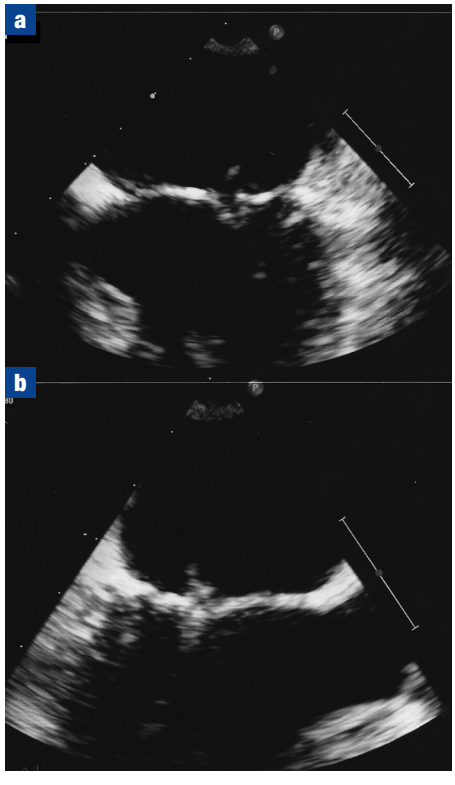
# A swollen leg and cerebral infarctions in a 49-year-old woman

## Introduction

The antiphospholipid syndrome is an acquired disorder of the immune system of unknown cause. It is characterized by the presence of antiphospholipid antibodies such as anti-cardiolipin or lupus anticoagulant which interfere with the homeostatic regulation of blood coagulation leading to a hypercoagulable state. Thrombosis may affect both venous and arterial circulations, with typical manifestations that include deep venous thrombosis, myocardial infarction and stroke (Levine et al, 2002).

Figure 1. Transoesophageal echocardiogram. **a.** The zoomed four-chamber view and **(b)** apical long axis view show a thickened mitral valve with verrucous lesions on the leaflet margins, typical of Libman–Sacks endocarditis.

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## Discussion

This case was diagnostic of primary antiphospholipid syndrome in its association of at least one of the clinical criteria (vascular thrombosis and/or pregnancy morbidity) and at least one of the laboratory criteria (detection of lupus anticoagulant, anticardiolipin, or anti-beta-2-glycoprotein 1 antibodies) without evidence of systemic lupus erythematosus (Ren et al, 2014). Libman–Sacks endocarditis was diagnosed, consistent with previous echocardiographic studies in which left-sided valvular abnormalities are found in about one third of cases of antiphospholipid syndrome (Hojnik et al, 1996). Whether antiphospholipid antibodies have a pathogenic role in Libman–Sacks endocarditis is unclear but reports of valvular disease in patients with

## CASE REPORT

A 49-year-old woman resident in East Africa presented with swelling of the right leg. A diagnosis of deep vein thrombosis was made on the basis of a positive D-dimer test and she was anticoagulated with rivaroxaban. She received no further investigation at that time but 3 months later a predisposition to headaches prompted cerebral magnetic resonance imaging. This was reported as showing multiple cerebral infarctions in various perfusion territories although there was no history of stroke and the neurological examination was normal. The magnetic resonance imaging findings suggested a cardioembolic source and she was referred for a cardiac opinion. Residual swelling of the right leg was noted but she had no systemic symptoms and the cardiac examination was unremarkable. She had a normal electrocardiogram.

Further investigation included a transthoracic echocardiogram. This showed normal left ventricular dimensions and contractile function but the mitral valve was thickened with mild regurgitation into a normal size left atrium. The right-sided chamber dimensions were normal. A transoesophageal echocardiogram confirmed an intact atrial septum. Verrucous lesions were observed on the mitral leaflet margins typical of Libman–Sacks endocarditis (*Figure 1*). Blood was sampled for measurement of the dilute Russell viper venom time. The ratio of patient to control clotting times was 1.97 and showed 45.9% correction with addition of phospholipid to the plasma samples, confirming the presence of lupus anticoagulant (Pengo et al, 2009). Further blood sampling more than 12 weeks later confirmed lupus anticoagulant but serological testing for systemic lupus erythematosus revealed only weakly positive anti-nuclear antibodies at 1/80 titre, while complement 3 and 4 and anticardiolipin antibodies were negative.

