Non-Bacterial Thrombotic Endocarditis of the Aortic Valve in a Young Woman

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A 40-year-old woman without heart disease suffered two embolic episodes in both legs due to a thrombus of the aortic valve. Transesophageal echocardiography performed after the first episode was considered normal, but a second study performed after the second embolism demonstrated a thrombus in the non-coronary leaflet that failed to resolve with the intravenous administration of heparin for two weeks. Surgical excision of the mass revealed a thrombus on an otherwise healthy aortic valve. The case is interesting because it is an exceptional cause of systemic embolism and the patient did not present a prothrombotic status in coagulation studies. The 3 years of follow-up was uneventful.

Key words: *Aortic valve thrombosis. Thrombotic endocarditis.*

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Endocarditis trombótica no bacteriana sobre válvula aórtica en mujer joven

Se describe el caso de una paciente joven que, sin cardiopatía previa, presentó 2 episodios embólicos en ambas piernas debido a un trombo en la válvula aórtica. Aunque el estudio con ecocardiograma transesofágico después del primer accidente embólico fue considerado normal, después de la segunda embolia aquél puso de manifiesto la presencia de una imagen vegetante de gran tamaño en la sigmoidea no coronaria, que no se resolvió con 2 semanas de anticoagulación con heparina sódica. Se decidió efectuar una escisión quirúrgica de la masa, comprobándose que se trataba de un trombo sobre la válvula aórtica sana. El caso es relevante por su infrecuencia y porque el estudio de trombofilia no evidenció estado protrombótico.

Palabras clave: *Trombosis valvular aórtica. Endocarditis trombótica no bacteriana.*

INTRODUCTION

Spontaneous thrombosis on the native aortic valve is an infrequent condition that is generally associated to fibrosis of the valve, after local trauma secondary to surgery or cardiac catheterization, or in procoagulant states like antiphospholipid syndrome or congenital protein S deficiency.

A case is reported of a young adult woman with 2 embolic accidents and the presence, confirmed by histomorphological study, of a thrombus on the healthy native aortic valve, without any thrombophilia state being demonstrated.

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CLINICAL CASE

A 40-year-old woman, who smoked and had been taking oral contraceptives for 10 years, had recurrent tonsillitis in childhood and no history of interest. In January 1998, she was hospitalized for clinical manifestations of pain, functional impotence, and intermittent claudication of the lower limb for 4 days, with absence of peripheral pulses, who was diagnosed as subacute arterial ischemia of the limb. Femoral arteriography showed amputation in the third popliteal region, which motivated embolectomy. After embolectomy, the clinical evolution was satisfactory and the anterior tibial pulse returned. No significant analytical findings were obtained, including the basic coagulation study (platelets 184 000/µg, fibrinogen 390 mg/dL, cephaloplasmin time 35.5 s, prothrombin time 79% [INR 1.2], activated partial thromboplastin time 33.9/30). From admission the patient showed stable sinus rhythm. A transthoracic echocardiogram revealed a non-hypertrophic, non-dilated left ventricle with

