

Idiopathic Acute Eosinophilic Pneumonia

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Idiopathic acute eosinophilic pneumonia (IAEP) is a rare disease but of clinical importance because of its good prognosis if treated promptly and appropriately. The etiology remains unknown and the temporal relationship between IAEP and a history of recent onset of cigarette smoking has been described. We report a typical case of a 21-year-old male with recent onset of smoking, who presented with acute febrile hypoxemic respiratory failure. High-resolution chest computed tomography scan revealed patchy ground glass opacity and ill-defined nodules, diffuse interlobar and interlobular septal thickening, and bilateral small amount of pleural effusion, which mimicked congestive heart failure except that the heart size was within normal limits. Bronchoalveolar lavage (BAL) was performed soon after the patient was admitted and remarkable eosinophilia was noted in BAL fluid. Clinical condition and chest radiographs improved dramatically after corticosteroid treatment. Because effective treatment and prompt institution of therapy can obviate unnecessary morbidity and mortality, IAEP should be kept in mind when treating patients presenting with diffuse parenchymal lung disease and acute respiratory failure. In that case, BAL is valuable and should be performed as soon as possible. [*J Chin Med Assoc* 2006;69(7):330–333]

Key Words: bronchoalveolar lavage, eosinophilic, pneumonia, smoking

Introduction

Idiopathic acute eosinophilic pneumonia (IAEP) is a rare disease and <100 cases have been reported to date, with the largest series including only 22 patients.¹ It is characterized by acute febrile hypoxic respiratory failure and diffuse pulmonary eosinophilia without concurring allergy or infection in the lung. Because the clinical presentation is very similar to acute interstitial pneumonitis (AIP) and acute respiratory distress syndrome (ARDS), it is easily misdiagnosed and delayed for treatment if bronchoalveolar lavage (BAL) is not performed promptly. The etiology remains unclear; however, as reported in previous studies,^{1,2} it is closely associated with recent onset of cigarette smoking. Corticosteroid remains the mainstay of therapy and relapses have not been reported.^{1,3,4} We present a young male who had a recent history of smoking and suffered from acute respiratory failure with rapid progression of chest radiographs. He showed spontaneous

partial improvement during hospitalization and responded to corticosteroid dramatically.

Case Report

A 21-year-old male college student called on a local hospital because of dry cough and high fever for 1 day. Chest radiograph was taken (Figure 1A) and he was discharged with oral antibiotics and symptom relievers. Within 24 hours, however, the fever returned and he became dyspneic progressively. He was sent to our emergency department with a pulse rate of 111 beats/minute, blood pressure of 113/66 mmHg, ear temperature of 38°C, and respiration rate of 20 breaths/minute. Breathing sound showed bilateral crackles. Chest radiograph revealed diffuse reticulo-nodular infiltrates in both lungs (Figure 1B). Chest computed tomography (CT) scan showed patchy ground glass opacity and ill-defined nodules, diffuse

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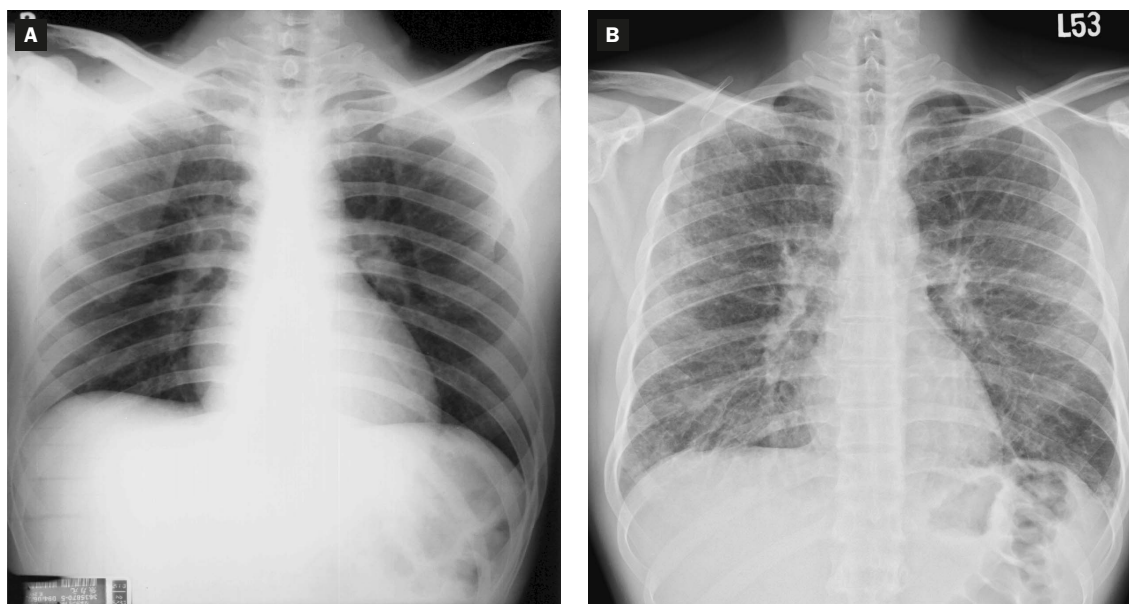


Figure 1. Rapid progression of chest radiographs. (A) Almost normal when patient was first presented in a local hospital. (B) Within 24 hours, diffuse reticulonodular infiltrates appeared in both lungs.

