A Case of Seronegative Goodpasture's syndrome associated with Organizing Pneumonia

Bae, Ju Young[1]; Retalis, Zachary[1]; Hussein, Khalil[1]; Leibert, Eric[1]; Greenberg, Alissa[1]; Archer, Herbert[1]

Department of Medicine, Greenwich Hospital, Yale New Haven Health System, Greenwich, CT, United States.

Clinical Presentation

CC: 79-year-old Dutch American male presents to the emergency department with a two-week history of dyspnea, non-productive cough, and confusion.

Past medical history: Prior 70 pack-year smoking history, mild dementia, hypertension, hyperlipidemia, and atrial fibrillation on Apixaban.

HPI/ROS: Denied chest pain, diarrhea, hemoptysis, abdominal pain, recent travel, or sick contacts.

Vitals: T 100.4 ºF, BP 166/77 mmHg, O2 sat 88% on RA

Exam: Irregularly irregular heart rhythm, crackles involving 2/3 of the bilateral lung fields, and pitting edema of the bilateral lower extremities

Early Diagnostics

Labs: WBC 11.1, Hgb 10.4 g/dL, Cr 2.05 mg/dL (baseline 0.95 mg/dL 3 years prior), procalcitonin 0.07 ng/mL, troponin I 0.028 ng/mL, lactic acid 0.9 mmol/L, pro-BNP 3807 pg/mL, and CRP 13.4 mg/L. Respiratory virus PCR panel was negative. UA found 2 RBC/hpf with negative sediments and 0 WBCs.

EKG: Atrial fibrillation with rate of 71 bpm.

Chest x-ray (Figure 1) demonstrated right upper lobe pneumonia with consolidation in the left perihilar region. Patient was started on ceftriaxone, doxycycline, and furosemide.

TTE: EF of 71-75%, moderate tricuspid regurgitation

CT chest without IV contrast (Figure 2): Severe symmetric bilateral ground glass opacities with areas of normal lung with upper zone predominance, and areas of confluent heterogenous airspace opacity in the right midlung and right lower lobe concerning for bacterial pneumonia.

Bronchoscopy with BAL and transbronchial lung biopsy: Increasing numbers of red blood cells (4,000 to 11,000 to 14,000) with preliminary pathology consistent with diffuse alveolar hemorrhage (DAH).

Patient's creatine first improved to 1.44 mg/dL but then progressively worsened, and dialysis was initiated. Inflammatory markers worsened despite antibiotic therapy, with infectious and rheumatologic workup as shown in table 1. Empiric therapy with corticosteroids was started, and patient went for VATS lung biopsy.

Final Diagnosis and Outcome

Pathology with immunohistochemistry confirmed anti-GBM disease of the right lower lobe while right upper lobe showed organizing pneumonia (figure 3) and lung damage without positive staining for anti-GBM disease.

Patient was started on daily plasmapheresis in addition to therapy with Cytoxan and corticosteroids, but his respiratory status worsened after 3 days and he also developed atrial fibrillation with rapid ventricular response and thrombocytopenia, and his goals of care were transitioned to comfort measures only by his family, and patient expired shortly afterwards.

Images/Figures

Figure 1. Chest x-ray on admission

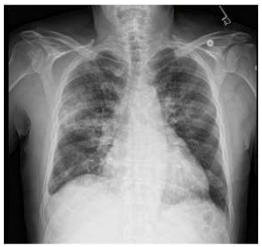


Figure 2. Initial CT Chest without contrast

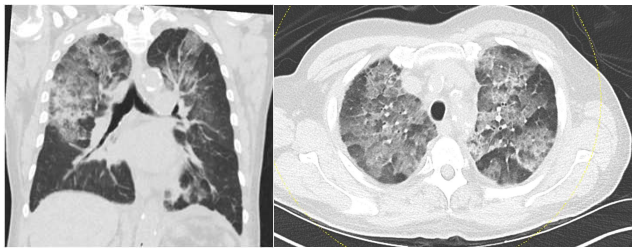
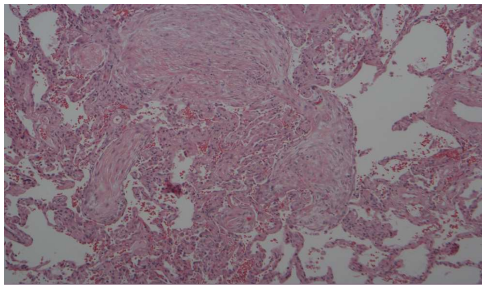


Table 1.

