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Case Report

Crystal Amphetamine Smoking-Induced Acute Eosinophilic Pneumonia and Diffuse Alveolar Damage: A Case Report and Literature Review

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Abstract

Eosinophilic pneumonia (EP) is a disease characterized by prominent infiltration of lung structures by eosinophils. The lung interstitium is infiltrated by eosinophils, and essentially the alveolar spaces are filled with eosinophils and a fibrinous exudate, with conservation of the global architecture of the lung. Diagnosis of EP relies on pathological demonstration of alveolar eosinophilia along with characteristic clinical manifestations of nonproductive cough, dyspnea, chest pain and/or unique imaging features. EP may be categorized according to the origin: EP of undetermined origin may overlap with well-individualized syndromes, while EP with a definite cause is mainly due to infections or drug abuse. Here, we report a case of an amphetamine abuser who developed acute EP and acute respiratory distress syndrome after amphetamine inhalation. Related studies on the pathogenesis of stimulant-related lung injury and treatment strategies are also discussed.

Key Words: acute eosinophilic pneumonia, amphetamine, diffuse alveolar damage, free radicals

Introduction

Eosinophilic pneumonia (EP), initially termed Loeffler syndrome, was first identified in 1932. This disease was described as an association between pulmonary infiltrates and peripheral eosinophilia. A vast number of drugs and toxic exposures have been associated with the development of pulmonary infiltrates and blood or pulmonary eosinophilia (7, 9). However, EP has seldom been reported in connection with inhalation substances. Possibility of EP was seldom considered when encountering inhaled drug abusers. However, EP can be life threatening, highlighting the importance of disease identification and forming correct treatment strategies. Diagnosis by histopathology is still the standard option, and the cornerstone of treatment is corticosteroid administration. However, antioxidant therapy has been suggested as a novel treatment option. Further studies are warranted for this disease.

Case Report

A previously healthy 31-year-old man presented with high fever, productive cough and dyspnea three days prior to admission. A chest radiograph obtained

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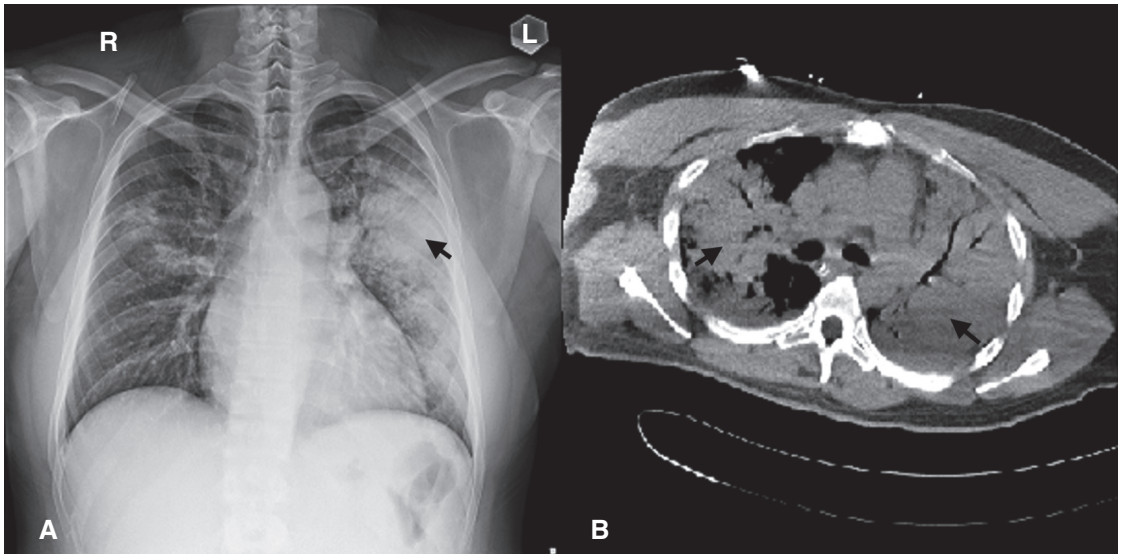

Fig. 1. Initial chest radiograph demonstrated (A) bilateral, peripherally predominant lung opacities (black arrow) and rapid progression of lung infiltrations after transferring to the ward. (B) Chest CT demonstrated bilateral consolidation with air-bronchogram (black arrows).

