A Case of Acute Eosinophilic Pneumonia Following Short-Term Passive Smoking: An Evidence of Very High Level of Urinary Cotinine

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ABSTRACT
Acute eosinophilic pneumonia (AEP) is characterized by febrile illness, diffuse pulmonary infiltrates with eosinophilia. The pathogenesis is not well understood. We report a case of 22-year-old men who never smoke presented with AEP 2 days after acute passive smoke exposure. He developed acute respiratory failure despite having no history of the disease. Computed tomography of the lung revealed diffuse bilateral pulmonary infiltrates. Lung biopsy specimens revealed marked eosinophil infiltration in the alveolar septa without signs of vasculitis.

Two days prior to the disease, he was exposed to cigarette smoke for 2 hours in a closed area. In the absence of other causes, passive smoking may cause lung inflammatory responses.

The level of urinary cotinine, which is a biomarker of smoke exposure, was considerably higher (0.198 μg/ml [201 ng/mg Creatinine]) than that in nonsmokers, but never detected following period. This case suggests that short-term passive smoking may cause AEP.

KEY WORDS
acute eosinophilic pneumonia, acute respiratory distress syndrome, lung biopsy specimens, passive smoking, urinary cotinine

ABBREVIATIONS
AEP, acute eosinophilic pneumonia; ARDS, acute respiratory distress syndrome; SpO2, arterial oxygen saturation measured by a oximetry; WBCs, white blood cells; CO, carbon monoxide.

INTRODUCTION
Acute eosinophilic pneumonia (AEP) is characterized by febrile illness, diffuse pulmonary infiltrates, and pulmonary eosinophilia. The pathogenesis is not well understood, but may relate to the exposure to exogenous substances. Several studies have proposed a causal relationship between cigarette smoking and AEP; however, no studies have provided direct evidence to support this hypothesis.

Herein is reported the first case showing the causal association between short-term period of passive smoking and AEP. The effects of passive smoking were assessed by the measurement of urinary cotinine and nicotine concentrations.

CASE REPORT
A case of a 22-year-old male was admitted to our hospital because of dyspnea, cough; his temperature was 37.2°C, and his respiratory rate was 40 breaths/min. High-flow oxygen of 15 L/min was administered via a reservoir mask to maintain the SpO2 at >90%. No wheezing was detected. Chest X radiographs and computed tomography of the lung revealed diffuse bi-
Chest X ray  Chest CT
April 16, 2009 (the onset of the disease)

Fig. 1 Chest radiograph on admission (left) revealing bilateral interstitial infiltrates Chest CT (right) on admission can revealing bilateral infiltrates with pleural effusion.

Fig. 2 (left) Bronchial lung biopsy specimen from left lung S8 (hematoxylin and eosin [H-E] staining; original magnification × 400) showing highly eosinophil and histiocyte infiltration in the alveoli. (right) Bronchial lung biopsy specimen from left lung S4 (hematoxylin and eosin [H-E] staining; original magnification × 400) showing eosinophil infiltration with fibrin exudation in the respiratory bronchioles and alveoli.

The patient has an atopic dermatitis and his serum IgE level is 239 IU/L.

DISCUSSION

We suspected that acute cigarette smoke exposure in a closed area may have caused the acute inflammatory response in the lungs of the current case, since lateral pulmonary infiltrates, intensified vascular bundles, and pleural effusion in the right lung (Fig. 1).

Fiberoptic bronchoscopy was performed under oxygen administration. Owing to his acute respiratory distress syndrome (ARDS) condition, we could not perform bronchoalveolar lavage. Transbronchial lung biopsy specimens revealed marked eosinophil infiltration in the alveolar septa and histiocyte and eosinophil infiltration in the alveoli without signs of vasculitis (Fig. 2).

He was given intravenous methyl prednisolone (1000 mg) for 3 consecutive days. On the 4th day, the abnormal shadows on the chest X-ray film improved remarkably, and it was no longer necessary to administer oxygen to treat hypoxemia.

Peripheral white blood cells (WBCs) showed progressive eosinophilia with 24% of total WBCs (3264/mm³) on day 5 to 40% of total WBCs (6400/mm³) on day 9, after which eosinophilia was gradually resolved. We diagnosed acute eosinophilic pneumonia on the basis of the clinical course and histological evidence. The patient has an atopic dermatitis and his serum IgE level is 239 IU/L.
causative agents such as drugs, allergens, parasites and fungi were not found in the patient.

Two days prior to the onset of the disease, the patient had attended a welcome party for the new members of a musical group, which was held in a fast food restaurant. He was the leader of the group and hesitated to move his seat from an area with high smoke exposure to one with low smoke exposure out of traditional Japanese courtesy. Although he experienced difficulty in breathing in the closed space, he remained in his seat for approximately 2 hours. This history prompted us to measure the exhaled carbon monoxide (CO) levels using a CO analyzer (Micro CO monitor®; Micro Medical, UK). However, exhaled CO was not detected (0 ppm). Because the inhaled CO by tobacco exposure was rapidly absorbed into pulmonary circulation, the measurement of exhaled CO may not be suitable to detect the burden of acute passive smoking. We next measured his urinary cotinine and nicotine levels, which are the biomarkers of tobacco smoke exposure within 3 days and more, to assess the effects of passive smoke exposure. The levels of cotinine, 0.198 μg/ml (201 ng/mg Creatinine), and nicotine, 0.025 μg/ml (25.4 ng/mg Cre) were considerably higher than those in non-smokers and greater than the recently reported cutoff value for passive smokers who have been exposed to environmental tobacco smoke (Table 1). Nicotine and cotinine were not detected in his urine in subsequent blood tests, which indicated that the acute cigarette smoke exposure might have occurred during the welcome party at the restaurant. Although the exposure to tobacco smoke was short term, it may have been condensed in the closed space and resulted in acute damage in the patient.

This is the first evidence of a significant association between acute cigarette smoke and the onset of AEP. Importantly, recent evidence has revealed that 1 h of passive smoke exposure at levels observed in bars or restaurants increases inflammatory cytokine levels, particularly in men. The smoke-induced inflammation persisted at elevated levels for at least 3 h after short-term exposure to passive smoke.

This case report suggests that passive smoking may be harmful for the cigarette smoke-naive young subjects. The causative relationship between the short-period time of exposure to tobacco smoke and AEP onset should be further determined by the comprehensive study including passive-smoking challenge test.

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REFERENCES