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Case Report

Libman–Sacks Endocarditis in Triple-Positive Antiphospholipid Syndrome Following Switch from Warfarin to Rivaroxaban: Improvement After Reinstitution of Warfarin and Escalation of Immunosuppression

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Abstract

Triple-positive antiphospholipid syndrome (APS) represents a high-risk serologic phenotype associated with recurrent thrombosis and systemic lupus erythematosus (SLE). Direct oral anticoagulants (DOACs), particularly rivaroxaban, have demonstrated inferior outcomes compared with vitamin K antagonists in this population. We report a case of a patient with long-standing SLE and persistently triple-positive APS who developed Libman–Sacks endocarditis following a switch from warfarin to rivaroxaban. The patient had biopsy-proven class V lupus nephritis and had remained clinically stable on long-term warfarin therapy for several years. Transthoracic echocardiography demonstrated underlying rheumatic mitral valve disease with newly developed mobile vegetations measuring 10-15 mm. Blood cultures obtained prior to antibiotic exposure were negative, and inflammatory markers were not suggestive of infection. Rivaroxaban was discontinued, and warfarin was reinstated with bridging therapy. Prednisolone (40 mg daily) was initiated, and follow-up echocardiography demonstrated a reduction in vegetation size with clinical improvement. This case highlights a temporal association between rivaroxaban use and valvular thrombotic lesions in high-risk APS. Improvement was likely multifactorial, reflecting combined effects of anticoagulation, escalation of immunosuppression, and underlying valvular disease. These findings support current recommendations favoring vitamin K antagonists over DOACs in patients with triple-positive APS.

Keywords: Antiphospholipid syndrome, Libman, rivaroxaban, Sacks endocarditis, systemic lupus erythematosus, warfarin

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Introduction

Antiphospholipid syndrome (APS) is an autoimmune prothrombotic disorder defined by vascular thrombosis occurring in the presence of persistent antiphospholipid antibodies including lupus anticoagulant, anticardiolipin, and anti-β2 glycoprotein I antibodies.[1]

Triple positivity confers the highest risk of recurrent thrombosis and adverse outcomes.[2,3]

Systemic lupus erythematosus (SLE) is closely associated with APS, and cardiac manifestations include Libman–Sacks endocarditis, a sterile form of non-bacterial thrombotic endocarditis.[4,5]

These vegetations most commonly involve the mitral valve and may lead to valvular dysfunction or embolic complications.[6]

The TRAPS trial demonstrated increased thrombotic recurrence in triple-positive APS patients treated with rivaroxaban compared with warfarin.[7]

Subsequent meta-analyses and international guidelines recommend vitamin K antagonists over direct oral anticoagulants (DOACs) in high-risk APS.[8,9]

Libman–Sacks endocarditis most commonly affects the mitral valve and may occur on previously abnormal valves, including those affected by rheumatic valvular disease.[6]

Case Presentation

The patient was diagnosed with SLE in October 2003, with renal biopsy confirming class V lupus nephritis. She also had a known history of rheumatic mitral valve disease. Baseline serological evaluation demonstrated antinuclear antibodies (ANA 1 : 640) and strongly positive anti–double-stranded DNA (315 IU/mL).

She demonstrated persistently positive antiphospholipid antibodies on repeated testing more than 12 weeks apart, fulfilling criteria for triple-positive APS.[1,2] Lupus anticoagulant was detected by dilute Russell viper venom test (DRVVT ratio 2.34), with elevated anticardiolipin IgG (120 GPL units) and anti-β2 glycoprotein I antibodies (IgG 99, IgM 88). Her clinical history also included 1 early pregnancy loss (<10 weeks).

She had a prior episode of deep venous thrombosis and was maintained on long-term warfarin with a target INR of 2-3 for several years without recurrence.[3]

In early 2025, anticoagulation was changed from warfarin to rivaroxaban at another institution by a hematologist.

Approximately 5 months later, she developed progressive dyspnea on exertion without fever or embolic symptoms.

At presentation, there was no evidence of active lupus flare, with ANA 1 : 80, anti-dsDNA <10 IU/mL, normal complement levels, and normal inflammatory markers (ESR and CRP).

