

# Lung injury associated with electronic cigarettes inhalation diagnosed by transbronchial lung biopsy

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## Keywords

Acute lung injury, bronchoalveolar lavage, electronic cigarette, lipid-laden macrophages, transbronchial lung biopsy.

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## Abstract

A 46-year-old healthy man developed respiratory distress, night sweats, fever, and weight loss after using electronic cigarettes (e-cigs) for approximately 1 month. He presented to the hospital when the symptoms worsened 2 months after onset. The findings of bronchoalveolar lavage (BAL) fluid examination and the following transbronchial lung biopsy examination led to the diagnosis of acute alveolitis: intra-alveolar fibrosis accompanied with exudate containing abundant lipid-laden macrophages, eosinophils, and neutrophils. Eventually, e-cig-induced acute lung injury was diagnosed. The symptoms were rapidly alleviated upon e-cig use termination and methylprednisolone pulse therapy, and no subsequent recurrence was observed. There have been only a few reported cases of e-cig-induced lung injury. In e-cig users presenting with atypical pneumonia, close examination by BAL and biopsy should be performed to verify the presence or absence of lipid-laden macrophages.

## Introduction

Electronic cigarettes (e-cigs) have gained in popularity in recent years.

The toxins in e-cig smoke are considered to be fewer than in cigarettes. However, lung injury caused by e-cig use, while rare, continues to be reported. E-cig-induced acute eosinophilic pneumonia (AEP) and lipid pneumonia have been reported [1–3]. Here, we report the clinical and pathological findings of a case of e-cig-induced acute lung injury (ALI) in which bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) were performed.

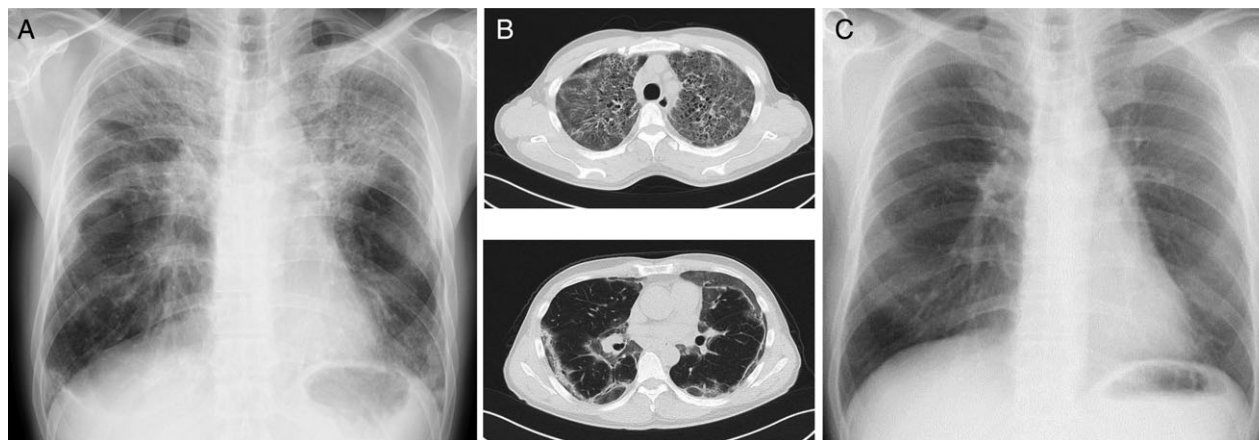
## Case Report

A 46-year-old man consulted our department for the chief complaint of exacerbation of respiratory distress of 2-month duration, with accompanying night sweats, fever, and weight loss. He was an electrician and had no history of dust inhalation, drug use, or pet birds. He was previously healthy with unremarkable medical history. He had been smoking 20 cigarettes per day from age 20 years. He

had quit paper cigarettes 3 months before, and smoked 20 cigarettes per day using an e-cig pen. He used the e-cigs until the day before examination. Physical findings at presentation revealed pallor, body temperature 37.1°C. Chest auscultation revealed mild fine crackles in both sides of the chest with normal heart sounds.

