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Libman-Sacks Endocarditis and Cerebral Infarction in Antiphospholipid Syndrome: A Case Report

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Valvular heart disease is a considerable finding in the antiphospholipid antibody syndrome (APS). The involvement of the mitral and aortic valves is more common in the form of leaflet thickening or aseptic verrucous vegetations called the Libman-Sacks endocarditis. In addition to the detrimental effects of endocarditis on the valves, it can lead to serious thromboembolic complications. Here we report our experience with a young woman, who had a history of transient ischemic attack 2 months earlier and referred to us due to severe vaginal bleeding. On echocardiography, several irregular masses were observed on the atrial side of both mitral valve leaflets. On rheumatologic work-up, she was found to have positive anticardiolipin IgG and lupus anticoagulant. During hospitalization, the patient suffered thrombotic stroke and computed tomography (CT) scan showed a parietal lobe ischemic lesion. With evidence of positive antiphospholipid antibodies and arterial thrombosis, negative blood culture, and no fever, the diagnosis of the Libman-Sacks endocarditis was established. The patient was discharged with good general condition and received Hydroxychloroquine, Warfarin, and Prednisolone. On follow-up echocardiography, intra-cardiac masses were not detected any more and no residual neurologic deficits were found.

Keywords: Libman-Sacks Endocarditis; Stroke; Thromboembolism; Echocardiography

1. Introduction

The antiphospholipid antibody syndrome (APS) is defined as the presence of at least two items of the following criteria: 1) presence of an antibody in the plasma known as antiphospholipid antibody (aPL = anticardiolipin antibodies, lupus anticoagulant, and antibodies to β2 glycoprotein-I); 2) arterial or venous thrombosis; and 3) recurrent fetal loss during pregnancy (1). The APS can be either primary or secondary to systemic lupus erythematous (SLE).

Cardiac valvular involvement in the APS has been previously reported. This can be either in the form of valve leaflet thickening or aseptic veracious vegetations called the Libman-Sacks endocarditis (2). It has an estimated prevalence of 30% in the APS patients and is considered as the most frequent cardiac manifestation in such patients (3). The Libman-Sacks endocarditis is an aseptic verrucous endocarditis described in patients with the APS or SLE. This endocarditis, in addition to detrimental effects on the involved valve, can cause thromboembolic events, in particular cerebrovascular embolization (2). Considering the young age of patients with the APS or SLE and the occurrence of endocarditis, proper diagnosis and management is important.

Here, we report our experience with a young female patient, who experienced stroke and then a bleeding diathesis and abnormal vegetation was found on her echocardiography.

2. Case Presentation

A 37-year-old woman presented to our hospital's gynecologic services with severe vaginal bleeding. She was considered for total abdominal hysterectomy. Her past medical history indicated hypertension and transient ischemic attack (TIA) 2 months earlier. During hospitalization in order to work-up her TIA, she refused to receive further medical investigations. She was receiving Atenolol, Clopidogrel, and Warfarin. She had two children and a positive history for one abortion. On examination, her vital signs were stable and she did not have oral ulcer, malar rash, or splinter hemorrhages. On cardiac auscultation, she had a grade II systolic murmur in the apex area. Electrocardiography (ECG) showed sinus rhythm. Lung auscultation was unremarkable. Abdominal examination did not reveal organomegaly. Her prothrombin time (PT) was 21 seconds and international normalized ratio (INR) was 3. In spite of the discontinuation of Warfarin and Clopidogrel, vaginal bleeding continued. Transvaginal ultrasound showed a uterine myoma measuring 3 × 3 cm. Regarding her cardiac murmur and a history of stroke, consultations with cardiology and rheumatology services were requested.

