中文題目：嗜伊紅性肉芽腫多發性血管炎併發肺栓塞及肺高壓:案例報告
英文題目：Eosinophilic granulomatosis with polyangiitis complicated with pulmonary embolism and pulmonary hypertension: A case report
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Introduction:

Eosinophilic granulomatosis with polyangiitis (EGPA) is a small-vessel necrotizing vasculitis with specific features like high asthma prevalence, eosinophilia and eosinophil infiltration in tissues. Thromboembolism is a complication of EGPA, and several factors, such as inflammatory diseases and eosinophilic inflammation may contribute to the association between EGPA and thromboembolism. Chronic thromboembolic pulmonary hypertension (CTEPH) resulted from pulmonary vascular thrombo-emboli, and is diagnosed by the evidence of pulmonary artery hypertension via cardiac catheterization and segmental perfusion defect on a perfusion/ventilation scan (V/Q scan). A comprehensive study of thromboembolism is necessary to provide patients with appropriate treatment and better outcomes. We presented a case of EGPA with an initial presentation of pulmonary embolism with CTEPH, treated by anti-coagulant therapy and anti-inflammation agents, including systemic steroid and mepolizumab.

Case presentation:

A 58-year-old woman with history of asthma and sinusitis presented to our hospital with a complaint of syncope for minutes when walking. She suffered from dyspnea on exertion when walking and postural change related dizziness for about 2 weeks. Chronic cough was also noted. After the episode of syncope, she developed shortness of breath and chest tightness. There was no fever, palpitation, head trauma, weakness, or drug use.

On physical examination, she had a Glasgow coma scale of 15 and was disoriented. Her vital signs were blood pressure 105/74 mmHg, respiratory rate 30/min with O_2 saturation of 79% on room air, pulse 105/min, and temperature 37.1°C. There were clear breathing sounds without crackles or wheezes, bilateral lower limbs pitting edema 1+, and no neurologic abnormalities. Laboratory examination showed no leukocytosis but eosinophilia (1,200 eosinophils per microliter), no anemia or electrolyte imbalance; pH, 7.44; pCO2, 32 mmHg; HCO3-act, 21.7 mmol/L; D-dimer,

6761.8 ng/mL(FEU). EKG showed low voltage QRS, poor R wave progression, and V1-V5 T wave inversion. Chest computed tomography (CT) revealed left pulmonary embolism (Fig. 1) with mosaic attenuation, a nodule about 1x 1.8 cm at RUL (right upper lobe), and multiple small subpleural ill-defined opacity in left lower lobe lung (Fig. 2).

Echocardiography showed impaired right ventricle contractility with tricuspid annular plane systolic excursion 15mm and dilated right atrium and ventricle. Peripheral sonography showed no deep vein thrombus. Lab data showed negative findings of the autoimmune profile including anti-nuclear antibody, rheumatoid factor, ds-DNA, SS-A/B, Scl-70, SM & RNP, antineutrophil cytoplasmic antibody, anticardiolipin antibody, lupus anticoagulant, cryoglobulin, and β-d-glucan. Levels of AFP, SCC, CEA, CA-125, CA-153, CA-199, anti-thrombin III, protein C, and protein S were all within the normal range. Cardiac catheterization disclosed moderate pulmonary hypertension with mean pressure of 39 mmHg of the pulmonary artery and 10 mmHg of pulmonary capillary wedge pressure, no response to 100% oxygen or vasodilator, and no congenital structure problem. V/Q scan revealed segmental perfusion defects involving multiple segments of both lungs (Fig. 3). She received a CT-guided biopsy after 15 days of presentation, and the pathology revealed mild chronic inflammatory cell infiltration including small lymphocytes, few plasma cells, eosinophils (up to 20 eosinophils/HPF) and granulation tissue (Fig. 4). As the presentations of asthma, sinusitis, peripheral eosinophilia, pulmonary infiltrates and extravascular eosinophilic infiltrates, EGPA was diagnosed. We prescribed rivaroxaban, sildenafil, steroid therapy, and Mepolizumab injection every 4 weeks. She had no recurrence of pulmonary embolism and gradual improvement of symptoms like dyspnea on exertion and hypoxemia.

Discussion:

EGPA is a small-vessel necrotizing vasculitis with specific clinical, biological, and histological features like high asthma prevalence, eosinophilia and eosinophil infiltration in tissues [1]. Depending on anti-myeloperoxidase (MPO)-ANCA, EGPA is divided into two phenotypes. Patients with MPO-ANCA+ have a more vasculitis phenotype such as purpura, peripheral neuropathy, renal involvement and biopsy-proven vasculitis [1]. In our patient, there was no ANCA, purpura, peripheral neuropathy or renal involvement noted.

