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A Case of Granulomatosis with Polyangiitis Masquerading as Community Acquired Pneumonia☆

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Abstract

Granulomatosis with polyangiitis (GPA) has a multitude of presentations, including appearing as a refractory community-acquired pneumonia (CAP) or an isolated localized pulmonary disease. This case describes a patient suspected to have a CAP before further workup and lung biopsy revealed his diagnosis of GPA. This case report demonstrates GPA's diverse presentations, critical complications such as diffuse alveolar hemorrhage (DAH) and cardiac tamponade, and nuanced management options.

Keywords: Granulomatosis with Polyangiitis, Pneumonia, c-ANCA, Vasculitis, Tamponade, Alveolar hemorrhage

1. Background

GPA is an ANCA-associated vasculitis (AAV) with diverse manifestations. The mechanism of this complex disease is based upon the proliferation of antineutrophil cytoplasmic antibodies, which target proteinase-3, leading to impaired neutrophil clearance, an uncontrolled pro-inflammatory environment, and ultimately vascular necrosis. GPA patients have increased expression of proteinase-3 positive neutrophils, promoting the inflammatory cascade and increased oxidative activity when bound by ANCA, which then lead to a necrotizing vasculitis with granuloma formations preferentially targeting small vessels.[1]

The literature's classic GPA presentation describes a vasculitis with necrotizing granulomas affecting the upper and lower respiratory tracts with hemoptysis and renal involvement. However, this description can be misleading, as clinical presentation varies significantly. Limited GPA involves one or two organ systems, whereas systemic GPA can involve multiple organs and thus have diverse presentations. The upper respiratory tract is involved in around 70–100% of GPA cases, usually affecting the nasal cavity and paranasal sinuses. Diagnosis is further complicated by a lack of rigid diagnostic criteria, often involving a synthesis of clinical, serological, radiological and histological evidence.[2]

2. Objective

To describe a unique case of GPA that was initially suspected to be CAP, and to review treatment options for severe GPA complications such as DAH and cardiac tamponade.

3. Case report

A 36-year-old male with a history of tobacco use presented with shortness of breath and pleuritic chest pain of one week's duration. He had associated symptoms of fevers and cough productive of sputum. He reported smoking 2–3 cigarettes per week but denied recreational drug use or vapor pen

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use. He has one sister with asthma, otherwise no family history of disease. Pertinent review of recent sick contacts, environmental exposures, pets at home, or recent travel is negative. He tested negative for SARS-CoV-2, and given his continued symptoms was admitted for management of suspected pneumonia.

Vital signs demonstrated a temperature of 103.2 °F, blood pressure 134/87 mmHg, respiratory rate 24 breaths per minute, heart rate 115 beats per minute, and oxygen saturation 100% on room air. On exam, he was visibly fatigued with increased work of breathing. Mucous membranes were dry with bilateral conjunctival injection. Crackles were heard in the left upper lung fields, and left chest was tender to palpation.

Laboratory findings revealed a white blood cell count of 12,600/mm^3 with 72.6% neutrophils, hemoglobin 9.9 g/dL, creatinine 0.8 mg/dL, blood urea nitrogen 11 mg/dL, C-reactive protein 42.3 mg/dL, erythrocyte sedimentation rate 121 mm/h, antineutrophil cytoplasmic antibody (c-ANCA) titer >8.0 AI units and rheumatoid factor level 35.3 IU/mL.

Computed tomography (CT) angiography of the chest with contrast showed no pulmonary embolism, but demonstrated an anterior left upper lobe (LUL) consolidation (Fig. 1). CT of the abdomen and pelvis showed no acute pathology. He received empiric antibiotics for presumed CAP; however, an extensive infectious workup was negative. After a week of fevers refractory to medical therapy he underwent left thoracotomy, adhesion takedown, and left upper lobe lobectomy with lymph node resection. Initial onsite pathology results were consistent with organizing pneumonia. Samples were sent to independent facility for further review given the severity of disease.

