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CASE REPORT

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Significance of early treatment in granulomatosis with polyangiitis vasculitis

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Abstract

Vasculitis is a multisystemic disease that affects vessels of different sizes. Its presentation can vary widely depending on the system involved. It may present with constitutional symptoms or with specific features of end-organ involvement. The diagnosis is built on a compatible pattern of clinical features supported by specific serological or radiological investigations and confirmatory biopsy. Tissue biopsy is vital to confirm the diagnosis of vasculitis; however, this should not delay treatment when presentation strongly suggests vasculitis. We describe a case of a 72-year-old man treated with steroids, plasma exchange, and rituximab for suspected granulomatosis with polyangiitis (GPA) given his clinical presentation including suspected scleritis of the right eye, hearing changes, sinusitis, diffuse alveolar hemorrhage, pulmonary lesions, kidney failure, palpable purpura, and radiological evidence of pansinusitis and pulmonary lesions without waiting for serology or tissue confirmation. This case highlights the importance of recognizing the clinical features of GPA to initiate prompt treatment as it can progress rapidly and be fatal.

KEYWORDS

GPA, granulomatosis with polyangiitis, mortality, vasculitis

1 | INTRODUCTION

Vasculitis is a multisystemic disease that is caused by inflammation of blood vessel walls, which affects vessels of different sizes.[1] Antineutrophil cytoplasmic antibodies (ANCAs) associated vasculitis (AAV) is a necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels associated with ANCA specific for myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA).[2] AAV consists of granulomatosis with polyangiitis (GPA), microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis.[3] GPA clinical presentation can vary widely but classically involves the upper respiratory tract, lungs, and kidneys.[4] GPA is associated with a high mortality rate, so prompt diagnosis and treatment is critical to avoid morbidity and mortality in these patients.[5]

We present a case of a patient that received treatment for GPA with significant improvement of symptoms without waiting for serology or tissue confirmation given high clinical suspicion for GPA.

2 | CASE PRESENTATION

Seventy-two-year-old Haitian, Creole-speaking male with a history of prostate cancer status post prostatectomy presented complaining of dyspnea. The patient had a recent diagnosis of pansinusitis, and multiple bilateral pulmonary lesions with a mass-like consolidation of the left upper lobe (Figure 1). He was receiving antibiotics for sinusitis and pneumonia with plans for outpatient bronchoscopy to rule out malignancy.

On presentation, the patient reported experiencing dyspnea for the past 2 days. Further questioning revealed increased fatigue and malaise over the course of 2 months. He also had difficulty hearing and described a sensation of echoing when speaking for 1 month. Additionally, he had a nonproductive cough, bilateral eye irritation, and blurry vision in the right eye for 2 weeks. Although, the patient had been using ciprofloxacin drops for 1 week to treat possible conjunctivitis, there was minimal improvement in eye redness.

On arrival, his vitals were as follows: temperature of 98.2°F, blood pressure of 154/100, heart rate of 82, respiratory rate of 17, and oxygen saturation of 87% on room air. He was placed on 2 L nasal cannula, increasing his oxygen saturation to 93%. Physical examination revealed palpable purpura on the upper and lower extremities, which the patient had noticed earlier that day. Initial laboratory tests revealed anemia, acute kidney injury, elevated inflammatory markers, and normal serum complement levels. Results included blood urea nitrogen level of 56, creatinine 3 (compared to a baseline of 1), glomerular filtration rate of 22.9, hemoglobin of 8.2 (compared to 10.8 2 months prior), C-reactive protein of 16.20, and sedimentation rate of 16.

Computer tomography of the chest revealed bilateral alveolar airspace disease with no evidence of pulmonary embolism (Figure 2). Broad spectrum antibiotics were started due to suspected infection. The patient was transferred to the intensive care unit (ICU) for ongoing care. He underwent bronchoscopy and remained intubated post procedure given progressive and rapid hypoxemia and worsening chest x-ray. Bronchoscopy revealed evidence of diffuse alveolar hemorrhage (Figure 3). Intravenous (IV) steroids were initiated post-bronchoscopy to treat suspected AAV based on the clinical and physical manifestations, which occurred on the second day of hospitalization. The patient received IV methylprednisolone pulse administration of 1 g/day, divided into 250 mg every 6 h for 3 days, followed by 1 mg/kg/day, divided into 40 mg every 12 h. Rheumatology was consulted and skin biopsy and/or renal biopsy was recommended for confirmation of GPA given his clinical presentation. Rheumatologic work-up was ordered during this time. IV steroid administration was continued, while the patient remained intubated. On the third day of hospitalization, plasma exchange and rituximab therapy were initiated. Plasma exchange was performed every other day for a total of seven sessions. Rituximab was administered in two doses of 1 g, spaced 2 weeks apart for induction therapy. On the fourth day of hospitalization, broad spectrum antibiotic was discontinued as the infectious work-up came back negative. The patient required hemodialysis (HD) due to worsening renal function. Nephrology recommended postponing renal biopsy until the patient was stable. While the patient was in the ICU, he was noted to have a left lower extremity deep vein thrombosis for which he underwent inferior vena cava filter placement given contraindications for anticoagulation. The patient was extubated on the fifth day of hospitalization after completing

