

Granulomatosis with polyangiitis mimicking multisystem pyoderma gangrenosum: A case report

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Abstract

Granulomatosis with polyangiitis, a type of small-medium vessel vasculitis, can pose diagnostic challenges due to its diverse clinical manifestations. We present a case that mimicked multisystem pyoderma gangrenosum with cutaneous ulceration, renal sparing, and antineutrophil cytoplasmic antibody negativity. Although antineutrophil cytoplasmic antibody is positive in approximately 90% of cases of granulomatosis with polyangiitis, its negativity should not exclude the diagnosis. Additionally, pyoderma gangrenosum-like cutaneous ulcers should prompt consideration of granulomatosis with polyangiitis, especially in the context of multisystem disease presentation. This case underscores the importance of maintaining a high suspicion for granulomatosis with polyangiitis in patients presenting with cutaneous ulceration and respiratory tract disease.

Keywords

Granulomatosis with polyangiitis, pyoderma gangrenosum, ANCA-negative

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Introduction

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis, is the most common type of anti-neutrophilic cytoplasmic antibody (ANCA)-associated vasculitis, affecting 10–20 individuals per one million worldwide annually.¹ The peak incidence of GPA occurs between the ages of 64 and 75. Characterized by a wide range of presentations that can involve various organ systems (Table 1),² GPA is associated with significant morbidity and mortality.¹ The life expectancy for individuals with untreated GPA is, on average, 5 months; however, remission can be achieved in more than 90% of patients with appropriate treatment.² Treatment of GPA involves immunosuppressive agents such as corticosteroids, cyclophosphamide, rituximab, methotrexate, azathioprine, and plasmapheresis.¹ Given its significant morbidity and mortality, timely diagnosis and management is imperative. We present a case of suspected ANCA-negative GPA that mimicked multisystem pyoderma gangrenosum (PG). This case highlights features of GPA to assist in future diagnoses, particularly when associated with ANCA-negativity or PG-like cutaneous lesions.

Case report

A 58-year-old male with a past medical history of intranasal cocaine use, chronic sinusitis, and epistaxis was being investigated by respiratory for cavitary lung lesions with radiologic progression despite antibiotics. Autoimmune workup was negative, including ANCA. Lung core biopsy #1 was taken (Table 2), leading to a potential diagnosis of organizing pneumonia. Prednisone 0.625 mg/kg daily was started, resulting in a significant decrease in the size of the lung lesions on computed tomography (CT).

One month later, during a prednisone taper, the patient developed painful bilateral lower extremity cutaneous ulcerations. Physical exam revealed multiple well-demarcated

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Table 1. Clinical features of GPA.

Organ	Clinical manifestations
General	Malaise, myalgia, arthralgia, anorexia, weight loss, fever, weight loss
Skin	Leukocytoclastic vasculitis, digital infarcts, purpura, cutaneous ulcers, and gangrene
Oral cavity	Oral ulcers, oral granulomatous lesions, gingival hyperplasia with strawberry-like aspect
Eye	Episcleritis, scleritis, conjunctivitis, keratitis, uveitis, retinal vasculitis, retinal arterial or venous thrombosis, retinal exudates, retinal hemorrhages, blurred vision, blindness, proptosis, orbital granulomatous masses, epiphora
Nose and paranasal sinus	Persistent-recurrent nasal discharge, blood-stained nasal discharge, epistaxis, crusting, mucosal ulceration, nasal bridge collapse, nasal granulomatous lesions, paranasal sinus inflammation, regional tenderness
Ear	Sensorineural or conductive hearing loss
Upper airway	Subglottic or tracheal stenosis
Lower airway	Cough, breathlessness, stridor, wheeze, small airway obstruction, pulmonary nodules, cavitating lung lesions, pleuritis, pleural effusions, pulmonary infiltrates, pulmonary hemorrhage, alveolar capillaritis, respiratory failure
Cardiovascular	Small vessel vasculitis, occlusive vascular disease, pericarditis, pericardial effusions, cardiomyopathy, valvular heart disease, ischemic heart disease, heart failure
Gastrointestinal	Acute abdomen secondary to peritonitis, bowel ischemia which may be secondary to mesenteric vasculitis
Kidney	Diffuse pauci-immune crescentic necrotizing glomerulonephritis, hematuria, proteinuria, cellular casts on urine cytology, renal impairment manifested as acute kidney injury, chronic kidney disease, or end-stage renal failure
Central and peripheral nervous system	Headache, meningitis, seizures, cerebrovascular accidents, spinal cord lesions, cranial nerve palsies, sensory or motor peripheral neuropathy, mononeuritis multiplex, sensorineural hearing loss, cerebral mass lesions
Musculoskeletal	Inflammatory arthritis, erosive or deforming

Source: Adapted from Greco et al.²

GPA, granulomatosis with polyangiitis; PG, pyoderma gangrenosum.

Table 2. Overview of pathology results.

Sample	Findings
Lung core biopsy #1	Negative for infection Consistent with organizing pneumonia with fibrosis and prominent infiltrate
Cutaneous ulcer punch biopsy	Nonspecific, neutrophil-rich inflammation with dermal/subcutaneous fibrosis and reactive changes
Nasal mucosa biopsy #1	Abundant purulent exudate and granulation tissue consistent with ulceration, nonspecific No granulomas or giant cells No fungus or malignancy Features of GPA not identified
Lung core biopsy #2	Nonspecific inflammation Rare neutrophils and eosinophils No giant cells or granulomas No vasculitis, necrosis, or malignancy
Lung wedge resections	Suppurative granulomatous change Non-necrotizing granulomas Few multinucleated giant cells No vasculitis Negative for malignancy Findings not typical for GPA Consistent with pulmonary involvement of PG Flow cytometry showed no abnormal hematologic cells or blasts
Nasal mucosa biopsy #2	Necrotic debris and granulation tissue Rare giant cells No definite granulomas Some vascular inflammation seen at ulcer base Occasional large, thrombosed vessels
Palate biopsy #1	Inflammatory infiltrate and neutrophils Consistent with palatal abscess/parulis No evidence of malignancy
Palate biopsy #2	Negative for fungi Scattered aggregates of gram-positive cocci admixed with neutrophils No granulomas or vasculitis Nonspecific inflammation

GPA, granulomatosis with polyangiitis.



