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Case report

Acute eosinophilic pneumonia with sepsis-like symptoms of arthralgia, joint stiffness and lymph node enlargement: A case report

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A B S T R A C T

Background: Acute eosinophilic pneumonia (AEP) is an acute febrile disease with good prognosis. It is often manifested as cough, dyspnea and fever, and sometimes may also as myalgia. However, there are no reports of AEP with sepsis-like symptoms of arthralgia, joint stiffness, lymph node enlargement, transient rashes and abnormal liver function in the literature.

Case summary: A male patient with AEP was admitted to our hospital. He presented with fever, cough, arthralgia and joint stiffness, and also had transient rashes, lymph node enlargement and mild abnormal liver function. The counts of white blood cells and eosinophils were increased in peripheral blood. It seemed like sepsis, but his percutaneous lung biopsy suggested eosinophil inflammation, which had a good response to corticosteroids instead of antibiotics.

Discussion: AEP is easily misdiagnosed as bacterial pneumonia with sepsis when it presents with lung infiltration on CT and atypical manifestations such as arthralgia, joint stiffness, lymph node enlargement, transient rashes and abnormal liver function. In this case, if a lot more antibiotics do not work, some of possible diseases including AEP may be considered. Increased eosinophils in peripheral blood and lung biopsy are helpful for the diagnosis of the disease.

1. Introduction

Acute eosinophilic pneumonia (AEP) categorized within the heterogenous group of eosinophilic lung diseases, is associated with airway and/or lung tissue eosinophilia which rules out other causes of eosinophilia such as vasculitis and fungal/parasitic infections. Different from simple pulmonary eosinophilic infiltration, it is regarded as an independent clinical disorder now. Since Allen and Badesch reported the first case of AEP in 1989 [1], a lot more previous studies have been performed in different countries, such as America, Japan, Korea, China and so on. Usually, it is manifested as cough, dyspnea and fever. To our knowledge, this case of AEP with the same manifestations as sepsis (fever, arthralgia, joint stiffness, lymph node enlargement and so on) hasn't been reported in the literatures.

2. Case description

A 47-year-old man was hospitalized in a hospital of Guiyang city in China 10 days ago for possible pulmonary infection. On admission, he presented with fever, cough, redness of the pharyngeal tonsils, stiffness and pain of four limbs joints without redness, swelling and heat before receiving antibiotics treatment and blood test. After a few days, he was transferred to our hospital for poor control of his symptoms. We found the highest body temperature was 39.8 °C and that he showed a clear mind without delirium, convulsion and drowsiness. He had a chronic 20-year history of smoking, and denied any drug or dust exposure history, asthma, nasosinusitis, allergic history or any other medical history. Chest auscultation revealed extensive bilateral coarse crackles. The arterial blood gas test indicated pH 7.49, arterial blood carbon dioxide partial pressure ($PaCO_2$) 34.0 mmHg, arterial partial pressure of oxygen (PaO_2) 67.0 mmHg (oxygen via nasal cannula at a rate of 2L/min) and PaO_2/Fraction of inspiration oxygen (FiO_2) 231 mmHg. The counts of white blood cells were 18.32×10^9/L, neutrophils were 12.02×10^9/L (65.6%), and eosinophils were 3.81×10^9/L(20.8%). The results of serum C-reactive protein(CRP) was 128.02 mg/dL, erythrocyte sedimentation rate (ESR) was 83 mm/hour and blood culture was negative. Blood biochemistry: alanine aminotransferase (ALT) 72u/L, aspartate amino transferase (AST) 33U/L, and lactic dehydrogenase (LDH) 257U/L (Indicating slight abnormality of liver function). Pulmonary function test indicated mild restrictive ventilation dysfunction and small airway obstruction. Computed tomography (CT) showed marked patchy infiltrate in the left upper lobes with small amount of pleural effusions.

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(Fig. 1).

He was thought to have lobar pneumonia accompanied with suspected sepsis, so intravenous amoxicillin/potassium clavulanate, moxifloxacin and meropenem were successively given. However, there was no significant improvement of the symptoms after antibiotics treatment. His fever of 38–39 °C remained. The generalized joint pain/stiffness was aggravated, so he was unable to move autonomously, accompanied by chest tightness, shortness of breath, pharyngeal pain, dysphagia and transient rashes. The blood test indicated that the counts of white blood cells were 20.31 $\times$ 10^9/L, neutrophils were 13.74 $\times$ 10^9/L (67.7%), and eosinophils were 3.4 $\times$ 10^9/L(16.7%). The liver function showed ALT 207U/L and AST 151U/L. CT (Fig. 2) indicated no improvement of infiltrate in the lungs. He was found to have normal kidney function while workup for urinalysis, blood culture, sputum culture, streptococcus 'O', rheumatoid factor, anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies (ANCA), complement factors 3 and 4, beta-D-glucan, Epstein-Barr virus and abdominal ultrasound was also negative except for the B-ultrasonography revealing bilateral enlarged supraclavicular lymph node.

