

CASE REPORT

Treatment of Libman-Sacks endocarditis by combination of warfarin and immunosuppressive therapy

Libman-Sacks endokarditinin warfarin ve immünsüpresif kombinasyon tedavisi ile iyileşmesi

✉ Mehmet Rasih Sonsöz, M.D.,¹ ✉ Rukiye Dilara Tekin, M.D.,² ✉ Ahmet Gül, M.D.,²
 ✉ Zehra Buğra, M.D.,¹ ✉ Dursun Atılğan, M.D.¹

¹Department of Cardiology, İstanbul University İstanbul Faculty of Medicine, İstanbul, Turkey

²Department of Rheumatology, İstanbul University İstanbul Faculty of Medicine, İstanbul, Turkey

Summary– Antiphospholipid syndrome (APS) is a clinical disorder that creates an increased risk of arterial or venous thrombotic events or pregnancy-associated complications and includes the presence of autoantibodies against negatively charged phospholipids. This syndrome is often associated with systemic autoimmune diseases, such as systemic lupus erythematosus (SLE). Libman-Sacks endocarditis is a form of non-bacterial thrombotic endocarditis and is infrequently seen in APS. There are few data documenting the echocardiographic response of APS valve disease to medical treatment. This is an unusual case of a young female patient with SLE and APS who had chorea and non-bacterial thrombotic aortic valve endocarditis. Echocardiography revealed that the vegetation had receded after a combination of warfarin and immunosuppressive therapy.

Özet– Antifosfolipid sendrom (AFS), negatif yüklü fosfolipidlere karşı gelişmiş antikorların varlığında arteriyel veya venöz trombotik olay ya da gebelik ilişkili komplikasyon riskini arttıran bir klinik tablodur. Bu sendrom sıklıkla sistemik lupus eritematozus (SLE) gibi diğer sistemik otoimmün hastalıklar ile ilişkilidir. Libman-Sacks endokarditi non-bakteriyel trombotik endokarditin bir formu olup AFS’de sık olmayarak ortaya çıkmaktadır. Literatürde AFS hastalarının kapak tutulumunda medikal tedavinin etkisi üzerine kısıtlı bilgi mevcuttur. Biz de kore ve Libman-Sacks endokarditi ile prezente olan SLE ve AFS tanılı genç bir kadın hastanın antikoagülan ve immünsüpresif tedavi ile vejetasyonunun ekokardiyografik olarak iyileştiğini bildirmekteyiz.

Antiphospholipid syndrome (APS) is a disorder that causes an increased risk of arterial or venous thrombotic events

or pregnancy-associated complications and includes the presence of autoantibodies against negatively charged phospholipids. This syndrome is often associated with other systemic autoimmune diseases such as systemic lupus erythematosus (SLE), but may occur without other autoimmune manifestations (primary APS).^[1]

Abbreviations:

APS	Antiphospholipid syndrome
Ig	Immunoglobulin
INR	International normalized ratio
NBTE	Non-bacterial thrombotic endocarditis
SLE	Systemic lupus erythematosus
TEE	Transesophageal echocardiography
TTE	Transthoracic echocardiography

APS frequently has cardiac manifestations, and vegetation is estimated to occur in 10% to 40% of patients.^[2] Non-bacterial thrombotic endocarditis (NBTE), also known as Libman–Sacks endocarditis, consists of sterile vegetation made up of fibrin and platelet aggregates on the cardiac valves. Establishing the diagnosis of NBTE in patients with APS is important in order to initiate rapid treatment and prevent valvular damage and systemic embolization.

Presently described is an unusual case of a young female with SLE and APS who had chorea and NTBE of the aortic valve. The clinical response to the treatment was evaluated with transesophageal echocardiography (TEE).

Received: December 10, 2018 Accepted: February 22, 2019

Correspondence: Dr. Mehmet Rasih Sonsöz. İstanbul Üniversitesi İstanbul Tıp Fakültesi, İç Hastalıkları Binası A Blok, Kardiyoloji Kliniği, 34093 Fatih, İstanbul, Turkey

Tel: +90212 - 414 20 00 / 31422 e-mail: mrsonsoz@gmail.com

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CASE REPORT

A 21-year-old female presented with a 1-month history of involuntary right hand movements. She was referred to the neurology department after an outpatient evaluation, and it was determined that she had chorea. Her heart rate was 90 bpm and her blood pressure was 130/85 mmHg. The physical examination demonstrated livedo reticularis in both legs, and a 2/6 diastolic murmur was present in the mesocardiac area. The results of a neurological examination were within normal limits. An electrocardiogram demonstrated a normal sinus rhythm. The initial laboratory work-up revealed a high erythrocyte sedimentation rate (73 mm/h) and low complement levels (C3c: 85 mg/dL, C4: 5 mg/dL). All of the other biochemical test results were within the normal range. A cranial magnetic resonance imaging scan was negative for significant patho-

