Case Report

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대한영상의학회지

Electronic Cigarette or Vaping Product Use-Associated Lung Injury: A Case Report

전자담배 관련 급성 폐 손상: 증례 보고

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Electronic cigarette (e-cigarette) or vaping product use-associated lung injury (EVALI) has emerged as a social issue as e-cigarette use is rapidly increasing worldwide and is related to many deaths in the United States. To our knowledge, this is the first case report of EVALI in South Korea of a 24-year-old man with acute respiratory symptoms and a history of e-cigarette use. Chest CT revealed diffuse bilateral ground-glass opacities with subpleural sparing, airspace consolidation, and centrilobular micronodules as typical patterns of EVALI with organizing pneumonia and diffuse alveolar damage. Infection was excluded with meticulous laboratory examinations, and the patients' illnesses were not attributed to other causes. EVALI was diagnosed by meeting the diagnostic criteria with consistent clinico-radiologic findings through a multidisciplinary approach. Radiologists should have good knowledge of EVALI radiologic findings and play a cardinal role in the proper diagnosis and management of EVALI.

Index terms Electronic Cigarette; Lung Injury; Vaping; E-Cigarette Vapor; South Korea

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INTRODUCTION

Electronic cigarette (e-cigarette) users have been rapidly increasing in the United States, reaching 41 million in 2018, and e-cigarettes have been proposed as an alternative to conventional cigarettes (1). Electronic cigarette or vaping product use-associated lung injury (EVALI) was first reported in the United States in 2019 as an outbreak of respiratory illness associated with vaping history and has emerged as a worldwide issue (2). EVALI is a diagnosis of exclusion: a history of vaping within 90 days from symptom onset, abnormality on chest imaging, and exclusion of other potential causes, including infection, malignancy, or autoimmune diseases (3). Lung biopsy is not mandatory to diagnose EVALI in cases that meet the diagnostic criteria. In South Korea, approximately 7% of adult smokers and 10% of adolescent smokers are reported to be e-ciga-

rette users (4). Herein, we report the first case of EVALI in South Korea.

CASE REPORT

This study was approved by the Institutional Review Board of our institution and the requirement for informed consent was waived (IRB No. SCHUH 2021-02-021).

A 24-year-old male presented to the emergency department (ED) with acute dyspnea and fever. The patient's symptoms appeared a week earlier and became aggravated three days prior. He had a history of arrhythmia that did not require medical treatment. He was a current smoker (0.5 pack for 10 years) and had lived in the United States for 16 years until a year ago. The patient's vital signs at presentation revealed a fever of 38.2°C and oxygen saturation of 86% in room air.

Initial chest radiography showed diffuse bilateral lung parenchymal opacification with dense airspace consolidations in the lower lungs, which were associated with mild interstitial thickening. No cardiomegaly was observed, and there was no evidence of pleural effusion (Fig. 1A). Initial laboratory findings in the ED revealed leukocytosis of 12400/μL with neutrophilia of 86.8%, elevation of inflammatory markers with a C-reactive protein level of 8.9 mg/dL, and an erythrocyte sedimentation rate of 120 mm/h. Elevation of the D-dimer level of 1204 ng/mL raised the possibility of pulmonary thromboembolism. The patient underwent chest CT with pulmonary angiography. However, there was no evidence of pulmonary thromboembolism. Lung window images (Fig. 1B) showed diffuse heterogeneous bilateral ground-glass opacities (GGOs) with sparing of the subpleural lungs and no craniocaudal predominance. Airspace consolidation was observed in the periphery of both lower lobes. Diffuse, poorly defined micronodules, and mild interlobular septal thickening were also suspected. Bilateral small mediastinal and hilar lymphadenopathy were observed. The primary radiologic diagnosis in our patient was an infection, such as miliary tuberculosis (TB) or other microbial causes of acute pneumonia with acute respiratory distress syndrome. Differential diagnoses included acute to subacute hypersensitivity pneumonitis, acute eosinophilic pneumonia, and diffuse alveolar hemorrhage. The patient was admitted to the pulmonology department for further diagnostic evaluation and treatment.

