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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Ischemic Stroke From Libman-Sacks Endocarditis Not Associated With Antiphospholipid Antibodies

Good Clinical Outcome Without Anticoagulation

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ABSTRACT

Libman-Sacks endocarditis (LSE), a cardiac complication of systemic lupus erythematosus, is commonly treated with anticoagulation for stroke prevention. We describe a patient with multifocal strokes secondary to LSE, treated with aspirin, without further recurrence. Our case highlights the importance of nuanced decision-making regarding antithrombotic choices for stroke prevention in LSE. (**Level of Difficulty: Intermediate.**)
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A 32-year-old woman with an 8-year history of systemic lupus erythematosus (SLE) presented to the hospital with subacute onset painful paresthesia of her right hemibody. Upon awakening, she described numbness along her right back that progressed over 1 h to involve her right leg, arm, and face. Three weeks before her presentation, the patient was diagnosed with lupus nephritis and started oral prednisone as well as cyclosporine, and continued on hydroxychloroquine. On neurological examination, the patient's primary sensory modalities were intact, but she described allodynia to touch along the right side of her face, back, and abdomen. The rest of her neurological examination was unremarkable. On systemic examination, there were no new rashes, arthritis, or stigmata of peripheral embolization.

LEARNING OBJECTIVES

- The benefits of glucocorticoids for the treatment of LSE remain unknown, but a short trial of high-dose steroids with the aim of reducing inflammation to mitigate further vegetation growth may be reasonable.
- Hydroxychloroquine is an important adjunctive therapy for patients with SLE and associated LSE due to its anti-inflammatory and antithrombotic effects.
- There is no evidence-based treatment for secondary stroke prevention in LSE. When APS is present, anticoagulation is recommended as a secondary thromboprophylaxis strategy. When APS is absent, aspirin may be considered as a therapeutic option.

MEDICAL HISTORY

Past complications of SLE included inflammatory arthritis and cardiac involvement with myopericarditis. She had no history of spontaneous abortions or thrombosis to suggest antiphospholipid antibody syndrome (APS). In addition, she had a

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ABBREVIATIONS AND ACRONYMS

aPLA = antiphospholipid antibody

APS = antiphospholipid antibody syndrome

LSE = Libman-Sacks endocarditis

SLE = systemic lupus erythematosus

TTE = transthoracic echocardiogram

history of hypertension and inactive myasthenia gravis.

DIFFERENTIAL DIAGNOSIS

There is a broad differential for ischemic stroke in patients with SLE, including vasculitis, hypercoagulability related to APS, infective endocarditis, arterial dissections, fibrin-platelet occlusion of intracranial arterioles, atherosclerosis of large vessels (e.g., middle cerebral artery), and Libman-Sacks endocarditis (LSE) (1).

INVESTIGATIONS

The patient's initial laboratory results revealed anemia with a hemoglobin level of 89 g/l (120 to 160 g/l), mild leukocytosis with a white blood cell count of 12.8 $\times$ 10^9/l (4 to 12.0 $\times$ 10^9/l), and normal platelet count of 200 $\times$ 10^9/l (150 to 400 $\times$ 10^9/l). Her C-reactive protein level was normal at 1.9 mg/l (0 to 10 mg/l), but the erythrocyte sedimentation rate was elevated at 97 mm/h (0 to 15 mm/h), and there was a depressed C3 level of 0.61 g/l (0.83 to 1.93 g/l) and an elevated double-stranded DNA level of 768 IU/ml (>25 IU/ml) suggesting active SLE. The patient's creatinine level was elevated at 124 μmol/l (50 to 110 μmol/l), in keeping with lupus nephritis.

Brain magnetic resonance imaging revealed numerous small cortical and subcortical acute infarcts in multiple vascular territories (**Figure 1**). A head and neck magnetic resonance angiogram was unremarkable. A lumbar puncture showed a normal cerebrospinal fluid profile. A hypercoagulable screen, including antiphospholipid antibodies (aPLAs), was negative. Transthoracic echocardiogram (TTE) and transesophageal echocardiogram showed an echobright linear strand on the aortic valve extending into the left ventricular outflow tract (**Figure 2**, Video 1). There was moderate aortic regurgitation, preserved ejection fraction, and no evidence of a patent foramen ovale. Infectious evaluation including multiple blood cultures, and results of serological testing for culture-negative endocarditis were negative. The patient was ultimately given a diagnosis of LSE of the aortic valve.

MANAGEMENT

Due to concern regarding a lupus flare, the patient was started on intravenous methylprednisolone 1 g daily for 3 days followed by an oral steroid taper, and continued on hydroxychloroquine and cyclosporine. For secondary stroke prevention, she was started on aspirin 81 mg daily.

