



Antiphospholipid syndrome associated with non-infective mitral valve endocarditis: a case report

Dragan Stevanović*, Denis Mačkić, Elvira Džambasović, Amir Čehajić, Faruk Čustović, Nijaz Tucaković

Department of Internal Medicine, General Hospital "Prim.dr Abdulah Nakaš", Sarajevo, Bosnia and Herzegovina

ABSTRACT

We present a rare case of antiphospholipid syndrome associated with non-infectious thrombotic endocarditis of the mitral valve. The patient was admitted to hospital for examination because of skin lesions manifested through a discoid skin rash. During the hospitalization antiphospholipid syndrome was diagnosed along with ultrasound verification of vegetations on the mitral valve, including both leaflets, with moderate to severe mitral regurgitation. Adequate and opportunely introduced therapy led to regression of all symptoms, including endocarditis of the mitral valve on checkup ultrasound verifications, with a prevention of arterial and/or venous thrombosis in patient's future.

Keywords: antiphospholipid syndrome, antiphospholipid antibodies, endocarditis.

INTRODUCTION

Antiphospholipid syndrome is a rare autoimmune disease characterized by antiphospholipid antibodies, clinically manifested in the form of recurrent arterial and/or venous thrombosis along with recurrent miscarriages. There are 20 or more different antiphospholipid antibodies which act against negatively charged proteins which bind to phospholipids. The antibodies with most clinical importance are lupus anticoagulant AB (LA), anticardiolipin antibodies and anti- β -2 glycoprotein I antibodies (a β 2gp-I). Antiphospholipid antibodies are easily

detected by ELISA tests. Even though they represent a heterogeneous group of antibodies, the main interest remains on those which are closely related to the clinical manifestations of the disease. Their most dominant activity is against serum phospholipid binding proteins, initially named co-factors, in comparison to reaction against phospholipids only. The most frequent of these proteins is β 2 glycoprotein which is bound to negatively charged phospholipids throughout a series of reactions. Physiological role of the β 2 glycoprotein is unknown, but it is assumed that it is a natural anticoagulant in-vivo, especially because of its ability to bind to the negatively charged phospholipids, inhibiting the activation of the intrinsic pathway of coagulation. It is considered that β 2 glycoprotein is the main target of the autoimmune antiphospholipid antibodies, but there are also other phospholipid binding proteins which play the similar role in the human body, and

*Corresponding author: Dragan Stevanović
Department of Internal Medicine, General Hospital "Prim. dr Abdulah Nakaš", Kranjčevićeva 12, 71000 Sarajevo, Bosnia and Herzegovina; Phone 387 33 285 100
E-mail: dragan.stevanovic@obs.ba

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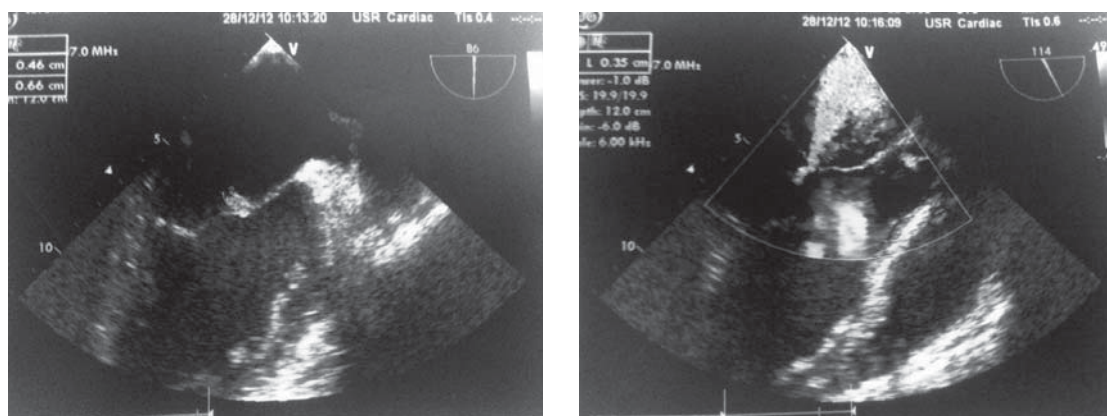


FIGURE 1. Transesophageal echocardiogram on mitral valve during first hospitalization

they include prothrombin, protein C, protein S and annexin V (1). Generally the diagnosis of the antiphospholipid syndrome is set when there is at least one clinical sign (vascular thrombosis and/or spontaneous miscarriage) along with increasing values of at least one type of antiphospholipid antibodies such as cardiolipin antibodies (aCL) or lupus anticoagulants antibodies (LA) (2). Patients diagnosed with antiphospholipid syndrome frequently have cardiovascular complications. It is most commonly present as coronary heart disease and non-infectious endocarditis of the mitral valve, followed by aortic and tricuspid valve. Described complications occur in two thirds of all cases (3). We present here a rare case of antiphospholipid syndrome associated with non-infectious thrombotic endocarditis of the mitral valve.