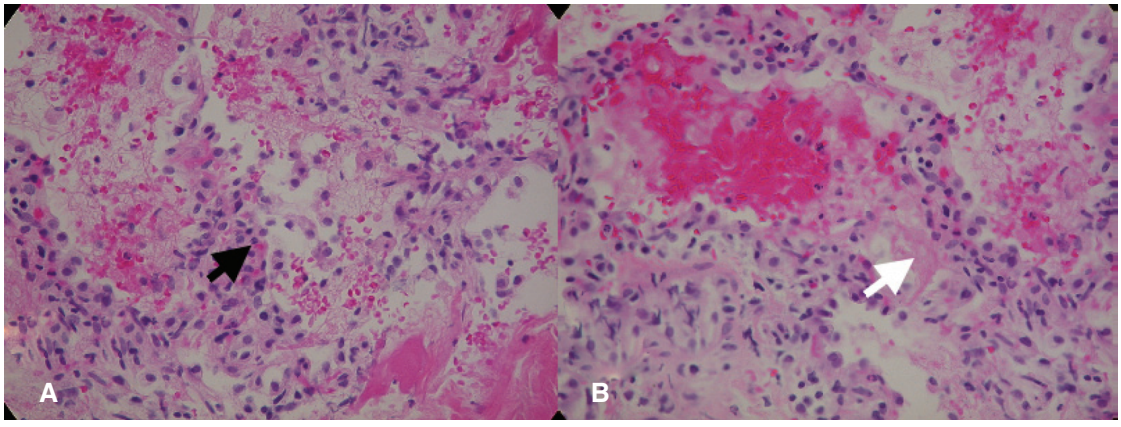

Fig. 2. Photomicrograph from sonography-guided lung biopsy showed (A) filling of alveolar spaces by eosinophils admixed with variable numbers of macrophage (black arrow) (400×, HE), and (B) proteinaceous exudate and necrosis of intraalveolar cellular infiltrate (diffuse alveolar damage) (white arrow) (400×, HE).

at the emergency room demonstrated bilateral, peripheral predominant opacities, while laboratory studies showed white blood cell count of 6900/mm^3 (neutrophil 85%, lymphocyte 6%, eosinophil 0%, band form 7%), C-reactive protein at 16.6 mg/dl and PaO_2 at 49 mmHg. Upon an initial diagnosis of severe community-acquired pneumonia, he was admitted to the intensive care unit (ICU).

After admission, broad-spectrum antibiotic therapy was started. The patient's symptoms improved after initial management, but he later became very agitated, and delirium was suspected. The patient was transferred to a ward on the second day of admission. However, he became desaturated just a few hours after transfer. A chest radiograph revealed progression of bilateral infiltrations, and chest computed tomography (CT) showed bilateral consolidation with an air-bronchogram (Fig. 1). The patient was intubated and mechanically ventilated.

After transferring back to the ICU, the patient's friends disclosed that the patient was an amphetamine user for more than a year and had smoked amphetamines just a few hours prior to the aggravation of his symptoms. This was confirmed by a subsequent urine amphetamine screening. Amphetamine smoking-induced acute lung injury was suspected, and the patient was administered 40 mg intravenous methylprednisolone every 8 h. Sonography-guided lung biopsy confirmed acute eosinophilic pneumonia (AEP) (Fig. 2). After corticosteroid treatment, the patient's conditions

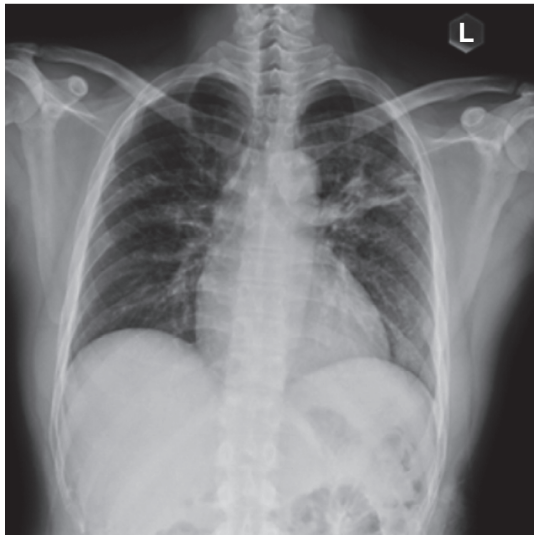

Fig. 3. There was almost complete resolution of lung infiltrations after corticosteroid treatment.

and lung infiltrations improved gradually (Fig. 3). He was successfully extubated on the 10th hospitalized day and was discharged 19 days later.

