Case report

Acute pulmonary embolism and deep vein thrombosis secondary to idiopathic hypereosinophilic syndrome

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ABSTRACT

Acute pulmonary embolism (PE) is a most dangerous complication that needs prompt treatment to reduce potentially death. There are many well-known prognostic factors indicate the morbidity and mortality in various thromboembolic events. Persistent eosinophilia in peripheral blood can lead to tissue infiltration and even organ damage, but the urgent event of thromboembolism in pulmonary provoked by eosinophil eosinophilia in idiopathic hypereosinophilic syndrome (HES) is relative an unusual presentation. In this paper, we present two cases of patients with multiple PE and deep vein thrombosis secondary to the idiopathic HES. Patients were all treated using anticoagulant therapy and corticosteroids successfully. Accordingly, eosinophilia is another risk and precipitating factor of pulmonary thromboembolism. It is necessary for physicians to make a diagnosis in hypereosinophilia as soon as possible for proper prognosis and in case of further thromboembolic events and prevent end-organ damage.

1. Introduction

Acute pulmonary embolism (PE) is a most dangerous complication that needs prompt treatment to reduce preventable deaths. Except anticoagulation, thrombolytic and embolectomy, removal of the reversible risk factors for venous thrombosis is also essential to improve the outcome [1,2]. Eosinophilia in peripheral blood is less known to promote a hypercoagulable state that may favor venous thrombosis [3]. Idiopathic hypereosinophilic syndrome (HES) is a leukoproliferative disorder, characterized by marked unexplained eosinophilia and organ damage led by tissue eosinophilia [4]. Several studies have suggested that the correlation between the thromboembolism and eosinophilia [5]. However, acute PE is relative an unusual presentation in pulmonary damages in idiopathic HES, which need to debulk the blood and tissue eosinophil burden as soon as possible for a proper prognosis.

Here, we describe two patients who had acute multiple PE and simultaneous deep venous thrombosis (DVT) secondary to idiopathic HES. The patients were treated successfully with anticoagulation and corticosteroids to decrease eosinophil count.

2. Case reports

2.1. Case 1

A 39-year-old man presented with a 3-days history of progressive chest pain, cough, hemoptysis, painless right lower limb swelling and a 10-days history of intermittent diarrhea. He had a transient 38.8 °C fever five days before admission. He did not present other symptoms or signs. Except for a 20-year-old cutaneous vitiligo, there was no history of immobilization, major trauma, or any other risk factors, or family history suggestive of inherited thrombophilia. He had a body mass index of 24. On physical examination, some irregular vitiligo patches on abdomen and back regions were observed. Chest auscultation revealed scattered bilateral coarse crepitations and decreased breath sounds in the bilateral lower lung fields. His right lower limb was swollen up to the groin, and there was tenderness over the calf.

On admission, laboratory assessment revealed markedly elevated leukocyte count (18.62 × 10⁹/L) and the eosinophil count (6.8 × 10⁹/L), D-dimer assay was > 20mg/L. Doppler ultrasonography showed multiple vein thrombosis in the right iliac, femoral and calf muscular vein. The computed tomography (CT) scan result for the chest with contrast enhancement suspected pulmonary embolism, diffuse bilateral...
patchy infiltrates and pleural effusion. Based on these findings, acute PE was suspected and computed tomographic pulmonary angiography (CTPA) scan was done immediately, which showed bilateral multiple pulmonary artery thrombosis and pulmonary infarction (Fig. 1A). Echocardiography was normal. The diagnosis of acute PE and DVT was made. Subcutaneous fondaparinux was administered to the patient for immediate anticoagulant treatment.

Because of high eosinophil count, the following additional tests were examined. The findings revealed that tumor markers and thyroid function were negative. A test for parasites in the stool and serum was negative. Tests for allergic and rheumatologic diseases, immunological studies, serum B12 level was negative. Bone marrow aspiration and biopsy revealed a normal cellular marrow with increased mature-appear- ing eosinophils (27.5%). BCR-ABL and Janus kinase 2(JAK-2) V617F were found to be negative by polymerase chain reaction. Flow cytometric evaluation showed no clonality, and Fip1-like1-platelet-derived growth factor receptor (FIP1L1-PDGFR)α fusion gene was negative by fluorescence in situ hybridization. The hematological malignancies were also excluded.

Based on the clinical evaluation and the patient’s peripheral eosinophilia, the multiple-organ dysfunction and the exclusion of other known causes of eosinophilia, a diagnosis of idiopathic HES with pneumonia was established. The patient was treated with corticosteroids (1mg/kg/d) and the eosinophil counts decreased to normal range within next five days. A follow-up CTPA scan, performed 15 days after the initial therapy, revealed the thrombi and pulmonary infarctions had significantly decreased (Fig. 1B). He was discharged in stable condition on rivaroxaban and corticosteroids therapy. The patient was symptom-free and doing well at about four months of follow-up (Fig. 1C).

2.2. Case 2

A 55-year-old man was admitted to our department for pain and swelling of right lower limb accompanied with 5-days hemoptysis. He had a history of the appendectomy at another hospital 11 days before admission to our hospital. The day after the appendectomy, the patient had pain and swelling of the right lower limb, hemoptysis subsequently came to him. He expectorated approximately 5–10 mL of bright red blood every day. Complete blood count showed a high eosinophil count (7.86 × 10^9/L) before appendectomy. Doppler ultrasonography showed vein thrombosis in the right femoral and popliteal vein. CT scan of the chest showed bilateral pneumonia and pleural effusion on the first day of hemoptysis. The D-dimer assay was 4.8 mg/L. The patient with a heavy smoking habit (120 pack-years) denied a personal history of other systemic complaints and family history. General examination revealed body temperature 38.6 °C, and systemic tests were normal except for the decreased breath sounds in the right lower lung field and swelling in the right lower limb.