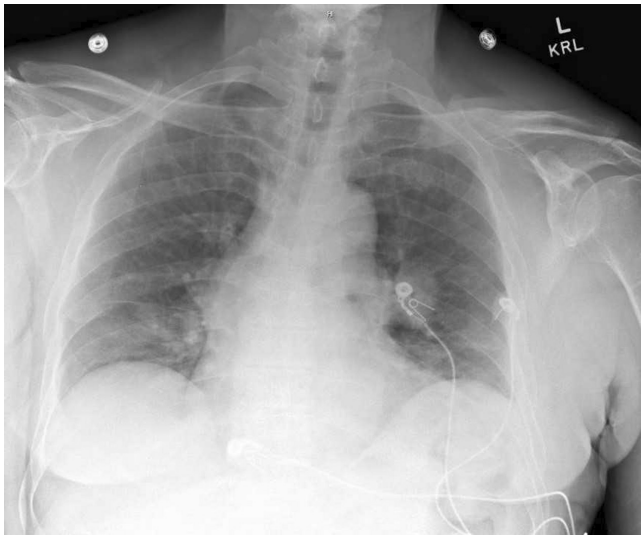

FIGURE 1 Initial chest x-ray showing a mass like consolidation on the left lung.

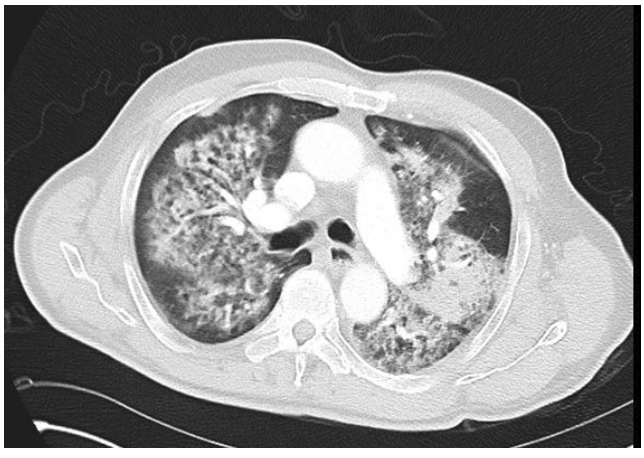

FIGURE 2 CT chest demonstrating bilateral airspace disease.

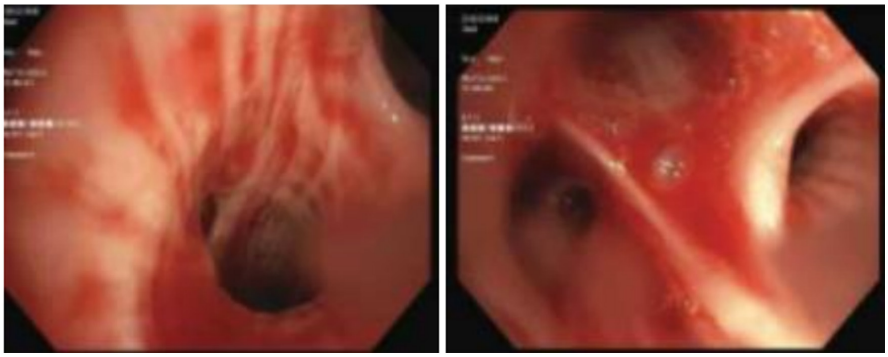

FIGURE 3 Diffuse alveolar hemorrhage in bronchoscopy.