Figure 1. Lower extremity ulcers following treatment with prednisone and cyclosporine, prior to initiation of infliximab.

ulcers with raised, violaceous borders. Repeat autoimmune workup was negative. Dermatology was consulted and diagnosed cutaneous PG. A skin biopsy was not performed at this time due to concern of pathergy. The ulcers responded well to prednisone 0.75 mg/kg daily and topical clobetasol ointment 0.05% with dressing changes.

A connection between the cutaneous PG-like lesions and lung nodules was considered. The patient did not have any signs or symptoms of inflammatory bowel disease, arthritis, or other autoimmune connective tissue diseases. The possibility of malignancy was also considered. Before further workup could be performed, his ulcers worsened during a prednisone taper, and he was admitted to the hospital for pain control.

While in the hospital, he was seen by dermatology, otolaryngology, respiratory, hematology, rheumatology, and infectious diseases. A cutaneous ulcer biopsy showed features consistent with PG with no evidence of vasculitis (Table 2). Serum protein electrophoresis and eosinophil levels were normal. Head CT showed opacification of the right maxillary sinus with loss of the medial sinus wall and a large midline septal defect. Nasal mucosa biopsy #1 and lung core biopsy #2 were performed (Table 2). Given the lack of diagnostic clarity, lung wedge resections were taken (Table 2). The findings were signed as consistent with PG given the clinical suspicion of the same in his skin. The patient was diagnosed with multisystem PG and was started on cyclosporine 5 mg/kg daily, which resulted in a temporary improvement of his cutaneous ulcers (Figure 1). Infliximab 5 mg/kg every 6 weeks



Figure 2. Lower extremity ulcers after treatment with prednisone, cyclosporine, and infliximab.

was subsequently initiated which resulted in dramatic ulcer healing (Figure 2).

In the year following discharge from the hospital, his ulcers worsened, and he developed sinus pain, progressive proptosis, and painful periocular swelling. Nasal mucosa biopsy #2 and palate biopsy #1 were taken (Table 2). Repeat ANCA was negative. Head CT showed right-sided pansinusitis and new destruction of the orbital floor and hard palate. Periocular discharge was drained and cultured, showing an abundance of neutrophils and no infection. Prednisone 1 mg/kg daily and infliximab 10 mg/kg every 4 weeks resulted in rapid improvements in his facial pain, proptosis, and periocular swelling. Given the bony necrosis and respiratory tract involvement, the patient was diagnosed with ANCA-negative GPA with PG-like cutaneous changes. The patient subsequently expired unexpectedly at home. An autopsy was declined by the family.

Discussion

We present a case of ANCA-negative GPA with renal sparing and PG-like cutaneous ulcers that mimicked multisystem PG. In GPA, up to 90% of cases are positive for ANCA.² Given this, it is imperative that physicians consider GPA in patients with multisystem inflammation or vasculitis, even in the context of a negative ANCA. Diagnosing ANCA-negative GPA can be further complicated when classic findings such as renal involvement are absent.

Renal sparing is often seen in patients with GPA, particularly early in the disease course or when ANCA is negative.^{1,3} The classic triad seen in GPA includes involvement of the upper respiratory tract, lower respiratory tract, and kidneys.¹ Although 80% of patients have renal involvement within 2 years of disease onset, only 10%–20% have renal involvement at the time of presentation.¹ Additionally, ANCA is negative in an estimated 40% of active, renal-sparing diseases.³ Similarly to renal involvement, other features of GPA are often absent on workup.

Histological findings of GPA can be absent. The histological findings in GPA include vasculitis, granulomas, and giant cells.⁴ In GPA, vasculitis and granulomatous inflammation may only be seen in 21% of head and neck biopsies.⁵ Further, only 47% of nasal biopsies in GPA reveal scattered giant cells. In the case presented, multiple biopsies were nonspecific and lacked features classic for GPA. GPA exhibits variable histological findings, and its clinical presentation, including cutaneous manifestations, can also vary significantly.

GPA can present with cutaneous changes, including PG-like ulcers. Although up to 50% of cases of GPA are found to have cutaneous involvement,¹ PG-like ulcers are a rare manifestation.^{6,7} PG is a rare neutrophilic inflammatory condition that classically presents as painful cutaneous pustules or nodules that evolve into ulcers with purulent drainage and violaceous, undermined borders.⁸ Extracutaneous manifestations of PG can also be seen, with pulmonary involvement being the most common.⁹ Similarly to GPA, there is a lack of gold standard diagnostic tests for PG.⁹ Findings of PG on histopathology are often nonspecific, with neutrophilic inflammation being the most common. It can thus be difficult to differentiate between multisystem PG and GPA with skin and pulmonary involvement.

In summary, diagnosing GPA can pose significant challenges, particularly when ANCA is negative. It is crucial for physicians to consider GPA when ANCA is negative, even if other typical features such as kidney involvement and histologic findings are absent. Additionally, GPA should be considered in patients presenting with PG-like ulcers, particularly when accompanied by inflammation or vasculitis affecting other systems.

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Patient consent

Informed verbal consent was obtained from the patient to share the case and photographs.

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