**Case Report**

Antiphospholipid syndrome with hemophilia B: A case report represented by recurrent thrombosis/bleeding attacks

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**ABSTRACT**

Antiphospholipid syndrome is an autoimmune disease characterized by thrombosis, thrombocytopenia and elevated titres of antiphospholipid antibodies (aPLs). Treatment is based on antiplatelet and anticoagulation drugs which is related to manifestations of the diseases. Although pulmonary embolism (PE) is the most common pulmonary manifestation of APS, intra-alveolar hemorrhage as well, can rarely be seen.

Haemophilia B is an X-linked chronic coagulation disorder which is characterized by factor IX deficiency. The severity of the disease is related to the antigen levels and coagulant activity of factor IX. We present the case of antiphospholipid syndrome with thrombotic complications after Cesarian delivery; after beginning antiplatelet medications complicated with severe bleeding because of accompanying hemophilia B.

**KEY WORDS:** Antiphospholipid syndrome, Hemophilia B, Thrombosis, Bleeding.

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**INTRODUCTION**

Antiphospholipid syndrome is an autoimmune disease characterized by thrombosis, thrombocytopenia and elevated titres of antiphospholipid antibodies (aPLs). Treatment is based on antiplatelet and anticoagulation drugs which is related to manifestations of the diseases. Although pulmonary embolism (PE) is the most common pulmonary manifestation of APS, intra-alveolar hemorrhage as well, can rarely be seen.

Haemophilia B is an X-linked chronic coagulation disorder which is characterized by factor IX deficiency. The severity of the disease is related to the antigen levels and coagulant activity of factor IX. We present the case of antiphospholipid syndrome with thrombotic complications after Cesarian delivery; after beginning antiplatelet medications complicated with severe bleeding because of accompanying hemophilia B.

**CASE REPORT**

A 31-year-old female patient had been admitted to our hospital with pulmonary embolism five days ago with continuing dyspnea. She had a history of hysterectomy due to massive uterine bleeding during removal of the dead fetus and postoperative deep venous thrombosis. She had been treated with warfarine for two years; after she stopped warfarine
herself, deep vein thrombosis and pulmonary embolism occurred five days ago. She had remarkable dyspnea (respiratory rate: 28/min.) and tachypnea (pulse rate: 122/min.). Oxygen saturation was low (sO₂: 88%). She was admitted to the intensive care unit. Oxygen, bronchodilator, low molecular weight heparin (subcutaneous enoxaparine 2x8000 anti-Xa IU daily) and aspirin (300 mg/day) were started.

Computed tomography (CT) pulmonary angiography (Figure 1, 2, 3) revealed an acute thrombus partially in the right main pulmonary artery. Doppler ultrasonography of the lower extremities (Figure 4) revealed thrombi seen in the proximal segment of the right saphenous vein. Echocardiography showed increased pulmonary arterial pressure (70 mmHg). The results of further analyses were as follows: Blood count parameters showed normal platelet and leucocyte count and mild anemia. Hemostatic parameters: INR: 1.2, prothrombin time (PT): 15.5 sec., aPTT: 82.3 (25-40) sec., fibrinogen: 960 mg/dl, D-dimer (quantitative): 700 ng/ml. Routine biochemical parameters were within normal ranges.

Anticardiolipin antibody levels were high; IgG (+): 57 GPL U/ml (<12 negative), IgM (+): 120 MPL U/ml (<12 negative). The results of lupus anticoagulant were also high: 134.9 sec (N: < 46.3 sec), lupus anticoagulant confirmation assay: 61.8 sec. (Normal < 40.8). The results of the screening tests performed for other genetic defects showed methylene tetrahydrofolate reductase gene mutation (MTHF-R 677 CC): heterozygote positive.

Fig-1: Thrombus beginning from the distal segment of the right main pulmonary artery extending through to the segment of the right inferior lobe.

