

Tanaffos (2008) 7(1), 71-74

©2008 NRITLD, National Research Institute of Tuberculosis and Lung Disease, Iran

Antiphospholipid Antibody Syndrome Presenting with Pulmonary Embolism

Nader Rezaei ¹, Mojdeh Zabihi Yeganeh ², Farideh Ahmadi ²

¹ Department of Pulmonary Medicine, ² Department of Rheumatology, Firouzgar Hospital, Iran University of Medical Sciences, TEHRAN-IRAN.

ABSTRACT

Antiphospholipid antibody syndrome (APS) is a recently-diagnosed syndrome presenting with arterial and venous thrombosis, recurrent miscarriages and thrombocytopenia in the presence of antiphospholipid antibodies.

A 16-year-old man referred due to right sided chest pain, dyspnea and cyanosis of two fingers presented for 2 months. After a complete workup, diagnosis of pulmonary thromboembolism was confirmed through clinical examination, spiral chest CT-scan and lower limb Doppler sonography.

He had positive anticardiolipin antibody, lupus anticoagulant, ANA and anti dsDNA. Based on these findings, diagnosis of APS (probably secondary to SLE) was made. Symptoms were improved by anticoagulant, prednisolone and chloroquine therapy. In a conclusion, pulmonary embolism may be the first presentation of APS, especially in young adults. (Tanaffos 2008; 7(1): 71-74)

Keywords: Antiphospholipid antibody syndrome, Pulmonary embolism, Systemic lupus erythematosus (SLE)

INTRODUCTION

Antiphospholipid antibody syndrome (APS) is a recently diagnosed clinical syndrome presenting either primarily or in association with other collagen vascular diseases mainly systemic lupus erythematosus (SLE) and also other conditions such as infections or cancer. Arterial and venous thrombosis and recurrent miscarriages are among the main manifestations of this syndrome (1). Vascular thrombosis due to these antibodies can be associated

with a high mortality and morbidity. Its clinical symptoms are nonspecific and most patients have undergone numerous laboratory tests and imaging methods several months before diagnosis. Sometimes, late diagnosis results in recurrent thrombosis in vital organs such as the CNS and the lungs of young patients which has serious consequences like permanent deformities and sometimes death. In case of involvement of more than one organ, there is a chance for development of catastrophic APS which is associated with a high mortality.

Pulmonary embolism may be the first manifestation of the APS and recurrent pulmonary

Correspondence to: Nader Rezaei

Address: Firouzgar Hospital, Iran University of Medical Sciences, TEHRAN-IRAN.

Email address: dnaderrezaei@yahoo.com

Received: 6 March 2007

Accepted: 2 July 2007

emboli may give rise to pulmonary hypertension.

In this article, a case of APS manifesting with pulmonary embolism is presented.

CASE PRESENTATION

A 16-year-old male student who had developed sudden right-sided chest pain radiating to the back of pleuritic origin lasting for 6 hours and accompanied by dyspnea and fever about 2 months prior to the hospitalization referred to the Firouzgar Hospital. Chest x-ray was obtained from the patient which was normal. Initial examinations did not show any specific findings. Pulmonary function test and HRCT were performed for the patient which were normal. One and a half months after the first attack, the patient suffered pleuritic chest pain again that lasted for about 4 hours and was accompanied by cough and sputum. Cefixim and pseudoephedrine were prescribed for the patient. New chest x-ray showed right side pleural effusion and the patient was hospitalized at the Firouzgar Hospital.

He had no history of diseases and no history of medication except for the above mentioned drugs. He was a non-smoker and non-alcoholic. On evaluation, pleuritic chest pain, exertional dyspnea, cough with sputum, and Raynaud's phenomenon were disclosed. But the patient had no history of hemoptysis, pain or swelling of the calves.