CASE REPORT

A 33 year old female patient was admitted to the hospital because of erythematous skin changes on her face, behind the right ear, on the left wrist and on the skin of both knees. The patient complained about fatigue and shortness of breath. She had a gall bladder resection surgery seven years ago and she has been diagnosed with an arterial hypertension grade I for 13 years. She is on medication therapy with carvedilol and enalapril. Two years ago the patient was diagnosed with cutaneous form of Discoid lupus erythematosus. Echocardiography on first admission revealed a thickening of both mitral

valve leaflets with verrucae on the ventricular side of mitral valve along with moderate to severe mitral regurgitation. Presence of mitral valve endocarditis with mitral regurgitation grade II/III found on transthoracic echocardiogram (TTE) was confirmed on transesophageal ultrasound (Figure 1).

Laboratory tests revealed highly positive anti-cardiolipin IgG titer higher than 100, anti-cardiolipin IgM 23.47, anti β 2-glycoprotein IgG also with high values over 100, anti β 2-glycoprotein IgM 3.71. The tests were repeated after one month: anticardiolipin IgG higher than 100, anticardiolipin IgM 23.45, anti β 2-glycoprotein IgG 59.42, anti β 2-glycoprotein IgM 4.03. IgG slightly elevated with a value of 19.10g/l, other immunoglobulins in reference ranges, C3 slightly decreased 0.889, C4 in referent ranges of 0.127 g/l, Anti-streptolysin O (ASTO) was mildly increased – 313 IU, increased erythrocyte sedimentation rate of 34 mm/hour.

Oral anticoagulants were introduced in therapy with a goal INR values between 2-3, methylprednisolone 1mg/kg and cytostatic therapy. Cyclophosphamide bolus was followed by a pulse therapy with cyclophosphamide premedication and postmedication, once a month for a period of 6 months, continued by a 3 month scheme, two doses, with gradual reduction of the dose of methylprednisolone at a maintenance dose of 8mg per day. Antihypertensive therapy was continued with carvedilol and enalapril. On follow up echocardiography the significant regression of verrucae formations were seen on both

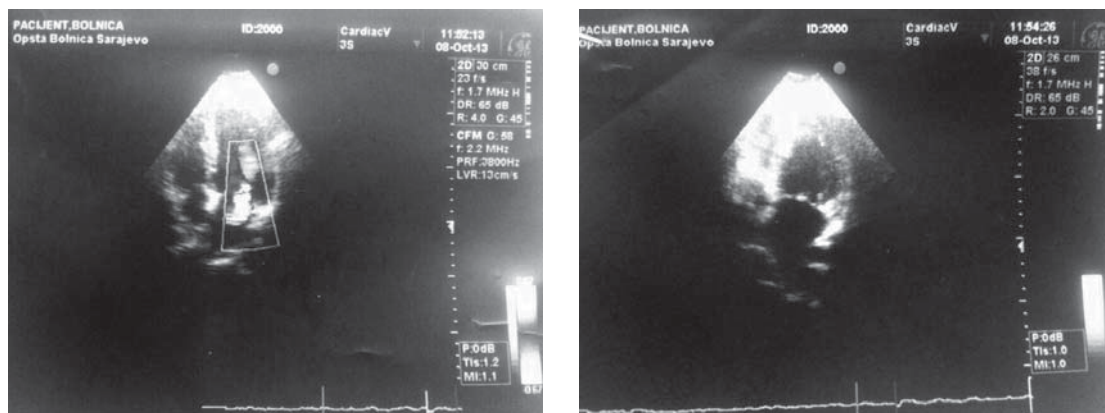


FIGURE 2. TTE findings on mitral valve at follow up examination after one year

mitral valve leaflets, with a reduction of valvular dysfunction and regression of skin changes, which were the primary reason for patient's hospitalization. Moderate to severe mitral regurgitation improved to a moderate to mild form (Figure 2).

On all ultrasound findings systolic (Ejection Fraction 60%) and diastolic function of the left ventricle was preserved. Also, after the immunosuppressive therapy in control findings a significant improvement was found: anticardiolipin IgG slightly positive 12.9, anticardiolipin IgM negative 5.0, anti- β 2-glycoprotein IgG negative 7.8, anti- β 2-glycoprotein IgM 5.96 with normal sedimentation rate of 4mm/hour.