Transthoracic echocardiography demonstrated underlying rheumatic mitral valve disease with features of rheumatic mitral stenosis and leaflet thickening. Mobile vegetations were visualized attached to the anterior mitral leaflet measuring approximately 10-15 mm, consistent with Libman–Sacks endocarditis (Figure 1).

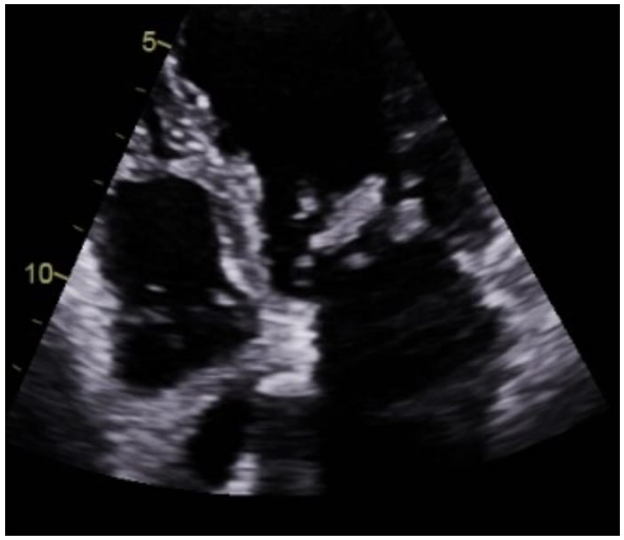

Figure 1. Transthoracic echocardiography demonstrating mobile vegetation attached to the anterior mitral leaflet during rivaroxaban therapy.

The vegetations were associated with worsening mitral valve dysfunction, including an increased mitral stenosis gradient and mitral regurgitation, which likely contributed to the patient's progressive dyspnea on exertion. Multiple blood cultures were obtained prior to antibiotic exposure and remained negative. Inflammatory markers were not suggestive of infection, and modified Duke criteria for infective endocarditis were not fulfilled. The patient was maintained on mycophenolate sodium (Myfortic), 720 mg twice daily and was not receiving corticosteroids prior to presentation. Hydroxychloroquine had been discontinued due to retinal toxicity.

Figure 2. Follow-up transthoracic echocardiography showing reduction in vegetation size and improvement in mitral valve function after reinstitution of warfarin therapy.

Main Points

- Libman–Sacks endocarditis is an important cardiac manifestation of systemic lupus erythematosus and antiphospholipid syndrome (APS).
- Direct oral anticoagulants such as rivaroxaban may be ineffective in high-risk triple-positive APS.
- Improvement may occur following combined anticoagulation and immunosuppressive therapy.

Rivaroxaban was discontinued, and warfarin was reinstituted with appropriate anticoagulation bridging. Corticosteroid therapy was escalated with prednisolone 40 mg daily.

Follow-up echocardiography demonstrated reduction in vegetation size and improvement in mitral valve hemodynamics (Figure 2).

Clinically, the patient experienced resolution of dyspnea on exertion. At 6 months of follow-up, she remained clinically stable without embolic events, with sustained echocardiographic improvement.

A summary of the patient's clinical timeline is provided in Table 1.

Table 1. Clinical Timeline

Time	Event
October 2003	SLE diagnosis; class V lupus nephritis
2003 onward	Persistent triple-positive APS; long-term warfarin therapy
Early 2025	Switched from warfarin to rivaroxaban
June 2025	Progressive dyspnea; mitral vegetations detected
July 2025	Warfarin restarted; corticosteroids escalated
August 2025	Reduction in vegetation size and improvement in mitral valve hemodynamics

APS, antiphospholipid syndrome; SLE, systemic lupus erythematosus.

Discussion

Triple-positive APS is associated with the highest recurrence rate of thrombosis and is considered a high-risk phenotype.[2,3]

The TRAPS randomized trial demonstrated increased arterial and recurrent thrombotic events in triple-positive APS patients treated with rivaroxaban compared with warfarin.[7]

Meta-analyses confirmed inferior efficacy of DOACs in high-risk APS populations.[9,10]

Current European Alliance of Associations for Rheumatology(EULAR) and international recommendations advise against DOAC use in triple-positive APS.[8]

Key evidence comparing DOACs and warfarin in high-risk APS populations is summarized in Table 2.[11]

Patients with triple-positive APS represent a particularly high-risk subgroup with increased rates of recurrent thrombosis and multi-organ involvement.[1,2,12]

Libman–Sacks endocarditis represents a form of non-infective valvular involvement in SLE, characterized by sterile platelet-fibrin deposits associated with immune complex–mediated injury.[4,6,13,14]

The presence of underlying rheumatic mitral valve disease in this patient may have contributed to increased susceptibility to valvular thrombotic deposition in the setting of APS. This highlights the potential role of underlying structural valve disease as a predisposing factor for thrombotic deposition in the prothrombotic milieu of APS.

