Wegener's Granulomatosis (WG) – Case Report

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Prevalence: Approximately 1 in 30 000 people[1].

Etiology

The cause of WG remains unknown, but it appears to develop as a result of an initial inflammation-causing event that triggers an abnormal reaction from the immune system[2]. Scientists speculate that the initial event may be an infection, an environmental toxin, a genetic predisposition to the condition, or a combination of all of these[2]. (WG is <u>not</u> an infection, nor is it a type of cancer) [2].

Description

WG causes inflammation of the blood vessels, which restricts blood flow to various organs[2]. This disorder most commonly affects the kidneys, lungs and upper respiratory tract[2]. If blood flow to these organs is restricted, damage can occur[2]. WG also produces inflammatory tissue called granuloma, which is found around the blood vessels and can destroy normal tissue[2].

Clinical Presentation

Symptoms may either develop suddenly or gradually and the first symptoms usually involve the respiratory tract[2]. The kidneys, if involved, don't usually cause symptoms early in the disease and therefore kidney involvement can only be detected by blood and urine tests[2]. However, this condition often worsens rapidly, affecting blood vessels and the organs they supply[2]. With time, kidney involvement leads to kidney failure and anemia[2]. Signs and symptoms of WG may include[2]:

- Constantly runny nose
- Nosebleeds
- Sinus pain and inflammation (sinusitis)
- Ear infections
- Cough
- Coughing up blood
- Shortness of breath
- General ill feeling (malaise)
- Appetite loss
- Joint aches and swelling
- Skin sores
- Eye redness, burning or pain
- Double or decreased vision
- Fever
- Weakness and fatigue, possibly associated with low red blood cell count (anemia)

Diagnosis

WG is diagnosed based on the patient's signs & symptoms, a physical exam, a medical history, and may also include any of the following[2]:

<u>Blood Tests:</u>
- To check for certain proteins called anti-neutrophil cytoplasmic autoantibdodies (ANCA) in the blood. The presence of these autoantibodies supports a WG diagnosis but this alone can't confirm it.
- To measure erythrocyte sedimentation rate (sed rate or ESR), which indicates the levels of inflammation in the body.
- To check for anemia.
- To measure creatinine levels to assess how the kidneys are functioning.

<u>Urine Tests:</u>
- To evaluate kidney function.

<u>Chest X-ray:</u>
- To look for cavities or masses in the lungs. (Can't distinguish WG from other lung diseases).

Biopsy of Affected Tissue:
- To look for the presence of vasculitis and granulomas. This is the only sure way to confirm a diagnosis of WG.

Prognosis

- Although there is no cure for WG, early diagnosis and proper treatment can effectively bring the disease into remission with complete absence of all signs of the disease, and can last up to 5-20 years[3]. Some patients will even achieve a drug-free remission[3]. Long-term remission can be maintained with medications, close management and regular lab tests[3].
- Unfortunately, relapses are common[3]. They can be caught at their earliest and most treatable stage by paying attention to the patient's symptoms and lab tests[3].
- Without treatment, WG can be fatal, most commonly from kidney failure[2].

Treatment

Goals: Induce & Maintain Remission

First Line Medications[3]

Prednisone:
- Given initially in high doses (60–100 mg/d) then in 2-4 weeks may be tapered to alternate-day regimen, and gradually discontinued over 2–6 months, depending on clinical course.

Cyclophosphamide:
- Initial dose: 4 mg/kg/d IV for 2–3 days then 2 mg/kg/d PO or start at 2 mg/kg/d PO
- Dosage adjustments based on patient response and toxicity (ie: bone marrow suppression).
- Usually continued for 1–2 years after patient is felt to be in remission, and then tapered slowly, with careful monitoring for reactivation of disease.

Methotrexate:
- 15–25 mg/wk PO has been successful in maintaining remission following cyclophosphamide.
- Methotrexate may replace cyclophosphamide if there's no pulmonary or renal involvement.

Second Line Medications[3]

Azathioprine: Used if history of severe bone marrow toxicity or hemorrhagic cystitis from cyclophosphamide.