Lab	Reference Range, Adults	Result
Fungitell (1-3) B D Glucan Assay	<60 pg/mL	<31
GBM-Ab IgG	0.0-0.9 AI	<0.2
Mycoplasma pneumonia by PCR		Not detected
HIV-1/HIV-2 ab/antigen screen		Negative
Cold Agglutinins Titer	<1:32	<1:32
Respiratory syncytial virus antigen		Negative
Respiratory virus PCR panel		Not detected
SS-A/B Sjogrens Ab	0.0-0.9 AI	<0.2
Sm antibody	0.0-0.9 AI	<0.2
RNP antibody	0.0-0.9 AI	<0.2
Anti-SM/RNP	0.0-0.9 AI	<0.2
Anti-Ribosomal P	0.0-0.9 AI	<0.2
Scleroderma (Scl-70) ab	0.0-0.9 AI	<0.2
Jo- IgG antibody	0.0-0.9 AI	<0.2
Chromatin (histone) ab	0.0-0.9 AI	<0.2
Centromere antibody screen	0.0-0.9 AI	<0.2
DsDNA antibody	0.0-4.0 IU/mL	1.0
ANA titer	<1:160	1:160
ANCA vasculitis IgG ab	0.0-0.9 AI	<0.2
ANA		Positive
C3 Complement	90-180 mg/dL	133
Angiotensin Converting Enzyme	8-52 U/L	10
Quantiferon-TB		Indeterminate

Figure 3.
Pathology demonstration of right upper lobe areas of organizing pneumonia containing typical plugs of recent fibroblast proliferation that fill airspaces



Discussion of Practice Guidelines

Usually, diagnosis of Goodpasture's syndrome is confirmed either by presence of serum anti-GBM antibody which is highly sensitive and specific (>95%) or by renal biopsy demonstrating IgG in linear pattern of deposition along the glomerular basement membrane by immunofluorescence consistent with crescentic glomerulonephritis. In patients with isolated pulmonary disease or delayed/minor renal presentations, lung biopsy may be indicated.

Regardless of the clinical presentation or the seropositivity, therapy includes 3 agents: plasmapheresis to remove circulating autoantibodies, an immunosuppressant such as cyclophosphamide, and corticosteroids to halt production of the responsible antibodies. The guideline published by the American Society for Apheresis in 2016 recommends treatment with plasmapheresis daily or every other day for a course of ten to twenty days. In patients who cannot tolerate cyclophosphamide due to side effects or allergies, rituximab (anti-CD20 monoclonal antibody) is efficacious. One-year survival rate was reported to be between 75% to 90% in a recent case series.

Case Discussion

An estimated 2-3% of cases of Goodpasture's syndrome are seronegative, and these patients without anti-GBM antibodies present with more indolent symptoms and thus more difficult to diagnose.

Our case has unique characteristics including an atypical presentation with non-specific pulmonary symptoms including shortness of breath and non-productive cough in the absence of hemoptysis. While the patient initially presented with acute kidney injury, his renal function steadily improved early in his hospitalization, and he had no evidence of hematuria. Later in his hospital course, he developed acute kidney injury requiring hemodialysis with repeat UA still grossly unremarkable.

The absence of anti-GBM antibodies in setting of delayed renal disease made the diagnosis more challenging as the work up was driven worsening pulmonary status with bronchoscopy and later surgical lung biopsy with pathology confirming the disease.

Learning Points

1. We advise clinicians to have high index of suspicion for Goodpasture's syndrome in the setting of pulmo-renal presentation, particularly if environment risk factors are present such as tobacco smoke, cocaine, and hydrocarbon chemical exposure are present.

2. Clinicians should be aware that atypical presentations with only renal manifestations or only pulmonary manifestations may represent up to 40% of cases, and these cases are at risk of being diagnosed later in the disease course, which would delay the treatment.

3. In the setting of unexplained severe pulmonary or renal disease, Goodpasture's syndrome should remain on the differential even in the setting of negative anti-GBM antibody testing.