# A Case Report

## Accute Wegener's Granulomatosis:

*Dr Aneela Chaudhary[*], Prof Zafar Hussain Iqbal[*]*

**ABSTRACT** - Wegener's granulomatous is distinct Clinico-pathological entity characterized by systemic vasculitis and necrotizing granulomatous inflammation. It is a multi systemic disease mainly involving upper and lower respiratory tracts and kidneys. We present a case of 36-year old male patient admitted with complaints of headache, muco purulent blood stained nasal discharge associated with low grade fever, cough and haemoptysis. Initially he was treated on the lines of sinusitis with necrotizing pneumonia. The chest X-ray revealed multiple cavitatory lesions in both lung fields. He had high levels of serum anti neutrophilic cytoplasmic antibody (C-ANCA). His nasal biopsy revealed granulomatous inflammatory response. Based on these findings, diagnosis of Wegener's Granulomatosis was made and combined therapy of steroids and cyclophosphamide started. He couldn't tolerate cyclophosphamide and was switched to Azathioprine. The patient showed dramatic improvement and recovered clinically and radiologically.

**KEY WORDS**: Wegener's Granulomatosis, Vasculitis, C-ANCA

## CASE HISTORY

A 36 year old male, was admitted in Pulmonology department of Jinnah hospital with 2 weeks history of frontal headache, post nasal drip and purulent blood stained nasal discharge. It was followed by dry cough which subsequently became productive of blood stained purulent sputum. Developed low grade fever without rigors, chills, and evening rise of fever or sweating.

---

**Department of Pulmonology, Jinnah Hospital Lahore*

Amoxicillin was prescribed by local GP. Due to lack of response Clarithromycin was added. At the start of 2nd week of illness, prior to admission, his White cell count was 14.8 per cubic millimeter with 66% Neutrophils, 13.5 % Lymphocytes and 11% Eosinophils. His C- reactive protein was 316, ESR 101. Renal and liver functions were within normal range. His CXR showed multiple rounded/nodular opacities with few cavitatory lesions involving both lungs.

By the end of 2nd week, patient deteriorated and developed shortness of breath, recurrent episodes of epistaxis and marked weakness for which he was referred to hospital and was admitted. He denied any previous episodes of sinusitis or rhinitis. He had no risk factors for HIV infection. He was a non addict and had never smoked. There was no history of dysuria, hematuria, diabetes mellitus, asthma, Tb contact or exposure to birds.

On admission his pulse was 90, blood pressure 110/70 mm Hg, respiratory rate 20, temperature 37.9°C, Oxygen saturation was 94 % on room air. General physical examination was unremarkable. Chest auscultation revealed normal vesicular breathing and crepitation bilaterally. Heart sounds were normal. Abdominal and neurologic examination was unremarkable. We started Tazobactum/piperacillin and Vancomycin immediately. His repeat blood picture revealed total white cell count of 14 with neutrophilic predominance and ESR was 120. Total protein, serum albumin, LDH, blood sugar levels and urine complete were all normal. ANA and RA factor were negative. Serum IgE levels were within normal limits. Cultures of blood and nasal discharge didn't reveal any significant growth of pathogens. Three consecutive Sputum smears were negative for AFB, malignant cells and no bacterial or fungal growth was obtained from sputum culture. Ultrasound abdomen was normal. CT chest obtained the next day of admission showed multiple nodules, some of which had cavitated. CT scan of paranasal sinuses showed changes of pan sinusitis. Detailed ENT examination revealed a lot of nasal crusting. We planned for nasal biopsy

and C-ANCA levels. In spite of getting broad spectrum antibiotics, patient continued to deteriorate and developed left sided chest pain and two mouth ulcers. Bronchoscopy was done and bronchial washing turned out to be negative for AFB, fungal hyphae and eosinophilia.

