Biventricular Thrombus and Endomyocardial Fibrosis in Antiphospholipid Syndrome

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Introduction

The antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by plasma detection of antiphospholipid antibodies such as anticardiolipin and lupus anticoagulant, which clinically manifests as: recurrent arterial and/or venous thrombosis, thrombocytopenia, recurrent miscarriage and autoimmune hemolytic anemia, in addition to cardiac, neurological and skin alterations[1]. It constitutes the main acquired cause of hypercoagulability, occurring in 2% of the general population and has high morbidity and mortality[2].

It can be classified as primary when there is no other underlying disease as secondary when it occurs associated with other pathologies, such as systemic lupus erythematosus (SLE). The cardiac alterations are frequently observed, especially valvular heart disease (thickening and vegetations) and coronary artery disease (CAD)[2-4]; the presence of thrombi has been also reported[5]. However, myocardial involvement is rarely described in this pathology[6].

This report describes the case of a lupus patient with APS and biventricular cavitary thrombus, diagnosed by MRI. The presence of endomyocardial delayed enhancement was also observed, which may be early onset of the occurrence of endomyocardial fibrosis (EMF).

Case report

This patient was a 22-year-old female with SLE, admitted to the hospital with complaints of malaise, and progressive dyspnea. Laboratory tests showed hemoglobin of 6.9 g/dL, hematocrit of 24%, elevated levels of indirect bilirubin and lactate dehydrogenase and positive Coombs test, thus consistent with autoimmune hemolytic anemia. The patient was submitted to blood transfusion associated with corticosteroid therapy. However, the patient developed worsening of dyspnea and decreased central venous O_2 saturation, suggesting clinical picture of low output.

The resting electrocardiogram showed sinus tachycardia, diffuse ventricular repolarization alterations and "slow" progression of "R" waves in the precordial leads. The transthoracic Doppler echocardiography performed in a Hewlett-Packard/Phillips SONOS 5500 equipment, with a transducer of 2.5 and 5 to 7.5 mHz, showed cardiac chambers with normal dimensions, preserved wall thickness and systolic function of left ventricle (LV) moderate LV diastolic dysfunction and mild pulmonary hypertension (systolic pulmonary pressure estimated at 40 mmHg). It was also observed the presence of obstruction in the apices of the two ventricles; it was not possible, however, to differentiate between thrombus and endomyocardial fibrosis, in spite of the use of color flow mapping and a high frequency transducer.

To achieve the diagnosis, MRI was then performed (Figure 1) in a Philips Achieva equipment with 1.5 T. Cine sequences were obtained (balance Steady-StateFreePrecession - BSSFP) and delayed enhancement (turbo-field-echo with inversion pulse and recovery, 10 minutes after the injection of 0.2 mmol/ kg of Gd contrast, TE: 6.1, TR 3.0). We observed reduced ventricular cavities at the longitudinal axes, due to the filling of their apices by thrombi (5.0 x 2.5 cm in LV and 2.0 x 1.0 cm in the RV). Additionally, we observed the presence of subendocardial delayed enhancement in the biventricular apical portions in the affected segments.

To explain the presence of intracavitary thrombus the hypothesis of APS was raised, and then confirmed by the detection of antiphospholipid antibodies and anticardiolipin antibodies in the patient's serum. The finding of delayed enhancement could be explained by endomyocardial disease or CAD. However, coronary angiography showed epicardial coronary arteries free of obstruction. The patient was submitted to anticoagulation with low molecular-weight heparin, followed by an adequate dose of warfarin to maintain INR values (TP) from 2.0 to 3.0. The patient showed progressive clinical improvement.

Three weeks after start of therapy, the control MRI was performed (Figure 2), which disclosed thrombi with regular contours and irregular enhancement, suggesting organization and a significant decrease in size (LV: 2.5 x 2.1 cm, RV: 0 9 x 0.7 cm). There was persistence of endocardial contrast, thus reinforcing the suspicion of associated endomyocardial disease. An endomyocardial biopsy was discarded due to the risk of thrombus embolization with catheter manipulation

Keywords

Antiphospholipid Syndrome; Antibodies; Antiphospholipid; Endomyocardial Fibrosis; thrombosis; Magnetic Resonance Spectroscopy.