The final diagnosis was antiphospholipid syndrome, the hypercoagulable state accounting for her presentation with venous thrombosis in the leg and her predisposition to cerebral thromboembolism in relation to mitral valve Libman–Sacks endocarditis. The main differential diagnosis was Lambl's excrescences but the echocardiogram was less characteristic of this degenerative abnormality, classically described as filiform fronds on the atrial surface of the mitral valve. Lambl's excrescences are normally asymptomatic but may rarely be associated with stroke. They show no association with lupus anticoagulant or deep vein thrombosis.

Haematological advice recommended continuing anticoagulation with rivaroxaban rather than warfarin because of concerns about the feasibility and safety of monitoring arrangements in the patient's homeland. Hydroxychloroquine was recommended for protection against systemic lupus erythematosus as well as its proposed antithrombotic properties in antiphospholipid syndrome.

systemic lupus erythematosus who are negative for antiphospholipid antibodies makes this unlikely (Hojnik et al, 1996).

The valvular abnormalities in antiphospholipid syndrome are usually clinically silent and progressive valvular dysfunction is rare (Hojnik et al, 1996). Occasionally, however, significant valvular dysfunction occurs and there are reports of cardiac failure requiring valve replacement surgery (Bouma et al, 2010). Embolic phenomena are uncommon but, like this case, can be a cause of cerebral infarction as well as other systemic complications (Hojnik et al, 1996).

It may be relevant that this patient was positive for lupus anticoagulant which is a stronger risk factor for thrombosis than anticardiolipin antibodies in patients with antiphospholipid syndrome (Galli et al, 2003). Her presentation with deep vein thrombosis and cardioembolic cerebral infarction emphasizes the need for effective anticoagulation to prevent further thrombotic events. Continuing treatment with rivaroxaban was chosen because of uncertainty about the availability and safety of warfarin therapy in her homeland. Rivaroxaban is a factor Xa inhibitor and studies of its effectiveness in antiphospholipid syndrome are currently in progress. Early signs are good and an antiphospholipid syndrome study showed greater suppression of complement levels compared with warfarin leading to speculation that, in addition to its anticoagulant effect, rivaroxaban may benefit patients by limiting the activation of complement (Arachchillage et al, 2016). Hydroxychloroquine was added for protection against systemic lupus erythematosus and its proposed antithrombotic effects (Belizna, 2015). **BJHM**

### LEARNING POINTS

- An aetiological diagnosis should always be sought in patients who present with deep vein thrombosis.
- Libman–Sacks endocarditis is not always a benign disorder and may be a source of cerebral thromboembolism.
- Associations of Libman–Sacks endocarditis with systemic lupus erythematosus are variable and may be absent.


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Galli M, Luciani D, Bertolini G, Barbui T. Lupus anticoagulants are stronger risk factors for thrombosis than anticardiolipin antibodies in the antiphospholipid syndrome: a systematic review of the literature. Blood. 2003 Mar 1;101(5):1827–1832. https://doi.org/10.1182/blood-2002-02-0441

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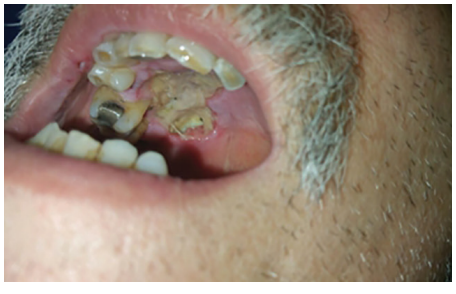
# A man with black–brown nasal discharge

A 56-year-old man presented to the emergency department with a history of nasal fullness, brown nasal discharge and facial pain, and a past medical history of poorly controlled diabetes mellitus. His physical examination was significant for low grade fever, black and brown discharges and necrotic tissue on both walls of the nasal cavities, and necrotic scars on the hard palate (*Figure 1*). A computed tomography scan of the head and paranasal sinuses revealed mucosal thickening in the right ethmoid, maxillary and frontal sinuses, with soft tissue swelling around both orbits which supported the diagnosis of mucormycosis.

Figure 1. Necrotic scars on the hard palate.



Mucormycosis refers to several life-threatening diseases caused by fungal infection (mostly *Rhizopus* species) (Petrikkos et al, 2012). The patient was commenced on antimicrobial therapy (amphotericin B) and underwent immediate debridement of infected and necrotic tissue. Unfortunately he died 1 month later. **BJHM**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