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Lung injury associated with an e-cigarette (vaping) use during the COVID-19 pandemic

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Abstract

In recent years, the excessive use of electronic cigarettes (e-cigarettes), and vaping, as a replacement for traditional tobacco cigarettes, have highlighted potential health risks for users. One such risk is the development of "electronic cigarette (vaping) product use-associated lung injury" (EVALI). This type of lung injury has an unclear cause that may be related to the various components found in e-cigarette fluids. The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection (coronavirus disease 2019 or COVID-19) may worsen EVALI symptoms in individuals with both conditions. This could be due to the increased oxidative stress and inflammation caused by e-cigarette use, as research shows increased levels of reactive oxygen species (ROS) and decreased glutathione. In this paper, we present two critical cases of COVID-19 patients with a history of chronic e-cigarette smoking and describe their clinical progression during hospitalization. The findings suggest that their prolonged use of e-cigarettes may have significantly impacted the severity of the disease.

Key words: COVID-19, SARS-CoV-2, EVALI, vape, e-cigarette, smoking.

Introduction

Electronic cigarettes (e-cigarettes) have gained widespread popularity as a substitute for traditional tobacco smoking. Initially marketed as a means of quitting smoking, e-cigarettes have since come under scrutiny due to reports of adverse health effects. (1-4) Reports have linked electronic cigarette use to multiple different respiratory diseases, including diffuse alveolar hemorrhage, hypersensitivity pneumonitis, acute eosinophilic pneumonia, and lipoid pneumonia. (1-4) Vape pen aerosols have been found to have several toxic compounds, including carbonyls, toluene, benzene, acrolein, and propylene oxide. (5,6) Furthermore, it has been demonstrated that exposure of healthy subjects to vaping aerosols increased alveolar neutrophil elastase and metalloprotease to levels comparable to tobacco smoking. (7) The most recent pathology correlated with e-cigarette use identified by the Center for Disease Control and Prevention (CDC) is “electronic cigarette (vaping) product use–associated lung injury” (EVALI), which is defined as respiratory failure with symptom onset within 90 days of e-cigarette use, with pulmonary infiltrates on imaging, the absence of infection, and no evidence of alternate causes of respiratory failure. (8)

The emergence of the coronavirus disease 2019 (COVID-19) pandemic had a notable impact on smoking individuals. Although no conclusive evidence indicates that chronic e-cigarette users are

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more susceptible to COVID-19 infections, it is well-established that both tobacco smoking and e-cigarette use can trigger marked oxidative stress and inflammation in the lung, which may exacerbate symptoms if they occur in tandem with an infection. (9-11) The airway epithelium that had been exposed to e-cigarette aerosols has been shown to experience increased oxidative stress, pro-inflammatory cytokine production, cytotoxicity, and oxidative deoxyribonucleic acid (DNA) damage, which can increase susceptibility to more severe COVID-19 infection and severity by up to five times as reported in multiple studies. (12-17) Also, decreased expression of some pattern recognition receptors, such as scavenger receptor A1 (SR-A1) and toll-like receptor-2 (TLR-2), has been found to cause a state of immune susceptibility to pathogens. (18,19)

In this article, we present two cases of COVID-19 patients who had a history of e-cigarette use. The cases demonstrate a severe disease progression with significant damage in the lung parenchyma. We hypothesize that their history of chronic e-cigarette use significantly impacted the severity of their hospital course and the radiological evidence observed.

Case 1

A 43-year-old Caucasian gentleman was admitted to the intensive care unit (ICU) due to intractable shortness of breath worsening over one week. He presented to the emergency department (ED) with an oxygen saturation of 86% while breathing room air and a respiratory rate of 24 rpm. On admission, he was unvaccinated for COVID-19 and tested positive for the disease in January 2022 by reverse transcription polymerase chain reaction (RT-PCR). The patient had no significant surgical history and denied drinking alcohol or using tobacco cigarettes but was admitted to frequent use of e-cigarettes containing tetrahydrocannabinol (THC). He reported that he had the vaping pen and had used it at his discretion for years.

Chest computed tomography (CT) scan without contrast on admission showed extensive ground glass consolidation throughout the lung parenchyma bilaterally, with consolidation being particularly dense in the lower lobes in addition to advanced pneumomediastinum with emphysema extending to the soft neck tissue (**Figure 1**). To avoid hypoxemia, this patient required constant awake pronation to maintain oxygen saturation in the mid-90s, as the supine position caused oxygen saturation to drop to the low 70s or high 60s. During his hospital stay, the patient needed respiratory support and was managed by alternating between a high-flow nasal cannula (HFNC) and non-invasive mechanical ventilation (NIMV). All efforts were taken to delay invasive mechanical ventilation (IMV); eventually, the patient never needed it. Progressively it was possible to switch to a nasal cannula with adequate oxygen saturation (between 89-95%), with evidence of partial resolution of pneumomediastinum on chest CT (**Figure 2**). The patient was discharged with a four liters nasal cannula and followed in the outpatient clinic, where he showed significant improvements. During the 11 months of outpatient care, the patient recovered to the point where there was a significant reduction in shortness of breath, chest pain, and productive cough. Home oxygen was no longer needed, and a chest CT scan without contrast showed significant improvement in the lung parenchyma (**Figure 3**). During the most recent follow-up in 2023, the patient had gained 35 lbs and fully resumed his regular daily activities, suggesting a return to good health and a normal quality of life.