The potent broad-spectrum antibiotics therapy was ineffective and leukocytes and eosinophils abnormally increased, but neutrophils didn't, we had his percutaneous lung puncture biopsy performed for diagnosis, which showed obvious eosinophilic infiltration without loose connective tissue, necrotizing or granulomatous vasculitis. (Fig. 3). Then the patient was diagnosed with AEP, initiated with intravenous methylprednisolone at 40mg/day, and antibiotics were discontinued. The patient felt much better with significant improvement of the fever, cough, chest tightness, shortness of breath and joint dysfunction the next day. Before discharged from hospital, blood examination including peripheral blood cells counts, arterial blood gas test and liver function returned to normal and CT (Fig. 4) demonstrated improvement of the pulmonary infiltrate.Enlarged lymphnode shrank. The patient was initiated with intravenous methylprednisolone at 40mg/day for 4 days, then switched to oral prednisone on the fifth day (45mg/day) and tapered within 1 month by reducing 5mg every three days. On follow-up in clinic 1 month later, the patient was noted to have significant improvement in blood test (white blood cells 16.01 $\times$ 10^9/L, neutrophils 11.09 $\times$ 10^9/L(69.3%), and eosinophils 1.71 $\times$ 10^9/L(10.7%)) and chest radiography (CR) (Fig. 5).

3. Discussion

AEP is a pulmonary eosinophilic disease, and may represent an acute type I hypersensitivity reaction triggered. It is hypothesized to occur due to respiratory epithelial injury with subsequent eosinophil recruitment, degranulation and inflammation [2]. Its typical manifestations are cough, dyspnea and fever. Some patients may suffer from respiratory failure, even need mechanical ventilation. A few patients may feel myalgia, night sweat, chills, chest pain, arthralgia and even abdominal pain [3–5]. CT shows bilateral patchy areas of ground-glass attenuation, frequently accompanied by consolidation opacities and smooth interlobular septal thickening and small to moderate-sized bilateral pleural effusions [4,6,7]. Eosinophils count increases in BALF and/or peripheral blood, and lung biopsy eosinophils infiltration can be found [2]. It has good response to corticosteroids and the patient may recover rapidly. The diagnostic criteria [8]are as follows:1) acute respiratory illness of less than or equal to 1 month duration; 2) pulmonary infiltrates on CR or CT; 3) hypoxemia, with PaO2 on room air less than 60 mmHg, and/or PaO2/FiO2 less than or equal to 300 in arterial blood gas, and/or oxygen saturation on room air less than 90%; 4) pulmonary eosinophilia as demonstrated by more than 25% eosinophils in BALF (can be accompanied by variably increased percentages of lymphocytes and neutrophils) or eosinophilic pneumonia on lung biopsy (bronchoscopic or surgical) and 5) absence of other specific pulmonary eosinophilic diseases, including eosinophilic granulomatosis with polyangiitis (Churg Strauss syndrome), hypereosinophilic syndrome, and allergic bronchopulmonary aspergillosis. However, cases of AEP combined with lobe consolidation, arthralgia, joint stiffness, lymphnode enlargement, abnormal liver function, transient rashes and markedly elevated white blood cells have not been reported yet in the world. It is important to distinguish this disease with those with the similar manifestations.