Repeat CT chest 10 days after admission showed progression of the pulmonary disease. Almost all nodules had cavitated with development of few new lesions. His C-ANCA (anti PR 3) levels were raised to 126.25 U/mL. Nasal mucosal biopsy revealed granulomatous inflammation. So we diagnosed him for having Wegener's Granulomatosis and started him on steroids and oral cyclophosphamide. One week after starting cyclophosphamide, his LFTs and RFTs were deranged. Cyclophosphamide was stopped. LFTs and RFTs settled within a week. Due to this hypersensitivity to cyclophosphamide, patient was started on Azathioprine as an alternative. Patient improved clinically as well as radiologically with combination of Azathioprine and steroids

**Discussion:**

Wegener Granulomatosis (WG) is a rare autoimmune disease of unknown etiology and was first described by Klinger in 1933, followed Friedrich Wegener, who was a German pathologist .It is characterized by necrotizing granulomatous inflammation of small- and medium-sized blood vessels [1] . Mostly it involves upper and lower respiratory tracts and kidneys as well [2]. The pathogenesis of WG has not been fully elucidated, but both cellular and humoral immunity are thought to be involved. Pathologically it causes Vasculitis of the small- to medium-sized vessels, necrosis, and granulomatous inflammation, particularly in the airways. WG is usually associated with the presence of diffuse staining cytoplasmic ANCA (C-ANCA) directed against serine proteinase 3 antigen (PR3-ANCA), the so-called Wegener auto antigen [3] .Average age of onset is 35-55 years .Patients may present with fever, night sweats, fatigue, lethargy and Weight loss. Ocular findings include scleritis, keratitis, uveitis, episcleritis, and conjunctivitis. Proptosis may

signal retrobulbar granuloma. Otitis media, hearing loss and Purulent or sanguinous nasal discharge may be seen. Saddle nose deformity may be present. Pulmonary disease may cause cough, Hoarseness, hemoptysis, chest discomfort, and dyspnea. Diffuse alveolar hemorrhage (DAH) can also be seen. Musculoskeletal symptoms are common. Renal disease is asymptomatic initially but can progress to renal failure. It is present in 17% at initial diagnosis and is usually asymptomatic. Renal failure occurs in 11% at presentation. It manifests as crescentic necrotizing glomerulonephritis characterized by urinary RBC or erythrocyte casts. The nervous system is affected by Vasculitis can present as mononeuritis multiplex and cranial nerve abnormalities. Skin is involved in 45% of patients.

In our patient the onset of purulent rhino sinusitis was very acute and ultimately lower respiratory tract was also involved. Because acute purulent rhino sinusitis is mostly a bacterial disease and can cause necrotizing pneumonias, we started Tazobactum /piperacillin and Vancomycin immediately. As there was no response to antibiotics and nodular lung lesions progressed and cavitated, we wanted to rule out Wegener's Granulomatosis. C-ANCA and nasal biopsy confirmed our diagnosis.

**Diagnosis:**

In 1990, when ANCA testing was not in widespread use as a diagnostic test for WG, American College of Rheumatology proposed a clinical criteria to facilitate standardization of patients enrolled in studies of WG.[4]

- Nasal or oral inflammation-Painful / painless oral ulcers or purulent / bloody nasal discharge
- Abnormal chest radiography - showing nodules, fixed infiltrates, or cavities
- Urinary sediment - Microhematuria (>5 RBCs per HPF) or RBC casts in urine sediment

- Granulomatous inflammation on biopsy - within the wall of an artery or perivascular

Presence of any 2 or more of the following criteria yields a sensitivity of 88.2% and a specificity of 92%. Classic necrotizing granulomatous vasculitis on tissue biopsy is not an absolute requirement for the diagnosis of WG, nor is it required to initiate therapy[4].Common abnormalities include leukocytosis with neutrophil predominance thrombocytosis, markedly raised ESR and C-reactive protein levels, and normochromic, normocytic anemia.

**Antineutrophil cytoplasmic antibodies:** Diagnosis of WG is suggested from the clinical and laboratory findings and by the presence of circulating antineutrophil cytoplasmic antibodies (ANCA). 90 to 95% of patients with active, generalized WG are ANCA-positive. 80 to 90 % have PR3-ANCA, and the remaining patients have MPO-ANCA[5]**.**

**Tissue biopsy:** Biopsy of an affected organ such as the nasal mucosa, skin, kidney or lung reveals an acute and chronic inflammation, often with granulomatous features. Kidney biopsy typically reveals a segmental necrotizing glomerulonephritis[6].