two out of seven sessions of plasma exchange. Rheumatological work-up eventually resulted in positive cytoplasmic ANCA (c-ANCA) pattern and autoantibodies to PR3. Skin biopsy was initially delayed and performed later in the hospital course, given the lack of specially trained medical professionals available to perform it inpatient. Ultimately, skin biopsy results returned normal. The patient received the diagnosis of GPA based on clinical features of suspected scleritis of the right eye, hearing changes, sinusitis, diffuse alveolar hemorrhage, pulmonary lesions, kidney failure and palpable purpura, specific serology of positive c-ANCA and PR-3 antibodies as well as radiological evidence of sinusitis and pulmonary lesions. The patient demonstrated improvement throughout the clinical course and was discharged after the second rituximab dose. Following discharge, the patient maintained close follow-up with rheumatology and ophthalmology for evaluation of right vision loss. Additionally, the patient underwent HD for 3 months until renal function improved.

3 | DISCUSSION

AAV is characterized by inflammation that affects small blood vessels. Several risk factors have been associated with the development of AAV. Genetic, infection and environmental risk factors have been attributed to contribute to the onset of AAV and the production of ANCA.[6] AAV is a rare disorder. According to a meta-analysis that retrieved almost 5000 published studies from the year of 1995–2020, the global pooled incidence of AAV was 17.2 per million person years and the global pooled prevalence was 198.0 per million persons. The pooled incidence per million person years for GPA was 9.0 and the individual pooled prevalence per million persons was 96.8. AAV more commonly affected men than women, and the mean age was higher than 56 years.[7] The clinical presentation of ANCA vasculitis can vary considerably depending on the system involved. It may present with constitutional symptoms or with specific features of end-organ involvement.[8] Symptoms can be nonspecific. ANCA vasculitis may mimic an infectious process, but frequently the clinical course is atypical, often with an extended, generalized, nonspecific, prodromal illness in which repeated courses of antibiotics have failed to produce the expected improvement.[9] GPA is a specific type of AAV. GPA classically involves the upper respiratory tract, lungs, and kidneys. Although the clinical manifestations can be variable. Multiple organs can be affected, including the skin, kidneys, upper and lower respiratory tract as well as nervous system.[4] The diagnosis is built on a compatible pattern of clinical features supported by specific serological or radiological investigations and confirmatory biopsy.[10] ANCA is 66% sensitive and 98% specific for GPA and is present in 80%–90% of patients with active multisystemic disease.[4] The major autoantigens of ANCA are MPO and PR3. Those who are PR3-ANCA+ more often have a presentation consistent with GPA, whereas those who are MPO-ANCA+ tend to have features of MPA. Approximately 10% of GPA patients are MPO-ANCA+ and 5% are ANCA negative.[11] A negative ANCA does not exclude the diagnosis of GPA, therefore, the diagnosis of GPA is generally confirmed with a tissue biopsy from an affected organ. In this particular case, the diagnosis was established approximately 2.5 months after the onset of the initial constitutional symptoms. Diagnosing GPA can be challenging due to the nonspecific nature of its initial signs and symptoms, and often it takes longer to diagnose. A retrospective analysis from a single center in South India reported an average duration of symptoms before diagnosis of 4.5 months, ranging from 0 to 32 months.[12] Vasculitis can progress rapidly and be fatal. Disease management is imperative given the mortality rate of up to 90% at 2 years of multisystemic GPA if left untreated.[9] In this case, the patient received the diagnosis of GPA based on clinical features of suspected scleritis of the right eye, hearing changes, sinusitis, diffuse alveolar hemorrhage, pulmonary lesions, kidney failure and palpable purpura, specific serology of positive c-ANCA and PR3 antibodies as well as radiological evidence of sinusitis and pulmonary lesions. The patient received treatment for GPA with plasma exchange and rituximab without waiting for serology or tissue confirmation given high clinical

suspicion for GPA. Early recognition of vasculitis is crucial to allow initiation of therapy and avoid poor outcomes.

4 | CONCLUSION

We recognize that tissue biopsy is vital for diagnosis of vasculitis; however, this should not delay treatment when clinical presentation is suggestive of vasculitis. This is important to recognize especially in a setting with limited access to inpatient specialists such as rheumatologists, dermatologists, or pathologists. Reducing delays in diagnosis can reduce morbidity and mortality and improve clinical outcomes.

AUTHOR CONTRIBUTIONS

Jenifer Centeno Gavica: Conceptualization; writing – original draft; writing – review and editing. **Leslie Raymond:** Supervision; writing – review and editing.

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The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this case report are from previously reported studies and datasets, which have been cited.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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