



A Case of Antiphospholipid Syndrome (APS)-Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

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Abstract

Chronic Thromboembolic Pulmonary Hypertension (CTEPH) is the group 4 pulmonary hypertension, related to blood clots blocking the arteries of the lung. CTEPH can be a complication of APS. Patient with CTEPH can develop various symptoms, which are not specific. So the diagnosis of CTEPH is difficult. Once CTEPH diagnosed, anticoagulation should be used for the patient. Pulmonary thromboendarterectomy (PTE) is the optimal therapeutic schedule for CTEPH now. Hereby we present a case of a CTEPH patient with APS. From this case, we found that when acute PE appeared on an APS patient, CTEPH should be considered. We also found that PTE is effective on CTEPH developed from APS.

Introduction

Chronic Thromboembolic Pulmonary Hypertension (CTEPH) is the group 4 pulmonary hypertension, which is caused by chronic blood clots blocking the arteries of the lung. In the course of disease, major vessel thromboembolism developed, then contributed to obstructive PA remodelling. Antiphospholipid syndrome (APS) is a disease that manifests clinically as vascular thrombosis (arterial, venous, or small vessel thrombosis) and/or abortion, as well as characteristic laboratory results (persistently elevated levels of antiphospholipid antibodies (aPL)) [1]. Patients with APS can develop CTEPH. CTEPH patients can develop clinical manifestation like chest pain, fatigue, edema, cough and hemoptysis. Then because of the appearance of right heart failure, jugular venous distention, hepatomegaly, ascites can be found on physical examination. The symptoms of CTEPH are not specific, so sometimes it is difficult to diagnose CTEPH at early stage of the disease. Once CTEPH diagnosed, long term anticoagulation and consideration of pulmonary thromboendarterectomy (PTE) surgery should go ahead [2]. PTE is the optimal therapeutic schedule for CTEPH.

Case Presentation

A 29-year-old man was admitted to this hospital because of chest pain, decrease of exercise capacity, and hemoptysis. The patient had been well until September 2015, when chest pain, dull pain on the left shoulder and back, and paroxysmal cough developed. Computed Tomography Pulmonary Angiography (CTPA) revealed a left inferior lobe pulmonary embolism. Rivaroxaban 20 mg Qd was prescribed and the patient got a pain remission.

One month later, the patient felt symptoms repeated and shortness of breath after some activities developed. He went to hospital and the result of lupus anticoagulant (LA), anticardiolipin antibody (ACL), and anti-beta₂-glycoprotein (anti-β₂GPI) are above normal, which showed the diagnosis of primary antiphospholipid syndrome (PAPS). A transthoracic echocardiogram (ECG) showed the size of the right ventricle and right atrium was large; the pulmonary artery systolic pressure was 98 mmHg, with an ejection fraction of 63%. He was considered as chronic thromboembolic pulmonary hypertension (CTEPH) and hydroxychloroquine 200 mg Qd as well as sildenafil 20 mg Tid was added. Then the patient felt relief of symptoms.

Three months later, the patient went to the hospital again because of hemoptysis. The erythrocyte sedimentation rate was 87 mm/h. A computed tomographic (CT) scan of the chest showed a 4.5x5.4 cm high density, clear boundary shadow in the apex of the left lung. The lobes of right lung showed

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Figure 1: CTPA showed multiple PE, the left pulmonary artery was completely embolized and the branches of right pulmonary artery were embolized.



Figure 2: Excised pulmonary artery intima.

multiple ill-defined patchy ground glass opacities and nodules.

The patient didn't have rash, joint pain, photosensitization, dryness of mouth and eye in the disease duration. He had smoked 15 cigarettes per day for many years but had quit for 8 months.