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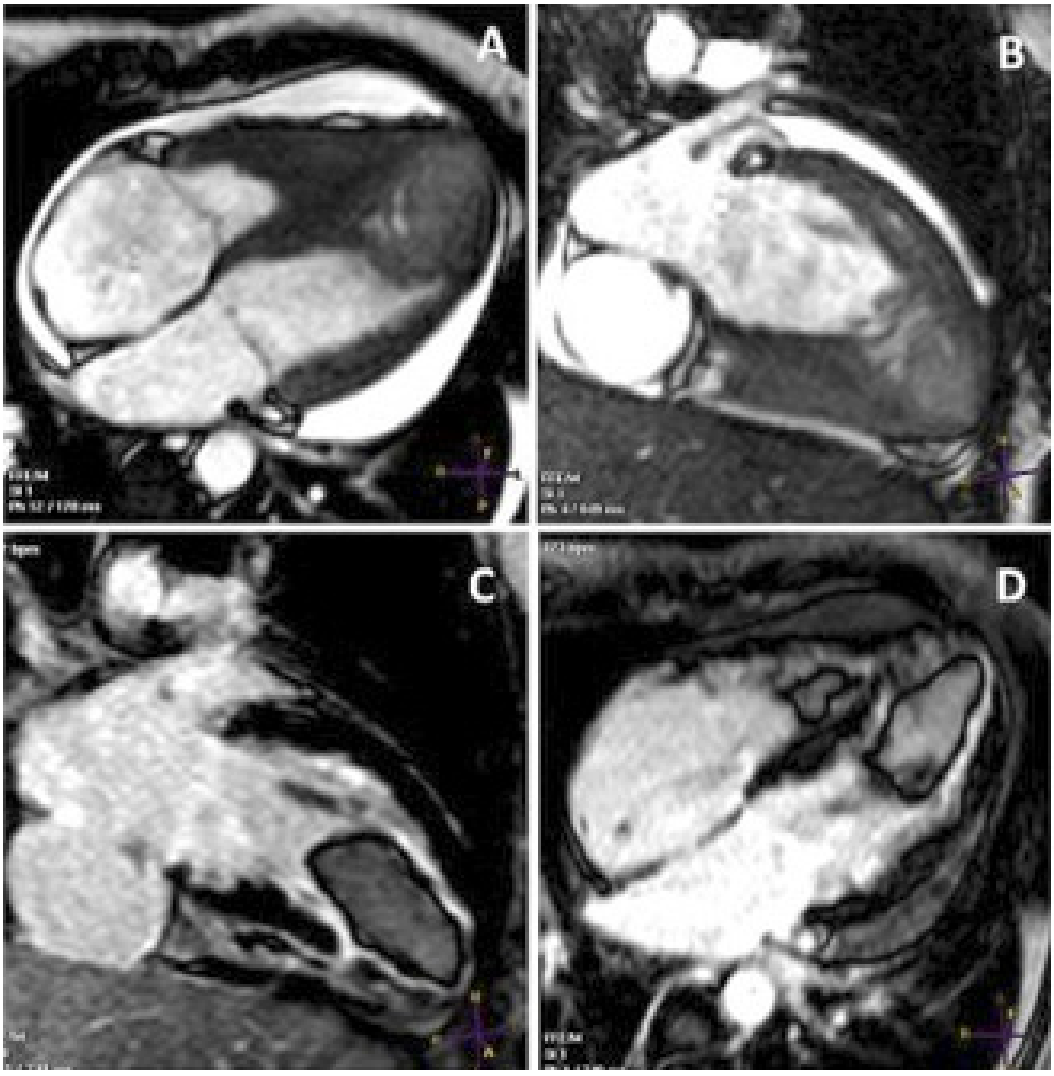

Figure 1 - *CMR: Magnetic resonance angiography (MRA) Sequences (A and B) and Delayed enhancement (C and D) showing apical biventricular filling by thrombus, in addition to endocardial enhancement in the same segments. Mild pericardial effusion can also be observed.*

and, above all, because this procedure would not change the therapeutic approach. The patient was discharged to outpatient follow-up.

Discussion

Venous thromboembolism is the most common clinical presentation of APS, occurring in 30-70% of patients[3]. In relation to arteries, the carotid arteries are the main affected vessels and their thrombi may develop into a stroke. The main cardiac manifestations found in this syndrome are valvular diseases and CAD, representing two thirds of cases[4].

Intracardiac thrombosis rarely occurs, except in the presence of ventricular dysfunction; it can be found in any heart chamber, being, however, more common on the right side of the heart and constituting potential cause of systemic or pulmonary embolism[5]. To the best of our knowledge, this is the first report of the presence of an intracavitary thrombus associated with biventricular APS, diagnosed by MRI.

It is yet to be clarified what constitutes the best therapy for these patients - heparin administration, thrombolysis, anticoagulation with warfarin or surgical excision of the thrombus[6]. Our patient was submitted to anticoagulation with heparin followed by warfarin, showing satisfactory progress.

Endomyocardial involvement is also rare in patients with APS. Azeem et al.[7] described a case of EMF causing right heart failure in a 50-year-old patient that had APS. This type of cardiomyopathy still has an unknown etiology and is associated with several neurohumoral and growth factors[8]. Some authors suggest that EMF results from the primary lesion of the coronary microcirculation, the myocyte, the subendocardial fibroblast or the endocardium itself. Antibodies have also been detected in

