

Acute eosinophilic pneumonia triggered by secondhand cigarette smoke exposure in an elderly man

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Abstract

The spectrum of eosinophilic lung diseases comprises a diverse group of pulmonary disorders associated with tissue or peripheral eosinophilia. Acute eosinophilic pneumonia (AEP) is an uncommon eosinophilic lung disease that can be idiopathic, but identifiable causes include medications, inhalational exposures and infections. Most cases in the literature are associated with first-time cigarette smoking or resuming smoking. Herein, we present a case of AEP in an elderly man triggered by exposure to secondhand tobacco smoke, in whom a transbronchial biopsy was diagnostic. The patient recovered fully with glucocorticoid therapy without recurrence after avoiding further secondhand smoke.

Introduction

Acute eosinophilic pneumonia (AEP) is an uncommon eosinophilic lung disease. Diagnosis is based on an acute onset of symptoms, lung opacities on chest imaging and pulmonary eosinophilia. Commonly confused with community-acquired pneumonia, this condition improves within days with corticosteroid treatment. While some cases are idiopathic, multiple causes have been identified, most importantly tobacco smoking, along with other toxins, medications and infection [1]. Exposure to secondhand smoke has been reported in only two cases [2,3].

We present a case of an elderly patient with AEP triggered by exposure to secondhand tobacco smoke diagnosed by transbronchial biopsy.

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Case Report

A 72-year-old man experienced 2 weeks of progressive dyspnea with exertion, 1 week of malaise, fatigue, palpitations, cough productive of clear sputum, and 3 days of fever. He reported dyspnea with minimal activity on admission. He was generally healthy at baseline, and had quit cigarette smoking 25 years ago (15 pack-year history). He occasionally smoked marijuana without any recent change in pattern or intensity. He reported very bothersome and recent exposure to heavy secondhand tobacco smoke in enclosed rooms at home after starting a new relationship with someone who smoked cigarettes heavily.

On admission, temperature was 38.3 C and white blood cell count (WBC) was 24.4 K/mL cell differential: eosinophils 20.1% (4.9 K/mL), neutrophils 41.8%, lymphocytes 32.7%, monocytes 5.2% and basophils 0.2%. SpO₂ was 92%; nasal cannula (NC) oxygen 2 L/min was started. Scattered rhonchi, decreased breath sounds at bases, crackles in mid lungs, normal respiratory effort and a systolic murmur grade 3/6 in the right upper sternal border were noted. Chest x-ray showed bibasilar patchy airspace opacities, and computed tomography showed areas of consolidation in all lobes most evident in the lower lobes, bronchovascular bundle thickening, septal markings, enlarged hilar and subcarinal lymph nodes and a small right pleural effusion (Figure 1). The findings were most compatible with pneumonia, but sarcoidosis or lymphoma were in the differential.

The patient was started on ceftazidime and vancomycin for possible community acquired pneumonia and sepsis. Blood and sputum cultures, respiratory viral panel, *Legionella* and *Streptococcus pneumoniae* urinary antigens were all negative.

Because of the peripheral eosinophilia, eosinophilic lung disease, in particular AEP was also suspected. Immunoglobulin (Ig)E, anti-neutrophil cytoplasmic antibody panel, C-reactive protein and erythrocyte sedimentation rate were normal except for total IgE elevated at 484 IU/ml. Echocardiogram demonstrated severe calcific aortic stenosis with valve area 0.8 cm² and moderate pulmonary hypertension; bronchoscopy was postponed pending cardiac evaluation. Over the next 2 days there was marked clinical deterioration: WBC peaked at 48.8 K/mcL, with worsening bibasilar opacification and new bilateral pleural effusions on chest x-ray, increased work of breathing and tachypnea. Arterial blood gas showed severe hypoxemia: pH 7.36, PCO₂ 42, PO₂ 62, SaO₂ 88 on 5 l/min oxygen NC. Antibiotics were switched to linezolid and piperacillin-tazobactam, and due to imminent respiratory failure methylprednisolone 60 mg intravenously every 12 h was started. Ultrasound revealed a moderate right and large left pleural effusion, with 850 ml serosanguineous fluid removed via a left thoracentesis. Because of prior good functional status, the patient was deemed stable from a cardiac standpoint for bronchoscopy.