He improved significantly following thoracotomy and was discharged on oral antibiotics and steroids. He returned to the hospital three weeks later complaining of chest pain and fevers. He completed his course of oral antibiotics but continued to have fevers, dyspnea, a nonproductive cough, and endorsed persistent, severe chest pain. On physical exam, he had labored breathing and bilateral conjunctival injection again noted, but now had muffled heart sounds, with crackles auscultated in bilateral lung fields. Heart rate was 137, BP 146/86, temperature 102.7 Fahrenheit, oxygen saturation 97% on 2 L nasal cannula. Labs showed a white blood cell count of 16,000, hemoglobin 7.8, hematocrit 25.2%, creatinine 1.40, blood urea nitrogen 18, C-reactive protein 25.8 and erythrocyte sedimentation rate 125. Troponin I was negative and electrocardiogram showed sinus tachycardia.

Creatinine reached a peak level of 1.7, with an estimated glomerular filtration rate of 55 mL/min/1.73^2. Urine studies was notable 100 mg/dL of protein and >100 red blood cells/hpf measured on urinalysis collection, however no casts, bacteria, nitrites or leukocyte esterase. Calculated fractional excretion of sodium was approximated to be 0.1%. No obstruction or hydronephrosis was noted on imaging.

Infectious workup was again negative. CT chest without contrast revealed bilateral ground glass opacities and a moderate size pericardial effusion. Transthoracic echocardiogram showed ejection fraction 60–65%, peak pulmonary artery pressure of 61 mmHg, and a moderate-large pericardial effusion with tamponade physiology (Fig. 2). Lung biopsy from previous visit underwent evaluation at outside facility which reported irregular zones of necrotizing granulomatous inflammation and diffuse pulmonary capillaritis, consistent with GPA (Fig. 3).

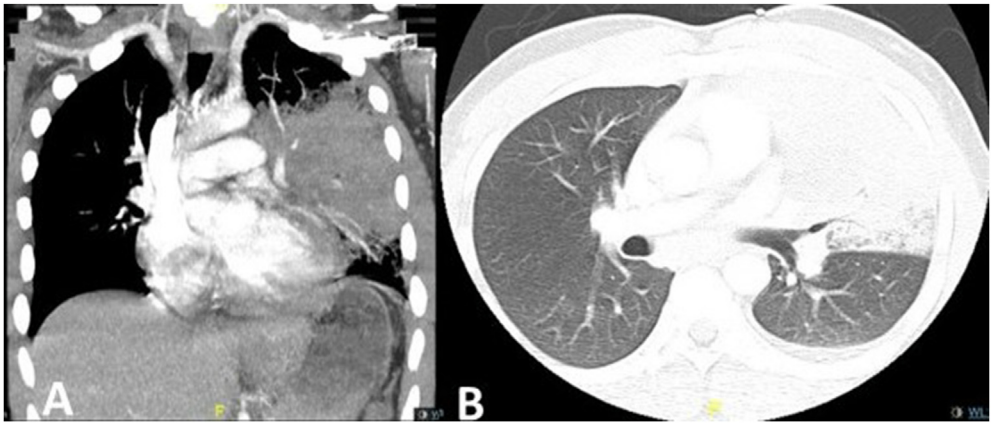

Fig. 1. CTA of the chest (1A and 1B) demonstrating a large anterior left upper lobe consolidation.