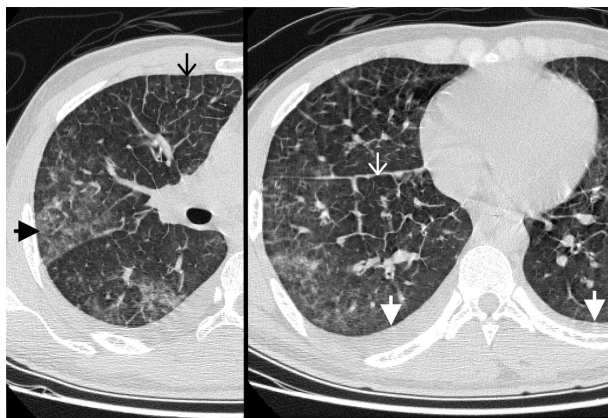


Figure 2. High-resolution chest computed tomography revealed patchy ground glass opacity and ill-defined nodules (large black arrow), diffuse thickening of interlobar (small white arrow) and interlobular septa (small black arrow), and bilateral small amount of pleural effusion (large white arrow). The heart size was within normal limits.

thickening of interlobar and interlobular septa, and bilateral small amount of pleural effusion (Figure 2). The laboratory examination revealed a white blood cell count of $17,900/\text{mm}^3$, with 95% neutrophils and 5% lymphocytes. Serum total IgE was 152 kU/L (normal, $<300 \text{ kU/L}$). The results of serologic tests were negative for HIV, chlamydia, mycoplasma, herpes simplex virus, Epstein-Barr virus, and cytomegalovirus. The arterial blood gas measurements performed in room air were as follows: pH, 7.424; PaO_2 , 59 mmHg; PaCO_2 , 37 mmHg. The patient was a student and

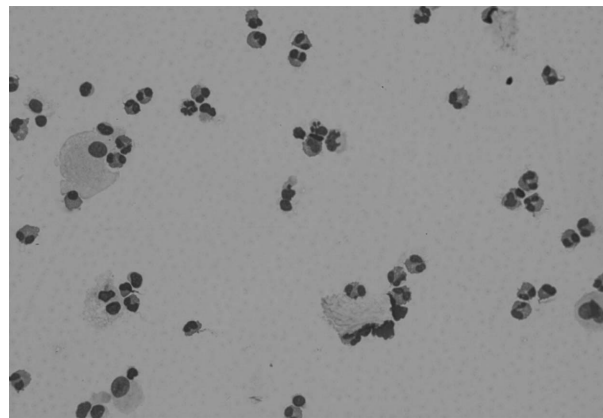


Figure 3. Liu-stained smear of bronchoalveolar lavage fluid showed a markedly increased percentage of eosinophils.

had worked in a barbecue restaurant as a waiter for 8 months. He denied any history of drug abuse, insect bite or travel history in the past 3 months, but admitted to smoking half a pack of cigarettes per day since about 2 weeks prior to this episode. Treatment started on admission with oxygen and empiric antibiotic with moxifloxacin. Thoracocentesis yielded exudate with 95% neutrophils and 5% lymphocytes. BAL with 150 mL normal saline was performed in the anterior segmental bronchus of the right upper lobe to demonstrate an increased total cell count ($14.9 \times 10^6/40 \text{ mL}$) with 52% eosinophils, 29.5% macrophages, 14% lymphocytes, and 4% neutrophils (Figure 3). The $\text{CD4}^+:\text{CD8}^+$ lymphocytes ratio was 1.7. Culture of the BAL fluid was negative for bacteria,

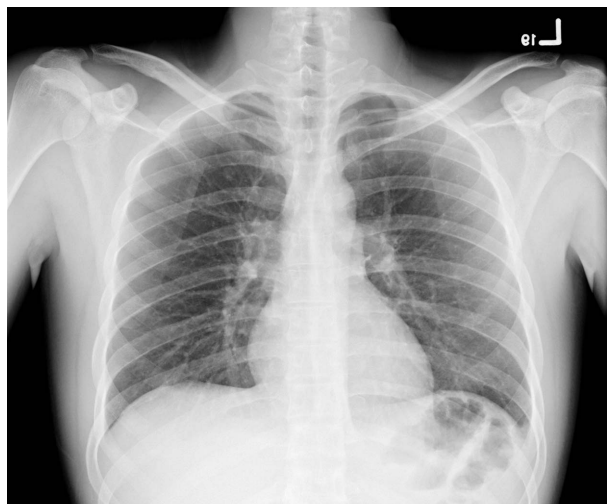


Figure 4. Rapid resolution of chest radiograph taken 4 days after corticosteroid treatment.

fungus, mycobacterium, and virus. Cytologic examination revealed no malignant cells or pneumocystis carinii. Pathologic examination of tissue obtained by bronchoscopic biopsy revealed nonspecific epithelial hyperplasia. Under the impression of IAEP, methylprednisolone (2 mg/kg/day) was prescribed and the clinical condition improved within 1 day. The chest radiograph taken 4 days after steroid treatment showed nearly complete resolution of the infiltration (Figure 4). We treated the patient with empiric antibiotics first, followed by corticosteroid after BAL. Because of the rapid resolution observed in chest radiographs, we could affirm that corticosteroid played a major role in the treatment response in this case. The patient was discharged with oral prednisolone and the follow-up radiographs taken 2 months later revealed no sequelae.