Case 2

A 34-year-old Caucasian lady was admitted to the general ward with intractable shortness of breath, at which time she tested positive for COVID-19 with RT-PCR. She has a history of seronegative rheumatoid arthritis under treatment with hydroxychloroquine and prednisone, anxiety, depression, fibromyalgia, and daily use of THC-containing e-cigarettes (more than five times a day) for two years. Initial chest CT scan on admission showed ground glass opacities in both pulmonary fields (**Figure 4**). However, her condition deteriorated despite supplementary oxygen and appropriate supportive treatment over the next month. A new chest CT scan showed worsening of the ground glass opacities (**Figures 5a** and **5b**). She was admitted to the ICU 28 days after admission, with severe hypoxia requiring IMV. Her ICU stay was complicated by further deterioration of lung parenchyma as seen on repeated chest CT scans (**Figures 6a, 6b, 6c**), pulmonary embolism, and right ventricular thrombus requiring heparin drip. Two months later, the patient's condition improved with supportive treatment, and he was discharged with home oxygen. After 12 months of follow-up in the outpatient clinic, the patient showed significant improvement in symptoms, lung function, and chest CT findings (**Figure 7a, 7b**, and **7c**) and no longer required supplemental oxygen. On the latest follow-up in 2023, the patient had returned to normal everyday functioning.

Discussion

Lung injury is the most widely recognized adverse effect of e-cigarettes capturing the attention of the CDC before the onset of the COVID-19 pandemic.

(20,21) E-cigarette liquid typically contains three primary components, namely a diluting agent (most commonly vitamin E acetate), a carrier agent (most commonly propylene glycol), and a flavoring agent (most commonly diacetyl or 2,3-pentanedione). These components have been implicated as potential causes of EVALI, particularly in patients who use THC as part of their e-cigarette liquid. (22) Propylene glycol, responsible for producing the vapor effect in vaping, has been reported by the CDC to cause significant respiratory irritation in theater workers exposed to it during theatrical fog production. (23,24) Moreover, the inhalation of high concentrations of diacetyl or 2,3-pentanedione flavoring agents have been linked to outbreaks of bronchiolitis obliterans in workers at microwave popcorn facilities that use it as a flavoring additive. This was done with in vitro analysis of airway epithelial cells exposed to diacetyl or 2,3-pentanedione, demonstrating disruptions in the growth and function of cilia. (25)

Before the COVID-19 pandemic, e-cigarette-related illnesses were the prevailing public health concern. However, the incidence of EVALI went from a peak in September 2019 to a low in February 2020, after the start of the COVID-19 pandemic as the CDC decided to discontinue the collection of EVALI case reports. (25) Therefore, the drop in the number of reported e-cigarette-related cases could result from a narrow diagnostic tendency during a pandemic surge in the population leading to availability bias. Indeed, features of COVID-19 pneumonia and e-cigarette-related lung damage overlap considerably, making diagnosis challenging. (26) Both COVID-19 and e-cigarette use have been associated with a marked inflammatory response in the lungs, characterized by elevated levels of various proinflammatory cytokines, including interleukin 1β (IL-1β), interleukin 6 (IL-6), interleukin 10 (IL-10), and interleukin 8 (IL-8). Therefore, in patients with both conditions, the co-occurrence of these inflammatory responses may lead to a further exacerbation of lung inflammation by accentuating airway inflammation and fibrotic scarring. (27,28) In fact, it has been hypothesized that using e-cigarettes increases individuals' susceptibility to respiratory infections. This is believed to occur due to the activation of several immunosuppressive pathways in the lungs following exposure to e-cigarette components. For instance, it has been suggested that the expression of pattern recognition receptors, including scavenger receptor A1 (SR-A1) and toll-like receptor-2 (TLR-2), may be reduced, thereby compromising the ability of the lungs to recognize and respond to infections. This potential dysregulation of the immune response may contribute to an increased risk of contracting respiratory infections among e-cigarette users. (19,25)

While both conditions present in a very similar manner clinically, several strategies have been proposed to differentiate between them. For instance, COVID-19 diagnosis relies on detecting SARS-CoV-2 by RT-PCR, while EVALI remains a diagnosis of exclusion. (6) EVALI is most commonly a disease of young age as e-cigarettes are most commonly used by younger adults, while severe COVID-19 symptoms requiring hospitalization are less commonly seen in the younger population. Furthermore, chest CT scans of COVID-19 patients typically present with ground glass opacities, while EVALI is commonly associated with organizing pneumonia. (5) Additionally, EVALI can present with leukocytosis, while COVID-19 often presents with lymphopenia. (5)

The cases of our two patients illustrate the potential impact of e-cigarette use on the severity of the COVID-19 hospital course. Both patients had no significant pre-existing medical conditions before contracting COVID-19, yet their hospital course was severe. While more research is needed to fully understand the relationship between e-cigarette use and outcomes of pulmonary infections like COVID-19, this publication sheds light on how e-cigarettes may exacerbate the damage caused by COVID-19 to the lungs, potentially leading to more severe presentation and worse clinical outcomes.

