erythematosus, Behcet disease, Sjogren's disease, and rheumatoid arthritis. Inflammation of blood vessels that supply the nervous system can occur due to infections such as endocarditis (infection of heart valves), herpes zoster or upper face chicken pox, mycoplasma, and tuberculosis.

What research is being done?

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. The NINDS is a component of the National Institutes of Health (NIH), the leading biomedical research organization in the world.

Several NINDS-funded investigators are studying blood vessel damage and cerebral blood flow as it relates to stroke. A better understanding of the mechanisms involved in injury and repair of blood vessels in the brain may lead to improvements in the treatment and prevention of other vascular disorders.

The Vasculitis Translational Research Program at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) is dedicated to performing clinical and translational research in all types of vasculitis. People aged 5 or older who have or are thought to have vasculitis are eligible to participate. Objectives of the program are to follow people with vasculitis over time to see how the disease affects them and to discover new aspects of vasculitis that will help doctors learn how to better care for individuals with vasculitis. Investigators in this program work in collaboration with investigators at NINDS and with the Vasculitis Clinical Research Consortium. For more information, see: https://clinicaltrials.gov/ct2/show/NCT02257866.

The NIH supports The Vasculitis Clinical Research Consortium (VCRC, www.rarediseasesnetwork.org/vcrc/), a network of academic medical centers, patient support organizations, and clinical research resources dedicated to conducting clinical research and improving the care of individuals with various vasculitis disorders, including polyarteritis nodosa, Takayasu's arteritis, and giant cell arteritis. Currently, 15 medical centers participating in the Consortium are located in the United States, Canada, and Turkey. The Consortium's internet site provides information about clinical research and clinical trial opportunities and helps individuals connect with expert doctors and patient support groups.

Other NIH institutes that support research on vasculitis include the National Heart, Lung, and Blood Institute and the National Institute of Arthritis and Musculoskeletal and Skin Diseases. More information about NIH-funded research on vasculitis and other disorders can be found using NIH RePORTER (http://projectreporter.nih.gov), a searchable database of current and past research projects supported by NIH and other federal agencies. RePORTER also includes links to publications and resources from these projects.

Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
800-352-9424
www.ninds.nih.gov

Information also is available from the following organizations:

American Autoimmune Related Diseases Association
22100 Gratiot Avenue
Eastpointe, MI 48021-2227
586-776-3900
800-598-4668
www.aarda.org

National Organization for Rare Disorders (NORD)
P.O. Box 1968
55 Kenosia Avenue
Danbury, CT 06813-1968
203-744-0100 Voice Mail
800-999-NORD (6673)
www.rarediseases.org

National Heart, Lung and Blood Institute (NHLBI) Health Information Center
National Institutes of Health, DHHS
P.O. Box 30105
Bethesda, MD 20824-0105
301-592-8573
www.nhlbi.nih.gov

National Institute of Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse
National Institutes of Health, DHHS
1 AMS Circle
Bethesda, MD 20892-3675
877-226-4267
www.niams.nih.gov

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