Vital signs were normal. No chest deformity was detected on chest x-ray. The nervous system was normal as well. Tactile fremitus had decreased on the right lower half of the lung. On chest percussion, the right lower half of the lung was dull. On chest auscultation, breath sounds and vocal fremitus had decreased in the right lower segment of the lung. The heart and abdomen were normal on examination. The patient's right hand was colder than the left hand. Splinter hemorrhage was seen under the nails of the 2nd and 3rd fingers of the right hand. Both fingers showed obvious changes in color and were cyanotic (Figure 1).



Figure 1. Splinter hemorrhage under the nails.

Spiral chest CT-scan with contrast showed that the right pulmonary artery was dilated and filling defect was evident inside the lumen. Right side pleural effusion was seen as well. Several mass-like densities were seen in the periphery of the right lung attached to the pleura (Figure 2).



Figure 2. Chest CT-Scan of the patient..

Pleural fluid of the patient was exudative and yellow in color and its culture and smear were both negative.

Since subacute infectious endocarditis was suspected, trans-thoracic echocardiography was performed which was normal. On trans-esophageal

echocardiography, mitral valve prolapse was reported. No vegetations or clot were seen. Pulmonary artery pressure was normal.

Color Doppler sonography of the lower extremities was also performed which disclosed deep thrombosis in the veins of the right lower extremity.

Laboratory tests: Peripheral cell blood count was normal. Other laboratory tests were as follows:

ANA=1/80 peripheral, ESR=37 mm/h, CRP=2+, RF=Negative, anti-dsDNA=147 (positive >40), anti cardiolipin antibody IgG= 158 GPL (up to 12), and anticardiolipin antibody IgM= 5.5 MPL (up to 10). Cardiolipin test repeated 6 weeks later also showed similar results.

ANCA was negative and lupus anti-coagulant was 88" (18"-55"), S and C protein, antithrombin III and serum homocystine were normal. Considering the above mentioned tests, the patient underwent treatment with heparin and warfarin with an INR ranging between 2.6 and 3.5 with the diagnosis of anti-phospholipid syndrome probably secondary to systemic lupus erythematosus. Prednisolone and chloroquine were also started for the patient. Chest pain, dyspnea and cyanosis of the fingers improved upon treatment. The patient is still under follow-up.

DISCUSSION

Antiphospholipid antibody syndrome (APS) is characterized by the presence of symptoms comprising of numerous arterial and venous thrombosis, recurrent miscarriages or preterm delivery and mild thrombocytopenia in the presence of anti-phospholipid antibodies (APL) including lupus anticoagulant (LA), anticardiolipin (ACL) or both. Anti-beta 2 glycoprotein I, antimitochondrial, antiendothelial, antiplatelet and anti-erythrocyte antibodies are also found.

APS patients can develop a broad spectrum of pulmonary disease. Pulmonary embolism and pulmonary artery hypertension are the most prevalent complications of this syndrome. Although, less

prevalent complications such as pulmonary microvascular thrombosis, pulmonary capillaritis and alveolar hemorrhage have been reported as well (2). Physicians should be familiar with all forms of pulmonary involvement in this syndrome and if an APS patient presents with dyspnea, fever and pulmonary infiltration, physicians should consider APS. Recurrent pulmonary embolism can result in pulmonary artery hypertension and in severe cases, tricuspid valve insufficiency. Therefore, pulmonary embolism can be the first manifestation of antiphospholipid antibody syndrome (2).

APS is divided into two forms of primary and secondary based on the association with other diseases. In normal population, a high percentage of people has anti-cardiolipin antibody. The prevalence of positive anticardiolipin rises with age (1,3).

The risk of pulmonary embolism in patients with moderate and high titers of IgG anticardiolipin was 8 times greater than patients with negative test result. Also, almost 10% of patients with stroke especially in young ages have antiphospholipid antibodies (1,4).

According to various studies, the frequency of anti-phospholipid antibodies in systemic lupus erythematosus ranges between 6-80%. A part of this difference is due to the different sensitivity of different measurement methods. Some studies have indicated that 30-40% of SLE patients have APL and one third to half of them will develop APS (1).