Thromboembolism is known as a complication of EGPA with the incidence of venous thromboembolism ranging from 5.8% to 30.0% and may be found in larger vessels unaffected by vasculitis [2, 3]. Several factors are proposed to explain the association between EGPA and thromboembolism, such as inflammatory diseases and eosinophilic inflammation. A possible explanation could be the ability of eosinophil cationic protein to activate the intrinsic pathway of coagulation through a factor XII-dependent mechanism [4]. Besides, the anticoagulant activities of vascular endothelial cells are inhibited by major basic protein binding to thrombomodulin and damage of eosinophil peroxidase, which promotes the formation of thrombosis [5].

Pulmonary arterial hypertension (PAH) is a rare condition of ANCA-associated vasculitis, and EGPA patients had PAH more frequently than controls in a retrospective and cross-sectional study [6]. Few literatures reported PAH secondary to EGPA without evidence of chronic thrombo-emboli [7, 8]. Pulmonary vascular thrombo-emboli can result in pulmonary hypertension, and it is known as CTEPH. CTEPH is diagnosed by the evidence of pulmonary artery hypertension via cardiac catheterization and the presentation of segmental perfusion defect on a V/Q scan.

Our patient had the event of acute pulmonary embolism, but the initial V/Q scan showed multiple segmental perfusion defects, which means CTEPH was favored. To our knowledge, this is the first report of EGPA patients with initial presentation of pulmonary embolism with CTEPH. Except for the standard of anti-coagulant therapy, we added anti-inflammation agents such as steroid and anti-IL5 monoclonal antibody (mepolizumab) therapy to treat EGPA.

A comprehensive study of the etiology of thromboembolism is necessary to approach the more benefit to the patient. Herein, we present a case of pulmonary embolism with CTEPH, who was diagnosed as EGPA with characteristics of asthma, peripheral eosinophilia, pulmonary infiltrates, and extravascular eosinophilic infiltration.

Conclusion:

EGPA is a small-vessel necrotizing vasculitis with specific features like asthma, eosinophilia and extravascular eosinophil infiltration. Thromboembolism is a complication of EGPA with several factors, such as inflammatory diseases and eosinophilic inflammation. CTEPH resulted from pulmonary vascular thrombo-emboli, and is diagnosed by cardiac catheterization and V/Q scan. Clinicians should

approach the appropriate treatment via clinical suspicion and detailed evaluation to get a better clinical improvement.

