Cambridge City Publishers

Case Reports in Clinical Cardiology Journal

Case Report | Vol 5 Iss 2

A Complex Presentation of Subacute Cerebrovascular Accident Revealing Libman-Sacks Endocarditis in a Middle-Aged Patient

Laura Gonazalez-Reyes[1], Godfrey Tabowei[1*], Prashanth Gumpu[1], Shahmeer Lodhi[1], Abi Watts[2], Carlos Matute-Martinez[2] and Evbu Enakpene[2]

[1]Texas Tech University Health Science Center, Permian Basin, Department of Internal Medicine, Odessa, TX, USA

[2]Texas Tech University Health Science Center, Permian Basin, Department of Cardiology, Odessa, TX, USA

[*]**Corresponding author:** Godfrey Tabowei, Texas Tech University Health Science Center, Permian Basin, Department of Internal Medicine, Odessa, TX, USA. E-mail: Godfrey.Tabowei@ttuhsc.edu

Received: February 13, 2025; **Accepted:** February 25, 2025; **Published:** March 15, 2025

Abstract

A middle-aged man presented with headache, nausea, dizziness, and vision changes for one month duration worsening in the past few days. Imaging revealed multiple embolic infarcts involving the right parietal lobe, left inferior cerebellar hemisphere, and a near-complete blockage of the right internal carotid artery. Additionally, an aortic valve vegetation and a small atrial septal defect was found in a transesophageal echocardiogram. Nonbacterial thrombotic endocarditis was suspected due to negative blood cultures. Elevated autoimmune markers suggested antiphospholipid syndrome. Warfarin and high-dose steroids were started. There was no evidence of atrial fibrillation during a 15-day hospitalization. Follow-up imaging confirmed Libman Sacks endocarditis and ruled out vasculitis. This complex case underscores the importance of interdisciplinary collaboration and thorough investigation in order to achieve a comprehensive diagnosis and effective management of rare conditions like Libman Sacks endocarditis.

Keywords: Libman-Sacks Endocarditis; Embolic strokes; Autoimmune disease

Case Presentation

A man in his forties with a past medical history of hypertension and positive rapid plasma reagin test (RPR), initially presented to a referring facility due to complaints of headache, nausea, and dizziness with vision changes of one-month duration. He also reported memory difficulties, which started before the onset of the previously mentioned symptoms. There was no history of trauma prior to the onset of symptoms. On evaluation, he was found to have a subacute right parietal cerebrovascular accident seen on computed tomography (CT), the reason why he was transferred to our facility. On arrival, he was found to be hypertensive (blood pressure 175/106 mmHg), heart rate 98 bpm, and afebrile (36.9 Celsius degrees), saturating on room air above 94%. The physical exam was unremarkable, with no neurological deficits. The review of systems was noncontributory. Family history was noncontributory. He had a past history of occasional tobacco use but quit about 8 months ago.

CT head without contrast done in our facility showed acute to subacute appearing medium-sized infarct in the right posterior middle cerebral artery territory (Figure 1). There was also an acute to subacute appearing multifocal small infarct in the right anterior superior frontal lobe. Finally, likely an old focal infarct in the left inferior cerebellar hemisphere. Prompting a neurology consult, the patient started on aspirin and atorvastatin. The laboratory performed at that time included a complete blood count, complete metabolic panel, screening for syphilis, inflammatory markers, and urinalysis with drug screen (Table 1).