Laboratory data at hospital arrival included white blood cell count 15,200/mm<sup>3</sup> (77.5% neutrophils, 11.5% lymphocytes, and 4.0% eosinophils). C-reactive protein levels (11.81 mg/dL) were elevated and Krebs von den Lungen 6 (KL-6) was high at 1841 U/mL. Blood gas analysis findings in room air revealed pH 7.504, PaCO<sub>2</sub> 29.0 Torr, PaO<sub>2</sub> 52.6 Torr, HCO<sub>3</sub> 22.7 mmol/L, and base excess 0.7. Pulmonary function testing (PFT) revealed the %vital capacity of 50.6%, indicating restrictive impairment.

Chest radiography revealed opacities in the bilateral upper lung fields with extensive bilateral ground-glass opacity (GGO) predominantly around the lateral segments of the lungs (Fig. 1A). Chest computed tomography (CT) revealed GGO and traction bronchiectasis throughout the entire bilateral upper lobes; non-segmental GGO



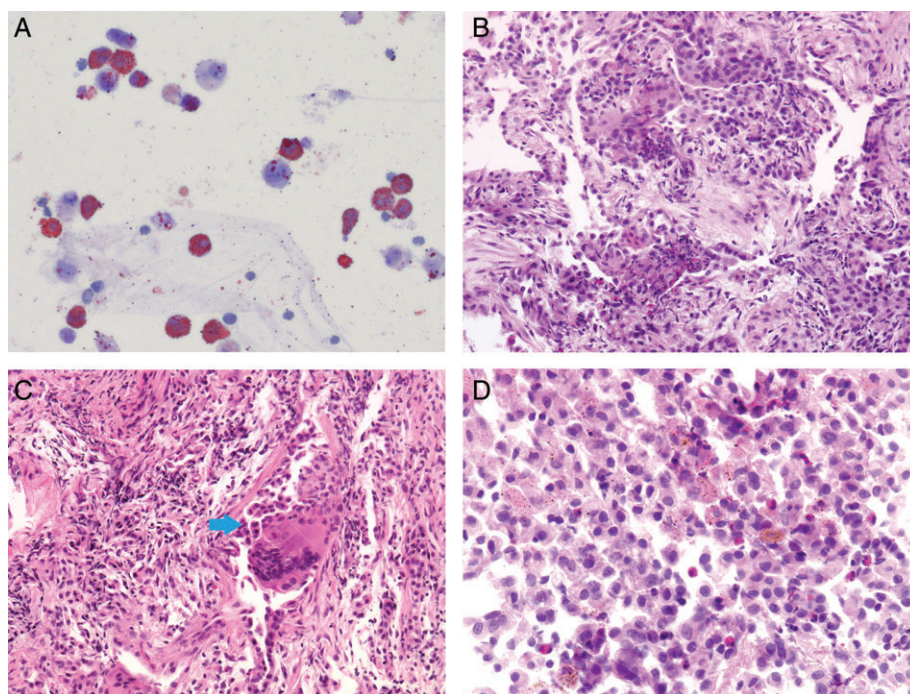
**Figure 1.** (A) Radiography at admission revealed extensive ground-glass opacity (GGO) in the bilateral upper lung fields, and GGO predominantly on the lateral segments of the lungs. (B) Computed tomography at the time of examination. Extensive GGO is seen in the upper lobes, accompanied with traction bronchiectasis. Non-segmental GGO is seen in the lateral segments of lungs bilaterally, and a curvilinear shadow can be seen. (C) Chest radiography taken after 4 weeks of treatment. The opacity has almost disappeared.

with curvilinear shadow was also observed in the middle lobe, lingula, and bilateral lower lobes (Fig. 1B).

