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Case Report

Splinters in the fingernails, heart and brain: thromboembolic complications of non-bacterial thrombotic endocarditis despite treatment with a direct-acting oral anticoagulant

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Abstract

Non-bacterial thrombotic endocarditis (NBTE) is a rare condition characterized by non-infectious vegetations affecting the cardiac valves. Although systemic thromboembolism is a commonly associated condition, antiphospholipid syndrome is less common. Nevertheless, treatment generally involves long-term anticoagulation. We report a case of a patient with previously undiagnosed NBTE who suffered systemic thromboembolic events despite pre-existing treatment with a direct-acting oral anticoagulant.

INTRODUCTION

Non-bacterial thrombotic endocarditis (NBTE) is a rare condition characterized by non-infectious lesions affecting the cardiac valves [1]. NBTE is strongly associated with malignancy and can also be associated with autoimmune disorders such as systemic lupus erythematosus and antiphospholipid syndrome (APS) [1]. Systemic thromboembolism is a common manifestation of NBTE and occurs in up to 50% of patients [2]. Valvular dysfunction may also occur, occasionally requiring surgical valvular intervention [1]. Treatment with anticoagulation is recommended; however, the optimal strategy is unclear [3]. We report a case of a patient with previously undiagnosed NBTE who presented with multi-organ systemic thromboembolism despite pre-existing treatment with a direct-acting oral anticoagulant.

CASE REPORT

A 56-year-old man with a history of persistent atrial fibrillation and previous lower limb deep vein thrombosis presented at hospital with a 1-day history of transient left-sided arm paraesthesia in the absence of chest pain. His regular medications included apixaban 5 mg twice daily and digoxin 125 micrograms daily. He was normotensive, had a resting heart rate of 105/min and was afebrile. A systolic murmur was noted over the aortic area without radiation to the carotid area. There were no clinical signs of cardiac failure. Neurological examination demonstrated normal upper and lower limb tone, power, reflexes, sensation and coordination. Splinter haemorrhages were noted in his fingernails (Fig. 1).

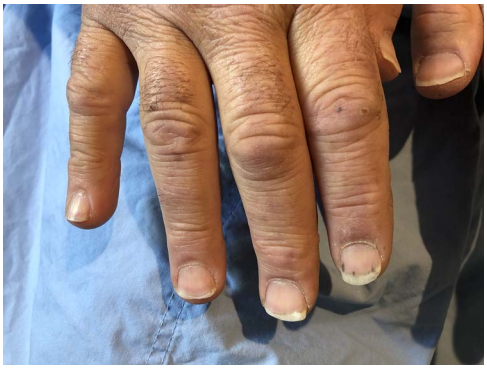

Figure 1. Splinter haemorrhages

The patient is an electrician by occupation and there was no history of tobacco smoking, excessive alcohol consumption or recreational drug usage. There was no

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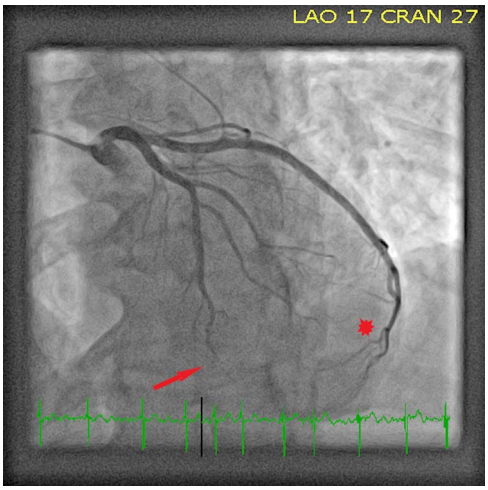

Figure 2. Coronary angiogram (cranial view) demonstrating slow antegrade flow (incomplete filling) in the left anterior descending artery (red arrow) compared with normal opacification of the left circumflex artery (red asterisk), suggestive of coronary artery embolism.

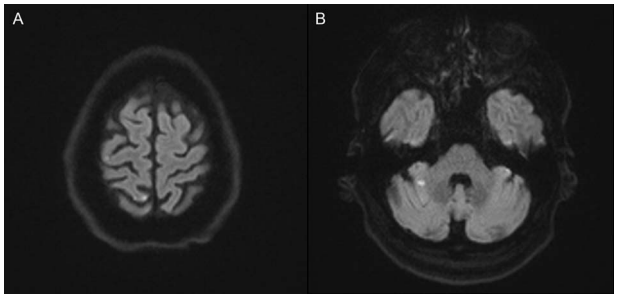

Figure 3. Brain magnetic resonance imaging (diffusion weight imaging) demonstrating multi-territory foci of restricted diffusion, including two in the right parietal vertex (**A**) and one in the right cerebellar hemisphere (**B**), consistent with embolic stroke.

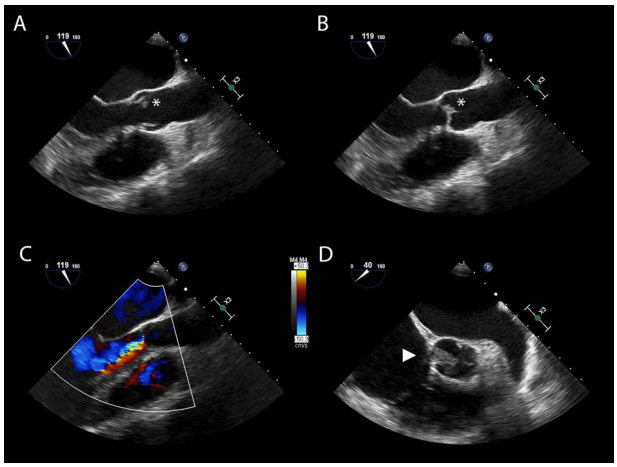

Figure 4. Transoesophageal echocardiography: Long-axis views of the left ventricular outflow tract and aortic valve in systole (**A**) and diastole (**B**) showing an echogenic mass in the non-coronary cusp of the aortic valve (indicated by asterisk). This was associated with moderate aortic regurgitation (**C**). (**D**) Short axis view of the aortic valve demonstrating the presence of a vegetation on the non-coronary cusp. Despite the presence of atrial fibrillation, the left atrial appendage was free of thrombus.

family history of prothrombotic disorders, and he did not have any prior investigation for prothrombotic disorders when he was diagnosed with an unprovoked deep venous thrombosis 2 years prior.