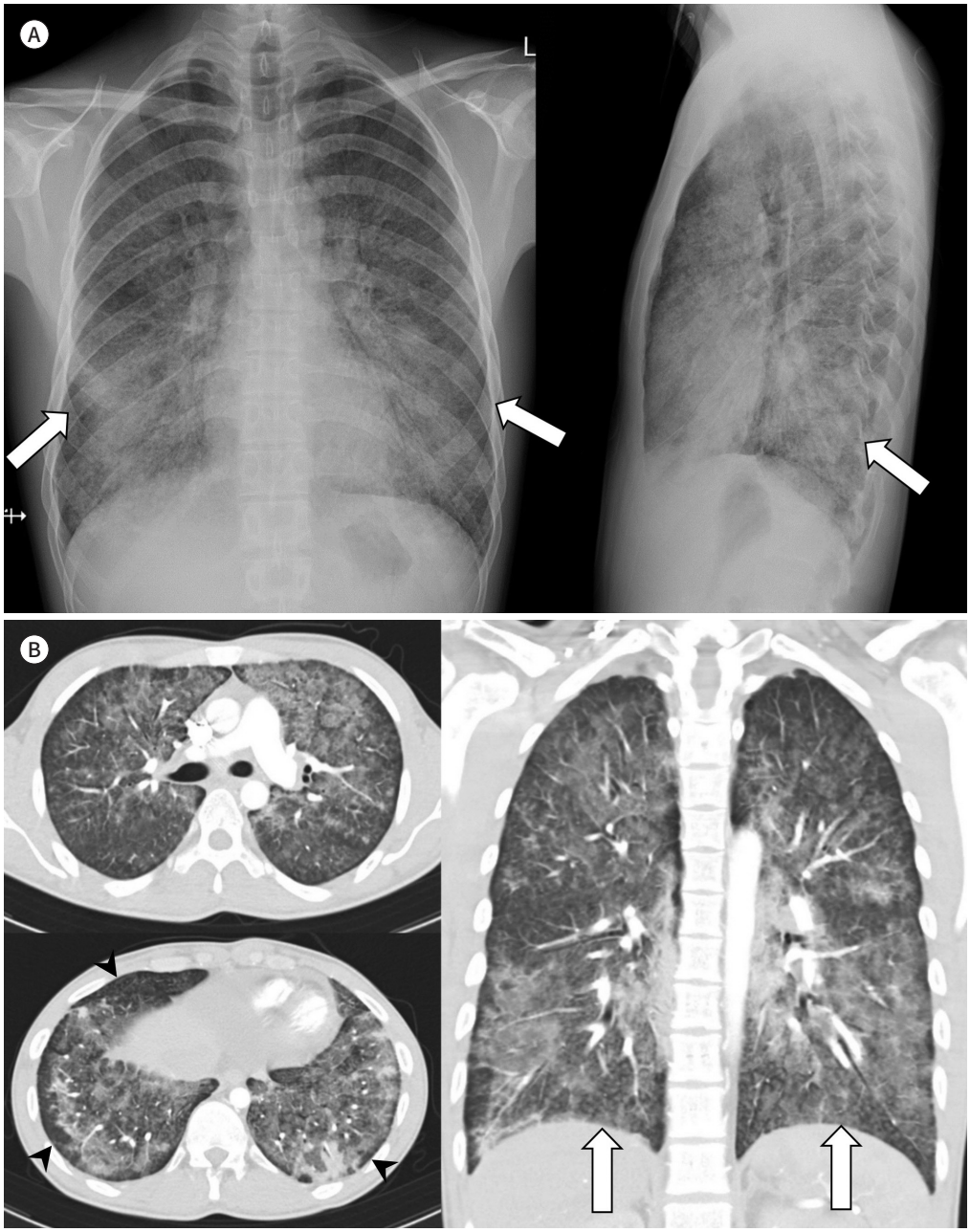
On admission, meticulous laboratory testing demonstrated no evidence of infection, including a negative respiratory viral panel, polymerase chain reaction (PCR) for influenza, pneumocystis, TB, urine antigen testing for *Streptococcus pneumoniae* and *Legionella*, and sputum/blood culture.

