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MITRAL VALVE VEGETATION AND EMBOLIC STROKE IN NEWLY DIAGNOSED GRANULOMATOSIS WITH POLYANGIITIS: A DIAGNOSTIC CHALLENGE MIMICKING CULTURE-NEGATIVE ENDOCARDITIS

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ABSTRACT

Introduction: Granulomatosis with polyangiitis (GPA) is an antineutrophil cytoplasmic antibody (ANCA)-associated small- to medium-vessel vasculitis that most commonly affects the respiratory tract and kidneys. Cardiac involvement is uncommon, and valvular manifestations are rare. Distinguishing GPA-related valvular involvement from infective endocarditis (IE) presents a significant diagnostic challenge, particularly because ANCA positivity may also occur in IE.

Case description: We report a 60-year-old man who presented with necrotic lower-extremity ulcers, acute kidney injury, and elevated inflammatory markers. Serologic evaluation demonstrated positive ANCA with proteinase-3 specificity, while kidney biopsy confirmed pauci-immune necrotizing crescentic glomerulonephritis, supporting a diagnosis of GPA. Despite initiation of immunosuppressive therapy, he developed acute focal neurologic deficits, and brain magnetic resonance imaging demonstrated multifocal ischemic infarcts consistent with an embolic process. Transoesophageal echocardiography revealed a mitral valve mass with moderate-to-severe regurgitation. Blood cultures and serologic evaluation for fastidious organisms remained negative.

Conclusion: This case highlights a rare presentation of GPA with suspected sterile valvular involvement complicated by embolic stroke and underscores the importance of distinguishing ANCA-associated vasculitis from culture-negative infective endocarditis.

KEYWORDS

ANCA-associated vasculitis, culture-negative endocarditis, mitral regurgitation, embolic stroke, cardiac involvement

LEARNING POINTS

- Antineutrophil cytoplasmic antibody (ANCA) positivity does not exclude infective endocarditis, as significant clinical overlap exists between these conditions.
- Kidney biopsy and careful microbiologic evaluation may help distinguish ANCA-associated vasculitis from infection-associated mimics.
- Cardiac imaging should be considered in patients with granulomatosis with polyangiitis who develop unexplained focal neurologic deficits.

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INTRODUCTION

Granulomatosis with polyangiitis (GPA) is an antineutrophil cytoplasmic antibody (ANCA)-associated necrotizing vasculitis affecting small- to medium-sized vessels, classically involving the upper respiratory tract, lungs, and kidneys[1]. Neurologic manifestations are less common and most frequently involve the peripheral nervous system, while central nervous system involvement is uncommon[2]. Cardiac involvement is similarly rare and may include pericarditis, myocarditis, coronary vasculitis, conduction abnormalities, and, infrequently, valvular disease[3].

Valvular involvement in GPA presents a significant diagnostic challenge because infective endocarditis (IE) may closely mimic ANCA-associated vasculitis. ANCA positivity, particularly anti-proteinase-3 antibodies, has been described in IE and may be accompanied by renal dysfunction, purpura, and inflammatory marker elevation, making distinction between these entities clinically difficult but therapeutically essential[4]. We describe a case of newly diagnosed GPA complicated by embolic ischemic stroke in the setting of a culture-negative mitral valve lesion.

CASE DESCRIPTION

A 60-year-old man with gastroesophageal reflux disease and type 2 diabetes mellitus presented with progressive bilateral lower extremity pain, swelling, and weakness. Physical examination demonstrated extensive necrotic ulcerations of both lower extremities with digital necrosis involving the left hand. Cardiopulmonary examination was unremarkable, and no peripheral stigmata of IE were identified.

Initial laboratory evaluation revealed leucocytosis (26.4 $\times 10^9$/l), elevated inflammatory markers (erythrocyte sedimentation rate 38 mm/h; C-reactive protein 31.4 mg/l), and acute kidney injury (creatinine 2.5 mg/dl) with haematuria and proteinuria. Doppler ultrasonography was negative for deep vein thrombosis. Given concern for severe infection, empiric broad-spectrum intravenous antibiotics were initiated; however, his clinical status failed to improve.

Further diagnostic evaluation demonstrated positive ANCA with proteinase-3 specificity, normal complement levels, and negative antiphospholipid antibodies. Kidney biopsy revealed pauci-immune segmental necrotizing and crescentic glomerulonephritis with minimal immunoglobulin/complement staining on immunofluorescence and no electron-dense deposits on electron microscopy, consistent with ANCA-associated glomerulonephritis. A diagnosis of GPA was established, and treatment with pulse-dose intravenous methylprednisolone and rituximab was initiated.

His hospitalization was complicated by worsening renal failure requiring temporary haemodialysis, as well as extensive lower-extremity wounds requiring surgical debridement and skin grafting, attributed to vasculitic ischemic injury.

During hospitalization, he developed acute right upper extremity weakness with worsening bilateral lower extremity weakness. Computed tomography scan of the head was unrevealing, but magnetic resonance imaging demonstrated multifocal ischemic infarcts in a distribution concerning for embolic disease. Given suspicion for a cardioembolic source, transoesophageal echocardiography was performed and demonstrated an echogenic mass attached to the posterior mitral leaflet with moderate-to-severe mitral regurgitation *(Fig. 1)*. Multiple blood cultures obtained before antibiotic administration remained negative. Serologic testing for fastidious culture-negative organisms, including *Coxiella burnetii*, *Bartonella*, and *Brucella*, was likewise negative.