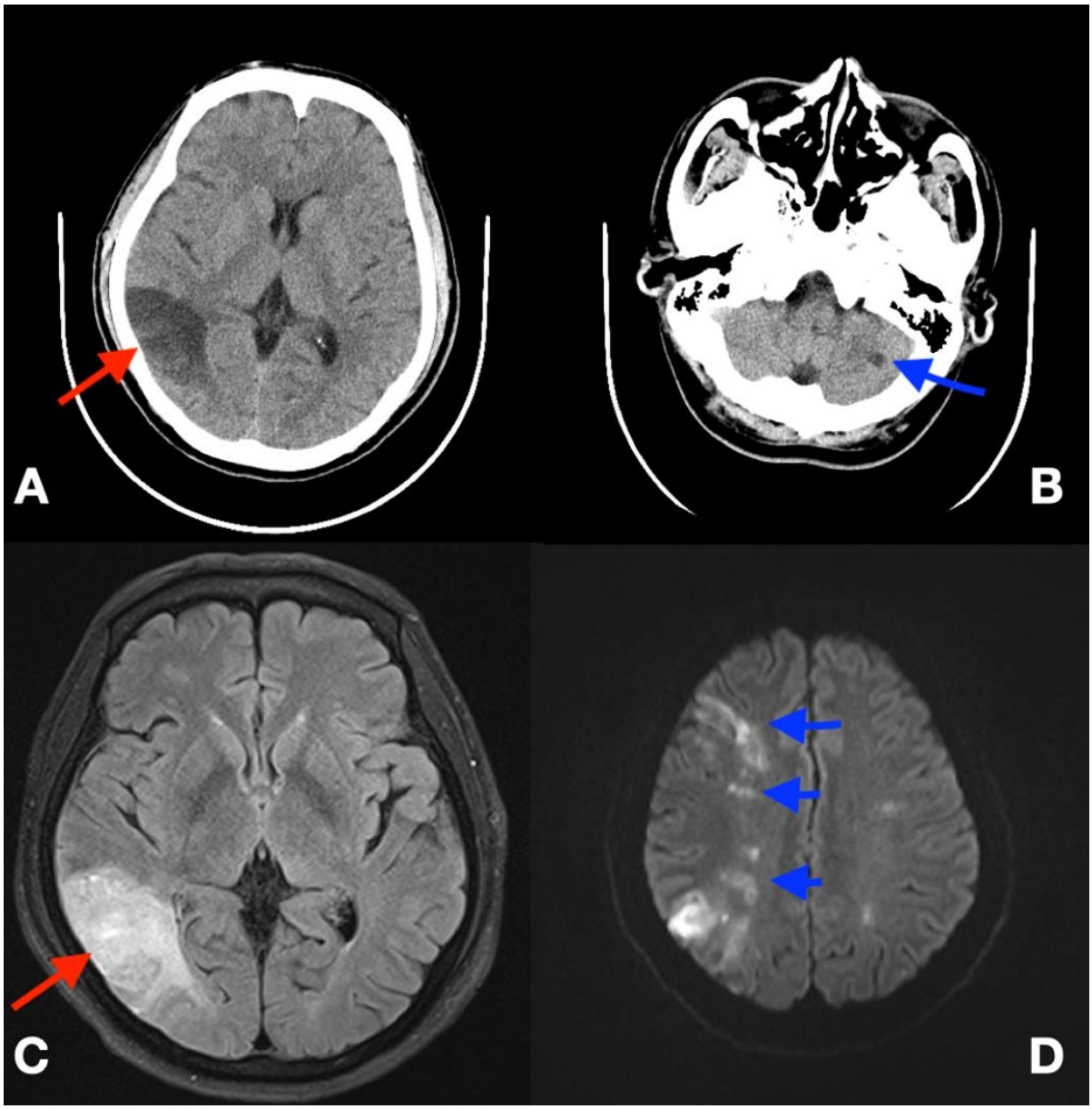

Figure 1: Brain imaging performed on day 1 of admission. Computed tomography of the brain axial views (A and B), showing infarct in the right posterior middle cerebral artery territory (red arrow in A); also, an old infarct in the left inferior cerebellar hemisphere (blue arrow in B). Magnetic resonance of the brain (C and D) showing acute to subacute infarct in the right posterior temporoparietal lobe (red arrow in C) and multiple subacute infarcts in the right frontoparietal area in watershed distribution (blue arrow in D).

Table 1: Laboratories performed during admission for diagnostic workup.