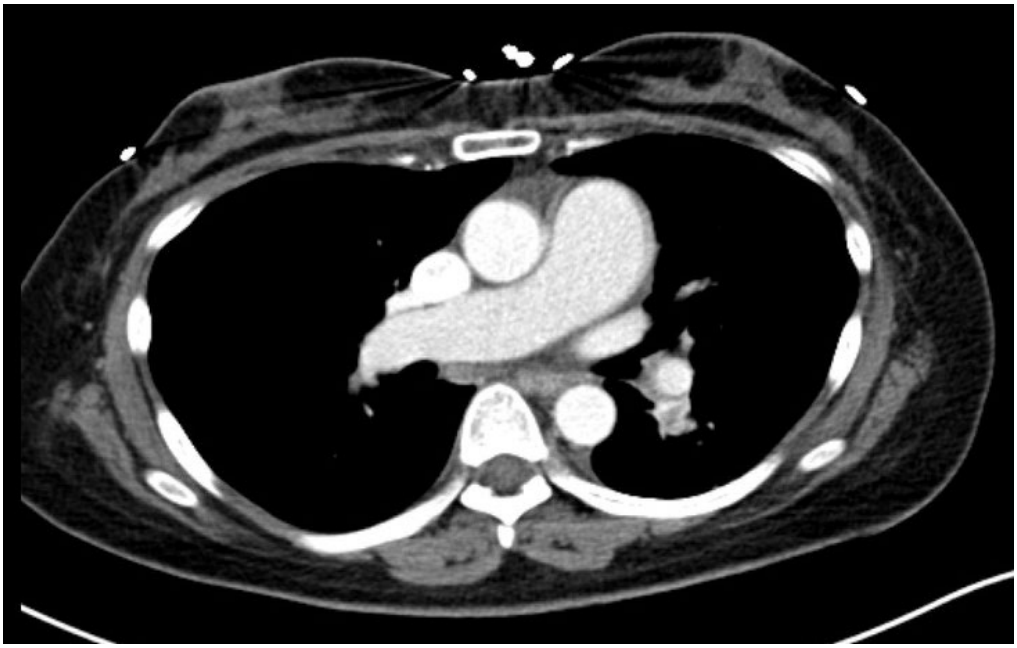


Fig. 1

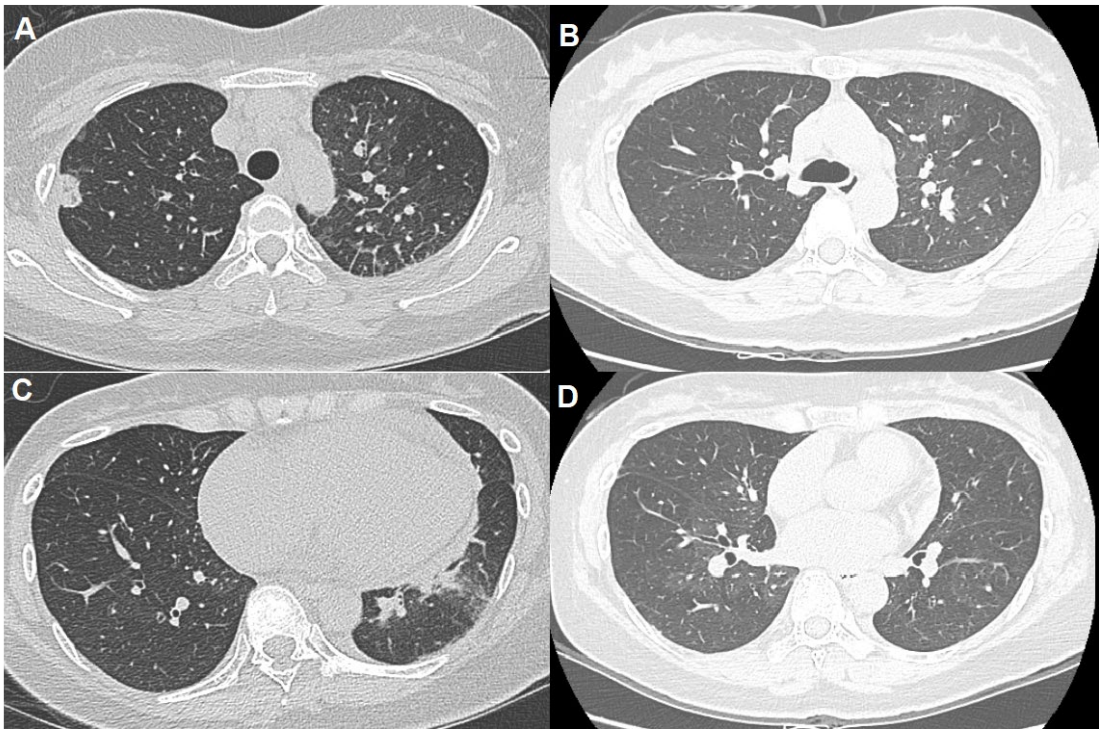
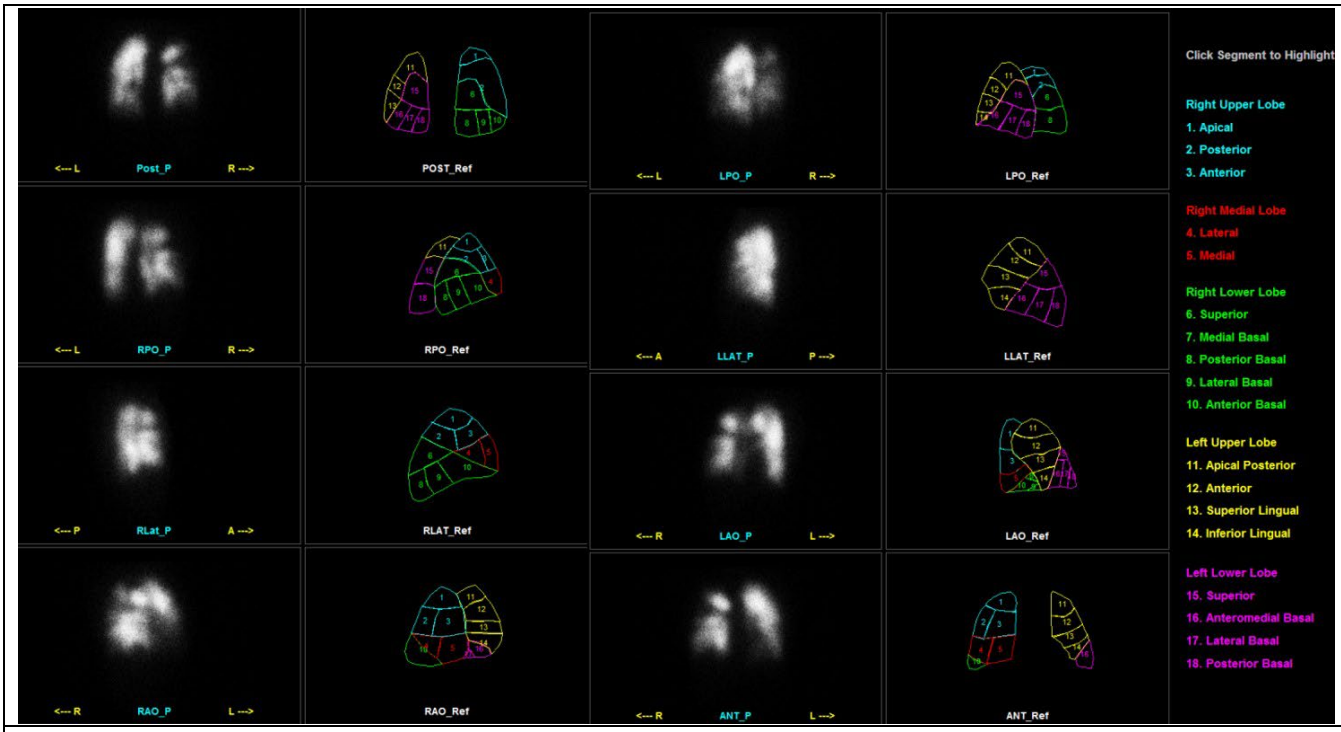