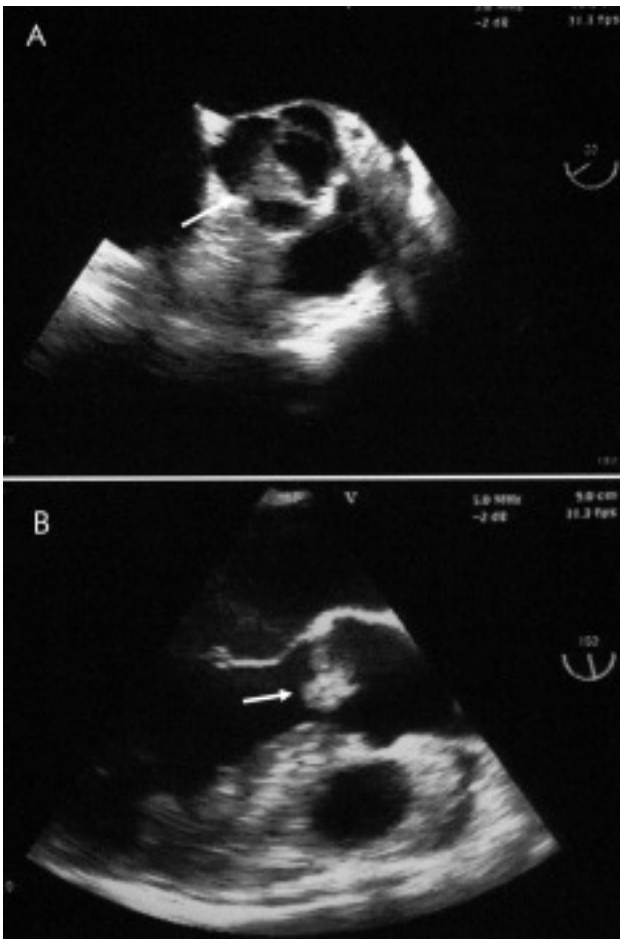

Fig. 1. Transesophageal echocardiogram demonstrating the presence of a large vegetation on the noncoronary sigmoid leaflet (arrows).

Fig. 2. Aortic valve resected during surgery and showing adhered thrombotic material.

conserved function and normal valvular planes and left atrium, without significant valvular regurgitation or thrombi. The transesophageal study confirmed these findings. She was released with anticoagulant treatment for 6 months.

A complete study of thrombophilia carried out 10 months later demonstrated antithrombin III, C protein S protein, and plasminogen concentrations within the limits of normality. The only significant finding was the presence of positive anticardiolipin IgM antibodies and lupus anticoagulant in low titers (18 MPL/mL and index 1.3, respectively). These findings were not confirmed in a later study. The study of autoantibodies and complement was also negative.

In January 1999, she was admitted again for a condition of acute ischemia of the right lower limb, confirming by angiographic study the presence of amputation of the superficial right femoral artery. Femoral thrombectomy was performed. The diagnostic histomorphological study of the thrombus disclosed mainly fibrin, with scant neutrophils. Sinus rhythm and the absence of fever or other findings compatible with an underlying infectious process were again confirmed. The transthoracic echocardiogram demonstrated the presence of a vegetative mass on the aortic valve with mild aortic insufficiency. The microbiological study, including blood cultures, viral serology, and antibodies against *Coxiella burnetii, Chlamydia, Toxoplasma,* and *Legionella* were repeatedly negative. The transesophageal echocardiogram performed after two weeks of anticoagulation with sodium heparin confirmed the findings of transthoracic echocardiography, consisting of the presence of a vegetative mass on the non-coronary sigmoid cusp of the aortic valve, 11×12 mm (Figure 1).

Suspecting aseptic endocarditis, and in the presence of a vegetative aortic valve mass of considerable size in the patient, who had had two embolic accidents, the tumor was resected surgically. The operative finding was a vegetative mass (Figure 2) implanted on the non-coronary sigmoid leaflet that was impossible to excise, requiring implantation of a mechanical valvular prosthesis. The leaflets were thin, with no fusion of commissures. The result of the histomorphological

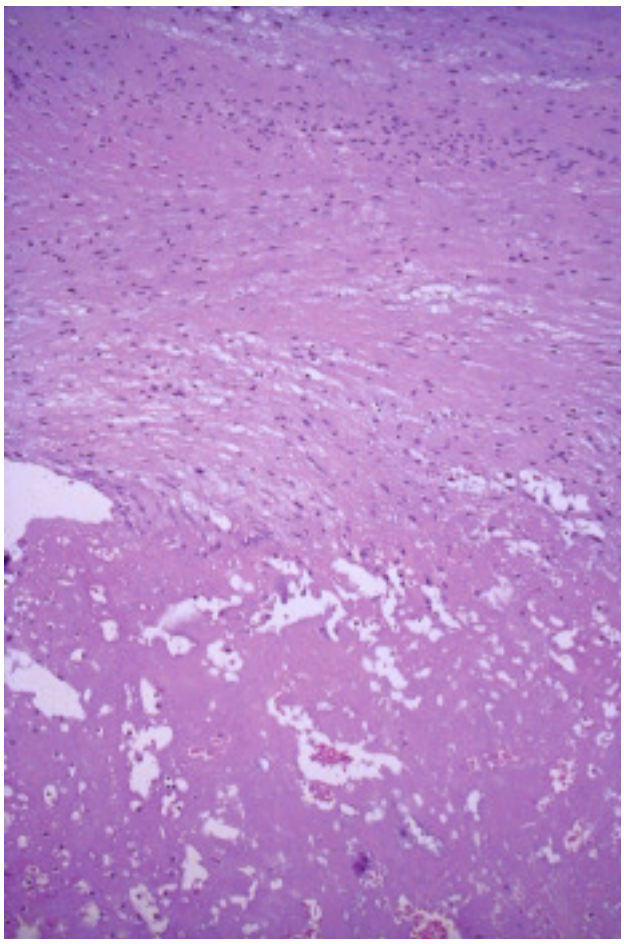

Fig. 3. Microscopic study revealed thrombotic material with fibrin and scant leukocytes.

study revealed thrombotic material, with no evidence of neoformation or an infectious process (Figure 3).

