Cleveland Clinic

Granulomatosis with Polyangiitis (GPA, formerly called Wegener's)

Granulomatosis with polyangiitis (formerly called Wegener's) is a rare disease of uncertain cause that can affect people of all ages. It is characterized by inflammation in various tissues, including blood vessels (vasculitis), but primarily parts of the respiratory tract and the kidneys.

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Overview

What is granulomatosis with polyangiitis

Granulomatosis with polyangiitis (GPA, formerly called Wegener's) is a rare disease of uncertain cause. It is the result of inflammation within the tissues called granulomatous inflammation and blood vessel inflammation ("vasculitis"), which can damage organ systems. The areas most commonly affected by GPA include the sinuses, lungs, and kidneys, but any site can be affected.

What is vasculitis?

Vasculitis is a general term that refers to inflammation of the blood vessels. When inflamed, the blood vessel may become weakened and stretch forming an aneurysm, or become so thin that it ruptures resulting in bleeding into the tissue. Vasculitis can also cause blood vessel narrowing

become damaged from loss of oxygen and nutrients that were being supplied by the blood.

What are the features of granulomatosis with polyangiitis (GPA)?

GPA primarily affects the upper respiratory tract (sinuses, nose, trachea [upper air tube]), lungs, and kidneys. Any other organ in the body can be affected as well.

The symptoms of GPA and their severity vary among patients. General signs of the disease may include:

- Loss of appetite
- Weight loss
- Fever
- Fatigue

Most patients first notice symptoms in the respiratory tract. Symptoms may include:

- Persistent runny nose (also called rhinorrhea) or the formation of nasal crusts and sores
- Nasal or facial pain
- Nose bleeds or unusual nasal discharge, caused by inflammation of the nose or sinuses
- Cough that might include bloody phlegm caused by upper airway or

- Chest discomfort with or without shortness of breath
- Middle ear inflammation (also called otitis media), pain, or hearing loss
- Voice change, wheezing, or shortness of breath caused by inflammation of the trachea

Other possible features include:

- Eye inflammation and/or pressure behind the eye, making eye movement difficult, with or without loss of vision
- Joint pain (arthritis) or muscle pain
- Rashes or skin sores
- Kidney inflammation (although kidney inflammation is common, it is not usually associated with symptoms, such as pain).

Who is affected by granulomatosis with

GPA can occur in people of all ages. The peak age groups affected are from 40-60 years. It appears to affect men and women equally.

Symptoms and Causes

What causes granulomatosis with polyangiitis (GPA)?

The cause of GPA is unknown. GPA is not a form of cancer, it is not contagious, and it does not usually occur within families. Evidence from research laboratories strongly supports the idea that the immune system plays a critical role in GPA such that the immune system causes blood vessel and tissue inflammation and damage.

How is granulomatosis with polyangiitis (GPA) diagnosed?

GPA has symptoms similar to a number of other disorders, which may make it difficult to diagnose. However, for the most effective and successful treatment, early diagnosis is critical.

Once the diagnosis of GPA is suspected, a biopsy (tissue sample) of an affected area is often performed to try to confirm the presence of vasculitis. Biopsies are only recommended for organ sites in which there are abnormal findings present by examination, laboratory tests, or imaging.

It is the combination of symptoms, results of physical examinations, laboratory tests, X-rays, and sometimes a biopsy (sample) of affected tissue (skin, nasal membranes, sinus, lung, kidney or other sites) that together prove the diagnosis of GPA. Following treatment, these factors are also critical in judging whether the disease is active or in remission.

A positive blood test for antineutrophil cytoplasmic antibodies (ANCA) can support a suspected diagnosis of the disease. However, this blood test does not by itself prove the diagnosis of GPA or determine disease activity.

GPA often affects the lungs. In patients with GPA that have no lung symptoms (coughing or shortness of breath), imaging tests (conventional X-rays or a CT scan) will show lung abnormalities in up to one third of cases. Therefore, it is important to have lung images performed if active GPA is suspected, even if you do not have any symptoms of lung disease.