Discussion

Amphetamines and their analogs are the most widely-used illicit drugs in the world. They are usually sold in capsules, tablets, or in powder forms that can be snorted, injected, ingested or smoked. Inhalation of chemical substances such as tobacco smoking is associated with various systemic complications (11). There has been at least one case report of methamphetamine inhalation-induced acute non-cardiogenic pulmonary edema and one fatal pulmonary hypertension case associated with amphetamine smoking (7, 9). Animal models also revealed systemic influences and deteriorations caused by amphetamine exposure (5). However, the clinical relationship between amphetamine inhalation and acute lung injury is unclear, and the mechanism of amphetamine-induced pulmonary complications remains unproven. In one animal study, de Oliveira *et al*. demonstrated the recruitment and subsequent increase in the number of inflammatory cells, including macrophages, neutrophils and eosinophils, in the bronchoalveolar (BAL) fluid after repeated treatment with aerosolized amphetamine in allergic rats (2). However, another animal study showed that a single exposure of amphetamine could down-regulate several parameters of lung inflammation, such as cellular migration, vascular permeability and tracheal responsiveness (3). The role of amphetamine in lung inflammation is still controversial.

EP includes all disorders characterized by infiltration of the lungs with eosinophils and are now recognized as a heterogeneous group of disorders characterized by varying degrees of pulmonary parenchymal or blood eosinophilia. A large number of drugs and toxic exposures have been documented to be associated with the development of EP (1). Among these, toxic inhalation-induced EP only accounts for a small part of the etiology. Therefore, the precise incidence of inhaled toxin-induced pulmonary eosinophilia is difficult to assess, considering that most of the literature contributing to these syndromes is published in the form of case reports (6, 12) rather than large series of controlled trials. Meanwhile, there is no literature which shows the relationship between amphetamine and AEP. For the same reason, the exact pathogenesis and the definition of the clinical syndromes associated with individual exposures are difficult to characterize.

Some investigators speculate that free radicals play an important role in amphetamine-induced lung injury. Sandra *et al.* have shown that acute inhalation exposure to relevant doses of volatilized methamphetamines is associated with elevated free radical formation and significant lung injury (13). Huang *et al.* showed that adding amphetamine into the perfusate caused pulmonary hypertension, lung weight gain and permeability changes in an isolated rat lung model (4). Huang *et al.* also disclosed that the source of free radicals could be the inflammatory cells or amphetamine itself (4). The *in vitro* experiments of the same study showed that exposure of neutrophils to amphetamine elicited a significant increase in free radicals. This result suggests that amphetamine can activate neutrophils to produce free radicals. However, inflammatory cells are not the only source of free radicals. In an isolated lung perfused with a physiologic salt solution without blood cells, amphetamine caused free radical-dependent tissue injuries (4). Thus, other sources may be involved in the generation of free radicals induced by amphetamine (4). In the present case report, the inflammatory cells were eosinophils, not neutrophils as in the aforementioned study. This difference suggests that free radical production in this case is directly due to amphetamine, rather than inflammatory cells such as eosinophils or neutrophils.

Although systemic corticosteroids remain the treatment of choice for severe lung injury, alternative treatment specific to free radical-related lung injuries may be effective. High concentration oxygen therapy, which was proved to be effective for resolution of pneumothorax in animal models, could be the alternative treatment or the potential effective therapy for free radical-related lung injury (10). The most common antioxidant in clinical medicine is N-acetylcysteine, which is mostly used as a prophylaxis for contrast-

induced nephropathy to prevent direct toxic effects caused by oxygen free radicals on renal tubular cells (8). Inhalation of N-acetylcysteine is very common in acute lung illness and may be effective in free radical-induced lung injury. Moreover, Huang *et al*. (4) also reported the effects of pre-treatment with the oxygen radical scavenger dimethylthiourea (DMTU), which significantly attenuates lung injury caused by amphetamine. However, these substances have only been used in animal models. Other studies are necessary before these substances can be used clinically.

In conclusion, lung injury is one of the most serious complications of inhaled amphetamine. As the condition responds dramatically to appropriate treatment, early identification is imperative. Further studies are warranted to fully understand the pathogenesis of AEP secondary to inhaled amphetamine.

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