

## Bronchiolitis Obliterans with Organizing Pneumonia in Wegener's Granulomatosis-Case Report

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### Abstract

Wegener Granulomatosis with Polyangiitis (GPA), formerly known as Wegener's Granulomatosis (WG), is a systemic vasculitis characterized by involvement of the upper airways, lungs, and kidneys and is related to ANCA-associated vasculitis. GPA is a multisystem disorder of unknown etiology affecting approximately 3 per 100,000 persons in the United States. It shows no sex preference and most patients are adults of Caucasian origin. It causes an inflammation, frequently leading histologically to tissue necrosis, granuloma formation, and vasculitis of the small to medium-sized vessels, and crescentic glomerulonephritis. Other body areas that may also be involved include ears, nose and throat, eyes, joints, and central nervous system. The classical histological features of Wegener's Granulomatosis in lung include necrotizing granulomatous inflammation and necrotizing vasculitis. The limited form of the disease involving the lung as Bronchiolitis Obliterans-Organizing Pneumonia (BOOP) has been described. Wegener's Granulomatosis with cardiac manifestations, such as pericarditis and coronary arteritis, compose 12% of the cases.

Here we describe a rare case of Wegener Granulomatosis and BOOP in a young healthy woman. C-ANCA (Anti-proteinase 3) was positive with active urinary sediment. Kidney biopsy was performed showing necrotizing vasculitis. Treatment with Cyclophosphamide and steroids for one year induced complete remission of kidney and lung function. ANCA titer returned to normal.

**Keywords:** Wegener vasculitis; BOOP; Cyclophosphamide

### Patient Description

This is a case report of a 53 year old Mediterranean Jewish woman, 3 months prior to her admittance in the Department of Internal Medicine on 29-05-201, at Poriya Medical center, she developed a fever of 38.2 that lasted 3 weeks and Erythrocyte Sedimentation Rate (ESR) was 100. Based on a chest X-ray she was diagnosed with pneumonia, which was treated with antibiotics. At discharge renal function tests were normal.

A month later she was readmitted at another hospital in Tel-Aviv because of persistent cough and fever. On physical examination, the patient is suffering with productive cough, blood pressure of 140/90 mmHg, Pulse 80/min, respiratory rate of 16/min and temperature 38.8°C. No cutaneous rash or peripheral edema.

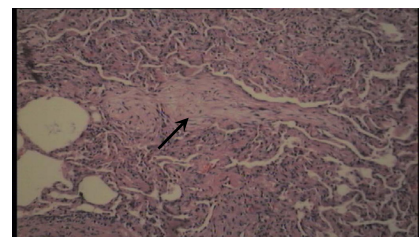
Based on blood analysis, elevated plasma Creatinine of 1.8 mg/dl (N=0.8-1 mg/dl) Urea of 60 mg/dl (N=10-20 mg/dl) were founded, and a high titer of C-ANCA of 15 U/ml measured by immunofluorescence (Normal=0.0-5 U/ml) with normal complement levels. Urine sediment showed dysmorphic erythrocytes and red blood casts, and Protein++. A 24 hours urine collection revealed a protein level of 3 grams.

A plain sinus radiograph and a CT of the sinuses failed to show findings suggesting WG, and a nasal mucosal biopsy was not performed, as the nasal mucosa was injured due to the invasive examinations performed to rule out TB. However, based on this clinical presentation, she received prednisone treatment 40 mg daily.

A month later she underwent an open lung biopsy, which demonstrated fibroblastic plugs ("Masson's bodies") composed of spindle mesenchymal cells obstructing the terminal bronchioles, a

morphological hallmark of Bronchiolitis Obliterans with Organizing Pneumonia (BOOP) (Figure 1).

The patient was admitted again to the Department of Internal Medicine, Poriya Medical Center, for a kidney biopsy due to a continuous deterioration in her kidney function and nephritic sediment. Physical examination was unremarkable except for abdominal tenderness in the right lower quadrant. Blood tests showed a mild leukocytosis with neutrophilia and a normocytic anemia with hemoglobin 8.8, which has



**Figure 1:** Open lung biopsy showing fibroblastic plugs ("Masson's bodies") composed of spindle mesenchymal cells obstructing the terminal bronchioles.

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developed over the prior 3 months, Creatinine was 1.5 and BUN 26. A urine test strip showed 30mg/dl of protein, nitrites +2, glucose +1 and erythrocytes +4. A chest X-ray and ECG were normal.