Echocardiography revealed normal findings. Bronchoscopy with bronchoalveolar lavage (BAL) revealed no endobronchial lesions and nonspecific findings on BAL specimen analysis (macrophages, 32.8%; neutrophils, 62.2%; eosinophils, 4.2%; lymphocytes, 0.4%; columnar epithelial cells, 0.4%; squamous epithelial cells, 0%).

Empiric antibiotics and anti-TB treatments were started after hospitalization, but the patient presented with persistent dyspnea, fever, and hypoxia. Follow-up chest CT was performed four days after hospitalization and showed some areas of mild partial improvement, but mostly persistent diffuse bilateral GGOs and airspace consolidations. Diffuse, poorly defined micronodules were better delineated and showed centrilobular distribution with sub-

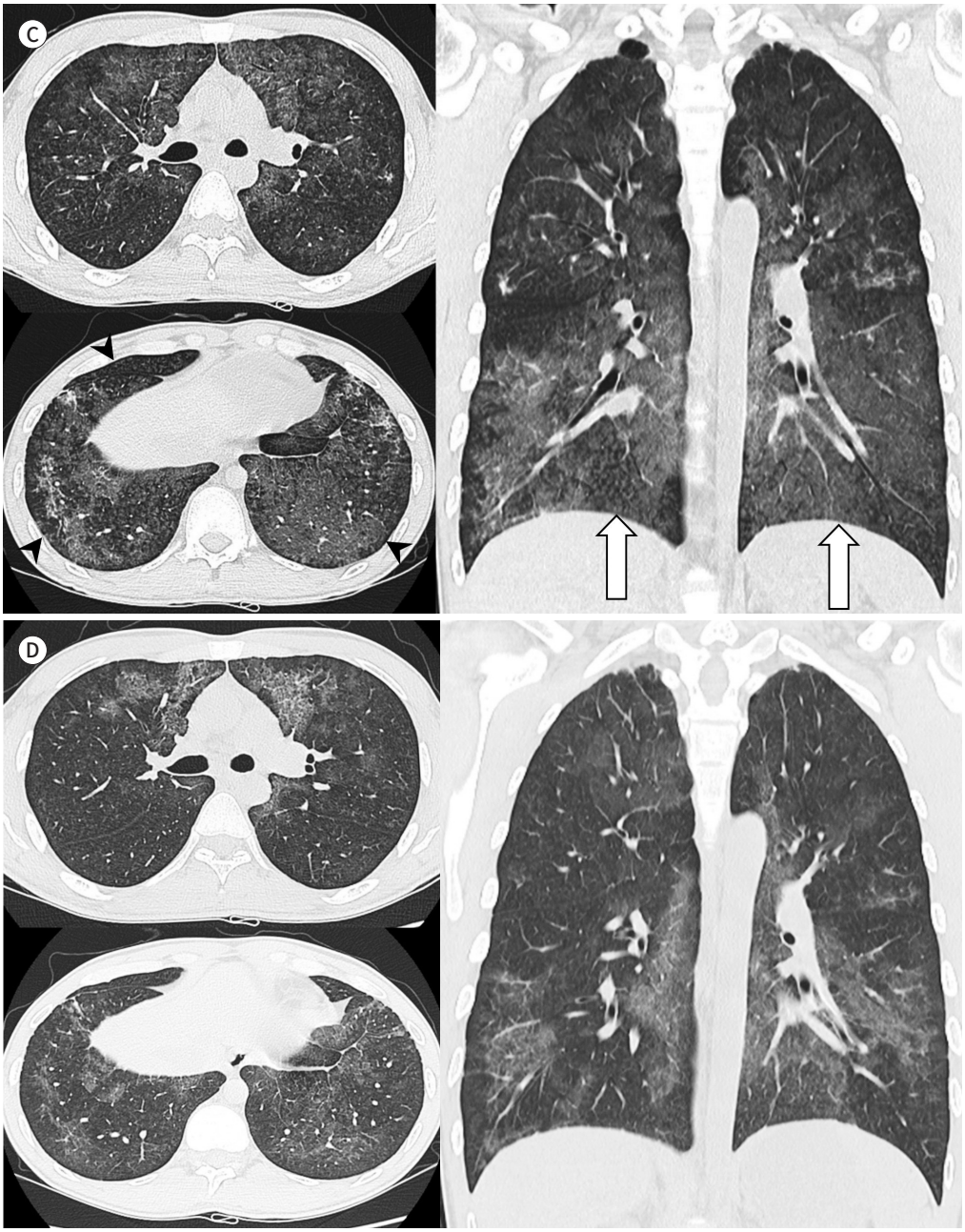
pleural sparing (Fig. 1C). Since the patient's symptoms did not respond to treatment, we started systemic steroid therapy following the follow-up CT scan. With the persevering efforts of the clinician, the patient disclosed a vaping history of three months before the onset