DISCUSSION

There are primary and secondary antiphospholipid syndrome, later one occurring in autoimmune diseases, primarily in systemic lupus erythematosus. There are described cases in which antiphospholipid syndrome occurs within malignant and infectious diseases or after certain drug use. The most common clinical manifestations of this syndrome are thrombosis, which can affect any blood vessel and any organ in the body. Libman-Sacks endocarditis is an uninfected valve damage, associated with autoimmune diseases such as antiphospholipid syndrome and systemic lupus erythematosus. Echocardiography studies suggest that abnormalities of cardiac valves are observed in one third of patients affected by primary antiphospholipid syndrome. Valvular le-

sions consist of non-infectious warts or thickening of the leaflets. These two forms can be combined during the same pathological process and both of them can be associated with different degrees of valvular dysfunction. The predominant functional abnormality is valvular insufficiency while stenosis is very rare. Mitral valve is the most affected one, followed by the aortic valve. Valvular dysfunction usually does not cause clinically manifested valvular disease. The presence of antiphospholipid antibodies increases the future risk for cerebrovascular complications such as stroke caused by an embolus from an affected valve. In the treatment of valvular lesions the most important thing is to establish an adequate anticoagulation using oral anticoagulant therapy along with corticosteroids and immunosuppressive agents (4). Antiphospholipid syndrome may be the cause of recurrent myocardial infarction. A case report from Snipelisky et al. shows a patient with antiphospholipid syndrome who had three myocardial infarctions over a period of two weeks, who was treated with primary percutaneous coronary intervention with stent implantation in the first myocardial infarction (5). The most frequent nonvalvular cardiac manifestation in patients with antiphospholipid syndrome is pulmonary hypertension (6). According to a follow-up echocardiography study by Kampolis et al. in patients with antiphospholipid syndrome and systemic lupus erythematosus, disease duration is an independent factor for the progression of valvular disease, and anticoagulants could not stop the advancement of the valvular dis-

ease or ventricular diastolic dysfunction (7). Sometimes acute myocardial infarction is the first manifestation of antiphospholipid syndrome (8). Although endocarditis within the antiphospholipid syndrome is usually mild and asymptomatic, complications can include an superimposed bacterial infection, thromboembolic complications and severe regurgitation and/or stenosis which requires cardiac surgery (9). Venous thrombosis, usually on lower extremities occur in 55% of cases within this syndrome. Arterial thrombosis involves brain in 50 % of the cases as a transient ischemic attack or stroke. Vascular occlusion may occur as a result of embolization from mitral or aortic valve, and have been reported in 4 % of cases. For the diagnosis of antiphospholipid syndrome according to "Saporo criteria", patients must have a vascular thrombosis or spontaneous miscarriage and proven presence of antiphospholipid antibodies, or anticardiolipin antibodies or positive lupus anticoagulant. Antibodies must be recorded at least twice at an interval of 6 weeks to distinguish persistent from transient autoimmune antibodies responses that can be caused by infectious diseases or use of certain medications. These criteria have a 71% sensitivity and a 98% specificity, suggesting that the threshold for making the diagnosis is high and that most of the cases who are subject to these criteria definitely have antiphospholipid syndrome (1). Echocardiographic valve abnormalities are present in about two-thirds of patients with antiphospholipid syndrome, although they are rarely presented as severe and do not have a very important clinical relevance. One of the most important complications of the disease are certainly recurrent miscarriages, and the risk of pregnancy loss is increased from the tenth week of gestation. This is in contrast with the loss of a pregnancy in the general population, which commonly occurs by the ninth week of pregnancy (1). A small number of patients have a so-called catastrophic antiphospholipid syndrome that some authors also refer to as the "thrombotic storm" (Catastrophic antiphospholipid syndrome - CAPS). In these patients blood vessels from at least three organic systems are affected, and there is a high mortality rate. The base of antiphospholipid therapy is full anticoagulation obtained using oral anticoagulants, with a preset INR. Based therapy of antiphospholipid syndrome is full anticoagulation

obtained with oral anticoagulants and targeted INR values in range from 2 to 3, along with the treatment of the underlying disease with immunomodulators. The case report of this patient demonstrated a very effective treatment strategy with oral anticoagulants, methylprednisolone and cyclophosphamide, which led to a significant regression of symptoms with almost complete correction of laboratory results and significant regression of non-infectious thrombotic endocarditis of the mitral valve with a notable decrease of dysfunction presented through a regression of mitral regurgitation.

CONCLUSION

We presented a successful diagnostic protocol that led to recognition and diagnosis of antiphospholipid syndrome, a rare disease with cardiac complications in the form of noninfectious thrombotic endocarditis of the mitral valve, manifested through a significant dysfunction of the mitral valve in the form of moderate to severe mitral regurgitation. Adequate diagnosis and appropriate and timely administered therapy resulted in a significant regression of the mitral valve endocarditis and prevention of the possible occurrence of venous or arterial thrombosis in the patient."

CONFLICT OF INTEREST

None to declare.

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