On transesophageal echocardiography (TEE), the left ventricle (LV) had a normal size with an ejection fraction (LVEF) of 50%. There were multiple irregular masses on the atrial side of both mitral leaflets, each measuring 8

× 4 mm, and immobile as well as mobile small particles suspected to be vegetation (Figure 1 and 2). There was also moderate to severe mitral regurgitation towards the lateral wall (Video 1 and 2). The mitral valve annulus was 35 mm. There was also mild tricuspid regurgitation, and the pulmonary artery pressure was 40 mmHg. The left atrium was dilated without any clot. With the initial diagnosis of infective endocarditis, consultation with infectious services was done and after getting blood culture, Ampicillin, Cefazolin , and Gentamicin were started for the patient.

Laboratory tests revealed positive anticardiolipin IgG of > 120 IU/mL (normal< 10 IU/mL) and normal anticardiolipin IgM (1.7 IU/mL, normal < 7 IU/mL). Serum complement protein C3 was 148 mg/dL (normal = 90-180 mg/dL), C4 was 21.8 mg/dL (normal = 10-40 mg/dL), and antibody against double-stranded DNA (anti-ds DNA) was 24 IU/mL (normal< 100 IU/mL). Protein C was low (23%, normal = 70-130%), protein S was low (8%, normal = 55-125%), and antithrombin III was low-borderline (8%, normal = 80-120%). Anti-SSA (Ro) was negative (4.1 U/mL, negative <15 U/mL) as well as anti-SSB (La) (2.6 U/mL, negative <15 U/mL). Anti-nuclear antibody (ANA) was negative. Antiphospholipid IgG was high (85 U/mL, negative < 10 U/mL). Complete blood count (CBC) values were within normal range.

The overall condition of the patient was good and she did not have fever or malaise. Since the blood cultures as well as the Wright and Coombs Wright tests were negative and the ESR was just 11 mm/hour, the diagnosis of infective endocarditis became questionable and instead the Libman-Sacks endocarditis gained more attention as the possible diagnosis regarding the history of TIA and positive anticardiolipin IgG. At this stage, steroid therapy (first pulse therapy and then oral Prednisolone) was initiated for her.

During the second week of hospitalization, the patient complained of left-sided hemiparesia. On brain CT scan, a right parietal lobe ischemic lesion was found. The patient underwent TEE for a second time, to evaluate any possible response of valvular lesions to steroids, which showed multiple irregular masses on the atrial side of both mitral leaflets, each measuring 7×4 mm, with moderate to severe mitral regurgitation. In the second rheumatologic biochemistry workup, lupus anticoagulant was also found to be positive. Her anti-ß2 glycoprotein IgG (82 U/mL, negative < 5 U/mL) as well as IgM (0.9 U/mL, negative < 5 U/mL) were found to be positive. Anti-RNP/Sm antibody was negative (6.7 U/mL, negative <15 U/mL).

The patient was prescribed with Hydroxychloroquine, Warfarin, and Prednisolone and was discharged with good general condition. On the last follow-up after about 6 months, the patient was in good general condition with no residual neurologic deficits. On transthoracic echocardiography (TTE) and TEE, no irregular masses were found on the mitral leaflets and mitral regurgitation was mild to moderate. Hysterectomy was not done for her, and the vaginal bleeding discontinued over time.

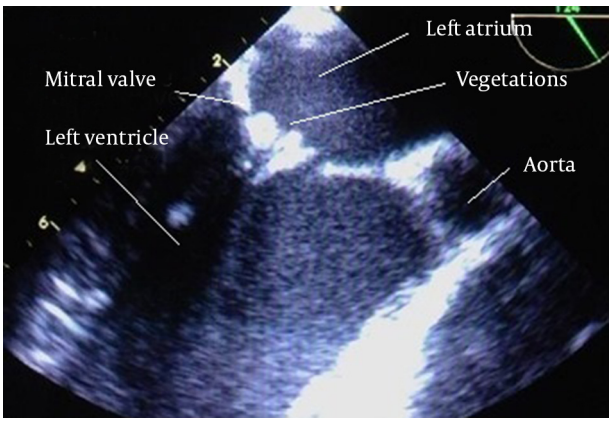

Figure 1. Long-Axis Transesophageal Echocardiography (TEE), Showing Multiple Irregular Masses on the Atrial Side of Both Mitral Leaflets