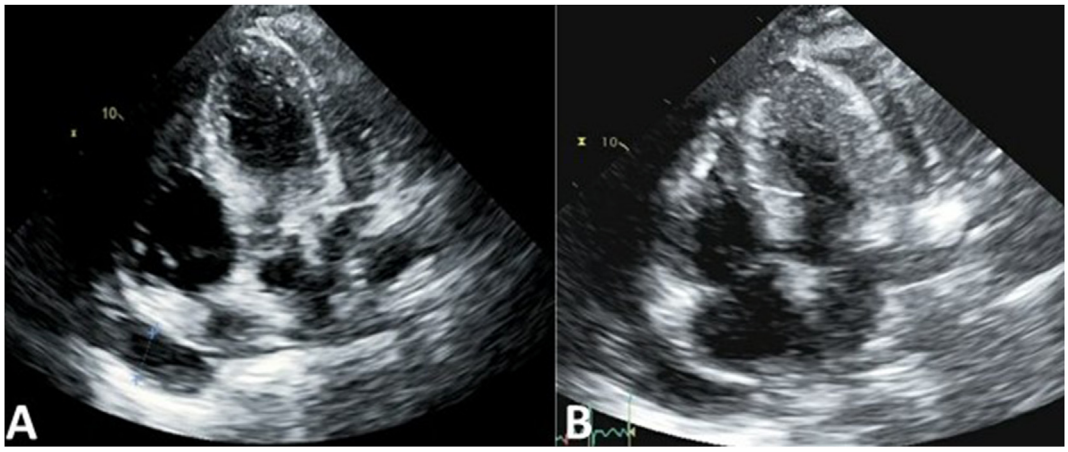

Fig. 2. Transthoracic echocardiogram demonstrating a moderate-large pericardial effusion with tamponade physiology (A and B).

He underwent successful pericardiocentesis with 300 mL of bloody pericardial fluid drained. Due to the emergent indication for pericardiocentesis, limited fluid studies were able to be obtained. Fluid cultures were negative.

He received intravenous (IV) pulse steroids, plasmapheresis and IV rituximab therapy. He subsequently developed acute hypoxic respiratory failure requiring high flow nasal cannula with worsening lung infiltrates and persistent hemoptysis.