Conflicts of interest

The authors have no conflict of interest in the preparation of this manuscript. This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Figure 1. Chest computed tomography scan shows extensive ground glass opacities in both lung fields compatible with pneumomediastinum

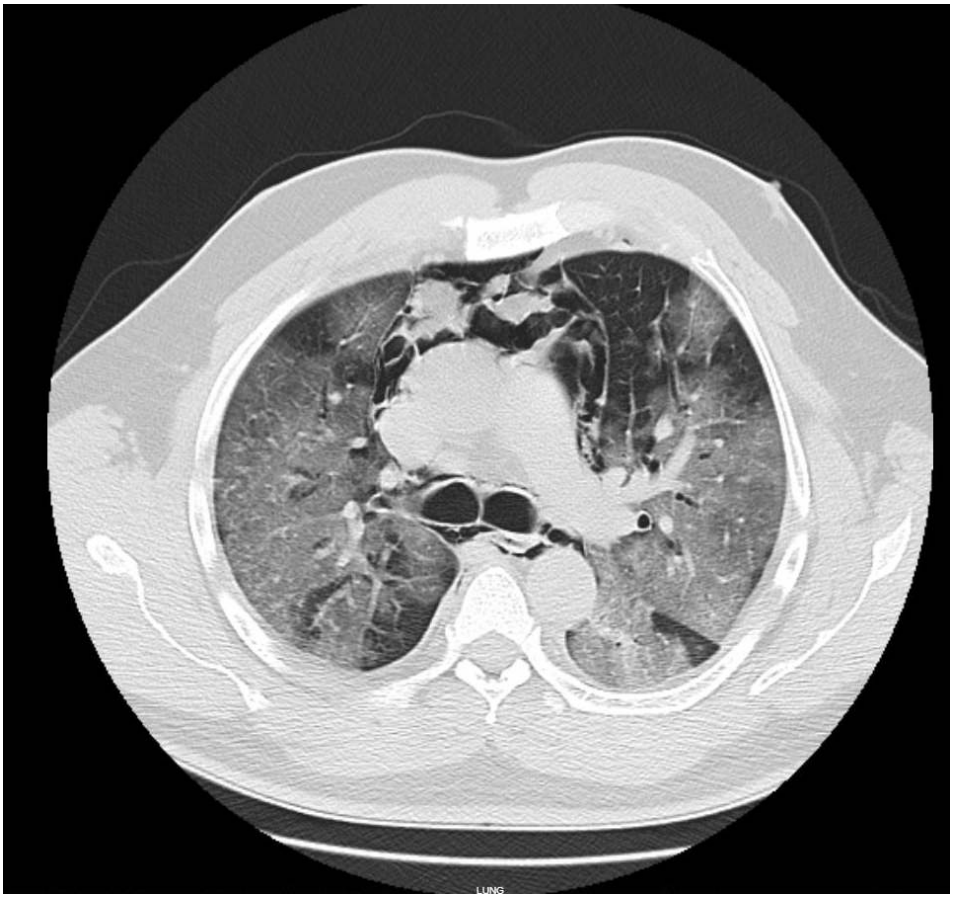


Figure 2. Chest computed tomography scan shows extensive ground glass opacities in both lung fields with consolidation in the left lower lobe