Variable	Reference Range	Day of admission	Day 2	Day 4
Hematology				
White blood cells (10*3/uL)	4.800-10.800	6.550		
Hemoglobin (g/dL)	13.5-17.5	12.0		
Plateles (10*3/uL)	150-400	148		
ESR (mm/hr)	1-20		73	
Autoimmune				
Complement 3 (mg/day)	85-165			81
Complement 4 (mg/day)	14-44			< 8
Anti-Nuclear Anibody IgG			Detected	
Cytoplasmic pattern			Speckled	
Cytoplasmic pattern titer			1:1280	
Beta 2 Glycoprotein IgG antibody (HI)	< 20		36	
Beta 2 Glycoprotein IgM and IgA antibody (HI)	< 20		< 10	
Cardiolipin Antibody IgA (HI)	< 11		<10	
Cardiolipin Antibody IgG (HI)	<14		50	
Cardiolipin Antibody IgM	<12		56	
Antithrombin III Activity (%)	70.0-120.0			104.6
Protein S Total (%)	84-134			130
Protein C Total (%)	63-153			88
Factor V Leiden Mutation				Negative
Thrombin Time (HI)	14.7-19.5			> 150.0
Prothrombin time (NA)	12.0-15.5			14.9
Lupus Anticoagulant			Detected	
Infectious disease				
RPR		Reactive		
T pallidum Antibody			Non-Reactive	
RPR Titer				1:128
HIV 1/2 Antibody screen		Negative		
SARS-CoV-2 IgG Antibody			Reactive	
Borrelia burdogferi Antibody IgG and IgM				Negative
Mycoplasma pneumonia antibody IgM (HI)	< 0.09			0.17
Mycoplasma pneumonia antibody IgG (NA)	< 0.76			0.02
Epstein Barr Virus by PCR				Detected
Cytomegalovirus				Not detected

We proceeded to perform further imaging, which included magnetic resonance of the brain with and without contrast, magnetic resonance angiography (MRA) of the head and neck revealed acute to subacute infarct in the right posterior temporoparietal lobe in the middle cerebral artery distribution, corresponding to the region of hypoattenuation on recent CT. There was associated laminar necrosis and petechial hemorrhage with no discrete parenchymal hematoma. Multiple small subacute infarcts were seen in the right frontoparietal white matter in an anterior cerebral artery and middle cerebral artery watershed distribution. Additionally, there were small, likely late subacute infarcts in the left frontal and parietal lobes and left cerebellum. There was near complete occlusion at the right internal carotid artery terminal bifurcation involving the origin of the right middle cerebral artery and anterior cerebral artery.

There were no hemodynamically significant stenosis, occlusion, or aneurysm of the arteries of the neck. Warfarin was started, and high-dose steroids were given for five days. The hematologist recommended continuing with the current treatment and repeating blood work in 3 months as per guidelines to diagnose APS. Aspirin was continued until the therapeutic range of INR was achieved, and a diagnosis of Libman Sacks endocarditis was made. The patient was discharged after being hospitalized for 15 days. His symptoms, including vision changes and dizziness, have now resolved. He was scheduled to follow up with the hematologist in three months to repeat the autoimmune panel for antiphospholipid syndrome. Additionally, he will have a follow-up appointment with his cardiologist in six weeks for a repeated transesophageal echocardiogram.

Differential Diagnosis

Considering a positive rapid plasma reagin (RPR) test, a confirmatory Treponema pallidum flurescent antibody absorption test was performed which resulted negative. Neurosyphilis could have presented with vision changes, nausea and vomiting, as well as our patient. The patient was also placed in telemetry monitoring since admission to screen for arrhythmias such as atrial fibrillation as the cause of embolic stroke.