Fig. 1. Electronic cigarette or vaping product use-associated lung injury with organizing pneumonia and diffuse alveolar damage pattern in a 24-year-old male.
A. Initial chest radiograph shows extensive bilateral lung parenchymal opacifications with dense airspace consolidations in the lower lungs (arrows), which are associated with mild interstitial thickening. No cardiomegaly is seen and there is no evidence of pleural effusion.
B. On axial and coronal reformatted lung window chest CT images with pulmonary angiography, diffuse heterogeneous bilateral ground-glass opacities are seen with sparing of the subpleural lungs (arrowheads) and no craniocaudal predominance. Airspace consolidations are noted in the periphery of both lower lobes, and there are also suspicious diffuse poorly defined micronodules (arrows) and mild interlobular septal thickening.



of symptoms, and continued to use e-cigarettes during hospitalization. The final diagnosis was electronic cigarette or vaping product use-associated lung injury (EVALI) as he met the diagnostic criteria consisting of a recent vaping history, compatible findings on chest radiog-

Fig. 1. Electronic cigarette or vaping product use-associated lung injury with organizing pneumonia and diffuse alveolar damage pattern in a 24-year-old male.
C. After four days of empirical antibiotics and anti-tuberculosis treatment, follow-up chest CT shows some areas of mild partial improvement, but mostly persistent bilateral ground-glass opacities and airspace consolidations with subpleural sparing (arrowheads). Diffuse poorly defined centrilobular micronodules (arrows) in both lungs are well delineated.
D. With steroid therapy for one month and cessation of vaping, follow-up chest CT demonstrates significantly improved bilateral lung parenchymal ground-glass opacities and poorly defined centrilobular micronodules with residual diseases, along with resolution of clinical symptoms, in our patient.



raphy and chest CT, exclusion of pulmonary infection, and no evidence of alternative plausible diagnoses of the patient's illnesses. After two weeks of intravenous administration of steroids followed by two weeks of oral steroid administration, a follow-up chest CT demonstrated significant improvement of the bilateral lung parenchymal GGOs and poorly defined centrilobular micronodules with residual diseases (Fig. 1D). The patient also showed resolution of clinical symptoms after the administration of steroids and cessation of vaping.

DISCUSSION

E-cigarettes were invented in China in 2003 and are an alternative to conventional smoking. E-cigarettes were introduced into the United States in 2007, and the number of e-cigarette users (vapers) strikingly increased to 41 million in 2018, with a noticeable rise in youth (1). EVALI was first identified in the United States in 2019 (1, 2), as with the outbreak of respiratory illness in patients with a vaping history in the days and weeks before symptom onset. As of February 2020, the Centers for Disease Control and Prevention (CDC) reported a total of 2807 cases of hospitalized patients with EVALI, with 68 deaths, more common in younger patients with a median age of 24 years (3).