FOLLOW-UP

Over the next week, the patient reported an improvement in her neurological symptoms and was discharged home. Five months later, a repeat TTE revealed a complete resolution of the previously described aortic vegetation, with no residual valvular fibrosis, calcification, stenosis, or insufficiency. There was no clinical recurrence of stroke or interval subclinical brain infarcts on subsequent brain magnetic resonance imaging.

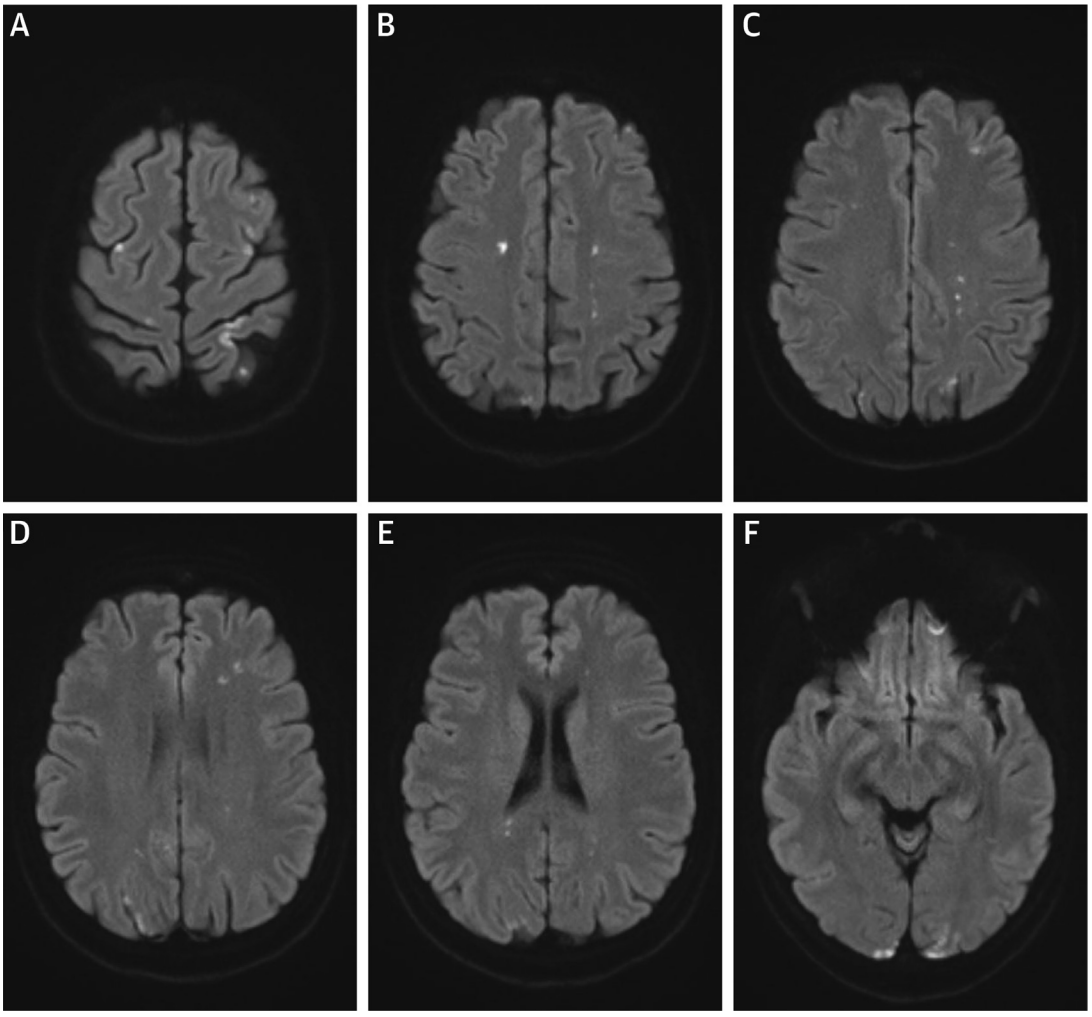
DISCUSSION

We present a patient with a history of SLE and multifocal ischemic strokes due to aortic valve LSE. There are 2 main features of the case that are noteworthy: 1) the complete resolution of the aortic valve vegetation without residual valvular damage; and 2) the prevention of stroke recurrence with aspirin treatment only.