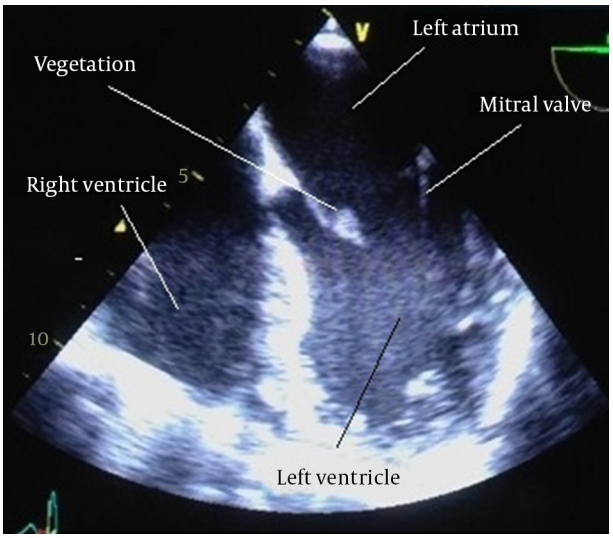

Figure 2. Four-Chamber Transesophageal Echocardiography, Showing Vegetations

3. Discussion

The patient described here shows some challenging findings in her history. First is her initial thrombotic stroke, which left her with muscular weakness, and in spite of her young age no suspicion was made to study the possible causes of her stroke. The next finding which warrants attention is her severe vaginal bleeding. Although the APS is well known by thrombosis, bleeding diatheses can also be seen in these patients, and in rare cases it can be the initial symptom. The possible pathogenesis of bleeding tendency in the APS patients has been related to factors, including severe thrombocytopenia, acquired thrombocytopathy, acquired factor VIII inhibitor, or acquired prothrombin deficiency. In the patient presented, platelet count was within normal limits, but based on transvaginal ultrasonography, she had a uterine myoma, which can be a contributing factor to her vaginal

bleeding (4). In our opinion, the vaginal bleeding in the presented case was due to the APS, as was evidenced by the continuation on earlier days of admission to hospital despite discontinuing Warfarin and Clopidogrel as well as gradual bleeding cease in the course of the disease. The finding of the arterial thrombotic event as well as positive anticardiolipin antibody, lupus anticoagulant, and anti-β2 glycoprotein IgG made the diagnosis of the APS. The masses on her left atrioventricular valve were suggestive of the Libman-Sacks endocarditis. It has been noted that deposition of immunoglobulins on the valve leaflets underlies the pathophysiology of the Libman-Sacks endocarditis (5). Antiphospholipid antibodies not only lead to the formation of verrucous vegetations but also can lead to the formation of valve thrombi and consequently serious complications such as cerebral thromboembolism can occur. This was demonstrated in our patient twice. This thromboembolic event is one of the most common manifestations in the APS patients who develop the Libman-Sacks endocarditis (2). Lonnebakken and Gerdts (2) reported a female patient similar to the case presented here. Their patient was a 46-year-old female with the initial manifestation of hemiparalysis. The difference is that our patient presented with severe vaginal bleeding and did not have familial history of thrombophilia, the findings which were reported by Lonnebakken et al. Another similar case was reported by Malvar et al. (6), who described a 33-year-old female who presented with muscular weakness and three episodes of visual loss during the preceding 3 months. Their patient underwent surgical removal of the masses and was prescribed Aspirin and Warfarin and the neurologic deficit was resolved. For the patient presented here, surgical intervention was not done. Only Hydroxychloroquine and Prednisolone were prescribed.

In conclusion, there should be a high suspicion for the APS in young females with thromboembolic events. TTE and TEE are helpful methods to demonstrate the Libman Sacks endocarditis, which can be the origin of thrombi formation.

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Authors' Contributions

Study concept and design: Farahnaz Nikdoust; acquisition of data: Farahnaz Nikdoust; drafting of the manuscript: Mansoureh Eghbalnezhad; critical revision of the manuscript for important intellectual content: Farahnaz Nikdoust.

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