Two days later, WBC was 39.8 K/mcl with normalization of eosinophil count to 0.4% (0.2 K/mcl). The patient felt much better on 3 l/min oxygen NC. Diagnostic bronchoscopy was performed while intubated. Diffuse tracheobronchomalacia with airway collapse was noted despite positive end-expiratory pressure 8 cm H₂O. Bronchoalveolar lavage (BAL) was performed in the lingula and left upper lobe with poor return in both sites. Transbronchial needle aspiration with endobronchial ultrasound of the enlarged lymph nodes and 6 transbronchial biopsies of the lung parenchyma were also performed without complications.

Over the following 2 days, WBC continued to decrease, oxygen was weaned off, and symptoms resolved with improved bibasilar opacities on chest x-ray. BAL was acellular and non-diagnostic. Lymph node cytology was normal. Pathology revealed

eosinophilic pneumonia (Figure 2), confirming the diagnosis of AEP. The patient was discharged on prednisone 40 mg daily with follow up in 4 weeks to initiate taper. He came off prednisone and avoided further exposure to secondhand smoke. One year later there was no recurrence (Figure 1).

Discussion

AEP is an uncommon eosinophilic lung disease. We present a case of an elderly patient with AEP triggered by exposure to secondhand tobacco smoke, confirmed by transbronchial biopsy. This patient developed AEP attributed to recent heavy indoor secondhand smoke exposure. There have been only two previously reported cases of secondhand smoke associated with AEP [2,3]. Other potential triggers were investigated. Although the patient occasionally smoked marijuana and this has been also associated with AEP in two cases [4,5], there had been no change in intensity or frequency of use. At 72 years old, the patient was also significantly older than the usual reported age of 20 to 40 years of age [1].

AEP is frequently confused with community-acquired pneumonia upon presentation. It is very important to make the correct diagnosis as this disease responds completely to corticosteroid treatment but can rapidly lead to respiratory failure and be fatal if misdiagnosed. The hallmark of AEP is pulmonary eosinophilia, with BAL >25% eosinophils in cell differential or eosinophilic pneumonia on lung biopsy required for diagnosis. Peripheral blood eosinophilia may not be present at presentation but eventually occurs in most cases [1]. In this case, both the recent inhalational exposure and peripheral eosinophilia were early clues to a possible AEP diagnosis.

