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Title	An unusual case of non-infective endocarditis in undiagnosed antiphospholipid syndrome
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An unusual case of non-infective endocarditis in undiagnosed antiphospholipid syndrome

Clinical record

A 57-year-old man presented with left facial droop and dysarthria due to a multiterritory ischaemic stroke affecting the right posterior and middle cerebral arteries. His previous history included a segmental pulmonary embolus in the setting of pneumonia. He was not taking any regular medications and denied recreational drug use. There was no relevant family history. He was haemodynamically stable, afebrile and euvolaemic. White cell count was normal at $7.8 \times 10^9/L$ (reference interval [RI], $4-12 \times 10^9/L$). C-reactive protein was mildly elevated at 9 mg/L (RI, < 5 mg/L). On day 1, transthoracic echocardiogram revealed a vegetation on the anterior mitral valve leaflet tip with moderate to severe mitral regurgitation, normal left atrial size and biventricular size and systolic function. Three sets of blood cultures were taken before commencing intravenous ceftriaxone and flucloxacillin. He was transferred to our hospital for surgical consideration.

On day 3, transoesophageal echocardiogram confirmed a 2 cm independently mobile lesion on the anterior mitral valve leaflet tip with severe central mitral regurgitation (Box 1). Extended 27-day blood cultures remained negative. Routine coagulation studies revealed an elevated activated partial thromboplastin time (aPTT) of 77 seconds (RI, 23–36 seconds) with normal international normalised ratio (INR). aPTT did not correct with mixing studies. Elevated dilute Russell viper venom time screen ratio of 2.63 (RI, < 1.2) confirmed presence of lupus anticoagulant. Thrombophilia screen confirmed high anticardiolipin IgG > 2024 (RI, < 20) and β 2-glycoprotein 1 antibody > 6100 (RI, < 20) suggestive of antiphospholipid syndrome. There were no clinical features of systemic lupus erythematosus and autoimmune screen was normal. Computed tomography of the chest, abdomen, and pelvis demonstrated no embolic events or malignancy. A diagnosis of non-infective endocarditis (NIE) due to presumed antiphospholipid syndrome was made. A multidisciplinary consensus opinion involving cardiology, cardiothoracic surgery, infectious diseases, haematology, and stroke teams was made for non-surgical management with warfarin (target INR, 2–3). Antibiotics were ceased. He was discharged home on day 10. Anticardiolipin IgG and β 2-glycoprotein 1 antibody remained elevated at 12 weeks, confirming antiphospholipid syndrome. Repeat transoesophageal

echocardiogram at 3 weeks demonstrated significantly reduced mitral valve lesion size with only mild mitral regurgitation (Box 2). The patient continues on lifelong warfarin with no residual stroke symptoms.

Discussion

While NIE is rarely diagnosed clinically,¹ in an autopsy study, NIE was three times more common than infective endocarditis.² NIE is associated with high morbidity and mortality mainly due to under-recognition. Causes include mechanical stress, hypercoagulable states such as malignancy, and autoimmune diseases including antiphospholipid syndrome.^{2,3} Turbulent blood flow in hypercoagulable states is hypothesised to induce endothelial cell injury leading to platelet and fibrin deposition interweaving to form vegetations,³ most commonly affecting the aortic and mitral valves.^{3,4} Systemic embolisation affects 40% of patients with NIE.⁴

Differentiating NIE from infective endocarditis can be challenging. Clinically, infective endocarditis usually manifests with fevers and weight loss, whereas NIE commonly presents as recurrent systemic embolisation.¹ Patients with NIE often have features suggestive of their underlying condition such as constitutional symptoms of occult malignancy, arthritis suggestive of systemic lupus erythematosus, or recurrent thromboses indicating antiphospholipid syndrome. Stroke is more common in NIE compared with infective endocarditis (33% v 13%),³ with NIE vegetations more likely to detach given minimal inflammation or adherence to the valve.⁴

Close scrutiny of laboratory markers is important, as abnormalities may indicate particular NIE-associated conditions. On echocardiogram, NIE lesions are typically 0.1–2 cm in diameter, broad-based, sessile and irregular.^{1,3} They usually attach to the leaflet closure line and move with the leaflets, compared with independently mobile infective endocarditis vegetations. Significant valvular regurgitation is rare in NIE.¹ Our case describes NIE in the setting of antiphospholipid syndrome. Despite unusual NIE echocardiographic features of an independently mobile mitral valve mass with severe mitral regurgitation, surgery was ultimately avoided with anticoagulation. Antiphospholipid syndrome is an autoimmune disease characterised by venous and arterial thromboses and recurrent miscarriages. Clinical features and laboratory criteria are crucial to diagnosis. The latter includes the identification of antiphospholipid antibodies or lupus anticoagulant on two occasions at least 12 weeks apart to minimise false positives. NIE occurs in up to 15% of patients with antiphospholipid syndrome.⁵

Mainstay NIE management involves treatment of the underlying condition and consideration of therapeutic anticoagulation to prevent recurrent embolisation.³ While warfarin is typically used in autoimmune-associated NIE,⁵ heparin and enoxaparin are superior in malignancy-related NIE. There is no consensus for use of direct oral anticoagulants or corticosteroids.³ Surgery is seldom necessary and reserved for severe valvular dysfunction, large vegetations, or recurrent embolism despite anticoagulation.

The diagnosis of NIE remains challenging based on clinical and echocardiographic features alone. Targeted history taking and scrutiny of investigations, including cultures, inflammatory markers, and coagulation studies, are paramount and may prevent unnecessary surgery. Our case exemplifies the value of a multidisciplinary approach to endocarditis.

Lessons from practice

- While uncommon, non-infective causes should be considered in all patients with endocarditis.
 - Non-infective endocarditis can be difficult to distinguish from infective endocarditis based on clinical and echocardiographic features alone, and targeted history taking and scrutiny of blood cultures, inflammatory markers, and coagulation studies is necessary.
 - The mainstay treatment of non-infective endocarditis is treatment of the underlying cause. Surgery is seldom required.
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[Insert Boxes]

[Box 1; lee_mja20.01268_gr1]

1 Initial transoesophageal echocardiogram demonstrating a 2 cm independently mobile linear lesion on the anterior mitral valve leaflet tip (arrow)

[Box 2; lee_mja20.01268_gr2]

2 Follow-up transoesophageal echocardiogram at 3 weeks after anticoagulation demonstrating a significant reduction in the size of the mitral valve lesion, now measuring 0.8 × 0.7 cm (arrow)



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