Hemoptisia (400ml) occurred twice in a day after 3rd day of admission. Computed pulmonary angiogram (Figure 5) showed disseminated interalveolar hemorrhage. The values of hemostatic tests were as follows: aPTT: 87 sec. and 75.4 sec., INR: 1.9, and PT: 23 second. The results of biochemical tests showed LDH level: 723 U/L, whereas other biochemical tests were within normal ranges. Complete blood count revealed normal platelet count. Oxygen saturation (pO₂) was found 65%. Enoxaparine was stopped and transfusions were performed for three days. The general status of the patient was partially stable. After

Fig-2: Thrombus beginning from the distal segment of the right main pulmonary artery extending through to the segment of the right inferior lobe.

Fig-3: Thrombus in the anterior and posterior sub-segments of the left pulmonary artery in the inferior lobe.
three days without antithrombotic drug, LMWH was started; because melena occurred at the same day, it was also discontinued. Gastroscopic examination showed the signs of superficial gastritis with patchy bleeding in the gastric mucosa. Blood tests for hemophilia were assessed and showed that factor VIII was 85% (50-150), factor IX was 35% (50-150), factor II (prothrombin) was 95%, factor X was 55%, factor V was 108%, and von Willebrand factor antigen was 114% (60-150). The result of factor IX analysis, done in another laboratory to confirm the previous result, was also slightly low (37%). After melena ceased; half-dose low molecular weight heparin and 2.5 mg Coumadin were recommended. INR level was about 1.5. On her seven-day follow-up, her respiratory rate and oxygen saturation was normal without taking oxygen. She was discharged on her own request and ambulatory follow-up was planned.

One month after the hospital discharge, severe pulmonary hypertension had occurred in the patient and the thrombosis in the pulmonary arteries persisted. She had undergone ‘pulmonary end-arterectomy’ and the thrombosis in the pulmonary arteries was removed surgically. Subsequent echocardiography revealed that pulmonary artery pressure decreased to 30 mmHg. Further clinical progression could not be followed due to the inadequate communication since the patient returned to her homeland.

**DISCUSSION**

APS is a thrombotic disease accounts for 20% of deep venous thromboses which may lead to pulmonary embolism. The prevention of recurrent thromboses may require long-term anticoagulation. In our case, factor IX was found 35% and 37% respectively in two consecutive analyses. We were unable to discontinue the antithrombotic medications completely because of disseminated thrombosis. After detecting a slight factor IX deficiency, further anticoagulants were planned to be given in low doses, and continued to be given as was planned.

There is a case report which revealed type I von Willebrand factor (VWF) deficiency, FVL and heterozygote factor V Leiden mutation, heterozygote methylene tetrahydrofolate reductase C677T (MTHFR) gene mutation, and activated protein C resistance.

Positive MTHFR C677C heterozygote gene mutation was identified in addition to the positive anticardiolipin antibody and to the positive lupus anticoagulant in our case. Thereby, it was thought that the presence of a combination of acquired and thrombophilic defects might be responsible for the clinical picture of thrombosis that was in the forefront despite the low factor level (35%).
However, the clinical picture of the present case is likely to result from the intra-alveolar hemorrhage due to APS. Pulmonary endarterectomy is a modern and current surgical method applied in case of pulmonary hypertension caused by massive thrombosis in the pulmonary arteries, particularly in the patients with massive thromboembolism with underlying thrombophilic defect. In our patient, symptoms related to pulmonary hypertension were resolved after pulmonary endarterectomy.

Life-long antithrombotic therapy is recommended in the presence of combined thrombophilic defect, thrombosis in vital regions or life-threatening thrombotic attack, recurrent thrombotic attacks and in the cases with APS. Close monitoring of these patient group is recommended.

APS is usually thought in gestational thrombotic complications. This disease may be the cause of recurrent thromboses; but coexistence of two thrombotic disorders should be considered in severe thrombotic attacks. If there is recurrent bleeding attacks with antithrombotic drugs, haemostatic defects should also be considered.

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REFERENCES