Structural valve abnormalities may provide a substrate for immune-mediated thrombotic deposition in patients with APS.

Mitral valve involvement is most common and may occur in up to 10% of SLE patients on systematic echocardiographic screening.[5]

The temporal association between switching from warfarin to rivaroxaban and the development of valvular vegetations in this patient is clinically notable. Although causality cannot be definitively established, the subsequent improvement following reinstitution of warfarin is consistent with concerns regarding the use of DOACs in high-risk triple-positive APS.[7,8] Importantly, the observed improvement is likely multifactorial, reflecting the combined effects of reinstitution of warfarin, escalation of immunosuppressive therapy, and the presence of underlying rheumatic valve disease.

Warfarin inhibits multiple vitamin K-dependent clotting factors and may provide broader anticoagulant coverage in complex autoimmune-mediated prothrombotic states.[15] This case also illustrates a potential double-hit scenario, where high-risk antiphospholipid antibody profile and underlying valvular pathology may synergistically contribute to disease expression.

Early recognition in this case likely prevented embolic stroke or other systemic embolic complications.[6,16]

Table 2. Evidence Comparing DOACs vs. Warfarin in Triple-Positive APS

Study	Design	Phenotype Enrolled	Main Thrombotic Outcomes / Key Findings
TRAPS trial (2018)	Randomized controlled trial	High-risk triple-positive thrombotic APS	Rivaroxaban was associated with more thromboembolic events, major bleeding, or vascular death than warfarin; concern was driven mainly by excess thrombotic events in the rivaroxaban arm.
Ordi-Ros et al. (2019)	Randomized controlled trial	Thrombotic APS	Recurrent thrombosis occurred more often with rivaroxaban than with vitamin K antagonists; arterial events, especially stroke, were numerically higher with rivaroxaban.
Khairani et al. (2023)	Systematic review and meta-analysis of randomized trials	Thrombotic APS	DOACs were associated with increased risk of arterial thrombosis vs. VKAs.
EULAR recommendations (2019)	Guideline/ recommendations	APS, especially high-risk profiles	Vitamin K antagonists are preferred over DOACs in high-risk APS, particularly triple-positive patients.

APS, antiphospholipid syndrome; DOACs, direct oral anticoagulants; VKAs, vitamin K antagonisits.

This case underscores the need for caution when considering DOAC therapy in triple-positive APS patients stable on warfarin.[7,8] These findings further support current guideline recommendations discouraging the use of DOACs in triple-positive APS patients.[17-20]

This case highlights the complex interaction between autoimmune thrombophilia, underlying valvular pathology, and anticoagulation strategy, emphasizing the importance of maintaining vitamin K antagonist therapy in high-risk triple-positive APS patients. This observation aligns with current international recommendations discouraging the use of DOACs in patients with triple-positive APS.

Conclusion

Triple-positive APS in SLE represents a particularly high-risk phenotype requiring careful anticoagulation strategy.

Development of Libman–Sacks endocarditis during rivaroxaban therapy, with subsequent improvement following reinstitution of warfarin and escalation of immunosuppressive therapy, highlights an important clinical association in high-risk triple-positive APS.[7]

The observed improvement is likely multifactorial and should not be attributed to anticoagulation alone.

Early recognition of Libman–Sacks endocarditis in patients with SLE and APS is essential to prevent embolic complications.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Artificial Intelligence Usage Statement: The authors declared that no artificial intelligence tool was used in the preparation of the manuscript.