E-cigarette devices consist of a battery, a reservoir containing substances, and a heating element that vaporizes the substances, which allows the users to inhale aerosolized (or vaporized) substances. E-cigarettes are customizable and enable users to add numerous substances (1). Vaping substances commonly include nicotine liquids dissolved in glycerine and propylene glycol, which are mostly mixed with flavoring aldehydes and alcohols. The exact components of vaping substances are often unknown and may contain undesirable contaminants, particularly in black market mixtures. It can also be used to deliver a variety of other recreational drugs such as tetrahydrocannabinol (THC), cannabidiol, and butane hash oils (also known as dabs). Although the causes of the reported illnesses are under investigation, products containing THC are most commonly reported among these patients, and one or more causative agents may be at play (1, 2). Many chemical constituents detected in e-cigarette liquids can cause acute and subacute adverse health effects. These constituents may also undergo thermal decomposition by metallic e-cigarette heating coils to produce new chemical compounds in aerosols (2, 3). Furthermore, the coils may also release metals such as manganese and zinc into the aerosol, which can be toxic when inhaled (2). Alone or in combination, these substances may result in a variety of respiratory diseases.

Until now, EVALI is a diagnosis of exclusion in cases with a history of vaping within 90 days of symptom onset, abnormality on chest imaging, and exclusion of other potential causes explaining patients' symptoms, including infection, malignancy, or autoimmune diseases (3). Clinical symptoms are nonspecific, and patients are mostly thought to have an acute viral infection with respiratory, constitutional, and gastrointestinal symptoms (2).

Radiologists play a significant role in the diagnosis of EVALI and are integral in the follow-up of patients for evaluation of improvement, worsening, and superimposed complications. Imaging patterns of lung injury in EVALI include organizing pneumonia (OP), diffuse alveolar damage (DAD), acute eosinophilic pneumonia (AEP), diffuse alveolar hemorrhage (DAH), exogenous lipoid pneumonia (ELP), and hypersensitivity pneumonitis (HP), along with path-

ological findings (1). OP and DAD are common patterns of acute lung injury (1). OP shows diffuse bilateral GGOs, usually with conspicuous subpleural sparing, septal thickening, and mild consolidation. Centrilobular nodules are a common and relatively minor finding, reflecting the bronchiolocentric distribution of injury, including airway-centered OP, DAH, or HP (5). DAD often presents with severe pulmonary injury, frequently requiring ventilatory support. During the acute exudative phase of DAD, chest imaging shows lower lobe predominant consolidation and GGO, progressing to the organizing phase with reticulation, increased bronchiectasis, and volume loss (6). Pathologically, AEP is a combination of DAD with interstitial and alveolar eosinophils. Eosinophilic degranulation causes permeability edema, seen in patients who have started smoking or have changed smoking habits (7). AEP shows an imaging appearance similar to that of DAD and OP, usually superimposed findings of fluid overload, such as septal thickening and small amount of pleural effusions (7). Patients with DAH often present with cough, fever, and dyspnea. Hemoptysis is common, but may be absent in one-third of cases (1, 2). Pulmonary hemorrhage appears as focal or diffuse consolidation and GGO sparing of the peripheral lung. Centrilobular nodules represent aspirated or retained blood in the distal bronchioles (1). Less common imaging patterns include ELP and HP (1). ELP shows GGO and consolidation with lower lobe predominance, septal thickening, and areas of fat attenuation (less than -30 HU) within consolidation or nodules on CT (8). Findings in patients with acute HP, with clinical symptoms within a few hours of exposure, include upper lung predominant, poorly defined centrilobular nodules, GGO, and consolidation in the mid to lower lungs. Patients with subacute to chronic HP, with clinical symptoms over weeks to months from prolonged exposure, show similar findings of acute HP, mostly associated with mosaic attenuation representing air trapping due to small airway injury (9).