Trimethoprim-sulfamethoxazole (TMP-SMX): Has success in some patients with limited disease (usually upper airway), and potential adjunctive therapy with prednisone and cyclophosphamide.

Rituximab: Has been reported to be useful in isolated cases or small series of patients.

IV Immunoglobulins (IVIg): Has been useful in case reports of patients with disease relapses.

Other*:* WG patients may also require medications to prevent osteoporosis, which may result from extended prednisone use. Many patients will also need the antibiotic TMP-SMX to help prevent secondary lung infections called Pneumocystis carinii pneumonia (PCP).

Case Report

The following is a case report of a rural Saskatchewan patient's experience with the process of being diagnosed and treated for Wegener's Granulomatosis. The patient will be referred to as JA throughout the case report. (The patient's initials have been changed to maintain confidentiality).

Background

No family history of WG
No significant illness/virus prior to symptoms

Description

Day 1: JA's symptoms began with an extremely painful sore throat and a bad cold. She was not concerned as it was the flu season and many people were experiencing similar symptoms. Later that month, JA began to cough up blood. (This continued until patient was hospitalized 3 months later).

Day 41: JA noticed a sharp pain in her left shoulder which progressed into her arm. That night, JA had taken someone else to the emergency department and decided to ask about the cause of her symptoms. A cardiac work-up appeared normal, but kidney tests (creatinine), blood tests (hemoglobin), and electrolytes (potassium) were found to be out of the normal range. Nothing was done at that time.

A few days after the pain had started, JA awoke early one morning to find that the pain had now moved over to her right shoulder. Then, a few days later the same pain had moved into the middle of the left side of her back.

Day 48: Due to the increasing severity of her symptoms, JA returned to the emergency department. JA's blood work again showed the same abnormalities (high creatinine, low hemoglobin, and low potassium). This time an erythrocyte sedimentation rate (ESR) test was also done and the results showed a level three times higher than normal, which indicated inflammation in her body. A CT scan and Chest X-ray were performed and found to be normal at this time.

Day 51: JA went for a kidney ultrasound.

As time progressed, JA continued feeling generally unwell, with symptoms including: aches, chills, and fatigue. Her legs and feet throbbed and ached. Her hands felt numb, tingled, and ached. The pain continued to worsen and by day 80 it was getting to the point where she found it hard to work. Although JA knew something was wrong, the fact that the pain kept changing locations seemed odd.

Day 86: While rubbing her legs in an attempt to soothe the pain, JA noticed a red, raised, warm, and painful lump (about 3 inches in size) on her shin, which she hadn't noticed before.

Day 87: JA's blood work was checked. Her creatinine levels came back more elevated than previously, ESR was still high, and hemoglobin was even more below range than the last test.

It was as this time that JA was diagnosed with WG. Following the diagnosis, JA was sent to a city hospital for specialized care.

While in the hospital, doctors noted that the knuckles of JA's hands and feet were swollen and sore (an arthritic type of appearance and symptoms).

Follow-up

- Once a diagnosis was finally given, JA was started on appropriate medications. The pain quickly began improving and continued to do so.
- Although JA did suffer some kidney damage, her disease was caught and treated early enough that the damage did not cause any severe long-term complications.
- JA could not return to work for at least 6 months after being discharged from the hospital due to factors involving her medications and the nature of her job.
- She continues to see a nephrologist (kidney specialist) for regular follow-up visits.

References:

1. Vasculitis Foundation. Wegener's Granulomatosis. 2006. Accessed Feb 19, 2010. <http:// www.vasculitisfoundation.org/wegenersgranulomatosis>

2. MayoClinic.com Wegener's Granulomatosis. September 2008. Accessed Feb 19, 2010. <http: //www.mayoclinic.com/health/wegeners-granulomatosis/DS00833>

3. 5-Minute Clinical Consult. Wegener Granulomatosis. February 2010. Accessed Feb 19, 2010. <http://www.5mcc.com/5mcc/ub/view/5-Minute-Clinical-Consult/116654/0.1/wegener _granulomatosis>