Working towards a greater understanding of Wegener’s Granulomatosis (GPA) and its ultimate cure

Until we can breathe again

What is Wegener’s Granulomatosis (GPA)?

- Wegener Granulomatosis (GPA or Granulomatosis with polyangiitis) is a rare condition of unknown cause that develops as a result of inflammation in the blood vessels.
- Around 500 people are diagnosed with the condition each year in the UK.
- It can occur at any age but is most often seen in middle age and distributed equally between men and women.
- It is rare for it to occur in two people in the same family, so there is not a strong genetic link.
- GPA can affect many different organs and systems including the sinuses, ears, throat, lungs, kidneys, nerves, brain and skin. Joint pains and eye symptoms can also occur.
- Less often the heart and bowels can become involved and some patients seem to be at a greater risk of developing blood clots in the leg or lung.
- Inflammation in the blood vessels occurs as the immune system, which usually works to fight infection, begins to attack your body. This is termed autoimmunity. The steps that lead to this occurring are not clearly understood.
- GPA is caused by a particular type of inflammation which has a characteristic pattern when tissues are examined under a microscope. This is a result of white blood cells arranging themselves in a certain way called a granuloma.

The Symptoms

Early in the disorder, symptoms are usually very non-specific and include:

- a general feeling of being unwell
- flu-like symptoms
- loss of appetite
- fevers
- night sweats
- severe fatigue
- weight loss.

The most common symptoms include:

- sinusitis
- a persistent runny nose
- nose bleeds
- mouth or nose ulcers
- a persistent cough
- painful joints and muscles
- skin rashes.

Other common symptoms are:

- hoarseness
- noisy breathing
- earache
- nasal bridge tenderness
- hearing loss
- recurrent ear infections
- discharge from the ears
- Patients may also experience shortness of breath or chest pain, and some people may cough up blood.

The symptoms that an individual experiences depend on which blood vessels are inflamed and can vary greatly. For example if the blood vessels in the skin are inflamed then skin rashes will be seen and if the blood vessels in the eyes or brain are affected then you may develop painful red eyes, headaches and heaviness or weakness in the arms and legs.
How is the diagnosis made?

Patients with generalised symptoms will need a full history and a thorough physical examination. You can help your doctor by trying to give as full an account of your symptoms as possible. A group of expert doctors have put together a list of typical features that are useful when making a diagnosis of GPA. In reality these do not always apply as each individual case tends to be unique and the diagnosis should be made by a trained specialist.

The presence of 2 or more of the following 4 findings is usually necessary for a specialist to consider a diagnosis of GPA.

1. Nose or mouth inflammation (painful or painless oral ulcers or purulent or bloody nasal discharge)
2. Abnormal chest x-ray showing nodules, shadows, or cavities
3. Abnormal laboratory tests — Blood count, kidney and liver tests and levels of blood inflammation such as the CRP (C-reactive Protein) and ESR. The urine should be tested for the presence of blood and protein.
4. Granulomatous inflammation (the typical white blood cell pattern seen under a microscope) on biopsy of an artery or area around a blood vessel. The tissue biopsy can be taken from the skin and nose and sometimes from the lungs or kidneys.

The ANCA blood test is also used to make the diagnosis, although up to 40 percent of patients with limited involvement may have a negative ANCA test.

Treatment of Wegener’s (GPA)

The aim of treatment is to rapidly get inflammation under control to limit organ damage. Treatment depends on whether there is limited or more widespread disease and how severe the condition is. For most seriously ill patients, a combination of drugs such as steroids and cyclophosphamide remains the best way of getting an early response — in many patients this can be life-saving. This is then followed by a more long-term approach using different drugs, for example azathioprine, to keep the patient in remission.

Steroids:
Corticosteroids (steroids) rapidly reduce inflammation throughout the body and are widely used in treating GPA. Prednisone and prednisolone are the most commonly used oral steroids. Doses are variable depending on the severity of the disease. Steroids are usually well tolerated although have long term side effects if used at high doses for over six months. These may include weight gain, mood swings, osteoporosis, high blood pressure and diabetes and your doctor will want to reduce your dose as quickly as possible.

To counteract some of these steroid side effects, your doctor may also prescribe Calcium supplements and a bisphosphonate, which prevents bone breakdown and is used in the treatment and prevention of osteoporosis.

Immunosuppressive Agents:
Steroid-sparing medications are frequently used to limit the dose and side-effects of steroids. They tend to work more slowly at modifying the inflammation but do not have the steroid side-effects. The use of these drugs frequently allows the dose of prednisolone to be reduced to very small doses that keep the condition under control and minimise long term side-effects. Frequently used medicines include Cyclophosphamide, Methotrexate, Azathioprine and Mycophenolate Mofetil.

Many of these drugs were first used in the treatment of cancer, and have a reputation as a ‘chemotherapy’ drug. Whilst side-effects are numerous and potentially serious, physicians have learned to use much smaller doses of these agents than those used in cancer with the result that these drugs are extremely effective but the side-effects are tolerable. These drugs do require regular monitoring of the blood, as the full blood count and liver function can be affected.

Using these combinations of drugs, up to 90% of patients may go into a remission from their disease. However, disease ‘flares’ occur frequently in GPA (between 60 and 80% of patients) and so treatment may last for many years and most patients will need very long term monitoring of their condition.

As GPA is a disease of the immunity and most of these medications affect the immune system, your ability to fight certain infections can be reduced. For this reason, doctors may prescribe an antibiotic, Co-Trimoxazole (Septrin), to reduce the risk of chest and sinus infections.

Newer Medications:
Rituximab has been found to be effective in some extreme cases of GPA and recent clinical trials have demonstrated very promising results. It works by reducing the number of B-cells (a type of white blood cell) that drive the inflammatory process.
DONATION FORM

Wegener’s Granulomatosis (GPA) is a rare condition that gets overlooked in the allocation of funding in the NHS. Donations to the Wegener’s Trust are therefore highly effective in furthering our understanding of the condition and of potential treatments.

For further information, patient stories or to donate to the St Thomas’ Wegener’s Trust, visit…

www.wegeners.org.uk

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