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Case Report
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A Rare Cause of Pulmonary Embolism and Seizure in a Young Man: Antiphospholipid Syndrome

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Pulmonary embolism (PE) is a complication of underlying vascular thrombosis. The causes of PE are multi-factorial, and patients with PE present with various symptoms. We herein have presented the case of a 21-year-old man who initially developed palpitation, dyspnea, and seizure. Computed tomography of the chest ultimately indicated PE, and antiphospholipid syndrome (APS) was diagnosed with clinical thrombosis events and series presence of antiphospholipid antibodies. APS commonly causes vascular thrombosis within the vascular tree; however, nonthrombotic manifestations, such as seizure, may also occur. Clinicians should be aware of such non-thrombotic manifestations of APS to avoid misdiagnosis and inappropriate management.

Key Words: Antiphospholipid syndrome • Pulmonary embolism • Seizure

INTRODUCTION

Pulmonary embolism (PE) typically arises from thrombi that originate in the venous system. After traveling to the lung, large thrombi can lodge in the pulmonary artery and cause hemodynamic compromise. The classic presentations of PE are an abrupt onset of pleuritic chest pain, shortness of breath and hypoxia.[1] However, patients with PE may present with atypical symptoms such as syncope, fever, productive cough, hemoptysis, abdominal pain and arrhythmia. In rare cases, this condition is associated with seizure.[2] The causes of PE are multi-factorial, including venous stasis, hypercoagulable states, immobilization, surgery and trauma, pregnancy, oral contraceptives and estrogen replacement, malignancy, hereditary factors, and acute medical illness.[3] In addition to these causes, antiphospholipid syndrome (APS) could be also a possible cause of PE.[4] Here, we have presented a rare case of APS associated with PE and seizure, which was treated successfully using anticoagulant.

CASE REPORT

A 21-year-old man presented to our emergency department with progressive palpitation and shortness of breath for 2-3 days. The patient had a history of type 2 diabetes mellitus controlled by oral anti-hyperglycemic agents for two years. Moreover, transient loss of consciousness, pale face, salivation, twitching and extension of the upper and lower limbs extension occurred twice within the 2 weeks prior to admission. Furthermore, the patient had experienced painful swelling in the right leg for 2 months, which improved after massage therapy by a physiotherapist. There was no history of fever, bleeding from any site, hemoptysis, trauma or any drug use except for oral anti-hyperglycemic agents.

The patient was afebrile (temperature, 36.3 °C) with a heart rate of 122 beats/minute, respiratory rate of 18

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breaths/minute, blood pressure of 137/84 mmHg, and oxygen saturation of 95% in room air. Chest examination revealed clear breathing sounds. Heart sounds were regular, however heart beats were rapid without apparent audible heart murmurs. The findings on neurological and musculoskeletal systems were normal, and routine blood testing revealed a normal cell count. Coagulogram test showed a prothrombin time of 10.7 seconds (international normalized ratio: 1.09), and an activated partial thromboplastin time of 26.4 seconds (control: approximately 24.3-32.7 seconds). However, elevated D-dimer levels (1160 ng/mL) were detected. The results of a renal function test, liver function test, and electrolyte and vein blood gas analyses were normal. But a routine urine test indicated the absence of proteinuria. A chest X-ray revealed enlargement of the bilateral pulmonary arteries. An electrocardiogram showed sinus tachycardia, right axis deviation, and T-wave inversion in V1-V5. Echocardiography demonstrated marked dilation of the right ventricle and right atrium, paradoxical motion of the interventricular septum with a D-shape deformity in the left ventricle during the diastolic phase (Figure 1), hypokinesis of the right ventricle free wall motion, and moderate-to-severe tricuspid regurgitation with a pulmonary artery systolic pressure of 82 mmHg. Further computed tomography of the chest demonstrated filling defects over bilateral pulmonary arteries (Figure 2), which are consistent with PE.

The patient received intravenous heparin infusion therapy in the intensive care unit. After heparinization, the patient received warfarin therapy with a target international normalized ratio (INR) of 2 to 3. During hospitalization, the patient suffered recurring transient loss of consciousness, pale face, salivation, and twitching and extension of the upper and lower limbs, which led to a diagnosis of seizure attack. However, the results ofbrain computed tomography and magnetic resonance imaging were unremarkable. Additional autoimmune test results were negative for the presence of antinuclear antibodies, anti-double-stranded antibodies, rheumatoid factor and normal complement (C3 and C4 levels), protein C and S levels. However, the patient's anticardiolipin (aCL) IgG level was elevated (43.0 GPL/mL) and remained so during the 3-month follow-up (41.0 GPL/mL), confirming the diagnosis of APS. The patient was followed-up uneventfully with an INR of 2 to 3, having undertaken warfarin therapy.