His electrocardiogram showed atrial fibrillation, with no acute ischaemic changes. Transthoracic echocardiography demonstrated a normal sized left ventricle with mild global impairment of left ventricular systolic function (ejection fraction of 45%). Serial high-sensitivity troponin I levels were elevated (320 ng/l and 288 ng/l, normal < 20 ng/l). Serum biochemistry, renal and liver function tests were normal. C-reactive protein was 6.5 mg/l (normal < 5.0 mg/l) and erythrocyte sedimentation rate was 11 mm/hour (normal 2–25 mm/hour).

Coronary angiography revealed slow flow in the distal LAD artery suggestive of a coronary artery embolism (Fig. 2). Cerebral magnetic resonance imaging demonstrated numerous foci of restricted diffusion, including two in the right parietal vertex and one in the right cerebellar hemisphere, consistent with embolic stroke (Fig. 3). The intracranial cerebral arteries demonstrated normal flow and were of normal calibre. Suspecting an intracardiac source of embolism, the patient underwent transoesophageal echocardiography. This revealed a broad-based vegetation (14 mm at the base and 9 mm in thickness) attached to the non-coronary cusp of the aortic valve, with several frond-like mobile elements and moderate aortic valve regurgitation (Fig. 4). There was no left atrial appendage thrombus. In the absence of septic features, NBTE was suspected. A procoagulant screen revealed strongly positive lupus anticoagulant tests (Russell's viper venom and tissue thromboplastin inhibition) and elevated β2-glycoprotein antibodies (91 CU, normal 0–19). The patient had normal anti-cardiolipin IgM and IgG levels (<1 and 18 CU, respectively, normal 0–19 CU). Anti-nuclear antibody titre was positive (1:160; speckled and homogenous), but no other diagnostic criteria for systemic lupus erythematosus were present. Computed tomography of the chest, abdomen and pelvis did not reveal any evidence of malignancy nor pulmonary embolism. Serum angiotensin-converting enzyme was within normal limits (61 U/l, normal 20–70 U/l), although lactate dehydrogenase was mildly elevated (301 U/l, normal 120–250 U/l). Serum electrophoresis and immunofixation was normal, with no evidence of paraproteinaemia.

The patient received intravenous unfractionated heparin. Because of the risks of recurrent systemic embolism, the patient underwent surgical aortic valve replacement with a bioprosthetic aortic prosthesis. A small vegetation noted on the P2 scallop of the mitral valve was also carefully excised. Pulmonary vein cryoablation and amputation of the left atrial appendage was performed. Histological examination of the excised aortic valve revealed hypocellular fibrinous material with organizing thrombus, and no evidence of acute inflammation, consistent with NBTE. Bacterial cultures were negative. Histological and cytogenic examination of a sampled mediastinal lymph nodes did not demonstrate any

features of sarcoidosis or lymphoproliferative disease. He was commenced on warfarin postoperatively (target INR 2.0–3.0). The patient made an excellent postoperative recovery and suffered no further thromboembolic events.

DISCUSSION

APS is a hypercoagulable state associated with both venous and arterial thrombotic and embolic complications [4]. This patient had recurrent venous thromboembolism as well as NBTE, complicated by embolic ischaemic stroke and coronary artery embolism. Antiphospholipid antibodies are thought to mediate valvular damage by promoting the formation of fibrin-platelet thrombi on altered valve surfaces, which results in NBTE, often appearing as verrucous lesions on left-sided heart valves [5]. Whilst atrial fibrillation is associated with an increased risk of systemic embolism, the absence of left atrial appendage thrombus and the presence of an aortic valve vegetation, suggests that his cardioembolic stroke was secondary to APS.

Unfractionated heparin or low molecular weight heparin are recommended in the acute setting [3], although the optimum long-term strategy is uncertain. Direct oral anticoagulants (DOACs) are less effective than warfarin in preventing recurrent thromboembolism in randomised-controlled trials [6, 7]. A recent meta-analysis of four studies comparing DOACs to vitamin K antagonists (VKAs) in patients with APS demonstrated an increased risk of recurrent arterial thrombosis (odds ratio 5.17), no increased risk in venous thrombosis and no difference in risk of bleeding [8]. VKAs remain the guideline-recommended treatment of choice in antiphospholipid syndrome, although current data do not specifically include patients with NBTE [3, 4].

The role of surgical valvular intervention is uncertain. Surgical valve replacement or vegetation excision with valvular repair may be performed for significant valvular dysfunction or to reduce the risk of thromboembolism. In a contemporary cohort study of 42 patients, 10 patients (24%) underwent cardiac surgery [1] and 7 of them did not have a history of malignancy. The prognosis of patients who underwent cardiac surgery without a history of malignancy was found to be excellent, whereas 3 patients with cancer-related NBTE all died within 2 years of surgery.

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None.

ETHICAL APPROVAL

This case is exempt from ethics approval at our institution.

CONSENT

Written informed consent was obtained from this patient and is available for review upon request.

GUARANTOR

Dr Justin Phan.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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