Two days after the initial examination, BAL and TBLB were performed. Bronchoscopic examinations revealed normal airways. The BAL fluid findings included CD4/CD8 0.6, total cell count  $4.0 \times 10^5/\text{mL}$ , and cell fractionation of 18% macrophages, 57.5% neutrophils, 6.0% lymphocytes, and 18.5% eosinophils. Bacterial culture examination revealed normal flora. Abundant lipid-laden

macrophages were observed upon Oil Red O staining of BAL fluid (Fig. 2A).

Lung histological examination revealed lesions with acute changes, alveolar septum swelling, and eosinophil and neutrophil invasion, with intra-alveolar invasion of eosinophils and neutrophils; in addition, abundant macrophages containing blackish-brown pigment and multinucleated foreign-body giant cells and intra-alveolar organization (Fig. 2B–D). These changes were considered



**Figure 2.** (A) Neutral lipid-laden macrophages in bronchoalveolar lavage fluid. (B) Intra-alveolar organization and multinucleated giant cells. With eosinophilic exudate, cuboid type II epithelial growth can be seen. (C) Multinucleated giant cells can be seen in the alveolar ducts (arrow). (D) Macrophages containing blackish-brown particles with eosinophilic and neutrophilic exudate can be seen in the alveolar space.

to be caused by inhalation of foreign bodies through the airways, which led to the histopathological diagnosis of acute alveolitis with intra-alveolar fibrosis caused by e-cig use. We diagnosed e-cig-induced ALI caused by inhalation.

After bronchoscopy, methylprednisolone was administered at a dose of 1 g/day for 3 days. The patient received high-dose steroids, because at the time of treatment he had severe hypoxia. Thereafter, the patient received maintenance therapy of 1 mg/kg prednisolone. Antibiotics were not prescribed. After 2 weeks of treatment, chest radiography showed that the extensive GGO had markedly ameliorated (Fig. 1C). After 4 weeks, PFT results returned to normal range. The subject was tapered off gradually from steroid therapy with follow-up observation and discharged from the hospital on Day 30. He completely quit e-cig smoking and no subsequent flare up of pneumonitis was observed on outpatient follow-up.

## Discussion

Compared to cigarettes, e-cigs contain much lesser amounts of toxic substances. Furthermore, e-cigs are reported to help people quit smoking [4]. However, in 2009, the U.S. Food and Drug Administration reported instances of nicotine detected in products labelled nicotine-free as well as detection of diethylene glycol, which is toxic when ingested [5]. Furthermore, reports of lung injury have emerged with the popularization of e-cigs, although such cases are extremely rare.

In two AEP cases reported in the past, the percentage of eosinophils in BAL fluid had clearly increased at 60% and 74%. In the present case, we observed an increase in the percentage of eosinophils to 18.5%, though not quite as high as that in other reports. The relationship between smoking and AEP is well known, and while it is suspected that the onset mechanism of e-cig-induced AEP works in a similar manner, the detailed pathology has not been elucidated.

Moreover, some e-cig vapour contains glycerin. We believe that this is attributed to the abundant lipid-laden macrophages observed in the BAL fluid findings of McCauley and of the present case.

Furthermore, in the present case, CT images differed from the typical findings of lipoid pneumonia and AEP

reported to date. And we required to make a differential diagnosis in the present case; therefore, we performed a lung biopsy.

Lung histology examination revealed that eosinophilic and neutrophilic invasion with exudate macrophages containing blackish-brown particles and multinucleated giant cells were observed in the alveolar space, which was thought to be a strong reaction to the inhaled substance. No underlying pulmonary disease was observed in the present case, and there was no inhalation of fat-containing substances apart from the e-cig that was used; hence, the patient was diagnosed with ALI due to e-cig use.

There are currently many different types of e-cigs commercially available. Consequently, the safety of e-cigs on the respiratory system has not been fully examined. Case reports on lung injury associated with e-cigs should continue to be compiled for future elucidation. Atypical pneumonitis arising while using e-cigs should be closely examined by alveolar lavage and lipid staining.

## Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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