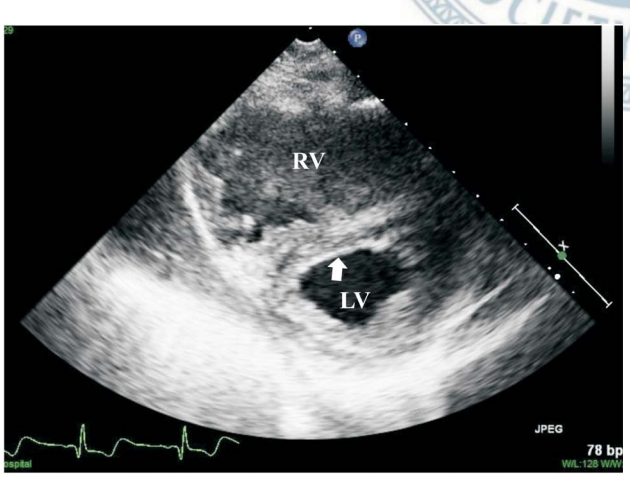

Figure 1. *2-D echocardiography of the patient demonstrated marked dilation of right ventricle and a D-shape deformity of the left ventricle during the diastolic phase (white arrow). LV indicates left ventricle; RV indicates right ventricle.*

DISCUSSION

We reported an unusual case of a young man with PE, which was ultimately proven to be associated with APS because of the series presence of antiphospholipid (aPL) antibodies. Moreover, in addition to typical manifestations of PE, such as palpitation and dyspnea, the patient presented with an atypical symptom of seizure. This indicated possible associations with these 3 disease manifestations.

APS, a disorder manifested clinically as recurrent venous or arterial thrombosis and/or fetal loss, is more common in women than in men.[4] APS is characterized by vascular thrombosis in the presence of aPL antibodies, which are autoantibodies directed against phospholipids or phospholipid-binding plasma proteins and can be distinguished into at least 3 distinct sub-

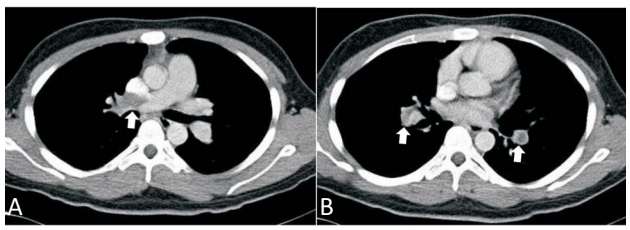

Figure 2. *Computed tomography of the chest revealed filling defects over bilateral pulmonary arteries (white arrow).*

types: aCL antibodies, anti-β_2 glycoprotein I antibodies, and lupus anticoagulant.[4] This condition can occur without any underlying autoimmune disorder (primary APS), or as a secondary condition to an underlying autoimmune disorder (secondary APS) such as systemic lupus erythematosus.[5] Clinical manifestations range from no symptoms to imminently life-threatening, such as deep vein thrombosis (31.7%), thrombocytopenia (21.9%), stroke (13.1%), superficial thrombophlebitis (9.1%), PE (9.0%), fetal loss (8.3%), transient ischemic attack (7.0%), and hemolytic anemia (6.6%).[4] Although most manifestations are related to vascular thrombosis, non-thrombotic presentations, such as cognitive dysfunction, psychiatric problems, migraine, seizure, chorea, multiple sclerosis-like syndrome, and transverse myelitis can be observed in aPL-positive patients, which leads to diagnostic challenges encountered in clinical practice.[6]

It has been reported that PE can be associated with seizure.[2] The pathophysiology underlying PE-related seizure suggests that massive PE causes transient right ventricular failure and decreased cardiac output, leading to transient global cerebral hypoperfusion.[2] In addition, massive PE with respiratory failure results in hypoxemia and acidosis, which can act as other possible contributors to seizures.[2] In this case, our patient presented with PE and seizure. Although PE can be explained by pulmonary vascular thrombotic events, thrombosis was absent in brain imaging. This observation indicated that the seizure in our patient may have been caused by non-thrombotic presentations of APS.

The prevalence of seizure in patients with APS ranges from 7-8.6%.[7] However, the pathogenesis of seizure in patients with APS remains unclear. Possible explanations include focal brain ischemic lesions, autoimmune diseases, or direct effects of aPL antibodies on the brain.[7] Positron emission tomography demonstrated decreased glucose metabolism in the perivascular areas in APS patients who experienced seizures with normal brain imaging, suggesting a subtle ischemic insult.[8] Moreover, several autoantibodies, such as autoantibodies to glutamic acid decarboxylase as well as aPL and aCL antibodies, were observed in patients with idiopathic epilepsy.[9] This finding suggests that seizure is caused as a direct effect of autoantibodies on the brain tissue, which is strongly supported by the findings of another study indicating that IgG aPL can directly permeabilize and depolarize brain synaptoneurosomes.[10]

In conclusion, we described a patient presenting with PE and seizure, secondary to APS. This case should remind clinicians to be aware of atypical presentation of PE and APS. Further investigation of the pathogenesis is necessary to provide optimal diagnostic and therapeutic strategies. Moreover, physicians should consider APS while surveying the possible underlying diseases in patients presenting with PE and seizure, even in a young man.

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