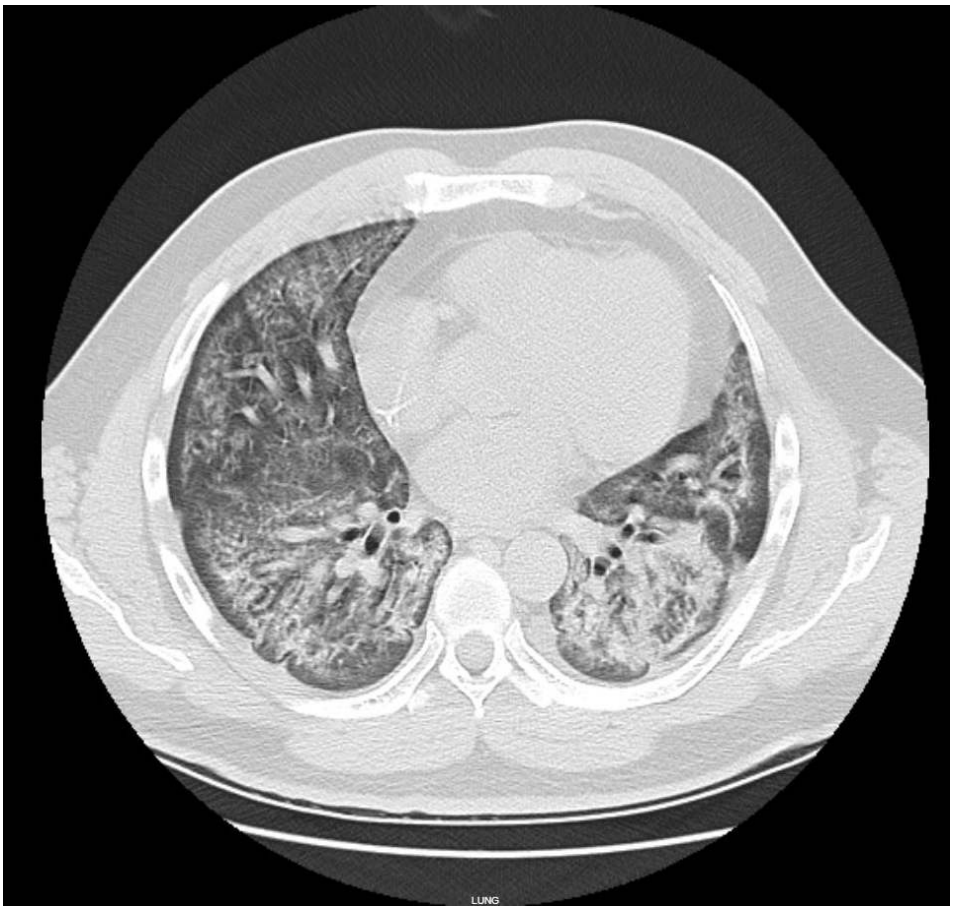


Figure 3. Multiple slides of chest computed tomography scan without contrast taken in November 2022 shows patchy but widespread ground glass opacities in bilateral upper lobes

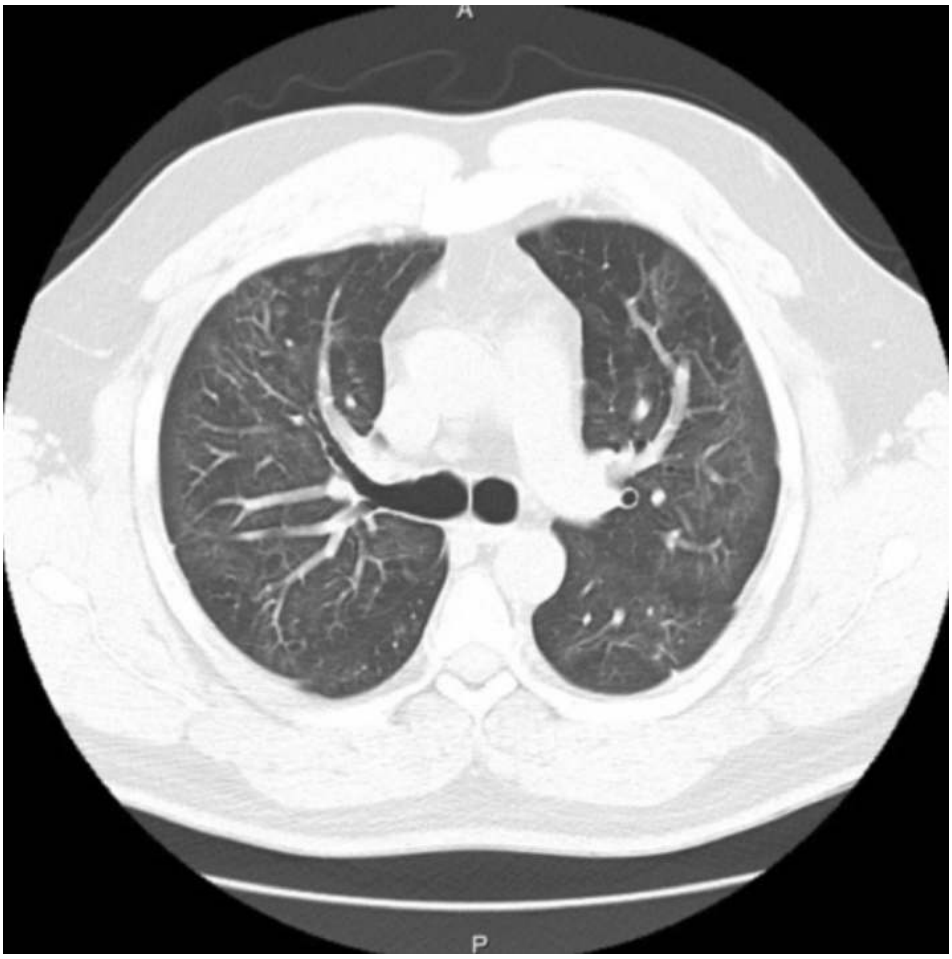


Figure 4. Chest computed tomography scan shows ground glass opacities in both lung apices