A complete study by computed tomography did not demonstrate an underlying neoplastic process, and a new autoantibody study again excluded systemic disease.

The patient has been taking anticoagulant treatment with dicoumarins. After 3 years of follow-up, there have been no new embolics episodes or had new masses found in the six-month echocardiograms.

DISCUSSION

The presence of embolic phenomena in a young patient, particularly if they are recurrent, require the a transthoracic echocardiographic study to be made, which often must be completed with a transesophageal study. In the absence of atrial fibrillation, cardiac valve diseases, intracavitary thrombi, patent foramen ovale, aneurysm of interatrial septum, intracardiac vegetations or tumors, or aortic disease must be excluded. The finding of thrombosis on the native aortic valve without valve disease must be considered exceptional.

Non-bacterial the thrombotic endocarditis has been described like one of the first histopathological stages in the pathogenesis of infectious endocarditis, as a result of the formation of a platelet aggregate on an endocardial lesion generated more frequently in the presence of underlying heart disease.[1] It has also been described in association with neoplasms, disseminated intravascular coagulation, or sepsis. The differential diagnosis in a patient with vegetations and a negative blood culture includes excluding infection by germs like *Brucella, Legionella, Coxiella,* and *Chlamydia, mycotic* endocarditis, and syndromes associated with antiphospholipid antibodies. In the present case, all these diagnoses were excluded. Outside these contexts, thrombosis on the native aortic valve is very infrequent and generally associated with valvular calcification and stenosis. For this reason, the series that communicate most cases are studies of surgical pieces obtained from surgery for aortic valve stenosis.[2-4] It is considered that, in the absence of a prothrombotic state and significant valvular lesion (including bicuspid aorta), spontaneous thrombosis on the native aortic valve occurs after local trauma, such as cardiac surgery and left heart catheterization, or as a complication of bacterial endocarditis. The hydrodynamic flow disturbance and the adjacent endothelial lesion constitute the clearest predisposing factors.[5] Finally, a case of sudden death due to obliteration of the left coronary tree secondary to a mobile thrombotic mass arising from a fibrotic chord has been described, probably of congenital origin.[6]

The prothrombotic state, as occurs in the primary antiphospholipid syndrome or in S protein deficiency, has been associated with the presence of non-bacterial thrombotic endocarditis.[7,8] It is possible that at present, the prothrombotic situations that can lead to the development of valvular thrombi are not absolutely defined, nor can they all be identified. The administration of contraceptives, especially in the presence of hypercholesterolemia, constitutes a risk factor for thromboembolic disease in young women. However, the absolute predominance of venous thrombosis should be noted, arterial thromboses being practically anecdotal. Thrombosis on the native aortic valve have not been described. Migraine and smoking are associated to a greater incidence of cerebrovascular accidents in young women who take oral contraceptives, although its cardioembolic origin cannot often be demonstrated. Likewise, some drugs, like fenfluramine, can condition valvular injuries, but no history of this sort was confirmed.

In our case it was not possible to confirm a local endothelial factor or a prothrombotic state that favored the formation of a thrombus on the aortic valve. Nevertheless, a state of thrombophilia not detectable with currently available analytic techniques cannot be ex-

cluded, or undetected local hemodynamic phenomena that predispose to this condition.

Given the controversy with regard to the attitude to take with respect to the presence of circulating anticoagulants that can predispose to thrombosis, it is first recommended that consistent prolongation of more than one coagulation test with an elevated titer of anticardiolipin immunoglobulins be demonstrated. Such consistent results could not be confirmed in our case. Secondly, the risk of thrombosis increases in patients with systemic lupus erythemathosus with respect to those that present LA activity (lupus anticoagulant) or idiopathic ACLA (anticardiolipin).

The surgical findings of a valve without organic disease and the histomorphological study of the mass mean that we consider our case as spontaneous thrombosis on a healthy native aortic valve that conditioned two episodes of systemic embolism. To the singularity of the case must be added the poor response to anticoagulant treatment, which made it necessary to perform cardiac surgery and implantation of an aortic valvve.

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