

# Rare Ocular Complication in a Case of Wegener's Granulomatosis

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## ABSTRACT

Wegener's Granulomatosis (WG) is a granulomatous necrotizing vasculitis characterized by a predilection to affect the upper and lower respiratory tracts and kidneys. Pulmonary involvement is seen in 85-90%, ear, nose and throat in 73%, eye in 52%,

skin lesions in 46% and renal disease in 77%. We report a female aged 39 years who presented with eye involvement in the form of nodular scleritis, subglottic stenosis, bilateral pulmonary nodules and consolidation with cavitation and glomerulonephritis.

**Key Words:** Wegener's Granulomatosis, Ocular manifestation

## INTRODUCTION

Wegener's granulomatosis (WG) is a systemic vasculitis of the medium and small arteries, venules, arterioles and the occasionally large arteries. After being initially reported by Klinger in 1931, this condition was later described in more detail by Wegener. In 1954, Goodman and Churg provided the definitive description of WG with their identification of a triad of pathological features, which included i) systemic necrotizing angiitis, ii) necrotizing granulomatous inflammation of the respiratory tract, and iii) necrotizing glomerulonephritis [1]. The largest reported experience with WG is that of Fauci and colleagues at the US National Institutes of Health [2]. We are reporting here, a case of Wegener's granulomatosis with a rare ocular manifestation.

## CASE REPORT

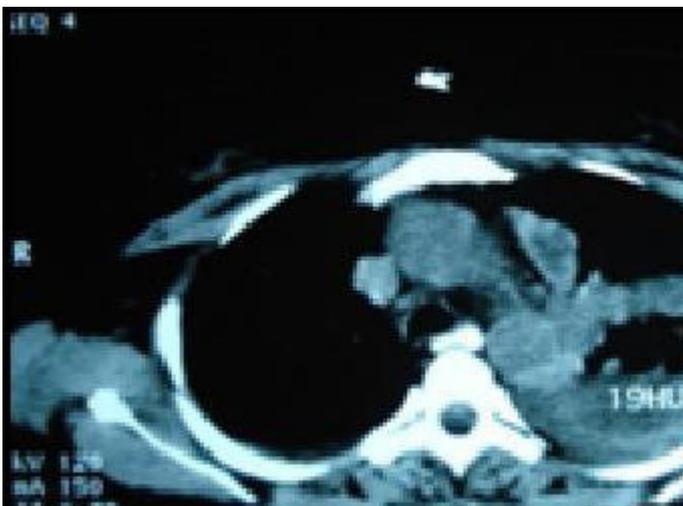
A female who was aged 39-years came with history of redness and nodules in the left eye one month back, which was diagnosed to be nodular scleritis by the ophthalmologist and for which scleral de-roofing surgery was done. On investigating for the aetiology, a left lung upper lobe opacity was detected and she was started on anti-tuberculous treatment empirically and was discharged. Ten days later, she developed sudden dyspnoea when she was at home and was taken to a nearby hospital, where emergency tracheostomy was done for stridor due to sub-glottic stenosis and she was referred to us for further management. There was no history of diabetes or hypertension. On examination, the patient was found to be moderately built and moderately nourished. There was no pallor, icterus, cyanosis, clubbing, pedal oedema or lymphadenopathy. Patient's vitals were normal. Tracheostomy tube insitu and bilateral creptitations were present. Other systemic examinations were normal. Right eye showed early changes of nodular scleritis [Table/Fig-1] showed a mucopurulent discharge, a congested conjunctiva, pupils not reacting to the light, scleral melt and uveovitreous prolapse. Haemoglobin was 11 gms%; TLC was 13,200/cu.mm,  $N_{72}$ , L20, M5, E3; platelet count was 3 lakhs/cu.mm; and ESR was 135mm/hr. A complete urine examination showed 40-50 dysmorphic RBCs/hpf. Mantoux test showed <5mm of induration. Cytoplasmic-antineutrophilic cytoplasmic antibody [c-ANCA]: -3+ IF



**[Table/Fig-1]:** Left eye showing Mucopurulent discharge, congested conjunctiva, pupils not reacting to light, scleral melt, uveovitreous prolapse



**[Table/Fig-2]:** Radiograph of Chest showing Left upperlobe consolidation.



**[Table/Fig-3]:** Contrast Enhanced Computed Tomography of Chest revealing multiple bilateral nodules consolidation and cavitation.



**[Table/Fig-4]:** MRI brain showing bilateral lacrimal gland enlargement

(immunofluorescence), level was 6.5 IU/ml (Normal-2 IU/ml) by ELISA. Her perinuclear-ANCA – IF 3+ level was 7.9 IU/ml (Normal-6 IU/ml) by ELISA. Bronchoscopy revealed normal vocal cords with subglottic stenosis. Radiograph of the chest [Table/Fig-2] showed left upper lobe consolidation. Contrast Enhanced Computed Tomography of the chest [Table/Fig-3] revealed multiple bilateral nodule consolidation and cavitation. MRI of the brain [Table/Fig-4] showed bilateral lacrimal gland enlargement. The patient was treated with cyclophosphamide 2mg/kg, methylprednisolone 1mg/kg/day and supportive care. A scleral patch graft was done for the left eye. The patient improved symptomatically and was discharged.