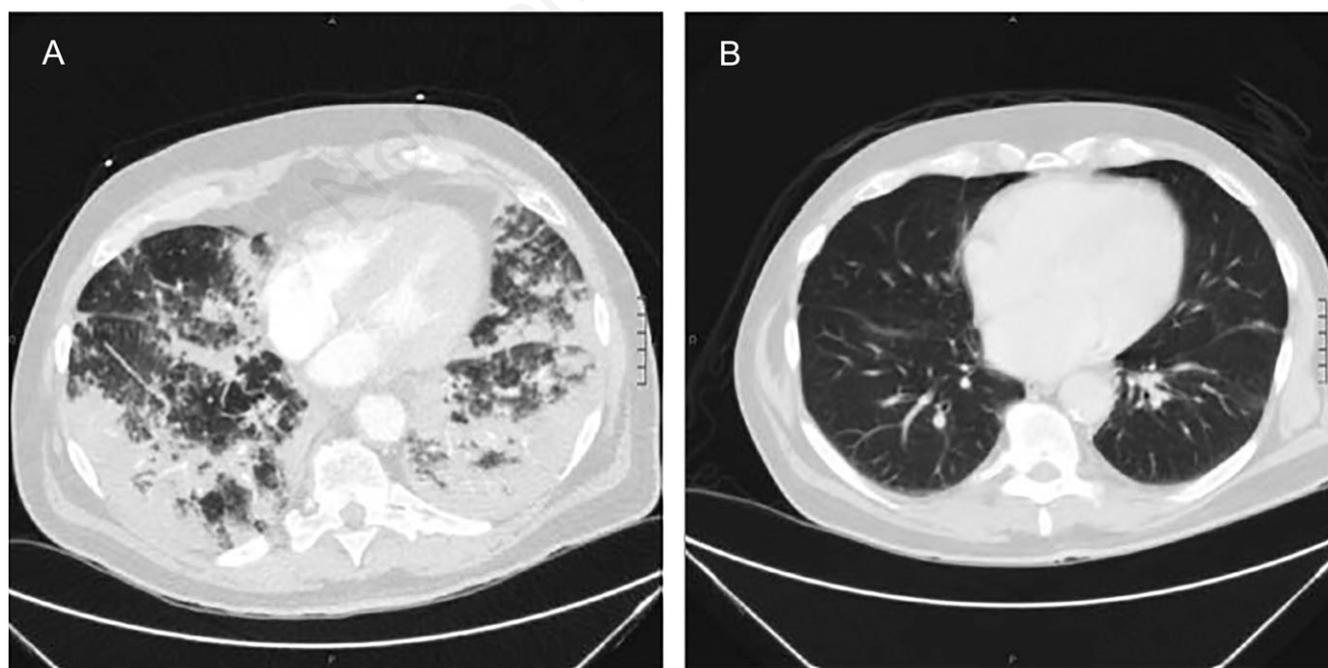


Figure 1. A) Computed tomography of the chest showing areas of dense parenchymal consolidation in the lower lobes, thickening of the bronchovascular bundle and septal markings. B) Five months later, findings resolved.

Lung biopsy -usually transbronchial- is less likely to be performed in AEP because the diagnosis can be made with BAL and patients may get ill quickly making biopsy riskier, but may be indicated when there are atypical features that suggest an alternative diagnosis [1]. In this case, imaging suggested the possibility of sarcoidosis or lymphoma, and thus the decision to perform biopsy, without which the diagnosis would have been missed. Given paucity of literature, it is difficult to provide a concrete number of passes required for achieving diagnosis of AEP. We recommend obtaining 4-8 transbronchial biopsies/pieces (with 4 adequate pieces) when evaluating patients with diffuse parenchymal opacities. We performed a total of 6 biopsies, which is similar to the number (6±2) performed in a study of 169 immunocompetent outpatients with various pulmonary diagnoses [6] and represents common practice amongst various pulmonologists.

There are potential pitfalls associated with relying only on BAL to make a diagnosis and start treatment for AEP. We favor that if a good quality BAL can be obtained resulting in a reliable cell count assessment, and clinical-radiological correlation favors AEP, a lower cut-off value of eosinophil count could be used as diagnostic criteria; but which cut-off value to use remains unclear. However, a high quality BAL (>50% return from representative lung segment, with visible surfactant) resulting in a reliable cell count may not be possible due to patient (airway collapsibility, cough interfering with wedge position of the scope, *etc.*) or operator factors, and in these situations transbronchial biopsies may be helpful provided the patient has no contraindications for the sampling and the procedure is feasible. BAL eosinophilia has also been shown to resolve a few days after the start of corticosteroid therapy [7]. Additionally, BAL eosinophils can be degranulated and demonstrate multiple nuclear lobes, resembling neutrophils, and this could potentially lead to a mistaken neutrophilic pattern on BAL [1]. In our case transbronchial biopsy was quite helpful in making a diagnosis.