On the day of admission, CTPA scan was done and showed multiple filling defects in bilateral multiple pulmonary artery and inferior pulmonary artery (Fig. 2A). The diagnosis of acute PE and DVT was made. The anticoagulant treatment was administered to the patient with fondaparinux. Laboratory tests revealed a high eosinophil count (5.4–7.86 × 10^9/L), low platelet count (38–52 × 10^9/L). The work-ups for allergic, parasitic, malignant, rheumatologic and immunological diseases were negative. Bone marrow examination showed no specific findings for myeloproliferative neoplasms but increased mature-appearing eosinophils (20.5%). FIP1L1-PDGFRα, JAK-2 V617F, and BCR-ABL fusion gene were negative. The patient was diagnosed with idiopathic HES. Corticosteroid treatment was initiated, the eosinophil and
platelet counts were all normal in 10 days. He was discharged in stable condition on warfarin and corticosteroids therapy. About three months after the home treatment, a CTPA scan showed the thrombi in pulmonary arteries resolved entirely (Fig. 2B). The eosinophil count was maintained at the normal level.

3. Discuss

Venous thromboembolism (VTE), including DVT and PE, is a multifactorial disease, involving interactions between all kinds of risk factors and predispositions to thrombosis, either acquired or inherited [6,7]. Identifying predisposing factors for VTE is significant in deciding the treatment modality, duration and preventive strategies for recurrence. In this report, we have described two cases of idiopathic HES with concomitant PE and DVT, and our experience suggests that eosinophilia may be an under-recognized risk factor for acute PE. Indeed, in two of our cases, extensive DVT and multiple PE were found incidentally with eosinophilia.

Eosinophilia is observed in patients with allergic conditions, various inflammatory and diverse hematologic malignancies. Idiopathic HES applies to all clinical presentations in which blood hypereosinophilia can be documented, and hypereosinophilia is directly linked to organ damage, after ruling out reactive or neoplastic (clonal) conditions/disorders. According to the Year 2011 Working Conference on Eosinophil Disorders and Syndromes, tissue hypereosinophilia should apply when one or more of the following is fulfilled. First, the percentage of eosinophils exceeds 20% of all nucleated cells in bone marrow sections. Second, a pathologist believes tissue infiltration by eosinophils is extensive when compared with the standard physiologic range, compared with other inflammatory cells, or both. Third, a specific stain directed against an established eosinophil granule protein reveals extensive extracellular deposition of eosinophil-derived proteins [8,9]. In our two cases, bone marrow infiltration and vein thromboembolism were consistent with tissue hypereosinophilia. Accordingly, the patients fulfilled the diagnostic criteria of idiopathic HES with the exception of duration. Though idiopathic HES is characterized by persistent elevation of absolute eosinophil count to 1.5 × 10⁹/L or above for a period of at least 6 months or on 2 examinations (interval ≥1 month) (2), but in the case of evolving life-threatening end-organ damage such as pulmonary embolism and cerebrovascular thromboembolism, the diagnosis can be made immediately to avoid delay in therapy [10].

In the majority of cases, PE originates from DVT in a limb like the patients in this report. However, there might be another possibility. In our two cases, CT of the chest showed diffuse bilateral patchy infiltrates and pleural effusion, which suggested the probability of simultaneously acute eosinophilic pneumonia. Though bronchoalveolar lavage was not conducted to the certificate, the pulmonary infiltrates, the improvement of clinical symptoms and radiographic findings demonstrated the diagnosis. In acute eosinophilic pneumonia, hypercoagulability can be promoted through hypercoagulable and platelet-activating effects of eosinophil granule proteins [7]. Accordingly, multiple embolisms in the pulmonary arteries in our cases suggested another probability of the local eosinophilic infiltration that resulted in hypercoagulability.

The goal of the therapy is to mitigate hypereosinophilia mediated organ damage. For patients with idiopathic HES, corticosteroids are the first-line therapy and are effective in producing rapid reductions in the eosinophil count [11], but the maintenance dose and the duration of therapy are different because of individual difference [12,13]. Corticosteroids can inhibit the production of the inflammatory mediators such as eosinophil cationic protein, major essential protein, eosinophil peroxidase and eosinophil-derived neurotoxin, which are thought to cause hypercoagulation [14]. Drug withdrawal prematurely may rebinding the eosinophil count. The presence of persistent hypereosinophilia may affect the decision on the duration of anticoagulation therapy. In these two patients, as soon as the diagnosis of idiopathic HES was established, corticosteroids (prednisone 1 mg/kg) were administered to debulk the blood and tissue eosinophil burden and prevent the recurrence of thromboembolism. The maintenance dose was 10 mg daily, and the duration of therapy was more than a half one year.

In conclusion, persistent eosinophilia can be a cause or precipitating factor of acute pulmonary thromboembolism in patients. It is necessary for physicians to make a diagnosis in hypereosinophilia as soon as possible in case of further thromboembolic events.

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Consent for publication

Written informed consent was obtained from the patients for publication of this case report and any accompanying images.

Competing interests

The authors reported no potential conflicts of interest.

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