The highest rates of diagnostic and therapeutic ambiguities are present in cases with APS secondary to SLE. In most cases it is difficult to find a correlation between clinical manifestations and antiphospholipid antibodies or SLE complications. For example, pregnancy complications can occur in case of presence of an underlying active renal disease or flare up of SLE.

Thrombosis can occur as the result of severe proteinuria independent of antiphospholipid antibodies. Distinction between these two is extremely important because of the different

treatment strategies.

Alarcon-Segovia et al. suggested a new classification for APS in which an intermediate group was added to the primary and secondary forms. This group of patients had all of the characteristics of primary APS syndrome, but did not meet all the SLE diagnostic criteria. This new group was named as antiphospholipid antibody syndrome with lupoid features (5).

Antiphospholipid antibody syndrome may affect any organ of the body such as central nervous system, cardiovascular, renal, pulmonary, hematologic, gastrointestinal tract and skin. Pulmonary manifestation of APS includes embolism and infarction, increased pulmonary artery pressure secondary to thromboembolism and pulmonary microvascular thrombosis. Also, cases of diffuse alveolar hemorrhage have been reported. Pulmonary embolism occurs in 30% of patients and may originate from the calf veins, inferior vena cava, tricuspid valve vegetation or intracardiac thromboses of the right heart. Adult respiratory distress syndrome (ARDS), primary thrombosis of pulmonary vessels and pulmonary capillaritis are among the other manifestations of this syndrome (1,2).

Treatment

Management of pulmonary thromboembolism is the same in patients with APS as in the general population. Patients require anticoagulation treatment with heparin followed by warfarin. It is recommended to maintain an INR ranging between 2.5 and 3.5 (2).

The mainstay of the treatment of antiphospholipid antibody syndrome is anticoagulants. The risk of developing a new thrombosis in a healthy individual who has antiphospholipid antibody is less than 1% per year. This rate in women with the history of recurrent miscarriages with no previous thrombosis is 10% while in those with a history of previous thrombosis who have discontinued using

anticoagulants sooner than 6 months is more than 10% a year. Also, in APS patients it is necessary to prescribe warfarin with an INR ranging between 2 and 3. According to several other articles INR of 2.6 and 3.5 (moderate intensity) is recommended for prevention of developing a new arterial or venous thrombosis. In case of APS in association with systemic lupus erythematosus, administration of hydroxy chloroquine has been effective in preventing new thrombotic events. Also use of this drug has been suggested for primary APS (6).

Effectiveness of chloroquine is implemented through affecting the activity of SLE, decreasing the level of antiphospholipid antibody and the anti-platelet effect (2).

In case of occurrence of catastrophic APS, high dose steroid therapy and cytotoxic treatment and in case of no treatment response, plasmapheresis and intravenous immunoglobulin prescription in addition to anticoagulants can be effective.

REFERENCES

1. Laskin CA, Clark CA, Spitzer KA. Antiphospholipid syndrome in systemic lupus erythematosus: is the whole greater than the sum of its parts? *Rheum Dis Clin North Am* 2005; 31 (2): 255- 72, vi.
2. Espinosa G, Cervera R, Font J, Asherson RA. The lung in the antiphospholipid syndrome. *Ann Rheum Dis* 2002; 61 (3): 195- 8.
3. Wilson WA. Classification criteria for antiphospholipid syndrome. *Rheum Dis Clin North Am* 2001; 27 (3): 499- 505.
4. Mehndiratta MM, Bhattacharya A, Gupta M, Khawaja GK, Puri V. Antiphospholipid antibodies syndrome in 'Stroke in young'. *Neurol India* 1999; 47 (2): 122- 6.
5. Alarcon-Segovia D, Cabral AR. The concept and classification of antiphospholipid/cofactor syndromes. *Lupus* 1996; 5:364-7.
6. Lim W, Crowther MA, Eikelboom JW. Management of antiphospholipid antibody syndrome: a systematic review. *JAMA* 2006; 295 (9): 1050- 7.