logical abnormalities. Transthoracic echocardiography (TTE) demonstrated vegetation attached to the aortic valve, which caused moderate regurgitation (vena contracta: 0.4 cm) and mildly elevated gradients. In order to obtain better images and not omit possible cardiac abnormalities, TEE was performed. (Fig. 1a-c; Video 1–3*) The findings indicated that the aortic valve had 3 cusps and that the vegetation was 0.9x1.6 cm in size and involved the right coronary cusp. Both the right and left coronary cusps were abnormally thickened (3 mm and 6 mm, respectively), and the non-coronary cusp was intact. The degree of regurgitation and stenosis observed was similar to that seen with the TTE examination. The mitral valve was also intact, and no other cardiac abnormality was identified.

Serological testing revealed positivity for anti-nuclear antibodies at 1:100 dilution with a speckled

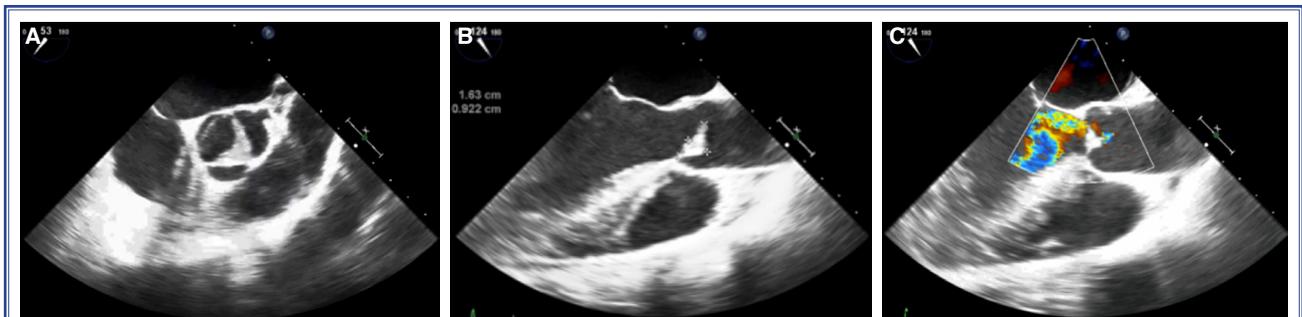


Figure 1. Two-dimensional transesophageal echocardiography images of Libman-Sacks endocarditis. **(A)** Left ventricular short axis view showing thickening of the aortic cusps and echo density. **(B)** Left ventricular long axis view demonstrating thickening of the aortic cusps. **(C)** Left ventricular long axis view demonstrating aortic regurgitation.

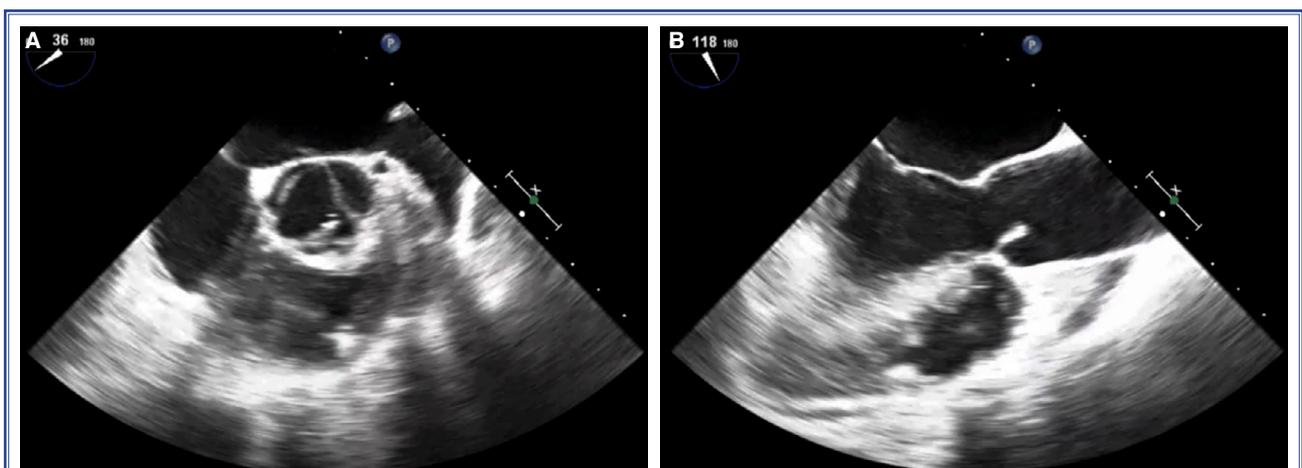


Figure 2. Two-dimensional transesophageal echocardiography images of Libman-Sacks endocarditis after medical treatment. **(A)** Left ventricular short axis view showing marked reduction in size of the echo density. **(B)** Left ventricular long axis view demonstrating reduction in thickness of the right coronary cusp.

pattern. Anti-cardiolipin immunoglobulin (Ig) G, anti-beta-2 glycoprotein-I IgM and IgG, and lupus anticoagulant results were positive. An antistreptolysin O titer was within the normal limits (52 IU/mL) and a throat swab culture was sterile. Blood cultures, a brucellosis tube agglutination test, and a Wright test were all negative. The serum Coxiella IgG level was non-significant.