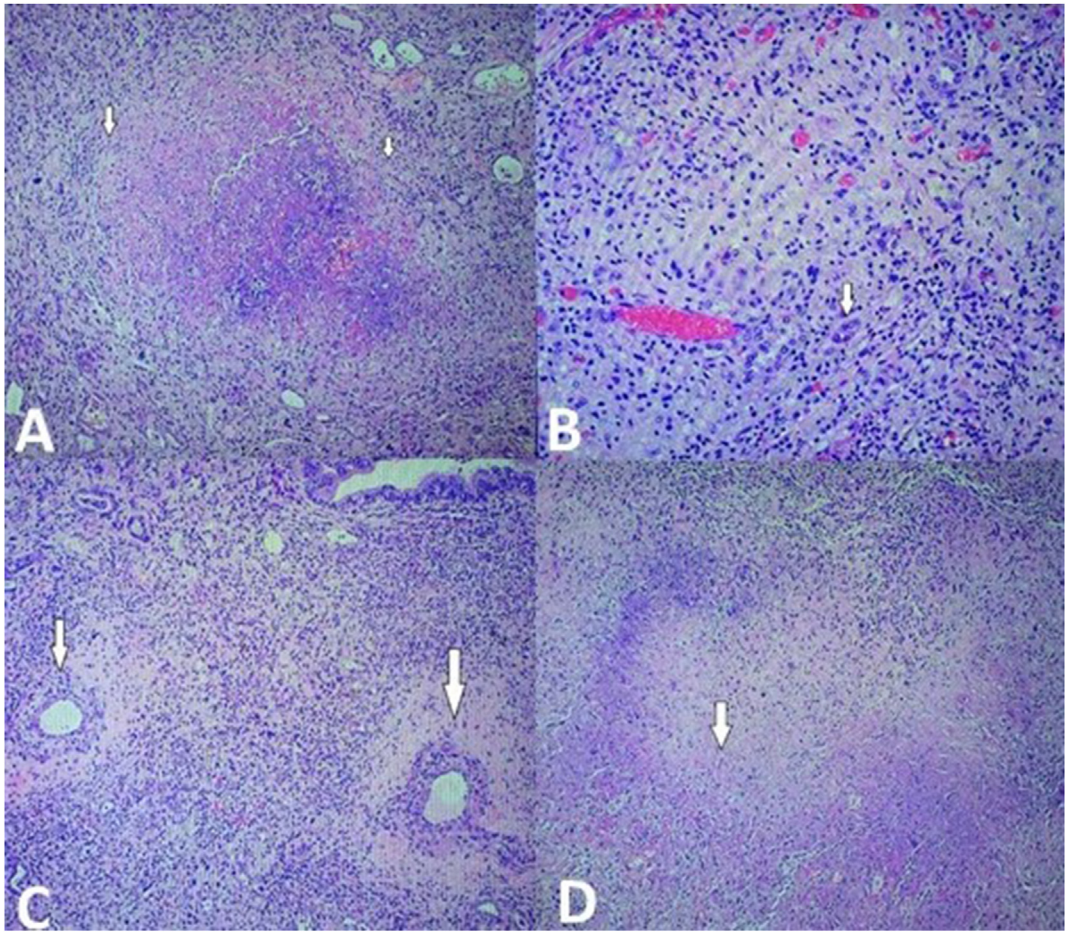

Fig. 3. Lung biopsy findings consistent with GPA, with the arrows demonstrating granulomatous inflammation (3A) containing multinucleated giant cells (3B), fibrinoid necrosis with angiocentric and angioinvasive patterns of vasculitis (3C), and geographic necrosis with a basophilic smudgy appearance (3D). Hematoxylin-eosin stain with magnification x10.

Bronchoscopy and lung biopsies were not performed in-house, but his concerning constellation of symptoms warranted a clinical diagnosis of DAH. Plasmapheresis and IV steroid therapy were restarted, and FVIIa was considered as additional therapy pending clinical response. He was transfused a total of five units of pack red blood cells. He underwent a total of eleven cycles of plasmapheresis. The initial five cycles were completed over the course of ten days following admission, with plasmapheresis performed every other day. Nine days later, the remaining six cycles took place over twelve days. Oxygen was weaned, hemoptysis resolved, and hemoglobin and kidney function stabilized. He was discharged with cyclophosphamide and prednisone. Close outpatient follow-up was arranged.

4. Discussion

This is a unique case of GPA whose presentation mimicked a CAP, as the patient had a LUL infiltrate associated with fevers and leukocytosis. AAV was low on the differential diagnosis despite elevated c-ANCA levels; diagnosis was further delayed due to local pathology lab reporting multifocal pneumonia. Reports of atypical GPA presentations are not uncommon; past reports have documented GPA initially appearing as a disease with an infectious, cardiovascular, or gastroenterological etiology among others.[3–5] Although prior GPA reports involved isolated pulmonary manifestations, these patients had hemoptysis and typical bilateral ground glass opacities on imaging,[6] whereas this patient had a focal infiltrate in the LUL only, an unusual pulmonary GPA presentation. Additionally, he developed cardiac tamponade, a very rare GPA complication, with a 2015 study reporting only 17 (3.3%) of 517 GPA patients in North America with cardiac complications altogether.[7]

GPA management depends upon the severity and extent of complications. Treatment involves induction and maintenance therapies; approximately 90% of patients achieve remission with standard therapy, but at least 50% relapse.[8] The 2021 American College of Rheumatology guidelines recommend a rituximab-based regimen as induction therapy for active, severe GPA. Rituximab is preferred over cyclophosphamide because of its safer side effect profile and similar efficacy, but after relapse, cyclophosphamide is recommended in patients who previously received rituximab. Routine addition of plasma exchange therapy is not advised, but may be considered in patients at increased risk of developing end-stage renal disease. The guidelines do not currently recommend plasma exchange added to remission induction therapy for patients with severe GPA and alveolar hemorrhage; however, it may be beneficial as rescue therapy in patients with glomerulonephritis or critical illness refractory to standard therapy.[9]

GPA patients may also acquire DAH, a life-threatening complication caused by inflammation of the lung microvasculature. Standard treatment of DAH with capillaritis in GPA involves immunosuppression, systemic glucocorticoids, and plasma exchange, but recombinant FVIIa can be considered for persistent hemorrhage. FVIIa counteracts the increased activity of tissue factor pathway inhibitors in DAH and also promotes the activity of factors IX and X on platelet surfaces. Although further research is needed to clarify the indications for recombinant FVIIa for DAH, and the impact of this therapy on mortality rates remain unclear, studies thus far have demonstrated its promising utility to control bleeding by inducing hemostasis.[10]

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