Fig. 2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8. Posterior Basal
9. Lateral Basal
10. Anterior Basal
Left Upper Lobe
11. Apical Posterior
12. Anterior
13. Superior Lingual
14. Inferior Lingual
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Fig. 3

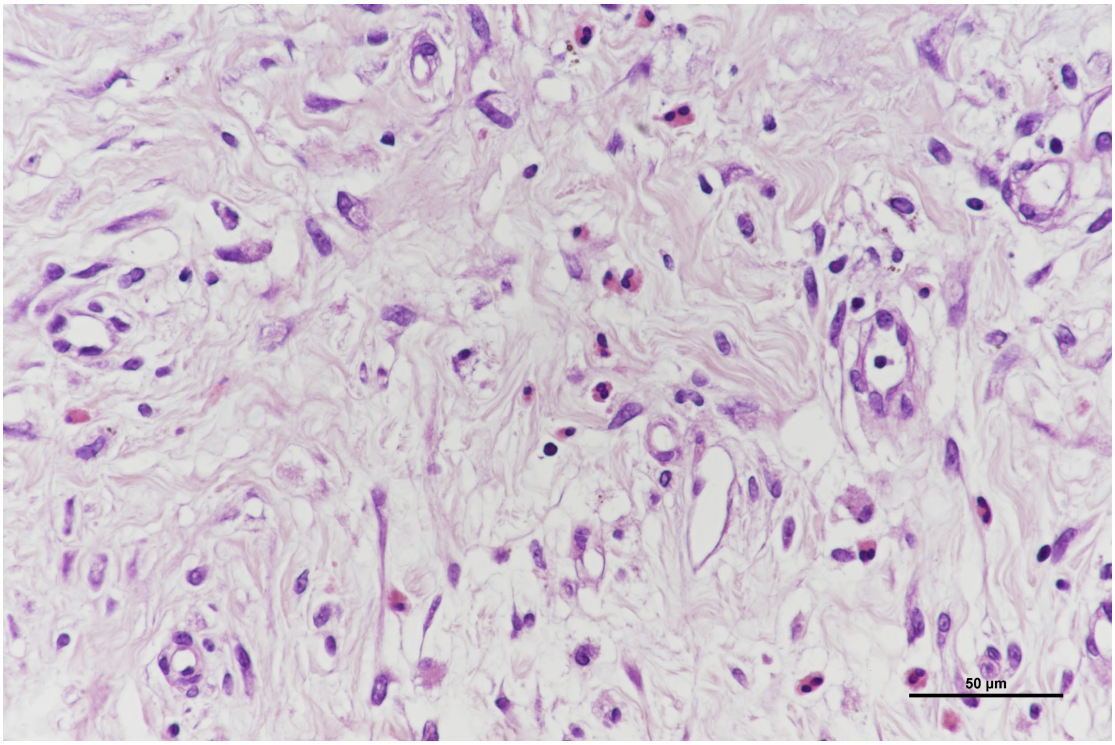
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Fig.4

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