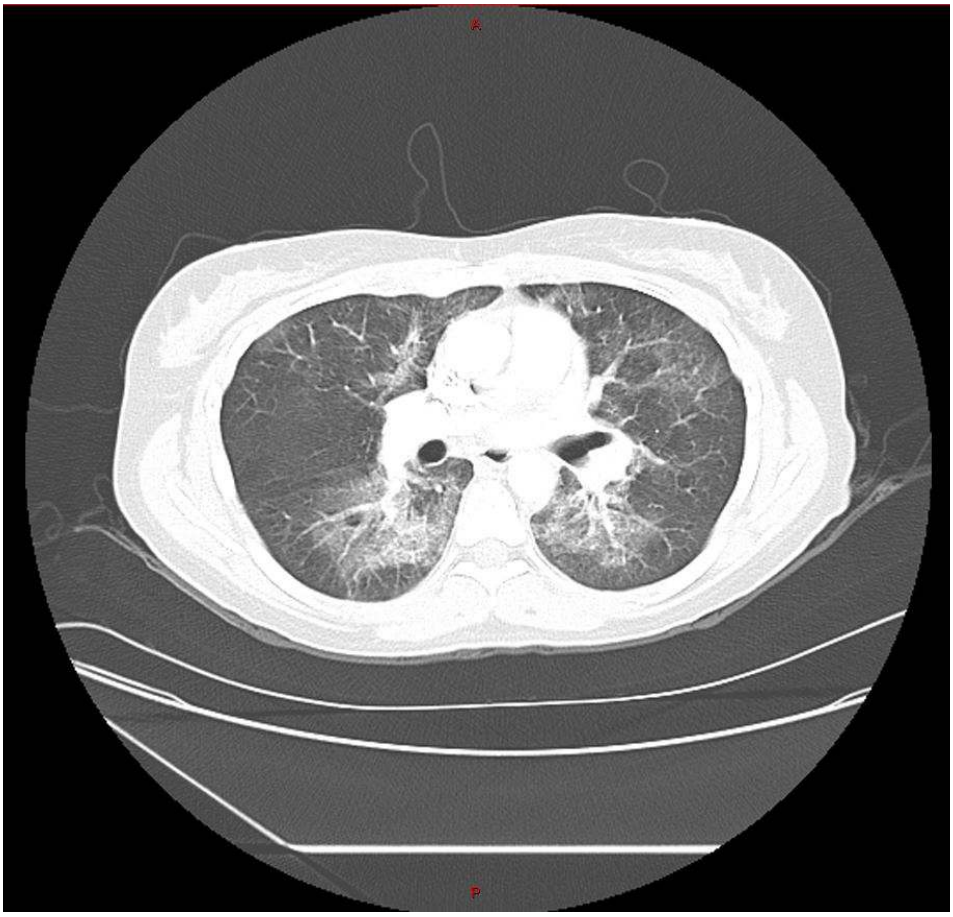


Figure 5a. Chest computed tomography scan shows extensive reticular infiltrates, ground glass opacities, bilateral lung consolidations, and left pleural effusion