The patient had a large, sessile, and immobile vegetation involving the right aortic coronary cusp. Both the right and left coronary cusps were quite thickened. The NBTE vegetation was not associated with bacteremia or with destructive valvular lesions, such as an abscess, fistula, or perforation. She had no history of previous antibiotic use and blood culture results were consistently negative. Serological tests were strongly compatible with SLE and APS. Treatment with warfarin 5mg and an international normalized ratio (INR) goal of 2–3, methylprednisolone 32 mg, azathioprine 100 mg, and hydroxychloroquine 200 mg were initiated at the rheumatology department with a diagnosis of APS and non-infective verrucous vegetation.

After 4 months, the patient underwent a control TEE and no measurable mass was detected on the aortic valve, and only the right coronary cusp was slightly thickened (4 mm). Moderate regurgitation persisted, which was probably caused by permanent destructive changes to the aortic cusps. (Fig. 2a, b, Video 4*). During the treatment and a close follow-up period of 4 months, no cardio embolic events or left ventricular systolic dysfunction and dilatation was observed.

DISCUSSION

This case illustrates how chorea and NBTE led to a diagnosis of APS, and how the vegetation resolved after combination therapy. Although some anecdotal reports^[3,4] have demonstrated echocardiographic resolution of valvular lesions with treatment, no specific therapy has yet been consistently shown in several small series to reverse the valvular vegetations seen in NBTE.^[5–7]

Libman-Sacks vegetations are sterile thrombi interwoven with fibrin and immune complexes around the heart valves.^[8] They most often affect the mitral and aortic valves.^[2] TTE is the first imaging procedure of choice for a diagnosis of NBTE. However, TEE

has superior sensitivity and specificity when detecting the valvular vegetations seen in Libman-Sacks endocarditis.^[9] The finding of valvular vegetations on an echocardiogram without evidence of systemic infection suggests a high risk of NBTE. These vegetations are often rounded, sessile, heterogenous, and >3 mm in size when visualized with echocardiography.^[2]

Since our patient had no symptoms of heart failure, acute valvular dysfunction, or recurrent embolization, a medical approach was preferred. According to the 2015 European Society of Cardiology guidelines for the management of infective endocarditis, anticoagulation therapy should be pursued for patients with NBTE if there is no contraindication.^[10] Warfarin with an INR goal of 2–3 has been considered the mainstay for treatment of patients with newly diagnosed APS presenting with their first thrombosis.^[11,12]

The data regarding the use of corticosteroids to treat NBTE are inconclusive. These agents decrease inflammation and improve the healing of lesions, but can also accelerate fibrosis on heart valves, leading to progressive valvular dysfunction.^[2] Nonetheless, steroids are a primary tool in the treatment of APS and may decrease the prevalence of Libman-Sacks endocarditis. Immunomodulatory and antimalarial agents were also added in the present case due to the severity of the clinical presentation.

Our patient responded well to combination therapy with anticoagulation and immunosuppression. The vegetation and mild aortic stenosis resolved, the right coronary cusp returned to its normal thickness. The left coronary cusp remained slightly thickened and moderate aortic regurgitation persisted.

This case demonstrated the response of NBTE to treatment with warfarin and immunosuppressive therapy. Questions still remain whether or not this approach could be applied to similar cases with reliable outcomes, and further studies needed to investigate this uncharted, challenging area of APS.

**Supplementary video files associated with this article can be found in the online version of the journal.*

Peer-review: Externally peer-reviewed.

Conflict-of-interest: None.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Authorship contributions: Concept: M.R.S., R.D.T., A.G., Z.B., D.A.; Design: M.R.S., A.G., Z.B., D.A.; Supervision: A.G., Z.B., D.A.; Materials: R.D.T.; Data collection: M.R.S., R.D.T.; Literature search: M.R.S.; Writing: M.R.S., A.G., Z.B., D.A.

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Keywords: Antiphospholipid syndrome; immunosuppressive therapy; Libman-Sacks endocarditis; systemic lupus erythematosus; warfarin.

Anahtar sözcükler: Antifosfolipid sendromu, immünsüpresif tedavi; Libman-Sacks endokarditi; sistemik lupus eritematozus; warfarin.