



Pulmonary Embolism with Antiphospholipid Syndrome: A Case Report

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Keyword

Pulmonary embolism, Antiphospholipid syndrome, Revised Geneva, Direct anticoagulant

Abstract

Antiphospholipid syndrome (APS) is a systemic autoimmune condition that is related to vascular thrombosis. Patients with APS are at risk for developing pulmonary embolism (PE) events. In this case, we present a 68 years old female with complaints of sudden onset of persistent shortness of breath for two days. No past medical history was identified. Physical and diagnostic examination revealed the presence of PE and antiphospholipid antibodies. Diagnosis of PE and APS were made. Patients then received initial anticoagulant using enoxaparin subcutaneously. Initial anticoagulants in patients with APS and PE should be administered. However, it is important to choose the right anticoagulant. Direct Oral Anticoagulant (DOAC) is contraindicated due to the increased risk of thromboembolic events.

Abstrak: Sindrom antifosfolipid (APS) adalah kondisi autoimun sistemik yang berhubungan dengan trombosis vaskular. Pasien dengan APS berisiko mengalami kejadian emboli paru (EP). Dalam kasus ini, seorang wanita berusia 68 tahun datang dengan keluhan sesak napas tiba-tiba selama dua hari. Tidak ada riwayat penyakit dahulu. Pemeriksaan fisik dan diagnostik menunjukkan adanya EP dan antibody antifosfolipid. Diagnosis EP dan APS ditegakkan. Pasien kemudian menerima antikoagulan menggunakan enoxaparin secara subkutan. Antikoagulan awal pada pasien dengan APS dan PE harus diberikan. Namun, penting untuk memilih antikoagulan yang tepat. DOAC dikontraindikasikan karena peningkatan risiko kejadian tromboemboli.

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Introduction

Pulmonary embolism (PE) is a life-threatening thromboembolic event and one of the most frequent acute cardiovascular disease behind myocardial infarction and stroke.^{1,2} Patients with unprovoked PE event had a higher recurrence rate. Antiphospholipid syndrome (APS) is one of many risk factors that are related to higher recurrence of PE.³ APS is a systemic autoimmune disorder characterized by the occurrence of vascular (venous or arterial) thrombosis with or without pregnancy morbidity in association with persistent antiphospholipid autoantibodies.⁴ Pulmonary embolism occurred in 2.1% of patients with APS.⁵ Treatment for patient with pulmonary embolism and antiphospholipid syndrome can be challenging. We describe patient with pulmonary embolism caused by antiphospholipid syndrome that came to our hospital.

Case Description

A 68 years old woman came with chief complaint sudden onset of shortness of breath that has been persistent for 2 days. There were no history of any other disease. She looked ill with GCS E4V5M6, his blood pressure was 120/70, pulse rate 127 beats/min, oxygen saturation 89% with room air, temperature was 36°C. Physical examination showed no abnormalities.

Laboratory test showed Hemoglobin 14,2mg/dl Leucocyte 10,55, creatinine 1,0 mg/dl ureum 46mg/dl, high sensitive cardiac troponin T (hs-CT) 269 ng/L, D-Dimer 10,71 mg/L, anti-B2-glicoprotein IgM positive (+), Lupus anticoagulant (1) 58,1 second (control 37,10 second), Lupus anticoagulant (2) 38,80 second (control 34,20 second).

Electrocardiography (ECG) showed atrial fibrillation rapid ventricular response, right axis deviation, right ventricular hypertrophy with strain pattern and S1Q3T3 pattern (Fig. 1).

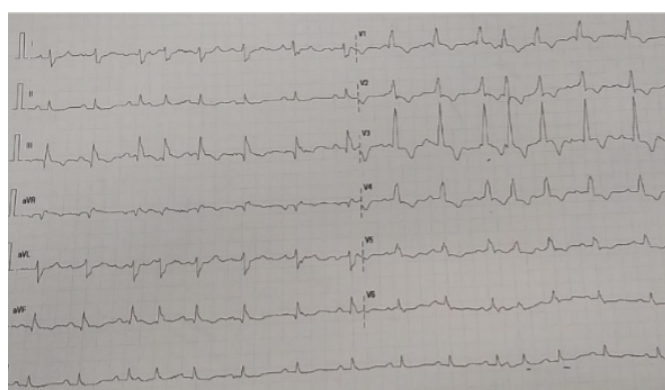


Figure 1. ECG showed atrial fibrillation rapid ventricular response with RVH and S1Q3T3 pattern

Echocardiography showed Ejection fraction (EF) 75% with Anteroseptal hypokinetic, Left ventricular (LV) with D shape appearance, Right ventricular (RV) dilatation, Mild Mitral regurgitation (MR), Mean pulmonary arterial pressure (mPAP) 43mmHg, mild impaired RV function (Fig. 2 and 3).