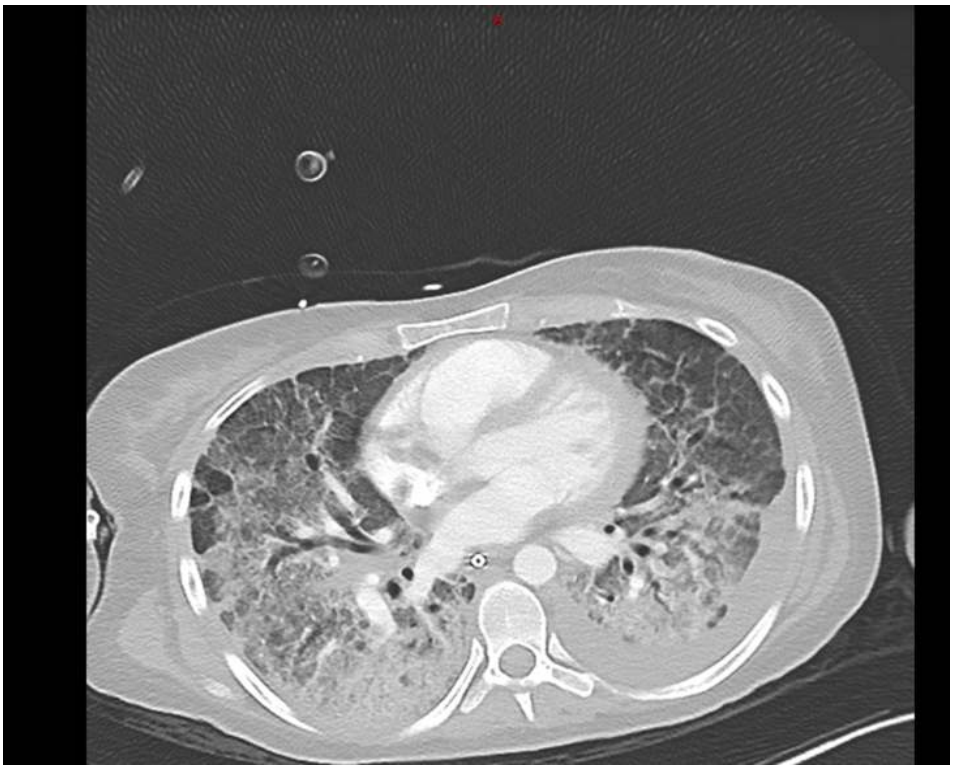
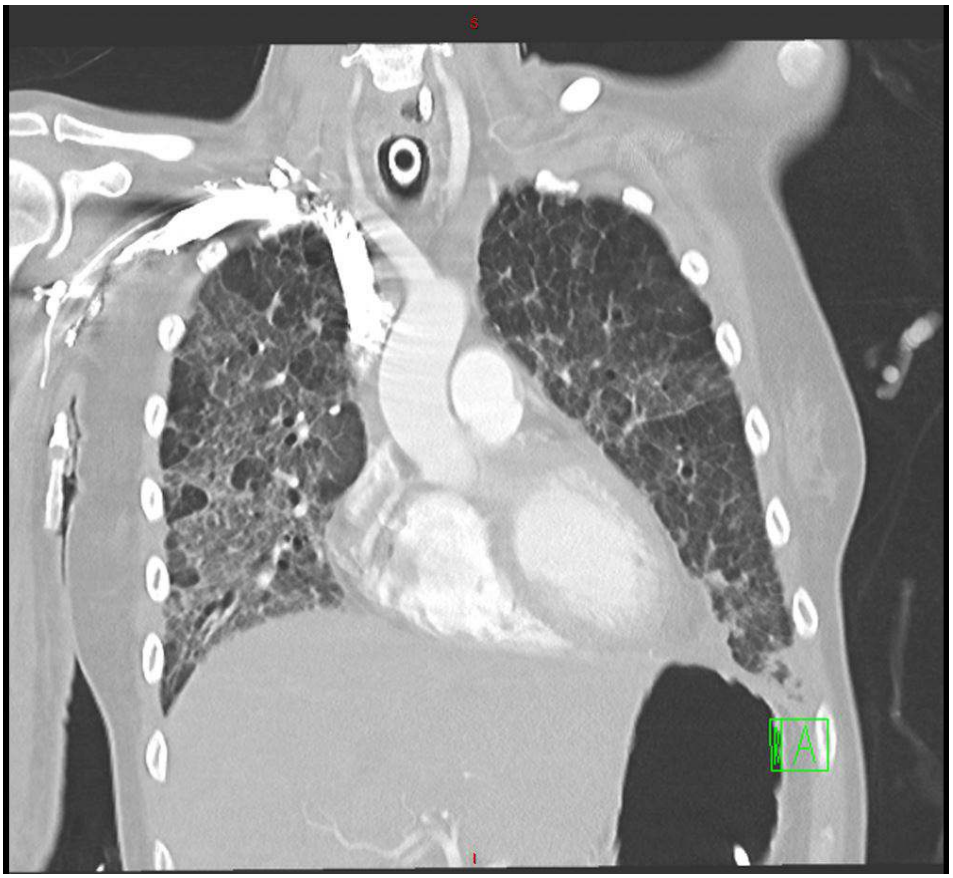
