Antiphospholipid Antibody Syndrome (AAS): Cardiac and Brain Presentation

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Introduction

The Antiphospholipid Antibody Syndrome (AAS) is a systemic autoimmune disease characterized by recurrent thromboses and/or gestational losses, associated with the presence of antiphospholipid antibodies. It is responsible for 15% - 20% of all events of deep venous thrombosis with or without pulmonary embolism; 33% of the new cerebrovascular accidents in patients younger than 50 years old; and 10% - 15% of women with recurrent fetal losses[1].

In this report, we will describe an uncommon case of primary AAS characterized by neurological clinical presentation (Ischemic Cerebrovascular Accident - CVA) accompanied by echocardiographic finding associated with Nonbacterial Thrombotic Endocarditis (NBTE).

Case Report

O. da R., 29 years, male, of brown color, was admitted to the hospital emergency with sudden aphasia and right-side hemiparesis. Smoker and without other comorbidities. In the physical examination, Glasgow coma scale 12/15, deviation of labial commissure to the left; no fever, Blood Pressure (BP) of 132/82 mmHg and heart rate of 93 bpm. Systolic murmur in the mitral valve focus grade +++/6+ irradiating to the armpit; reductions to strength and sensitivity in right upper limb and lower right limb.

Electrocardiography (ECG) with sinus rhythm and within normal limits (Figure 1A).

Nuclear Magnetic Resonance Imaging (MRI) of the skull revealed hyperintense areas in T2 and flair with restricted diffusion in basal nuclei, in the insula, front, temporal and parietal regions to the left compatible with subacute ischemic lesions (Figure 1B).

Transesophageal Echocardiography (TEE) registered vegetation adhered to the atrial face of the both cusps of the mitral valve (Figures 1C and 1D), presenting reduced mobility and higher dimension, up to 9 mm, causing moderate mitral insufficiency.

Keywords

Antiphospholipid Syndrome; Cerebrovascular Accident (CVA); Non-infective Endocarditis.

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After empirical antibiotic approach for two weeks for Infective Endocarditis (IE), the results of blood cultures and inflammatory activity tests were not conclusive about an infective clinical status.

Serial echocardiograms did not show any abnormality relating to aspect and dimension of mitral valve vegetation by the end of four weeks of antibiotic therapy.

Suspecting a nonbacterial thrombotic endocarditis, antibodies were tested for Antiphospholipid Antibody Syndrome (AAS) with positive results for anti-cardiolipin (262 glp/mL) and lupus anticoagulant, confirmed after an interval of 12 weeks. The antibodies for other autoimmune diseases (such as systemic lupus erythematosus), stratification for Acquired Immunodeficiency Syndrome (AIDS) and cancer were not conclusive, and the diagnosis of primary AAS was the most probable hypothesis.

After three months of full anticoagulation treatment with Warfarin, keeping INR between 2.5 and 3.5, there was a total disappearance of the mitral valve vegetation (Figure 1E), as well as of the mitral insufficiency. The neurological clinical status showed gradual and significant improvement after physical and speech therapy.

Discussion

AAS may be classified as primary or secondary. The primary one happens in the absence of associated or underlying diseases, and is more common than the secondary, which is characterized by the association with a wide array of recurrent diseases[1].

The current classification criteria for AAS require the use of three laboratory tests to detect antiphospholipid antibodies (Lupus Anticoagulant, Anti-β2GPI Antibodies and Anti-cardiolipin Antibodies), in the presence of at least one of the two main clinical manifestations (namely, thrombosis or pregnancy with morbidity)[2].

The diagnosis of AAS relies on the presence positive results for at least one of the following tests:

- Lupus Inhibitor (Lupus Anticoagulant) in the plasma, on two separate occasions over a period of 12 weeks, detected according to the recommendations of the International Society on Thrombosis and Haemostasis.

- Anti-cardiolipin IgM or IgG antibodies in the plasma or serum in moderate titers (> 40 GPL or MPL units, respectively) on two or more separate occasions over a period of 12 weeks, measured by ELISA.

- Anti-β2GPI antibodies present in the plasma or serum (in titers above the percentile 99) on two or more separate occasions over a period of 12 weeks, measured by ELISA[2].