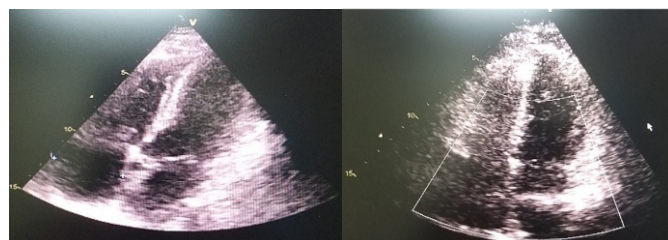


Figure 2. Echocardiography showed Left ventricular with D shape appearance and Right ventricular dilatation

Figure 3. Ten days after anticoagulation therapy echocardiography showed normal size of right ventricular and left ventricular

Peripheral Doppler ultrasound showed no abnormality. This showed pulmonary hypertension with preserved EF. Coronary angiography CT scan (Fig. 4 and 5) showed normal coronary artery with total calcium score: 0 and thrombus on bilateral pulmonary arterial which decrease 90% of arterial lumen. A diagnosis of pulmonary embolism (PE) and antiphospholipid syndrome (APS) were made.

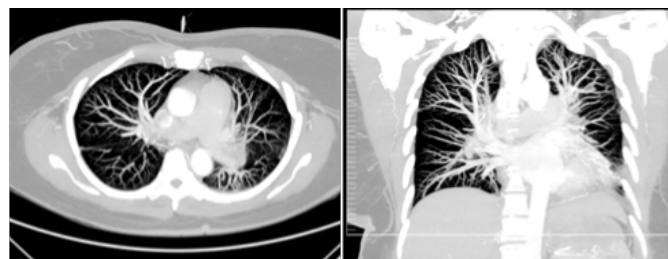


Figure 4. CT pulmonary angiography (coronal view) showed bilateral pulmonary arterial thrombus with decrease of arterial lumen

Figure 5. CT pulmonary angiography (sagittal view) showed bilateral pulmonary arterial thrombus with decrease of arterial lumen

Patient was treated with supplementary oxygen using non rebreathing mask (NRM) 15lpm, bisoprolol 1x5mg for rate control, subcutaneous enoxaparin 2x0,6ml and single antiplatelet for ten days. Post treatment D-dimer showed 3,32mg/L. Ten days after treatment patient underwent pulmonary angiography that showed no significant improvement with bilateral pulmonary arterial thrombus still decreased 90% of arterial lumen. Post treatment echocardiography showed global normokinetic, LVEF 77%, mPAP 30 mmHg, good RV function, Normal RV and LV size. After that, patient was discharged with continuous subcutaneous injection enoxaparin 2x0,6ml and would be monitored from the outpatient clinic.

Discussion

Pulmonary embolism (PE) is third most frequent acute cardiovascular syndrome behind myocardial infarction and stroke. PE annual incidence rates ranging 39-115 per 100,000 population.⁶ Predisposing factors for PE are categorized into strong, moderate and weak risk factor.

Strong risk factors include lower limb fracture, hospitalization for atrial flutter/fibrillation (within previous 3 months), previous venous thromboembolism (VTE) events, spinal cord injury, and history of myocardial infarction (within previous 3 months).⁷ Moderate risk factor include autoimmune disease, blood transfusion, arthroscopic knee surgery, chemotherapy, congestive heart failure, postpartum period, oral contraceptive therapy and thrombophilia.⁷ Weak risk factor include bed rest >3 days, diabetes mellitus (DM), increasing age, obesity, and pregnancy.⁷

PE can be associated with APS. APS is a systemic autoimmune disorder characterized by recurrent venous or arterial thrombosis with or without pregnancy morbidity in the presence of persistent antiphospholipid (aPL) autoantibodies. These include the lupus anticoagulant (LA), anticardiolipin (aCL), and anti-beta-2 glycoprotein (anti-β2GPI) autoantibodies.^{4,8} Diagnosis APS consists of clinical criteria (vascular thrombosis and pregnancy morbidity) and laboratory criteria (Lupus anticoagulant on plasma, anticardiolipin antibody isotype in serum and anti-β2 glycoprotein antibody of IgG or IgM in serum).⁹

Antiphospholipid antibodies can induce endothelial-cell, complement, platelet, neutrophil, and monocyte activation, leading to thrombosis. The major target of antiphospholipid antibody is β2-glycoprotein I (β2GPI), a plasma protein that binds avidly to phospho-lipid surfaces. Binding of antiphospholipid antibody and β2GPI on cellular surfaces will up regulates the expression of prothrombotic cellular adhesion molecule such as E-selectin and tissue factor. Antiphospholipid antibodies will then promote clot formation that can cause vascular thrombosis.¹⁰

PE can present in acute state that can interfere circulation and gas exchange. RV failure due to pressure overload is the primary cause of death in severe PE. Pulmonary arterial pressure increases if >30-50% pulmonary arterial bed is occluded by thromboembolic. PE will cause vasoconstriction, mediated by release of thromboxane A2 and serotonin contributes to the initial increase in pulmonary vascular resistance (PVR).¹¹ Increased PVR result in RV afterload, therefore increasing the tension of RV wall and RV dilation, which alter contractility causing RV dysfunction. Inotropic and chronotropic will be stimulated to maintain pulmonary artery and systemic circulation. These mechanisms will stabilize blood pressure and organ function. However, RV cannot generate mean PAP >40 mmHg.¹² RV dilation also causes the interventricular septum to be shifted toward the left ventricle.