In our patient with a diagnosis of EVALI, an initial chest radiograph and CT demonstrated extensive heterogeneous bilateral GGOs with sparing of the subpleural lungs. Airspace consolidations were observed in the periphery of both lower lobes, and we also suspected diffuse, poorly defined micronodules with centrilobular distribution (Fig. 1A, B). Follow-up chest CT after four days of empirical antibiotics and anti-TB treatment showed some area of mild partial improvement, but mostly persistent bilateral GGOs and airspace consolidations with more prominent poorly defined centrilobular micronodules (Fig. 1C) with persistent clinical symptoms. We believe that our case represents overlapping of OP and the early exudative phase of DAD patterns of acute lung injury on chest imaging. Poorly defined centrilobular nodules on chest CT are also reminiscent of a bronchiolocentric injury pattern of OP or an acute HP pattern. Follow-up chest CT following a month of steroid therapy and vaping cessation demonstrated significant improvement of bilateral lung parenchymal abnormalities (Fig. 1D), with resolution of clinical symptoms. The clinical course of patients with EVALI varied. Most patients show improvement following cessation of vaping and initiation of corticosteroids, as in our case. However, some patients show a progressive course with respiratory failure, even causing death (10). In South Korea, the Ministry of Health and Welfare and the CDC recommended stopping e-cigarette use since September 2019. Two cases of suspected EVALI were officially reported to the Korean CDC. Only one case met the diagnostic criteria after the expert review. To our knowledge, this is the first case report of EVALI with consistent clinical features and imaging findings.

In conclusion, electronic cigarettes have been proven to be associated with unexpected detrimental health effects, which can be serious and sometimes fatal. EVALI is defined as an acute lung injury with various histopathological and imaging patterns, including OP and DAD. Chest radiography and CT have considerable value in the diagnosis of EVALI. With our first case report and review, radiologists can be aware of the clinical manifestations and various imaging findings of EVALI and can suggest the diagnosis in the proper clinical context.

Author Contributions

Conceptualization, N.B.D.; data curation, L.J., N.B.D., H.J.H.; formal analysis, L.J., N.B.D., H.J.H.; funding acquisition, N.B.D.; investigation, all authors; methodology, K.Y., O.E., L.E.J.; project administration, N.B.D.; resources, N.B.D., H.J.H.; software, L.J., N.B.D.; supervision, N.B.D., H.J.H.; validation, K.Y., O.E., L.E.J.; visualization, L.J., N.B.D., H.J.H.; writing—original draft, L.J., N.B.D., H.J.H.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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대한영상의학회지

전자담배 관련 급성 폐 손상: 증례 보고

임지윤[1] · 남보다[1]* · 황정화[1] · 김양기[2] · 오은선[1] · 이은지[1]

세계적으로 전자담배 사용의 급속한 증가와 함께 미국을 중심으로 전자담배와 관련된 사망 보고들이 발생함에 따라 전자담배 관련 급성 폐 손상은 중요한 사회적 문제로 대두되었다. 이 증례 보고는 급성 호흡기 증상과 전자담배 흡연력이 있는 24세 남자 환자에서 전자담배 관련 급성 폐 손상을 진단한 국내 첫 사례이다. 흉부 CT에서 흉막하부 보존을 보이는 미만성 간유리음영과 폐경화 및 중심소엽성 미세결절의 소견을 보여 전자담배 관련 폐 손상의 특징적 형태인 기질화폐렴과 미만성폐포손상에 해당하는 증례로 생각되었고, 검사실 소견에서 감염이 배제되고, 환자의 질병을 설명할 다른 원인이 없었다. 따라서, 임상 소견 및 부합하는 영상 소견으로 진단 기준을 충족하여, 다학제 진료를 통해 전자담배 관련 급성 폐 손상을 진단하였다. 이를 통해 영상의학과 의사들이 전자담배 관련 급성 폐 손상의 진단에 중요한 역할을 할 수 있을 것으로 생각된다.

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