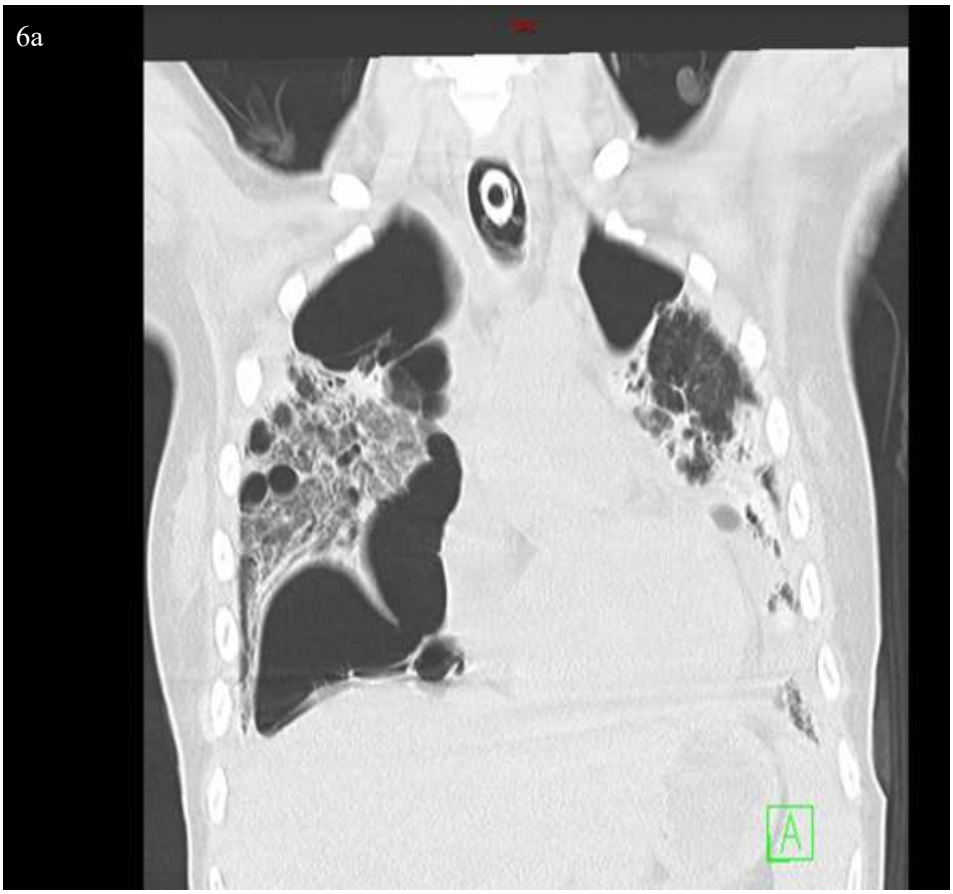
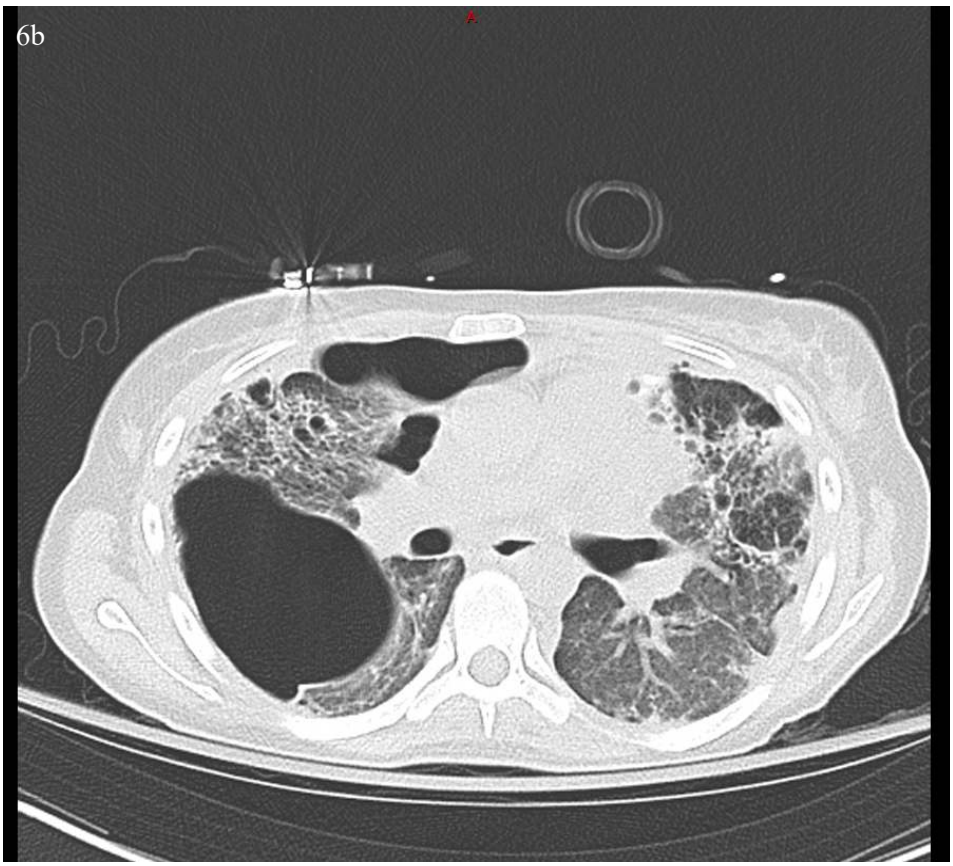