In the setting of systemic embolization and concern for a thrombotic valvular process, therapeutic anticoagulation with intravenous unfractionated heparin was initiated while immunosuppressive therapy for GPA was continued. Renal function gradually improved over the subsequent two months, allowing discontinuation of dialysis. Avacopan was initiated for remission maintenance.

DISCUSSION

This case illustrates an uncommon presentation of newly diagnosed GPA complicated by valvular involvement and embolic ischemic stroke, while highlighting the important diagnostic challenge of distinguishing ANCA-associated vasculitis from IE.

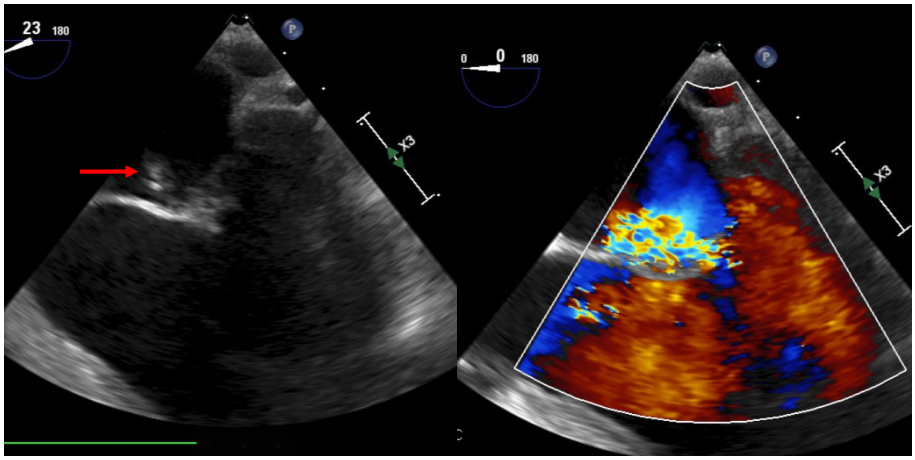


Figure 1. *Transoesophageal echocardiography: The left panel shows an arrow indicating the echogeneic structure attached to the posterior leaflet of the mitral valve. The right panel shows anteriorly directed jet of moderately severe mitral regurgitation.*

Cardiac manifestations of GPA are uncommon, reported in approximately 6% of patients, and include pericarditis, myocarditis, coronary vasculitis, arrhythmias, and valvular abnormalities[3]. Among reported cases of valvular involvement, the aortic valve is most frequently affected, while mitral valve disease appears substantially less common[3]. Although the precise mechanism remains incompletely understood, ANCA-mediated endothelial injury and systemic inflammation may promote a prothrombotic milieu predisposing to sterile valvular thrombus formation or inflammatory valvular injury[5-6].

The neurologic findings in this case were particularly notable. Central nervous system involvement in GPA occurs infrequently and is more commonly attributed to cerebral vasculitis[2]. In contrast, this patient's multifocal ischemic infarcts followed a distribution suggestive of embolic disease, prompting cardiac evaluation that identified a plausible embolic source.

A central diagnostic challenge was exclusion of IE, particularly given the well-recognized overlap between IE and ANCA-associated vasculitis. ANCA positivity, including anti-proteinase-3 antibodies, has been reported in IE and may be accompanied by renal dysfunction and cutaneous manifestations, closely mimicking primary vasculitis[4]. The bidirectional nature of this diagnostic challenge has been highlighted before in the case of a patient initially suspected to have IE who was ultimately diagnosed with GPA[7]. Our case illustrates the converse scenario, in which biopsy-confirmed GPA developed valvular pathology prompting reconsideration of IE.

Several findings favoured GPA-related disease rather than IE in this case. Kidney biopsy demonstrated a pauci-immune necrotizing crescentic glomerulonephritis without immune-complex deposition, supporting ANCA-associated glomerulonephritis rather than infection-associated immune-complex disease[8]. Multiple blood cultures obtained prior to antibiotic administration were negative, and targeted serologic testing for common fastidious causes of culture-negative endocarditis was unrevealing[9]. Normal complement levels further argued against infection-associated immune-complex glomerulonephritis[10]. The patient also demonstrated clinical improvement following immunosuppressive therapy, supporting an autoimmune rather than infectious etiology.

Despite these findings, definitive characterization of the valvular lesion remains limited by the absence of histopathologic confirmation. The lesion may represent sterile thrombotic vegetation, inflammatory valvular involvement related to GPA, or another non-infectious endocardial process. Repeat echocardiographic assessment demonstrating interval regression would have further strengthened the presumed diagnosis.

This case expands the recognized spectrum of cardiac manifestations in GPA and underscores the importance of considering cardiac evaluation in patients with ANCA-associated vasculitis who develop unexplained neurologic events. At the same time, clinicians must maintain diagnostic caution, as culture-negative IE remains a critical alternative diagnosis requiring exclusion.

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