Ethics Committee Approval: Ethical approval was waived for this case report according to institutional policy.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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References

1. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost*. 2006;4(2):295-306. [CrossRef]
2. Tektonidou MG, Andreoli L, Limper M, et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. *Ann Rheum Dis*. 2019;78(10):1296-1304. [CrossRef]
3. Dufrost V, Risse J, Reshetnyak T, et al. Increased risk of thrombosis in triple-positive antiphospholipid syndrome: a meta-analysis. *Autoimmun Rev*. 2018;17(8):814-822. [CrossRef]
4. Moyssakis I, Tektonidou MG, Vasilliou VA, Samarkos M, Votteas V, Moutsopoulos HM. Libman–Sacks endocarditis in systemic lupus erythematosus: prevalence, associations, and evolution. *Circulation*. 2007;116(4):1486-1494. [CrossRef]
5. Roldan CA, Qualls CR, Sopko KS, Sibbitt WL Jr. Transthoracic versus transesophageal echocardiography for detection of Libman–Sacks endocarditis. *J Am Coll Cardiol*. 1996;28(1):134-139. [CrossRef]
6. Cervera R, Piette JC, Font J, et al. Antiphospholipid syndrome: clinical and immunologic manifestations and patterns of disease expression. *Ann Rheum Dis*. 2009;68(9):1428-1432. [CrossRef]
7. Pengo V, Denas G, Zoppellaro G, et al. Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome. *N Engl J Med*. 2018;378(21):1923-1934. [CrossRef]
8. Ruiz-Irastorza G, Crowther M, Branch W, Khamashta MA. Antiphospholipid syndrome. *Lancet*. 2010;376(9751):1498-1509. [CrossRef]
9. Sciascia S, Lopez-Pedrera C, Cecchi I, Pecoraro C, Roccatello D, Cuadrado MJ. Non-vitamin K antagonist oral anticoagulants and antiphospholipid syndrome. *Blood*. 2018;132(13):1365-1371. [CrossRef]
10. Khairani CD, Kim J, Aljabri A, Tantry US, Gurbel PA. Direct oral anticoagulants in antiphospholipid syndrome: meta-analysis of randomized controlled trials. *Rheumatol (Oxf Engl)*. 2020;59(7):129-136. [CrossRef]
11. Ordi-Ros J, Sáez-Comet L, Pérez-Conesa M, Vidal X, Riera-Mestre A, Castro-Salomó A, et al. Rivaroxaban versus vitamin K antagonist in antiphospholipid syndrome. *Ann Intern Med*. 2019;171(10):685-694. [CrossRef]
12. Laurent C, Ricard L, Nguyen Y, et al. Triple positive profile in antiphospholipid syndrome: prognosis, relapse and management from a retrospective multicentre study. *RMD Open*. 2023;9(1):e002534. [CrossRef]
13. Pons-Estel GJ, Cervera R, Plasín MA, Gómez-Puerta JA. Cardiac manifestations in systemic lupus erythematosus. *Nat Rev Rheumatol*. 2017;13(11):676-692. [CrossRef]
14. Sanna G, Bertolaccini ML, Cuadrado MJ, Hughes GRV. Cardiac manifestations in APS. *Autoimmun Rev*. 2013;12(5):594-603. [CrossRef]
15. Garcia D, Ageno W, Libby E, Crowther MA. Prevention and treatment of thrombosis in antiphospholipid syndrome. *J Thromb Haemost*. 2020;18(6):1460-1467. [CrossRef]
16. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice guidelines. *Circulation*. 2017;135(25):e1159-e1195. [CrossRef]
17. Cohen H, Hunt BJ, Efthymiou M, et al. Rivaroxaban versus warfarin in antiphospholipid syndrome: a randomized controlled trial. *Blood*. 2021;137(11):3011-3022. [CrossRef]
18. Aljaberi N, Wenderfer SE, Mathur A, et al. Clinical measurement of lupus nephritis activity is inferior to biomarker-based activity assessment using the renal activity index for lupus nephritis in childhood-onset systemic lupus erythematosus. *Lupus Sci Med*. 2022;9(1):e000631. [CrossRef]
19. Erkan D, Lockshin MD. APS management beyond anticoagulation. *Arthritis Rheumatol*. 2020;72(2):189-198. [CrossRef]
20. Zuily S, Cohen H, Isenberg D, Woller SC, Crowther M, Dufrost V. Use of direct oral anticoagulants in patients with antiphospholipid syndrome. *Ann Rheum Dis*. 2020;79(6):685-699. [CrossRef]