While hospitalized, anticoagulant therapy was suspended, and pituitrin was used for hemostasis. The symptom of hemoptysis was getting better. 2 weeks later, the ECG reexamination showed that the pulmonary artery systolic pressure was 101 mmHg. And this time the CTPA showed multiple pulmonary embolism. Complete obstruction of left pulmonary artery and fresh thrombosis of right lung could be seen. Approach to this situation, the patient was given low molecular weight heparin 4000 iu IH Qd. But next day he presented hemoptysis again; and the amount of the blood was about 200-300ml. Bronchial arteriography (BAG) showed pulmono-bronchial shunt of the left lung. Embolism of bronchial artery was used to treat hemoptysis and it worked out. Anticoagulation was continued under close surveillance. 1 month later, PTE was operated on the patient. After the surgery, the patient felt an obvious increase of exercise capacity. ECG reexamination showed that the pulmonary artery systolic pressure was down into the normal range; with triple antiphospholipid antibodies (aPLs) positive.

Discussion

This young patient got left chest pain at the onset of the disease. The image results showed left inferior lobe pulmonary embolism many times. Except smoking history, there weren't certain risk factors for venous thromboembolism (VTE) like fat, hyperlipidemia, trauma, surgery etc, so some rare risk factors for thrombophilia should be considered. From laboratory tests results we could see LA, ACL, anti- β_2 GPI increased significantly and presented in high titer after 4 months, from which APS could be diagnosed. There was

no evidence exists to suggest other connective tissue diseases. So PAPS should be considered as a diagnosis. The patient used novel oral anticoagulant (NOVC) as standard regularly after developing acute PE; but developed thromboembolic events twice again. Then exercise intolerance, and hemoptysis were reported by the patient. CTPA showed multiple pulmonary embolism. Several times of ECG examination showed the increased size of the right ventricle and right atrium and high systolic pressure of the pulmonary artery. The diagnosis of CTEPH was made by his symptoms and imaging results.

Both venous and arterial thrombotic events can be presented in APS patients. Deep vein thrombosis and PE are most common thrombotic events. Most APS patient has more than one thrombus, and it is common to see recurrent thrombotic events on APS patient. According to other literature, the recurrence rate of thrombotic events is up to 30% [3]. The rate of CTEPH developed from acute PE ranges from 0.57%-4.7% from different studies. Some common risk factors for this process include unexplained PE, recurrent PE, big blood clot of PE, elderly, chronic inflammatory state, malignant tumor, etc [4]. Some research indicates that aPLs are not only the markers for APS, but also associated with the pathogen of CTEPH [5]. Proposed mechanisms include that aPLs may inhibit the cascade reactions catalyzed by phospholipids, which are also connected with the development of CTEPH. Another hypothesis is that the formation of microembolization in the course of APS makes a great contribution to CTEPH [6]. According to the results of several cohort studies [7,8], aPLs positive occurs in about 15-50% CTEPH patients. A high titer of LA is involved with microembolization in PAPS [9]. The higher titer of aPLs, the worse the prognosis is.

Effective, life-long anticoagulation is recommended for all CTEPH patients. There is no evidence to prove NOVC is effective as Warfarin [10]. In the early stage of disease, the patient didn't get a definite diagnose. He was considered as acute PE and only used Rivaroxaban. Anticoagulant efficacy wasn't evaluated regularly, which caused the patient miss the optimal therapeutic time. While going to the hospital, the patient experienced hemoptysis. The CTPA showed pulmono-bronchial shunt of the left lung, which was considered relative to CTEPH and was a difficult for anticoagulation. Patients with CTEPH are more easily to get hemoptysis. That's because thrombus blocks both proximal and distal pulmonary artery, and then led to the increase of blood supply provided by the bronchial artery to pulmonary, and the increase of blood flow volume in the capillary network between these two arteries. The capillary is easier to rupture. So the anticoagulation for CTEPH patients should under close surveillance to prevent bleed events.

Since pulmonary thromboendarterectomy (PTE) is the optimal therapeutic schedule for CTEPH now, it is important to create opportunity for operation. There is no clear evidence to prove that patients with APS-CTEPH have fair prognosis after PTE. After PTE, even though the patient still has triple antiphospholipid antibodies (aPLs) positive; he felt obviously symptom relieve; and ECG showed the recovery of cardiac structure and pulmonary arterial pressure on the six month follow-up. From this case we can say that APS-CTEPH is not a contraindication to PTE. After evaluate the risk of thrombosis in an experienced treatment center and standard anticoagulation treatment, patients with APS-CTEPH could accept PTE to get a good prognosis.

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