These pathologic mechanisms can cause diastolic dysfunction and a decreased in LV filling. All these decrease the cardiac output, thus resulting in decreased systemic blood pressure causing hypotension.¹³ RV infarction can happened after PE because imbalance oxygen supply and demand can result in cardiomyocytes damages and further decrease contractility forces. Respiratory failure is consequence of hemodynamic instability. The mechanism is affected by the characteristic of embolic material, degree of occlusion, and onset of embolization. Zones of reduced blood flow in

obstructed pulmonary arteries, combined with zones of overflowing blood flow in non-obstructed pulmonary arteries will cause ventilation-perfusion mismatch that will lead to hypoxia.¹⁴ Small distal emboli usually does not cause hemodynamic instability but may create areas of alveolar hemorrhage resulting in hemoptysis, pleural effusion, and pleuritis. This is known as pulmonary infarction.¹

Clinical sign and symptoms of PE range from dyspnea, chest pain, pre-syncope or syncope, or hemoptysis. PE can be asymptomatic or discovered incidentally while working up on another disease. Chest pain complaints is usually caused by pleural irritation due to obstruction of the distal pulmonary artery.¹ Chest x ray is sometimes abnormal although its finding are usually nonspecific for PE. ECG can be presented as RV strain (Inverted T waves in V1-V4 and Qr morphology in lead V1), incomplete or complete RBBB and S1Q3T3 pattern. Furthermore, T-wave inversions in precordial leads are related to severity of PE and the presence of RV dysfunction.¹²

Patients with suspected PE should be evaluated for the probability of PE. Clinical probability can be categorized into three level score (low: 0-3, intermediate 4-10, high ≥ 11) or two level score (PE unlikely 0-3, PE likely > 3).¹⁵

Pulmonary embolism rule out criteria (PERC) has been made to rule out PE embolism to avoid high cost and complication of unnecessary diagnostic workup. Eight clinical criteria has associated with absence of PE: age < 50 years; pulse < 100 beats per minute; SaO₂ >94%; no unilateral leg swelling; no history of hemoptysis; no recent trauma or surgery; no history of VTE; and no oral hormone use.¹⁶

D-dimer is a result from degradation of plasmin-mediated fibrin. D-dimer levels are increased in the presence of acute clotting due to simultaneous activation of coagulation and fibrinolysis.¹² D-dimer has a good negative predictive value but low positive predictive value to confirm the diagnosis of PE.¹²

CT pulmonary angiography (CTPA) is using for diagnosing PE based on direct visualization of thrombus, showing a filling defect in the artery.¹⁷ Echocardiography can also be used in diagnosing PE, but need further comprehensive evaluation. Some findings from echocardiography examination are the presence of RV dilation, RV free wall hypokinesia or akinesia (McConnell sign), 60/60 sign, RV/LV end-diastolic diameter >1, and decreased tricuspid annular plane systolic excursion (TAPSE) measured by m-mode (less than 16mm) may also be present in PE patients.¹⁷

Treatment in acute phase should be done to support haemodynamic and respiration system. This includes oxygen administration and ventilation, cautious volume loading, administration of vasopressors and inotropes, and mechanical circulatory support.⁷

Administration of initial anticoagulation should be done for patients with intermediate or high clinical probability of PE. Subcutaneous injection of low molecular weight heparin (LMWH) or fondaparinux are preferred over unfractionated heparin (UFH) because they have a decreased risk for major bleeding and heparin-induced thrombocytopenia.⁴ UFH can be administered in patients with renal impairment (Creatinine clearance ≤ 30mL/min) and patients with unstable hemodynamic status who will undergo reperfusion treatment.⁴ Warfarin and direct anticoagulant (DOAC) can be used in treatment for PE.

Reperfusion treatment on high risk PE patient consist of systemic thrombolysis (streptokinase, recombinant tissue plasminogen activator (rtPA), urokinase), percutaneous

catheter direct treatment or surgical embolectomy. Although DOAC is an alternative anticoagulation for patients with PE and does not require monitoring, the safety and efficacy of DOAC in PE patients with APS lack of evidence. DOAC did not show efficiency in preventing thrombosis in high-risk APS patients.¹⁸ Recent study, Trial of rivaroxaban in AntiPhospholipid syndrome (TRAPS), showed that thromboembolic event was increased in patient that taking rivaroxaban. Therefore, warfarin can be chosen and DOAC should be avoided in high-risk patient with antiphospholipid syndrome.¹⁹

Conclusion

Pulmonary embolism (PE) is third most frequent acute cardiovascular syndrome behind myocardial infarction and stroke. Patients with APS are at risk for developing PE. Predisposing factor for PE can be differentiated into strong, moderate and weak risk factor. Revised Geneva clinical prediction rule can be used for clinical probability of PE. Management includes hemodynamic and respiratory support, anticoagulation administration, and interventional management. In APS patients with PE, DOAC is contraindicated because it could increase the risk of thromboembolic event.

Conflict of Interest

None to be declared.

Acknowledgements

None

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