Cerebrovascular disease is a major cause of morbidity and mortality in SLE, accounting for 12% of deaths (2). In a large prospective cohort study of 342 patients with SLE who underwent TTE, LSE was observed in 11% of patients and was associated with longer disease duration, pericarditis, nephritis, and APS (3). With the exception of APS, the patient had all of these risk factors. Moreover, the presence of LSE is independently associated with elevated risk of recurrent stroke (4). The underlying pathophysiology of LSE involves endothelial damage through immunoglobulin, complement, and inflammatory cell deposition. The damaged endothelium subsequently promotes fibrin-platelet formation that may lead to thromboembolic complications (5). As such, LSE vegetation has 2 potentially treatable targets: the underlying inflammation that may lead to valvular damage, and a superimposed thrombotic competent that is at risk of embolization.

There is no universally accepted treatment for LSE. Although glucocorticoids help to reduce the valvular inflammatory reaction, there is limited evidence that they prevent thromboembolic events (6). There is also concern that chronic glucocorticoid use may lead to valvular dysfunction by promoting fibrosis (5), and case reports exist of acute valvular dysfunction after subsequent high-dose steroids (7). In distinction to the aforementioned studies, this report shows that a short course of high-dose steroids may be beneficial at mitigating vegetation growth without causing

FIGURE 1 **Brain Magnetic Resonance Imaging**



Magnetic resonance head diffusion weighted sequence from **(A)** dorsal to **(F)** ventral. Multiple cortical and subcortical small infarcts seen as restricted diffusivity.

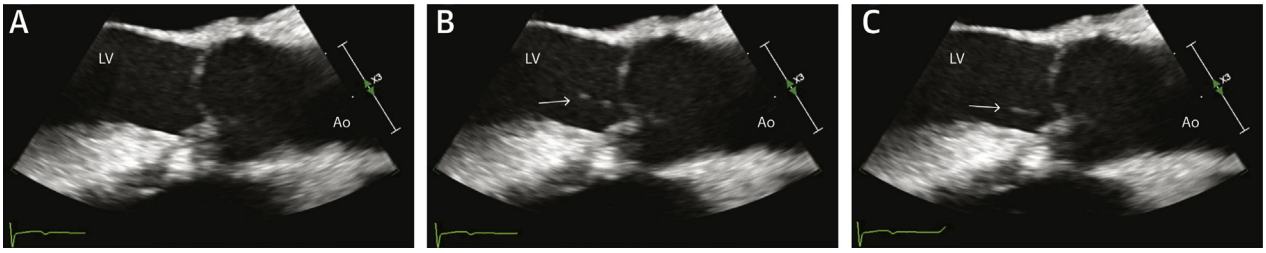
valvular damage. Our patient also received hydroxychloroquine, which is reportedly associated with good outcomes in patients with SLE and LSE due to its anti-inflammatory and antithrombotic properties (8).

Antithrombotic therapy is the most controversial point of contention in the treatment of LSE without APS, with few data comparing anticoagulation versus antiplatelet therapy. When LSE occurs in the presence of APS, anticoagulation is recommended as a secondary thromboprophylaxis strategy for APS (9), rather than for LSE. Importantly, as with the current case, up to 60% of LSE cases occur in the absence of APS, meaning that the selection of an antithrombotic agent is problematic in the majority of patients with LSE (3). Furthermore, patients with SLE often have medical comorbidities that increase the risk of hemorrhage on anticoagulation, which should be taken into account when deciding antithrombotic treatment. Our patient was negative for aPLAs and was at increased risk for anticoagulation-related hemorrhagic complications due to her chronic kidney disease and anemia.

CONCLUSIONS

The current case illustrates a good clinical outcome, with no recurrent strokes or silent brain infarcts,

FIGURE 2 Transesophageal Echocardiogram



White arrow in B and C demonstrates a vegetation on the aortic valve extending into the LV outflow tract consistent with Libman-Sacks endocarditis. See Video 1.
Ao = aorta; LV = left ventricle.

using only aspirin for secondary stroke prevention in LSE, and total resolution of the aortic vegetation in a patient treated with high-dose steroids, hydroxychloroquine, and cyclosporine. Physicians should be aware of the therapeutic equipoise in choice of antithrombotic treatment for ischemic stroke patients with LSE and negative aPLAs, and consider antiplatelet therapy if there are concerns regarding hemorrhagic risk with anticoagulation. Whether the risk of thromboembolic complications in patients with aortic LSE is lower than in those with mitral involvement is unknown. Future studies are needed to determine the optimal secondary stroke prevention strategy in patients with ischemic stroke due to LSE.

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KEY WORDS anticoagulation, antiplatelet, aortic valve, endocarditis, secondary prevention, stroke, thrombus, treatment

APPENDIX For a supplemental video, please see the online version of this paper.