**Treatment:** Untreated generalized or severe Wegener granulomatosis typically carries a dismal prognosis, with up to 90% of patients dying within 2 years, usually of respiratory or renal failure. Approximately 90% of patients respond to Cyclophosphamide, with approximately 75% experiencing complete remission.

**Localized disease:** generally requires milder therapy and may respond to a single agent e.g. corticosteroids, Azathioprine, or Methotrexate [7, 8].

**Generalized or severe disease:** A combination of Cyclophosphamide and glucocorticoids is recommended for induction of remission. Combination therapy with oral Cyclophosphamide 2 mg/kg/d (maximum 200 mg/d) and prednisone 1 mg/kg/d have been used for induction of

remission. Pulsed (intravenous) cyclophosphamide (15 mg/kg every 2 weeks for the first 3 pulses, then every 3 weeks for the next 3-6 pulses) is an alternative to daily oral cyclophosphamide .Therapy is usually continued for 3-12 months following remission. Methotrexate and Azathioprine are alternatives where Cyclophosphamide can't be used[9]. Prophylaxis against *Pneumocystis jiroveci* pneumonia should be given.

**Remission maintenance:** Long-term oral cyclophosphamide can cause significant toxicity, making it unattractive. As shown by the CYCAZAREM trial, Azathioprine (2 mg/kg/d) is safer than and as effective as cyclophosphamide in maintaining remission[10].

In this patient Cyclophosphamide and steroids were started but couldn't continue cyclophosphamide due to development of hypersensitivity against it. So Azathioprine was started and patient responded very well. Methotrexate is another option for maintenance of remission if the serum creatinine level is less than 1.5 mg/dL. Methotrexate has been shown to be similar to Azathioprine in terms of adverse effects, efficacy in maintaining remission, and rates of relapse. Leflunamide, Mycofenolate Moftinil, Infliximab, Rituximab have also been tried[11].

**REFRENCES:**


1. Hoffman GS, Kerr GS, Leavitt RY, et al. Wegener granulomatosis: an analysis of 158 patients. *Ann Intern Med*. Mar 15 1992; 116(6):488-98.
2. Cannady SB; Batra PS; Koening C; Lorenz RR; Citardi MJ; Langford C; Hoffman GS - Sinonasal Wegener Granulomatosis: a single-institution experience with 120 cases. Laryngoscope. 2009 Apr;119(4):757-61
3. Savage CO; Harper L; Holland M - New findings in pathogenesis of antineutrophil cytoplasm antibody-associated vasculitis. - Curr Opin Rheumatol 2002 Jan;14(1):15-22

4. Leavitt RY; Fauci AS; Bloch DA; Michel BA; Hunder GG; Arend WP; Calabrese LH; Fries JF; Lie J; et al - The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheum 1990 Aug; 33(8):1101-7.
5. Seo P; Stone JH -The antineutrophil cytoplasmic antibody-associated vasculitis .Am J Med 2004 Jul 1; 117(1):39-50.
6. Moosig F, Lamprecht P, Gross WL. Wegener's Granulomatosis: the current view. *Clin Rev Allergy Immunol*. October 2008;35(1-2):19-21
7. Mukhtyar C, Guillevin L, Cid MC, et al. EULAR recommendations for the management of primary small and medium vessel vasculitis. *Ann Rheum Dis*. March 2009;68:310-317
8. Frankel SK, Cosgrove GP, Fischer A. Update in the diagnosis and management of pulmonary vasculitis. *Chest*. February 2006; 129(2):452-65.
9. Pagnoux C, Mahr A, Hamidou MA, et al. Azathioprine or methotrexate maintenance for ANCA-associated vasculitis. *N Engl J Med*. December 2008;359:2790-2803
10. David J, Niels R, et al. A randomized trial of maintenance therapy for vacuities associated with antineutrophil cytoplasmic autoantibodies. N Engl J Med 2003; 349:36-44July 3, 2003
11. Lee RW, D'Cruz DP. Novel therapies for anti-neutrophil cytoplasmic antibody-associated vasculitis. *Drugs*. 2008;68:747-770
12. Klemmer PJ, Chalermskulrat W, Reif MS, Hogan SL, Henke DC, Falk RJ. Plasmapheresis therapy for diffuse alveolar haemorrhage in patients with small-vessel vasculitis. *Am J Kidney Dis*. December 2003; 42(6):1149-1153.