How is granulomatosis with polyangiitis (GPA) treated?

Because GPA is often a life-threatening disease, it is treated with a variety of powerful drugs that have been shown to be life-saving. Medications that suppress the immune system form the foundation of treatment for GPA. The severity of the disease in each individual case dictates what immunosuppressive medications are used. There are a variety of immunosuppressive medications that are used in GPA, each of which has individual side effects.

People with GPA who have critical organ system involvement are generally treated with corticosteroids combined with another immunosuppressive medication such as cyclophosphamide (Cytoxan ®) or rituximab (Rituxan®). In patients who have less severe GPA, corticosteroids and methotrexate can be used initially. The goal of treatment is to stop all injury that is occurring as a result of GPA. If disease activity can be completely "turned off," this is called "remission." Once it is apparent that the disease is improving, doctors slowly reduce the corticosteroid dose and eventually hope to discontinue it completely. When cyclophosphamide is used, it is only given until the time of remission (usually around 3 to 6 months), after which time it is switched to another immunosuppressive agent, such as methotrexate, azathioprine (Imuran®), or mycophenolate mofetil (Cellcept®) to maintain remission. The treatment duration of the maintenance immunosuppressive medication may vary between individuals. In most instances, it is given for a minimum of 2 years before consideration is given to slowly reduce the dose toward discontinuation.

transplant rejection. Methotrexate is used to treat rheumatoid arthritis and psoriasis. Both cyclophosphamide and methotrexate are given at high doses as a treatment for certain types of cancer and therefore are sometimes referred to as "chemotherapy." In cancer treatment, these medications work by killing or slowing the growth of rapidly multiplying cancer cells. In vasculitis, these medications are given at doses that are 10 to 100 times lower than those used to treat cancer, and their primary effect is to influence the behavior of the immune system in a manner that results in immunosuppression. Rituximab belongs to a class of medications called biologic agents that target a specific element of the immune system. Recent studies found that rituximab was as effective as cyclophosphamide for treating severe active GPA.

What are some side effects associated with treatment of granulomatosis with polyangiitis (GPA)?

Because these medications suppress the immune system, there is an increased risk of developing serious infections. Each immunosuppressive drug also has a unique set of potential side effects. Monitoring for the side effects associated with each drug is critical to prevent or minimize their occurrence. Also, the fact that a patient may initially tolerate treatment does not guarantee that tolerance will remain the same over time.

Regardless of the medication used, ongoing monitoring of the patient's lab work is essential while treating these diseases. Methotrexate, azathioprine, and cyclophosphamide can suppress the patient's ability to make blood

medication can be adjusted or discontinued depending on the severity. Cyclophosphamide also has important side effects, such as reduced fertility in younger patients, as well as an increased risk of developing bladder cancer. Rituximab use has a rare increased risk of a brain infection that can be life-threatening.

Outlook / Prognosis

What is the outlook for people with granulomatosis with polyangiitis (GPA)?

After achieving remission, it is possible for GPA to recur (often referred to as a "relapse"). Relapses may be similar to what the patient experienced at the time of their diagnosis, or the symptoms may be different. The likelihood of experiencing a severe relapse can be minimized by prompt reporting to the doctor of any new symptoms, regular doctor follow-up, and ongoing monitoring with laboratory tests and imaging. The treatment approach for relapses is similar to that of newly diagnosed disease.

GPA is a very serious disease, and its treatment carries significant risks. However, treatment can be life-saving when the diagnosis is made in a timely fashion and appropriate treatment initiated.

Prior to recognizing effective therapy in the 1970s, half of all patients with this illness died within 5 months of diagnosis. Today, more than 80% of treated patients are alive at least eight years later. For many people with GPA, long term survival has been seen with many able to lead relatively

Medically Reviewed

Last reviewed by a Cleveland Clinic medical professional on 07/16/2019.

Learn more about our editorial process.

References

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