While >25% BAL eosinophils is the diagnostic criteria if no biopsy, this level might also be too stringent. There have been several cases of AEP diagnosed with a lower eosinophil level or even

a normal count. There is a case report of a BAL with neutrophil predominance without eosinophils [8]. The diagnosis was confirmed with transbronchial biopsy and the authors speculated this may have been related to early disease. In a series of 22 patients with AEP, 3 patients (14%) also had a normal BAL eosinophil count (<1%) [9]. Other series have also reported values <25%. In 45 patients with AEP, only 36 (80%) had BAL eosinophils >25% [10]. A case series of AEP reported [11] >25% eosinophils in BAL in 2 out of 6 cases, and in only 16 out of 31 (52%) cases in its accompanying literature review. In another report involving 2 cases, one had BAL eosinophils of 17% [12]; the authors discussed the difficulty with the current diagnostic criteria [6,13], and argued that adherence to strict cut-offs may limit the number of diagnoses. They proposed substituting >25% BAL eosinophils with any abnormal value of BAL % eosinophils [12].

Conclusions

To our knowledge, the current case is the third report of a patient with AEP associated with secondhand tobacco smoke exposure. In addition, this was an elderly patient and the diagnosis was confirmed by transbronchial biopsy because of a nondiagnostic BAL. Bronchoscopy was delayed prompting the start of empiric corticosteroid therapy for impending respiratory failure with almost immediate clinical improvement. This illustrates the potential role for empiric therapy in suspected AEP after a careful risk/benefit assessment, in cases where diagnostic procedures are not feasible or nondiagnostic. This case and the review of the prior cases also bring attention to potential limitations of BAL testing to diagnose and, most importantly, initiate therapy in this disease, and suggest that current BAL diagnostic criteria for AEP may need to be reevaluated. The question of whether a specific cut-off value of BAL % eosinophils in an adequate sample would be diagnostic, or whether the addition of transbronchial biopsy may be required needs further study.

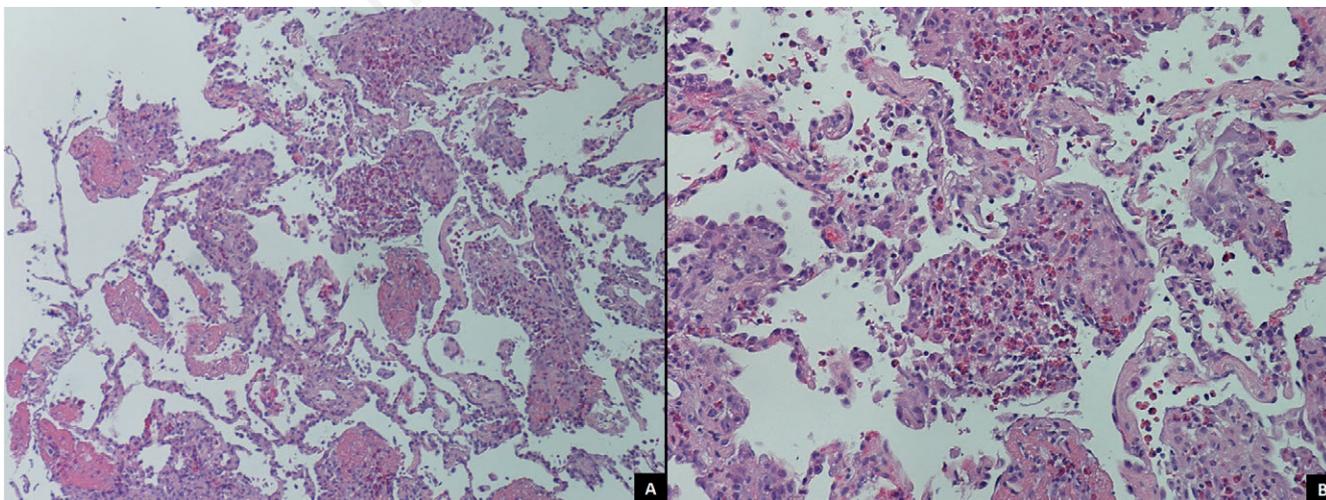


Figure 2. A) Low power view of the lung showing intra-alveolar eosinophils mixed with macrophages and fibrin; there is also interstitial eosinophilia with perivascular predilection; the bronchiole is spared showing no significant inflammation or eosinophilia; H&E, x100. B) Higher power view of the lung showing abundant interstitial and intra-alveolar eosinophils associated with reactive pneumocytes; H&E, x200.

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