The cardiology team performed a transesophageal echocardiogram, suspecting a cardioembolic source of his cerebrovascular accident, such as left ventricular thrombus, patent foramen ovale or valvular vegetation. The test revealed a large aortic vegetation and an atrial septal defect with a small left-to-right shunt (Figure 2). Two sets of blood cultures were drawn and vancomycin and piperacillin-tazobactam were given. After five days, blood cultures were negative, prompting the discontinuation of antibiotics. Further tests showed elevated erythrocyte sedimentation rate, c-reactive protein, antinuclear antibody, B-2-glycoprotein, as well as anticardiolipin antibodies IgG and IgM, and low complement levels (C3 and C4) (Table 1). Adding to this, patients with lupus could also present with false positive RPR, such as our young male. Nonbacterial thrombotic endocarditis was diagnosed, and antiphospholipid syndrome (APS) and potential vasculitis were considered. A repeat computed tomography with angiography of the head and neck was ordered but did not show any evidence of vasculitis.

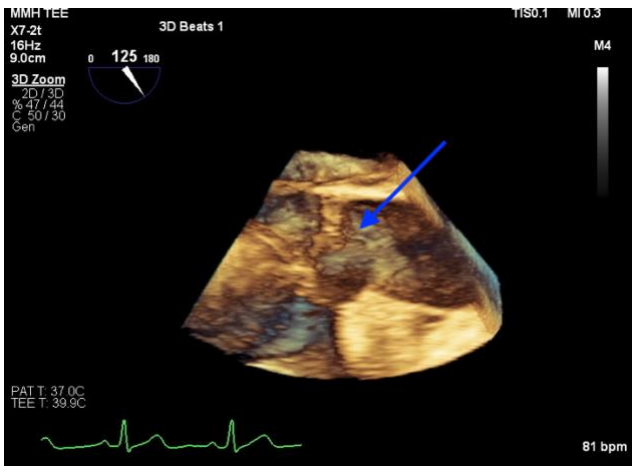

Figure 2: Aortic valve vegetation seen in transesophageal echocardiogram.

Discussion

We encountered a young patient who initially presented with symptoms concerning for a stroke. Subsequent CT imaging of the brain confirmed the presence of micro embolic strokes. In young patients like this one, the differential diagnosis should encompass seizures, migraines with aura, multiple sclerosis, tumors, infections such as syphilis and viral encephalitis, in addition to vasculitis and hypertensive encephalopathy. However, when embolic strokes are identified, the diagnostic focus shifts. A comprehensive work-up at this stage should include angiography to assess for both small and large vessel atherothrombotic strokes. An echocardiogram is vital to exclude potential causes of cardio-aortic embolic strokes, including intracardiac thrombus, endocarditis, valvular heart disease, and patent foramen ovale. Furthermore, electrophysiology studies are crucial for identifying arrhythmias, notably atrial fibrillation. In our patient, an echocardiogram pointed to the causative agent of our young patient embolic stroke.

Nonbacterial thrombotic endocarditis (NBTE) is a condition characterized by the presence of sterile vegetations on the cardiac valves without any signs of infections [6]. These sterile vegetations may be linked to malignancy or autoimmune disease [7]. The prevalence is 1.25% in patients with solid tumors (mainly adenocarcinoma) versus 0.25% in the general population [6]. When NBTE is observed in association with systemic lupus erythematosus (SLE) and antiphospholipid antibody syndrome (APS), it is known as Libman-Sacks (LS) endocarditis.

According to a study by Moyssakis et al. [8], around 11% of SLE patients suffer from this condition. They studied 342 patients and found that 11% of them had Libman-Sacks endocarditis through transthoracic echocardiogram [8]. However, an autopsy study reported the presence of NBTE in 50% of lupus cases [7]. Lupus duration, cerebrovascular events, disease activity, presence of anticardiolipin antibodies, and manifestations of antiphospholipid syndrome are all associated with the presence of this type of endocarditis [9]. Vegetations predominantly involved the mitral valve (61.9%), followed by the aortic valve (23.8%) according to a 20-year registry [10]. Similarly, Moyssakis et al. [8] found that 63% of patients had vegetation on the mitral valve and 34% on the aortic valve. Regurgitation is the most common functional lesion associated with this condition [8].