The patient underwent closed kidney biopsy which revealed Glomeruli with fibrocellular crescents and fibrin deposits, hence verifying WG (Figures 2 and 3). We continue steroid treatment 40 mg daily, tapering 5 mg every two weeks and maintained with 7.5 mg until one year of treatment and remission. Oral Cyclophosphamide (Cytoxan) 2 mg/kg for 6 months, and switched later to Imuran (Azathioprine) 100 mg daily for other 6 months. At the end of the treatment she was in excellent general condition without fever or cough. The plasma creatinine reversed to normal 0.9 mg/dl, without proteinuria and negative titer of C and PANCA.

## Discussion

Wegener Granulomatosis is a potentially life-threatening disease. Diagnosis of WG depends on several criteria defined by the American College of Rheumatology (ACR) [1] which includes pulmonary X-ray changes, abnormal urinary sediment, nasal or oral ulcers, and granulomatous inflammation on biopsy. The presence of two or more of these four criteria is associated with high sensitivity and specificity for WG. Characteristic laboratory findings include a markedly elevated ESR, mild anemia and leukocytosis, mild hypergammaglobulinemia (particularly of the IgA class), and mildly elevated rheumatoid factor. Thrombocytosis may be seen as an acute-phase reactant. Approximately 90% of patients with active Wegener's granulomatosis have positive antiproteinase-3 Anti-Neutrophil Cytoplasmic Autoantibodies (ANCA). However, ANCA is non-specific and may occur in a subset of patients with systemic small vessel vasculitis, including patients with microscopic polyangiitis (microscopic polyarteritis), and Churg-Strauss syndrome, as well as Bronchiolitis Obliterans

Organizing Pneumonia (BOOP) [2-5]. Histologic manifestations in the lung typically are characterized by the combination of necrotizing granulomatous inflammation with extensive parenchymal necrosis and a necrotizing vasculitis. In the 1980-2000 several histologic variants have been recognized, including cases manifesting bronchocentric inflammation, a marked eosinophil infiltrate, alveolar hemorrhage and capillaritis, and interstitial fibrosis [4,5].

Uner et al. [6] have encountered another variant in which BOOP-type fibrosis was the major histologic finding in 16 cases. Yano et al. [5] presented a case of a 19-year-old man with ulcerative colitis, who developed WG with BOOP-like variant, which was induced by mesalazine [6-8].

Here we describe a middle-aged woman with non-specific symptoms, whose lung biopsy demonstrated BOOP but was later diagnosed with WG based on a kidney biopsy.

Through this case we wish to emphasize the association between the pathological picture of WG and BOOP. Furthermore, it is cardinal to keep this association in mind as the clinical picture of these two diseases is overlapping and ANCA may be elevated in both, but the treatment differs between them.

Treatment with prednisone and daily cyclophosphamide is best treatment for induction and remission. However, this treatment did not prevent relapse, and with extended experience there became a greater recognition of the short-term and long term toxicities of cyclophosphamide.

Recent therapeutic strategies have investigated means to eliminate the need for cyclophosphamide. Methotrexate has been found to be as effective as cyclophosphamide to induce remission. In severe cases, Cyclophosphamide is given for 3 to 6 months to induce remission after which we switch to less toxic agents for maintenance such as Methotrexate and Azathioprine (Imuran) [9]. The most recent innovation in the treatment of severe GPA has been the introduction of rituximab (anti-CD20) and glucocorticoids.

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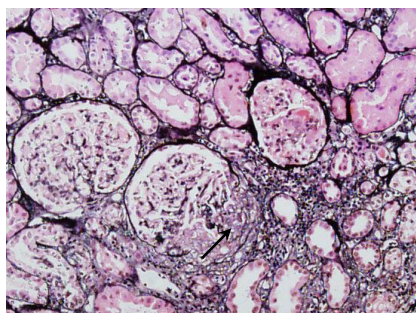


Figure 2: Kidney biopsy (Jones methenamine silver stain) showing fibrocellular crescent.

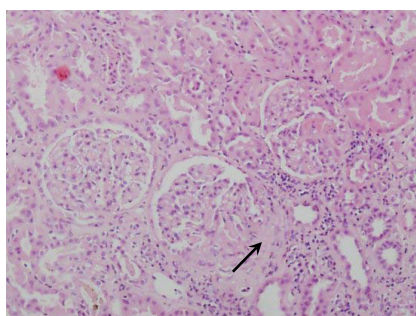


Figure 3: Kidney biopsy (Hematoxylin and eosin stain) showing Glomerular crescents with fibrocellular crescents and fibrin deposits.