Libman-Sacks endocarditis, antiphospholipid antibodies and arterial thrombosis in systemic lupus erythematosus: case report

Raul Amorim Marques1, Carolina Salim Gonçalves Freitas1, Romeo Ceccon2, Sandra Gofinet Pasotto3

ABSTRACT
Case report of a 38-year-old female patient with systemic lupus erythematosus (SLE) who presented an acute arterial thromboembolic event in the right lower limb. Investigation showed the presence of antiphospholipid antibodies and sterile vegetation in the mitral valve, Libman-Sacks endocarditis (LSE). Possible causes of thromboembolic events in SLE are discussed, with emphasis on current recommendations for diagnosis and treatment of LSE.

Keywords: Libman-Sacks endocarditis, antiphospholipid antibody syndrome, antiphospholipid antibodies, systemic lupus erythematosus.

INTRODUCTION
Libman-Sacks endocarditis (LSE), characterized by sterile vegetation in the heart valves, is detected by Doppler echocardiograms in 11% of the patients with systemic lupus erythematosus (SLE).1 It is usually asymptomatic; however, cases that needed valve replacement have been described.2 An association between LSE and antiphospholipid antibodies (APAs), with an increased risk of thromboembolic phenomena, has been observed in these patients.1 The present case report describes a patient with SLE, LSE, and antiphospholipid syndrome (APS) that had an acute peripheral arterial thromboembolic event. The possible causes of the event will be discussed, with emphasis on the current recommendations for LSE diagnosis and treatment.

CASE REPORT
The patient signed the informed consent for this case report publication. The patient was a 38-year-old Brazilian mulatto woman, nurse aide, followed at the Service of Rheumatology of HSPM since March/2005 with a diagnosis of SLE, when she presented malar rash, photosensitivity, symmetric non-erosive polyarthritis involving small and large joints, and lower-limb palpable purpura. Prior to diagnosis, she had had three pregnancies – 1st – full-term fetus born by caesarean section; 2nd – preeclampsia and caesarean-section premature birth on the 30th week of gestation; 3rd – miscarriage on the 8th week of gestation. After the second pregnancy, the patient developed systemic arterial hypertension (SAH); she was a smoker and did not take oral contraceptives.

Received on 09/08/2009. Approved on 10/04/2010. We declare no conflict of interest.
Discipline of Rheumatology of Faculdade de Medicina da Universidade de São Paulo – FMUSP.
Correspondence to: Dr. Sandra Gofinet Pasotto. Faculdade de Medicina da USP, Disciplina de Reumatologia. Av. Dr. Arnaldo, nº 455, 3° andar, sala 3190. Cerqueira César, São Paulo, SP, Brazil. CEP: 01246-903. E-mail: sandrapasoto@yahoo.com.br
At the time of the SLE diagnosis, she presented a normal blood count, with 250,000 platelets, normal urea/creatinine levels, increased ESR, decreased C3 fraction of complement, C4 at the lower normal range, and 24-hour proteinuria = 360 mg. The antinuclear antibodies (ANAs on HEp-2) were positive (dot, 1:1280); negative antinative DNA; positive anti-Sm, anti-RNP and anti-Ro/SS-A; and negative anti-La/SS-B. She also had positive anticardiolipin antibodies (IgG: 30 GPL, IgM: 70 MPL) and lupus anticoagulant antibodies. Histological assessment of the purpuric lesions disclosed leukocytoclastic vasculitis.

Treatment was initiated with prednisone 1 mg/kg/day, chloroquine diphosphate 250 mg/day, losartan, 100 mg/day, nifedipine 20 mg/day, and acetylsalicylic acid (ASA), 100 mg/day. However, the patient interrupted the treatment for one year and, spite of that, still presented clinical evolution and the corticoid dose was decreased. In January 2008, the patient had no complaints, with normal ESR, C3/ C4, under irregular use of prednisone 20 mg/day and ASA.

On 02/15/08, she sought medical help at the Emergency Room of HSPM due to pain in the right lower limb (RLL) for 15 days, which had worsened in the last two days. General health status was regular and the patient had normal skin color, no fever, BP = 160 x 100 mmHg. Pulmonary assessment was normal. On heart auscultation there was splitting of the second heart sound at pulmonary level. The RLL was cyanotic, cold (from the distal leg extremity) and no palpable pulses could be identified (foot and posterior tibial pulse). The left lower limb (LLL) had normal skin color and temperature and palpable distal pulses, albeit decreased. No skin or oropharyngeal lesions were observed, as well as arthritis or joint deformities.