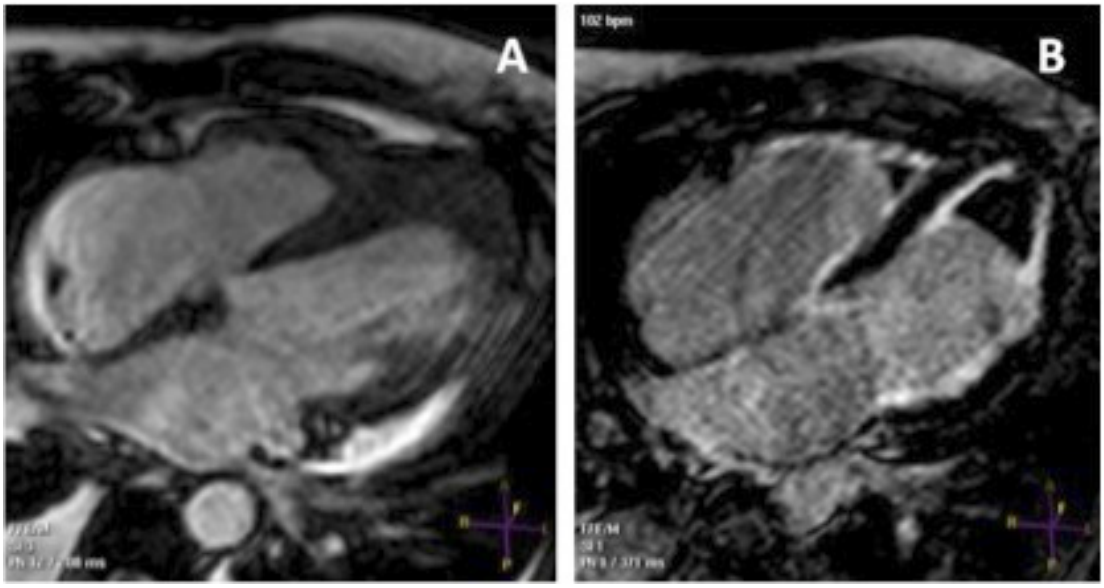

Figure 2 - *Control MRI [A- Magnetic resonance angiography (MRA) and B- Delayed enhancement] showing significant decrease in thrombi and persistence of endocardial enhancement.*

myocardial proteins of patients with this type of pathology, thus suggesting that the autoimmune response may be implicated in its etiopathogenesis[9].

The demonstration of delayed enhancement at the MRI has been associated with irreversible myocardial injury (fibrosis or necrosis), especially in patients with CAD; however, there has been a report that this methodology also allows the detection of subendocardial fibrosis, with good histopathological correlation in patients with EMF[10]. This finding allows, in theory, the diagnosis of EMF in its early stages, as it is a noninvasive and easy to perform examination.

Therefore, in this case, it is possible to speculate that the finding of delayed enhancement, in the absence of obstructive lesions in epicardial coronary arteries, reflect an early manifestation of EMF, in a patient with APS.

The biopsy would help to confirm this finding and to clarify the adjacent pathology, although it is a risky procedure as a result of intracavitary thrombosis, which would not alter the conduct.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

References

1. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, 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.
2. Tripodi A, Chantarangkul V, Clerici M, Negri B, Galli M, Mannucci PM. Laboratory control of oral anticoagulant treatment by the INR system in patients with the antiphospholipid syndrome and lupus anticoagulant. Results of a collaborative study involving nine commercial thromboplastins. Br J Haematol. 2001;115(3):672-8.
3. Gastineau DA, Kazmier FJ, Nichols WL, Bowie EJ. Lupus anticoagulant: an analysis of the clinical and laboratory features of 219 cases. Am J Hematol. 1985;19(3):265-75.
4. Hedge VA, Vivas Y, Shah H, Haybron D, Srinivasan V, Dua A, et al. Cardiovascular surgical outcomes in patients with the antiphospholipid syndrome- a case series. Heart Lung Circ. 2007;16(6):423-7.
5. Weiss S, Nyzio JB, Cines D, Detre J, Milas BL, Narula N, et al: Antiphospholipid syndrome: intraoperative and postoperative anticoagulation in cardiac surgery. J Cardiothorac Vasc Anesth. 2008,22(5):735-9.
6. Koniari J, Siminelakis SN, Baikoussis NG, Papadopoulos G, Goudevenos J, Apostolakis E. Antiphospholipid syndrome; its implication in cardiovascular disease: a review. J Cardiothorac Surg. 2010;5:101.
7. Azeem T, Vassallo M, Samani N. Images in cardiology. Endomyocardial fibrosis associated with antiphospholipid syndrome. Heart. 2000;84(2):156.
8. Kapoun AM, Liang F, O'Young G, Damm DL, Quon D, White RT, et al. B-type natriuretic peptide exerts broad functional opposition to transforming growth factor-beta in primary human cardiac fibroblasts: fibrosis, myofibroblast conversion, proliferation, and inflammation. Circ Res. 2004;94(4):453-61.

9. Mathai A, Kartha CC, Balakrishnan KG. Serum immunoglobulins inpatients with endomyocardial fibrosis. Indian Heart J. 1986;38(6):470-2.

10. Cury RC, Abbara S, Sandoval LJ, Houser S, Brady TJ, Palacios IF. Images in Cardiovascular Medicine. Visualization of endomyocardial fibrosis by delayed-enhancement magnetic resonance imaging. Circulation. 2005;111(9):e115-7.