The patient met the diagnostic criteria above: 1) fever and cough less than 1 month; 2) pulmonary infiltrates on CT; 3) peripheral blood eosinophilia and eosinophilia pneumonia confirmed by percutaneous lung biopsy; 4) arterial blood gas analysis indicated hypoxemia, 5) absence of other specific pulmonary eosinophilic diseases. After corticosteroid treatment, his symptoms and lung infiltration improved rapidly, so he was diagnosed with AEP. Since we could not find a cause for this disease, it was thought to be idiopathic. Different from other cases reported, the patient had joint stiffness, transient rash, superficial lymphnode enlargement, mild liver function damage and obvious increase of peripheral blood leukocytes at the same time in addition to fever, cough and arthralgia. It seems like eosinophilic granulomatosis with polyangiitis (EGPA), formerly called Churg-Strauss syndrome, a rare systemic, small-to-medium vessel vasculitis associated with asthma, sinusitis, blood and tissue eosinophilia [9]. However, the patient denied the history of asthma, sinusitis or allergy, and his ANCA were negative. The lung biopsy did not indicate necrotizing vasculitis, which didn't suggest the diagnosis of EGPA [10]. The syndrome of drug reaction with eosinophilia and systemic symptoms (DRESS) is also associated with eosinophil infiltration, lymphadenopathy, rash, liver dysfunction and respiratory failure, which has good response to corticosteroids therapy. Patients with pulmonary manifestations commonly present with dyspnea, cough and/or pleurisy [11]. It's usually misdiagnosed as pneumonia and treated with antimicrobials. But the disease is an acute, idiosyncratic, and potentially life-threatening drug reaction, usually starts abruptly 2–3 weeks after the introduction of the culprit drug containing antimicrobials, anticonvulsants, allopurinol and so on [12], which is quite different from AEP. In our study, the patient denied any drug exposure history before the first hospitalization, and we found his

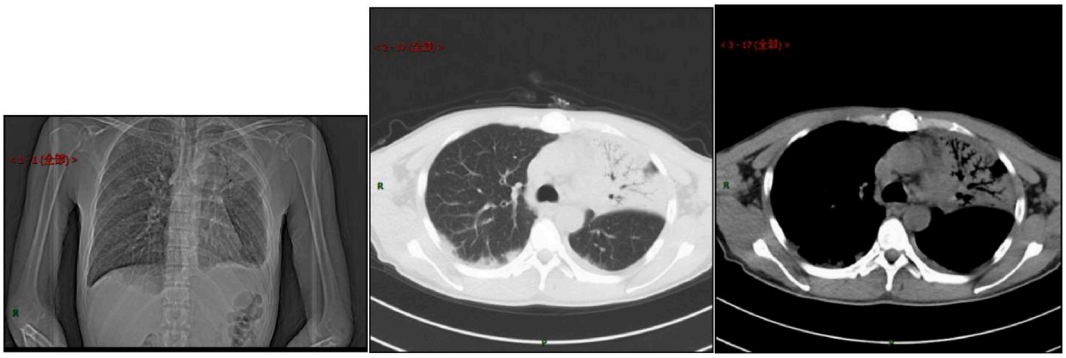

Fig. 1. CT showed marked patchy infiltrate in the left upper lobes with small amount of pleural effusions.

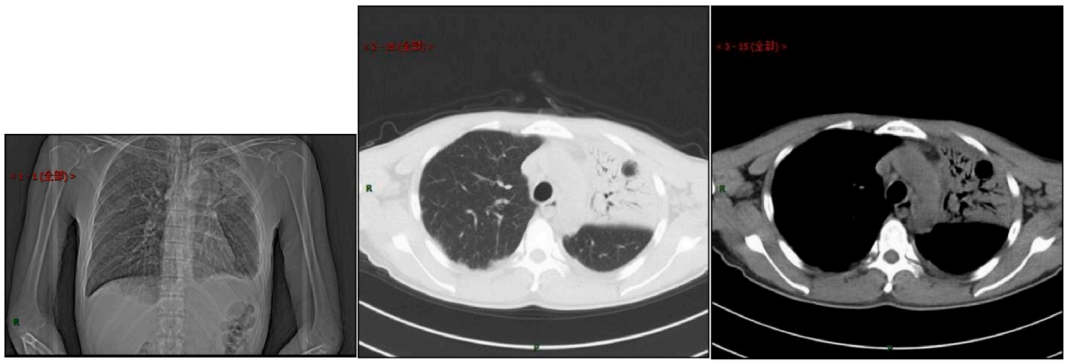

Fig. 2. CT done after antibiotics treatment showed no improvement in left lung.