Discussion

IAEP was first described as a cause of acute respiratory failure by Allen et al⁴ and Badesch et al⁵ in 1989. The criteria currently proposed for diagnosis are: (1) acute onset of symptoms, usually <7 days; (2) fever; (3) bilateral infiltrates on chest radiograph; (4) severe hypoxemia with $\text{PaO}_2 < 60$ mmHg, and/or an alveolar-arterial gradient > 40 mmHg; (5) pulmonary eosinophilia with $> 25\%$ eosinophils in BAL fluid; (6) no history of hypersensitivity to drugs, no evidence of infection, and no other known cause of eosinophilic lung disease. However, as suggested by Tazelaar et al,⁶ symptoms lasting > 7 days do not exclude the diagnosis of IAEP. In a study series on 22 patients by Philit et al,¹ the duration of symptoms ranged between 1 and 30 days

and exceeded 7 days in 7 patients. Thus, the diagnostic criteria of IAEP should include duration of symptoms for up to 1 month. A milder form of IAEP without respiratory failure should also be taken into account.

IAEP is a rare disease with < 100 cases reported to date, and the etiology remains unknown. A temporal relationship has been described between IAEP and a history of recent onset of cigarette smoking.^{7,8} In 18 case series of US military personnel deployed in and around Iraq,² all the patients reported tobacco smoking and 78% were new smokers with a median duration of 1 month prior to illness. Due to the high incidence of smoking and the rarity of IAEP, it is unlikely that smoking is the simple cause of IAEP; however, exposure to smoke or other environmental agents may induce an eosinophilic reaction.¹ In the previous studies, the patients were usually young, with an average age below 30 years, and predominantly male. Patients usually presented with fever and dyspnea. Chest radiographs showed bilateral infiltrates, which could be airspace opacities, interstitial reticulonodular densities, or mixed airspace and interstitial patterns.^{1,3,9} The high-resolution chest CT findings included diffuse areas of ground-glass attenuation, nodules, smooth interlobular septal thickening, and pleural effusion.¹⁰ It may mimic patterns seen in patients with congestive heart failure, except that the heart size is within normal limits. Pulmonary parenchymal infiltrate with eosinophils was the pathologic hallmark of IAEP. BAL was the major diagnostic tool for documentation of pulmonary eosinophilia.¹ Characteristically, analysis of BAL fluid showed an increased percentage ($> 25\%$) in the total number of eosinophils. In addition, it was not unusual to see an increased percentage of lymphocytes and neutrophils.^{1,3,11} The $\text{CD4}^+ : \text{CD8}^+$ lymphocytes ratio in BAL fluid was variable.¹¹ Surgical lung biopsy may be considered in immunocompromised patients with acute pneumonia of unknown etiology, particularly when fungal infection is suspected.³ However, BAL fluid analysis with a careful screening of medical history may provide a reliable diagnosis of IAEP in nonimmunocompromised patients and obviate the need for open lung biopsy.¹ Unlike idiopathic chronic eosinophilic pneumonia and other eosinophilic lung diseases, it is unusual to see peripheral hyper eosinophilia in IAEP patients. Elevated serum IgE level has been reported in some cases; however, it neither rules in nor rules out the diagnosis of IAEP.

Conventionally, IAEP is considered in patients presenting with acute febrile illness and hypoxic respiratory failure, which usually requires mechanical ventilation. IAEP is also characterized by responding dramatically

to corticosteroid therapy within 48 hours. The radiographic changes improved quickly, from 4 to 11 days in 1 series.² A milder form of IAEP has also been reported and some patients recovered spontaneously.^{1,2,12,13} Although the efficacy of corticosteroid has not been fully demonstrated, it is still recommended as a routine treatment in patients with life-threatening hypoxemia.¹ IAEP has a very similar clinical picture to AIP and ARDS. However, IAEP must be distinguished between AIP and ARDS since the prognosis of IAEP is excellent if corticosteroid therapy is instituted promptly.

We present a typical case of IAEP in a young man who had recent onset of smoking and presented with acute febrile hypoxemic respiratory failure. Clinical condition and chest radiographs improved dramatically after corticosteroid treatment. Although IAEP is a rare disease, it should be kept in mind, not only for pulmonary specialists but also for general internists, because there is an effective treatment and prompt institution of therapy which can obviate unnecessary morbidity and mortality. Thus, IAEP should be in the list of differential diagnoses in patients with diffuse parenchymal lung disease and acute respiratory failure, and BAL should be performed as soon as possible if IAEP is considered.

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