Arterial Doppler examination of the RLL showed an obstruction in the posterior tibial region (distal third). An arteriography disclosed a right distal-popliteal occlusion (Figure 1). The electrocardiogram was normal. A transthoracic echocardiogram disclosed vegetation in the mitral valve (16 x 3.9 mm) (Figure 2), pericardial effusion of 99 ml and ejection fraction of 66%. The transesophageal echocardiogram confirmed the presence of mitral vegetation; six pairs of blood culture samples were collected from different sites and all had negative results. Hemoglobin = 10.6 mg/dL, platelets = 275,000 and leukocytes = 7,000, urea = 23/ creatinine = 1.2 mg/dL, normal urinary sediment. Antinative-DNA antibody was negative and anticardiolipin IgG antibodies (13.6 GPL) were undetermined, whereas IgM (2.4 MPL) was negative, with com positive lupus anticoagulant antibodies. ESR = 69 mm, C-reactive protein (CRP) = 3.95 mg/L, C3 was decreased and C4 was normal.
Anticoagulation therapy with unfractionated heparin was started, which was later maintained with warfarin (INR 2.5-3.5). The patient also received prednisone (40 mg/day), chloroquine diphosphate, enalapril (40 mg/day) and nifedipine (30 mg/day). The patient’s evolution showed pain improvement and RLL perfusion (clinically and at the Doppler examination), with no tissue loss; the patient was discharged on 02/29/08. She was not submitted to echocardiographic control at hospital discharge.

DISCUSSION

The present is a case report of a patient with SLE (established according to the criteria of the American College of Rheumatology), who presented an acute arterial thromboembolic event in the RLL, which might have been caused by LSE or APS. In fact, the patient had aseptic vegetation in the mitral valve, in addition to a history of preeclampsia and premature birth in association with positive lupus anticoagulant antibodies in two different occasions, characterizing a diagnosis of APS. She probably also had atherosclerotic arteriopathy, of which onset appears to be an early one in SLE, mainly in association with SAH, smoking or chronic use of corticoids and which might have contributed to the vascular occlusion.

In a study with 342 SLE patients, LSE was detected by Doppler echocardiogram in 11% of the cases, more often in the mitral valve. After 4 years of follow-up, valve failure and/or stenosis were frequent, and two patients who were candidates to heart surgery died. Thus, the diagnosis of LSE is of utmost importance and the echocardiogram is currently the best imaging procedure. In a prospective, controlled and randomized study, the transesophageal echocardiogram showed to be more effective than the transthoracic echocardiogram in detecting LSE valve vegetations in SLE.

One must also recall that infectious endocarditis is not unusual in SLE patients with LSE and a differential diagnosis is mandatory. In this aspect, three laboratory data are important: leukocyte count, CRP levels, and APA levels. The leukocytes tend to decrease during lupus activity and the opposite occurs in infectious endocarditis. As for the APAs, it is unlikely that elevated levels be caused by infectious diseases, thus suggesting the presence of SLE. Very high CRP levels suggest an infectious cause, as lupus patients are less capable of presenting an exuberant response of this protein; however, for a definitive differential diagnosis, the blood cultures are more important. In the present case, a diagnosis of LSE was attained, as the leukocyte count was normal, the CRP was not very elevated, APA was positive and six pairs of blood culture samples had negative results.

An increased risk of thromboembolic events is observed in LSE, which might be in part due to the presence of the APAs. Patients with moderate to high titers of anticardiolipin IgG antibodies have a higher incidence of valve lesions, whereas there are patients with valve disease in whom lupus anticoagulant are the only anti-phospholipid antibodies detected.

More recently, moderate to high titers of anti-h2-glycoprotein-I antibodies have been associated with valve disease in APS. In our service, we do not perform the screening for this antibody, but we emphasize the importance of its assessment in patients suspected to have APS.

There is scarce information in the literature regarding treatment of LSE. It is known that the use of corticoids and immunosuppressive drugs seems to have no effect on valve lesions; however, anticoagulation therapy must be used for treatment of patients with thromboembolic events.

In a case report of a patient with SLE, APS, LSE with mitral vegetation and seizures, oral anticoagulation resulted in the resolution of seizures and vegetation detected through echocardiography. However, a study that analyzed patients with primary APS and valve lesions showed persistence of the latter, in spite of oral anticoagulation.

In the present case, the patient received warfarin to maintain the INR at 2.5-3.5, chloroquine diphosphate and as she had signs of disease activity (pericardial effusion, increased ESR and decreased C3), prednisone – 40 mg/day. In this aspect, it should be considered that prospective, controlled, and randomized studies have shown that moderate anticoagulation (INR 2.0-3.0), as well as a more intensive one (INR 3.0-4.0) with warfarin were similarly effective in preventing new thromboembolic events in patients with APS after the first thrombotic event. However, in these studies, patients with arterial events comprised less than half of the studied population and some specialists have recommended more intensive anticoagulation therapy for patients with APS and arterial thrombosis.

The potential usefulness of hydroxychloroquine in preventing events related to the APS remains in the case of SLE patients, particularly those with APAs, as there is evidence of fewer thrombotic events with its use.

REFERÊNCIAS

REFERENCES