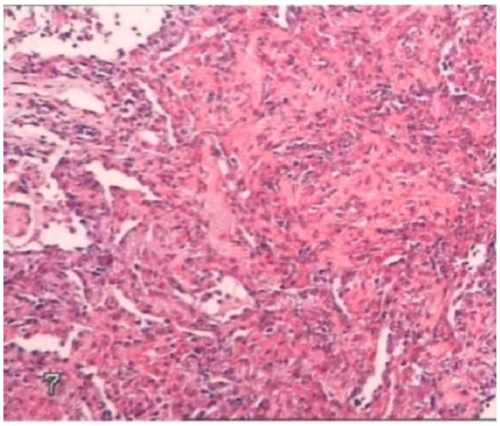

Fig. 3. Pathological biopsy of percutaneous lung biopsy showed eosinophilic pneumonia(× 100).

fever, cough and marked eosinophils in peripheral blood had already occurred before antibiotics use in the first hospital by looking through the medical record, indicating the occurrence of diseases had nothing to do with any drug. The course of the disease was less than 1 month, and no damage of nervous system was found. In addition, the rheumatoid factor, complement factors 3 and 4 and abdominal ultrasound were normal. So, hypereosinophilic syndrome was ruled out. Since the sputum culture and beta-D-glucan were negative and he hadn't received any antifungal treatment, allergic bronchopulmonary aspergillosis (ABPA) was not considered. Since loose connective tissue was not found in the lung biopsy, organizing pneumonia was also excluded. Unlike pneumonia with sepsis, the elevation of neutrophil was not obvious, repeated blood culture was negative, and potent broad-spectrum antibiotics therapy was ineffective. So, sepsis was excluded. This disease was also similar to adult onset Still's disease(AOSD) [13], which is a systemic inflammatory disorder of unknown etiology, characterized by a high spiking fever, evanescent salmon-colored maculopapular rash, arthritis, and leukocytosis [14], but the patient's eosinophilia was marked in the course of the disease, which was different from AOSD. Considering the diagnosis of AOSD was based on exclusion of other diseases, we final diagnosed him with AEP.

Author contributions

JJL and ZWS were responsible for the initial plan, study design, manuscript drafting and performance of the study.

BT and TMZ were responsible for data collection, supervision, and critical revision of the manuscript.

CZ act as the guarantors for this article and take full responsibility for this study.

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Registration of clinical trial

None.

Statement

All authors have read and approved the final manuscript.

Data sharing

No additional data available.

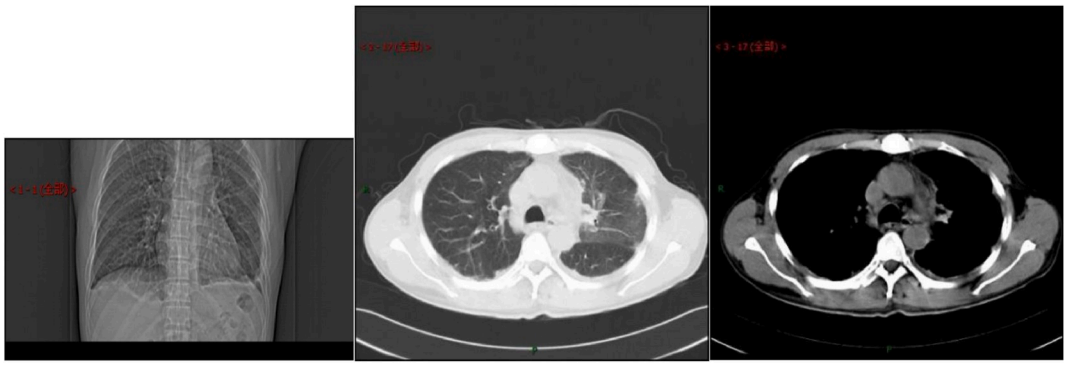

Fig. 4. CT done before discharged from hospital showed resolution of pulmonary infiltrate.

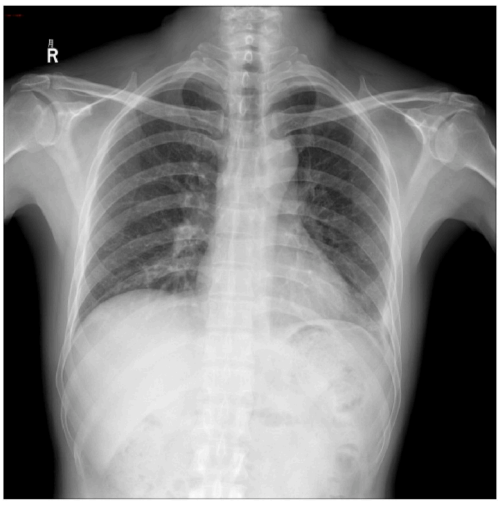

Fig. 5. CR showed no obvious abnormality.

Declaration of competing interest

The authors declare that they have no conflict of interest exits in the submission of this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2020.101072.

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