LS endocarditis involves damage to the endothelial cells through the deposition of immunoglobulin, complement, and inflammatory cells [8,11]. This damage can lead to a hypercoagulable state conducive to the formation of fibrin-platelet clot formation that may lead to thromboembolic complications [11,12]. The histopathology of LS shows fibroblast hyperplasia, fibrin deposition, angiogenesis, hematoxylin bodies, and nonbacterial inflammation [12].

Diagnosing NBTE can be difficult, as some patients may not show any symptoms, while in about 59% of cases, clinical symptoms appear following peripheral embolization from endocardial vegetations, particularly cerebrovascular accidents [10]. Embolic stroke affects around 20% of patients with infective endocarditis, but it occurs in a significantly higher proportion, up to 75%, of cases associated with NBTE [6]. A meta-analysis of 26 real-world observational studies showed that systemic lupus erythematosus is linked to an increased risk of ischemic stroke, with a pooled relative risk of 2.18 (95% confidence interval 1.78 to 2.67) [13]. Patients with vegetations have three times more cerebromicroembolic events per hour after simultaneously adjusting for patent foramen ovale, interatrial septal aneurysm, carotid or aortic atherosclerosis, and antiphospholipid antibodies [14].

The diagnosis of LS endocarditis is usually confirmed through an echocardiogram. A study conducted over a period of 20 years found that transesophageal echocardiogram (TEE) was more sensitive (97.1%) than transthoracic echocardiogram (45.2%) in detecting this condition [10]. Recent studies comparing 3D and 2D TEE have revealed that 3D TEEs are more effective in detecting mitral or aortic valve vegetation. They can detect more vegetation per study and are better at determining the size of the vegetation [9]. Libman-Sacks vegetations have been characterized by Roldan et al. [9] as sessile, oval or tubular, coalescent, nodular, or protuberant echogenic masses. They are usually located on the coaptation point of the leaflets but can extend through the leaflets into the opposite side [9]. Reports have shown that cardiac valve leaflets are diffusely thickened without commissural fusion and that this predominantly affects the base [10,15]. Unlike infective endocarditis, nonbacterial thrombotic endocarditis does not significantly damage the valvular apparatus. It is not associated with local complications such as abscesses, fistulae, or disruption of the leaflets and/or chordae [6]. Infective endocarditis vegetations, on the other hand, are characterized as being highly mobile, with narrow base attachment and elongated infective vegetations [9,15].

The primary treatment for Libman-Sacks endocarditis involves anti-inflammatory and anti-thrombotic medication, a recurrent follow-up with echocardiography for evaluation of resolution or progression. A study of 17 lupus patients with cerebrovascular disease found that those treated with such medication had a reduction in the number, size, and area of valve vegetation. They also experienced significant improvement in valve regurgitation, and valve thickening did not progress. Additionally, ischemic brain lesion load and neurocognitive dysfunction resolved or significantly improved [2].

Regarding anti-inflammatory therapy, hydroxychloroquine is the preferred choice, but some recommend a short course of high-dose glucocorticoids alongside hydroxychloroquine to reduce inflammation [11]. Intravenous unfractionated or subcutaneous heparin is used for anticoagulation in patients with malignancy [6,10], whereas warfarin is the anticoagulant of choice in antiphospholipid antibody syndrome [10]. In cases of lupus where antiphospholipid syndrome is absent, aspirin may be considered a therapeutic option, as reported in a case study [11].

When patients with severe valvular regurgitation, large mobile vegetation (usually >2 cm), and recurrent embolic strokes, despite adequate anticoagulation, are not responding to other treatments, surgical intervention may be necessary [10,12]. However, patients with Libman-Sacks endocarditis are at a higher risk of experiencing post-operative complications such as embolism of valve vegetations, prosthesis dehiscence, prosthetic valve stenosis and/or regurgitation due to thrombosis, premature degeneration, or pannus formation, infective endocarditis, autoimmune-mediated bioprosthetic valvulitis, perforation, or accelerated degeneration [2].