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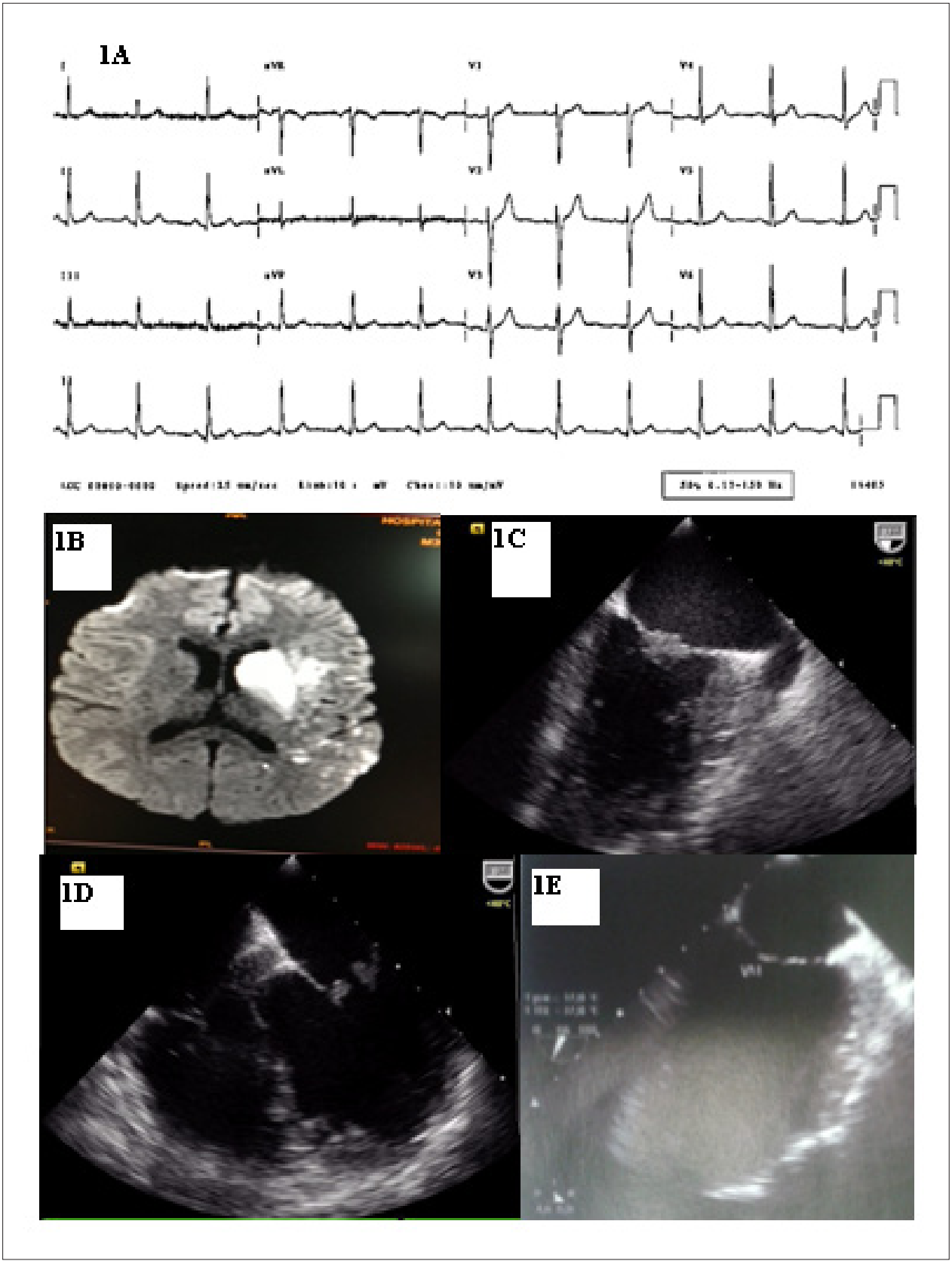

Figure 1A – *Normal electrocardiogram.* **Figure 1B -** *Subacute Cerebral Ischemic Lesions.* **Figures 1C and 1D -** *Vegetation in Mitral Valve.* **Figure 1E -** *Mitral Valve without Vegetations.*

Many of the clinical manifestations of AAS may be triggered by thromboembolism of large vessels, thrombotic microangiopathy or both. Therefore, the following are highlighted: transient ischemic attack and cerebrovascular (thrombotic or embolic) accidents, chorea, convulsions, multi-infarct dementia, transverse myelitis, encephalopathies, migraine, pseudotumor cerebri, cerebral venous thrombosis, amaurosis fugax or mononeuritis multiplex[3].

NBTE is a condition in which friable "vegetations" of fibrin of platelets and red blood cells affect cardiac valves, especially the mitral and aortic valves, and is differentiated from other forma of endocarditis due to its non-infective onset and to demonstrate little cell organization without signs of inflammatory process[4]. Its incidence, according to autopsy studies, has ranged from 0.3% to 9.3%[5].

Initially described in over one century by Ziegler as "thrombus-endocarditis," it is associated with some diseases, such as malignant neoplasms, acquired immunodeficiency syndrome, hypercoagulable states, as in the presence of antiphospholipid antibodies, happening in 10% - 15% of the patients with disseminated intravascular coagulation. The systemic embolization happens to up to 42% of the patients, with the brain as the main destination, reason due to which the first clinical manifestations are typically CVA or encephalopathy[6].

The echocardiography remains the main tool for clinical diagnosis and for predicting potential complications of NBTE. The presence of vegetations in the coaptation region without destruction of valvular tissue and the bilateral heart involvement of the valves or the right heart involvement are highly suggestive of NBTE[7]. The transesophageal modality (TEE) is the most sensitive (90% vs. 70% of the transthoracic modality (TTE)) for its detection, especially if the diameter is for < 5 mm. Because of this, TEE should be performed only upon a high index of suspicion. Although embolism risks are unknown, characteristics that allow stratifying the risk of NBTE have not been described yet[8].

In the first place, the purpose of treatment is to prevent recurrent embolization. In the case of patients with AAS, the anticoagulant therapeutics is recommended regardless of the presence or absence of valvular involvement, owing to the hypercoagulable state to which these patients are subject[9].

Isolated cases of resolution of NBTE with Warfarin have been described[9]; nonetheless, studies reveal there is no response of valvular lesions to anticoagulant therapeutics, reporting even that they present progression[10].

The use of anticoagulants to prevent the recurrence of embolizations and even the disappearance of vegetations has already been reported[10]. Nevertheless, the effectiveness of this approach was not described by any study.

Although there are no formal recommendations regarding indications and the optimal moment for surgical approach, the existence of severe valve dysfunction or the recurrence of embolic events are currently accepted criteria for resorting to surgical procedures[9].

In this case, we report the favorable outcome of primary AAS with brain and heart complications, which, after diagnosis, led to a change of treatment, as well as the indication of a conservative approach to the mitral valve through full anticoagulation.

Authors' Contribution

Manuscript Drafting: Leme Neto AC, Dalmonico AC, Leme KMMC, Carvalho MTM; Critical review of the manuscript regarding important intellectual content: Leme Neto AC, Dalmonico AC, Leme KMMC .

Potential Conflicts of Interest

No relevant potential conflicts of interest.

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Academic Association

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