## DISCUSSION

The complete form of WG is characterized by a triad of necrotizing granuloma of the upper and lower respiratory tract, systemic vasculitis, and focal necrotizing glomerulonephritis [1]. The limited form is characterized by isolated organ involvement, commonly involving the lungs and the airways. Ocular involvement has been reported in few of the earlier reports [3-6]. Various ocular manifestations like keratitis, conjunctivitis, scleritis, episcleritis, nasolacrimal duct obstruction, uveitis, retro-orbital pseudotumor with proptosis, retinal vessel occlusion, and optic neuritis have all been described in WG [4,5,7,8]. Vision loss may occur in as many

as 8% of the patients. A complete ophthalmologic examination is an important part of the diagnostic evaluation.

In patients with proptosis, CT or MRI of the orbits and sinuses may provide useful anatomic information. Ocular disease may also occur as a complication of the therapy. Glucocorticoid and cyclophosphamide therapies have been associated with opportunistic ocular infections which include cytomegalovirus retinitis and herpes zoster ophthalmicus.

The routine laboratory tests are non-specific and they include leukocytosis, thrombocytosis (>400,000/ $\mu$ L), marked elevation of the erythrocyte sedimentation rate and the C-reactive protein level, and normocytic normochromic anaemia. Anaemia is present in up to 50% of patients. A peripheral blood smear may show schistocytes and burr cells. Leukocytosis is observed with a neutrophilic predominance in the differential cell count. Eosinophilia is not a feature of WG. In patients with renal involvement, urinalysis can reveal proteinuria, microscopic haematuria, and the presence of red blood cell casts. A nephrotic-range proteinuria can be observed. The chest radiograph findings may include one or more nodules which may cavitate, alveolar opacities, pleural opacities and diffuse hazy opacities, (which reflect alveolar haemorrhage). The CT scans may show a sharper definition of the pulmonary lesions and of the orbital or paranasal sinus involvement [9]. (www.MedicalCriteria.com).

The serum antibodies against the cytoplasmic component of the neutrophils and the monocytes (cANCA) form useful adjuncts in the diagnosis of WG [4,10,11]. Indirect immuno-fluorescence is currently the standard test for the ANCA screening [5]. 80-95% of all the ANCA which is found in WG is cANCA. The specificity of ANCA in WG is about 98% and its sensitivity depends on the extent of the disease and the disease activity [6]. The combination of a C-ANCA pattern with immunofluorescence testing and serine proteinase 3-ANCA by immunoassay is associated with WG [12,13].

The diagnosis of Wegener's granulomatosis is confirmed by detecting both granulomas and vasculitis in a biopsy of the tissue which is involved [14] [www.Medicinenet.com]. The biopsy of a nasopharyngeal lesion which demonstrates a culture-negative granulomatous inflammation is suggestive of the diagnosis. Renal biopsy reveals segmental crescentic necrotizing glomerulonephritis with little or no immunoglobulin or complement deposition, with immunofluorescence (pauci-immune). Lung biopsy may reveal the typical findings of vasculitis and granulomatous inflammation, although the chronic infections should be excluded.

Two or more positive criteria have a sensitivity of 88.2% and a specificity of 92% in describing Wegener's granulomatosis [9] [www.MedicalCriteria.com]. Our patient fulfilled three of the above criteria; however, a biopsy could not be done because of the patient's poor general condition.

The management of WG requires a multi-systemic approach in close co-ordination with an internist. The 3 phases of the treatment of WG are (1) induction of remission, (2) maintenance of the remission, and (3) treatment of the relapse. Long-lasting remissions can be induced in most of the patients with cytotoxic agents, particularly cyclophosphamide which is administered in combination with corticosteroids. Approximately 90% of the patients respond to cyclophosphamide, approximately 75% experience complete remission and a 5-year patient survival is seen in over 80% of the patients [14]. Subsequently, 30-50% of those who respond have at least one relapse, which requires another course of therapy

[4,5,8,15]. In patients who present with rapidly progressive glomerulonephritis, alveolar haemorrhage or both, intravenous glucocorticoids should be administered at a much higher dose. In patients who did not tolerate cyclophosphamide, other cytotoxic agents such as azathioprine, chlorambucil, or methotrexate have been used [4,7,8,15]. Plasmapheresis generally produces no added benefit, although it may be beneficial in patients who are dependent on dialysis, who have severe pulmonary haemorrhage, or who have concurrent anti-glomerular basement membrane antibody disease. The roles of intravenous immunoglobulin, mycophenolate mofetil, leflunomide, and etanercept are controversial. The prognosis which is associated with untreated systemic WG is poor, with up to 90% of patients dying within 2 years, usually from respiratory or renal failure. With aggressive therapy, the mortality rates have been found to improve [15]. An inflammatory insult leads to tissue necrosis and fibrotic damage to the nose, the subglottic areas, the trachea, and the bronchi, which require surgical intervention.

## CONCLUSIONS

Ophthalmic manifestations are frequently encountered and they can result in significant morbidity and even blindness. Wegener's granulomatosis presenting with eye manifestations at the onset is unusual. A scleral melt with a uveal prolapse is still rare. The management is challenging and it often requires a multidisciplinary approach. This is an important clinical entity that needs to be recognized early and treated appropriately, thereby requiring a high index of clinical suspicion.

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