Learning Points

- Embolic strokes necessitate a thorough work-up, including angiography for small and large vessel assessment, echocardiogram to exclude cardio-aortic embolic causes, and electrophysiology studies to identify arrhythmias.
- Since nonbacterial thrombotic endocarditis is known to be associated with cerebrovascular events, it is crucial for healthcare professionals to conduct thorough clinical assessments and employ appropriate diagnostic tools to ensure early detection and proper treatment.
- Libman-Sacks endocarditis is treated with a combination of anti-inflammatory and anti-thrombotic medications, and monitoring treatment outcomes with recurrent echocardiography is crucial.

REFERENCES

1. Galve E, Candell-Riera J, Pigrau C, et al. Prevalence, morphologic types, and evolution of cardiac valvular disease in systemic lupus erythematosus. The New England Journal of Medicine. 1988; 319: 817-823.
2. Roldan CA, Sibbitt WL Jr, Greene ER, et al. Libman-Sacks endocarditis and associated cerebrovascular disease: The role of medical therapy. PLoS One. 2021; 16: e0247052.
3. Miller CS, Egan RM, Falace DA, et al. Prevalence of Infective Endocarditis In Patients with Systemic Lupus Erythematosus. Journal of the American Dental Association. 1999; 130: 387-392.
4. Mattos P, Santiago MB. Association of antiphospholipid antibodies with valvulopathy in systemic lupus erythematosus: a systematic review. Clinical Rheumatology. 2011; 30: 165-171.
5. Zuily S, Régnault V, Selton-Suty C, et al. Increased risk for heart valve disease associated with antiphospholipid antibodies in patients with systemic lupus erythematosus. Circulation. 2011; 124: 215-224.
6. Tonutti A, Scarfò I, La Canna G, et al. Diagnostic Work-Up in Patients with Nonbacterial Thrombotic Endocarditis. J Clin Med. 2023; 12: 5819.
7. Ibrahim AM, Siddique MS. Libman-Sacks Endocarditis. 2023 Sep 4. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
8. Moyssakis I, Tektonidou MG, Vasilliou VA, et al. Libman-Sacks endocarditis in systemic lupus erythematosus: prevalence, associations, and evolution. Am J Med. 2007; 120: 636-642.
9. Roldan CA, Tolstrup K, Macias L, et al. Libman-Sacks Endocarditis: Detection, Characterization, and Clinical Correlates by Three-Dimensional Transesophageal Echocardiography. J Am Soc Echocardiogr. 2015; 28: 770-779.
10. Zmaili MA, Alzubi JM, Kocyigit D, et al. A Contemporary 20-Year Cleveland Clinic Experience of Nonbacterial Thrombotic Endocarditis: Etiology, Echocardiographic Imaging, Management, and Outcomes. Am J Med. 2021; 134: 361-369.
11. Krawczyk M, Budhram A, Sposato LA. Ischemic Stroke from Libman-Sacks Endocarditis Not Associated with Antiphospholipid Antibodies: Good Clinical Outcome Without Anticoagulation. JACC Case Rep. 2019; 11: 297-300.
12. Takeuchi K, Izumi T, Nanaura H, et al. Mitral Valve Replacement for Enlarged Libman-Sacks Endocarditis in a Patient with Persistent Primary Antiphospholipid Syndrome and Recurrent Stroke: A Case Report. Am J Case Rep. 2023; 24: e938930.
13. Yazdany J, Pooley N, Langham J, et al. Systemic lupus erythematosus; stroke and myocardial infarction risk: a systematic review and meta-analysis. RMD Open. 2020; 6: e001247.
14. Roldan CA, Sibbitt WL Jr, Qualls CR, et al. Libman-Sacks endocarditis and embolic cerebrovascular disease. JACC Cardiovasc Imaging. 2013; 6: 973-983.
15. Arnautovic JZ, Yamasaki H, Rosman HS. Multiple embolic strokes as a result of Libman-Sacks endocarditis associated with lupus and secondary antiphospholipid antibody syndrome: a case report. Eur Heart J Case Rep. 2018; 17: 94.