Figure 5b. Coronal chest computed tomography scan shows extensive reticular infiltrates and changes suggestive of initial fibrotic changes that were worse in the right lung



Figures 6a-c. Chest computed tomography scans show extensive destruction of the lung parenchyma, worse in all right lung lobes. Large bullous was visualized in the apical-posterior segment of the left lung, and extensive fibrotic changes in the remaining lung parenchyma were noted.

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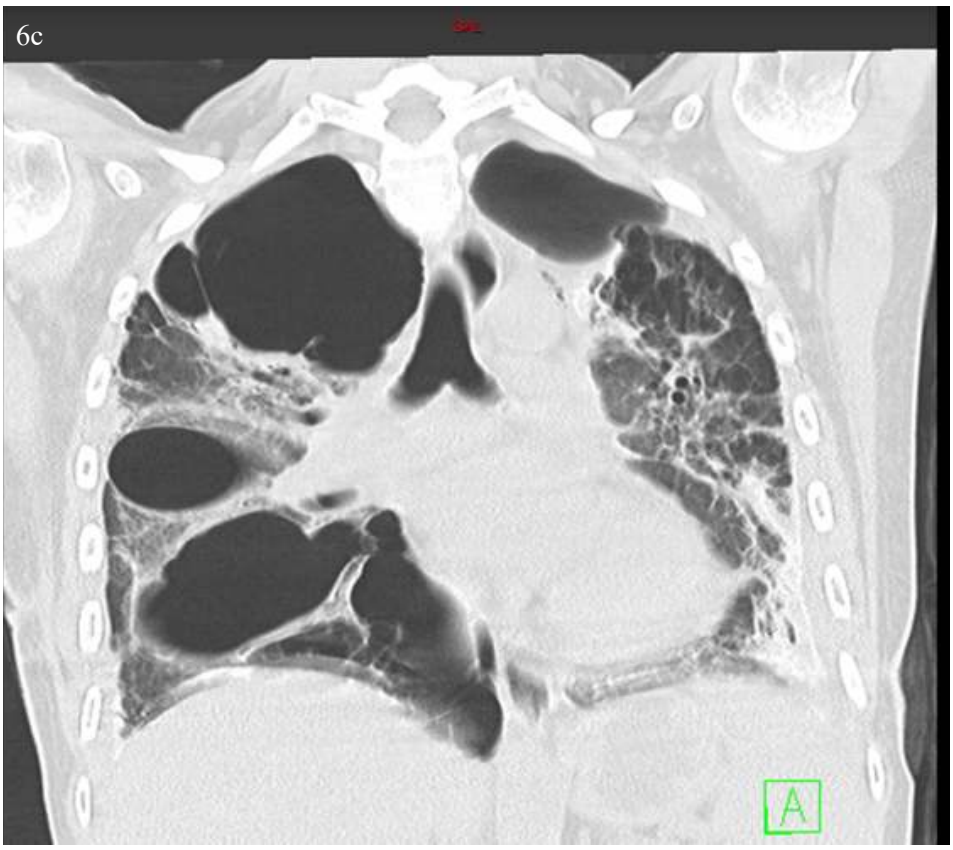
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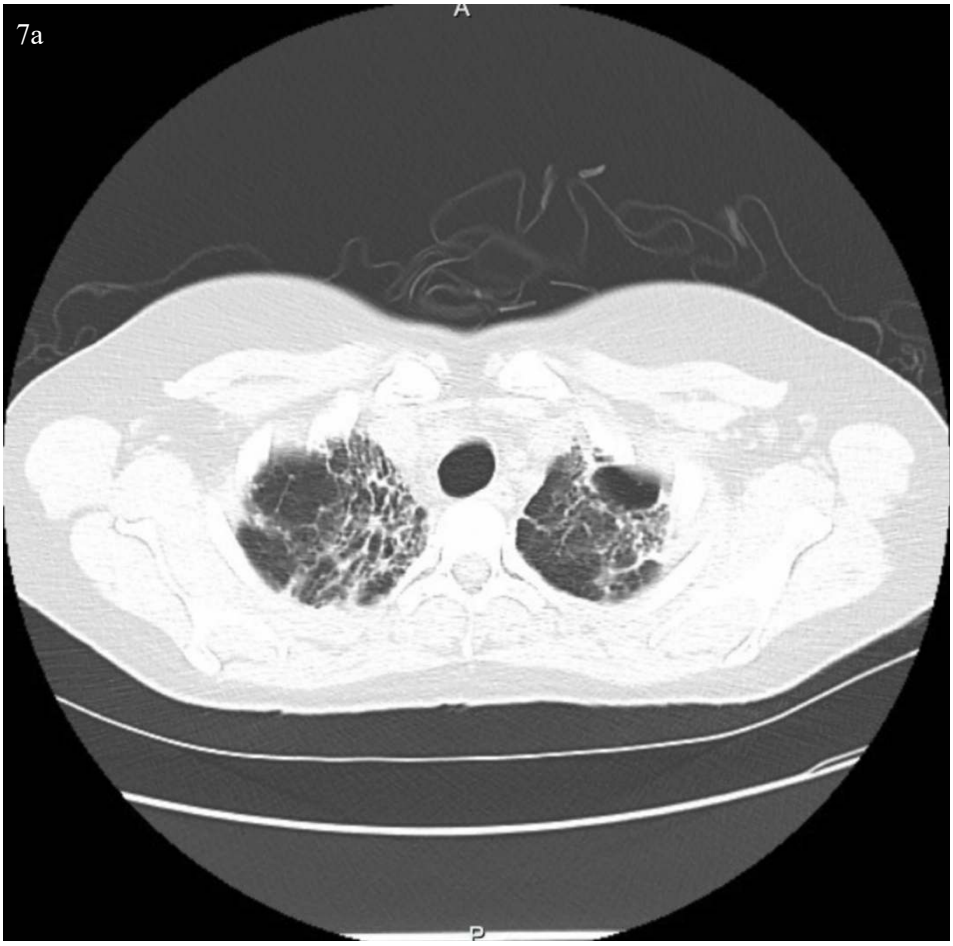
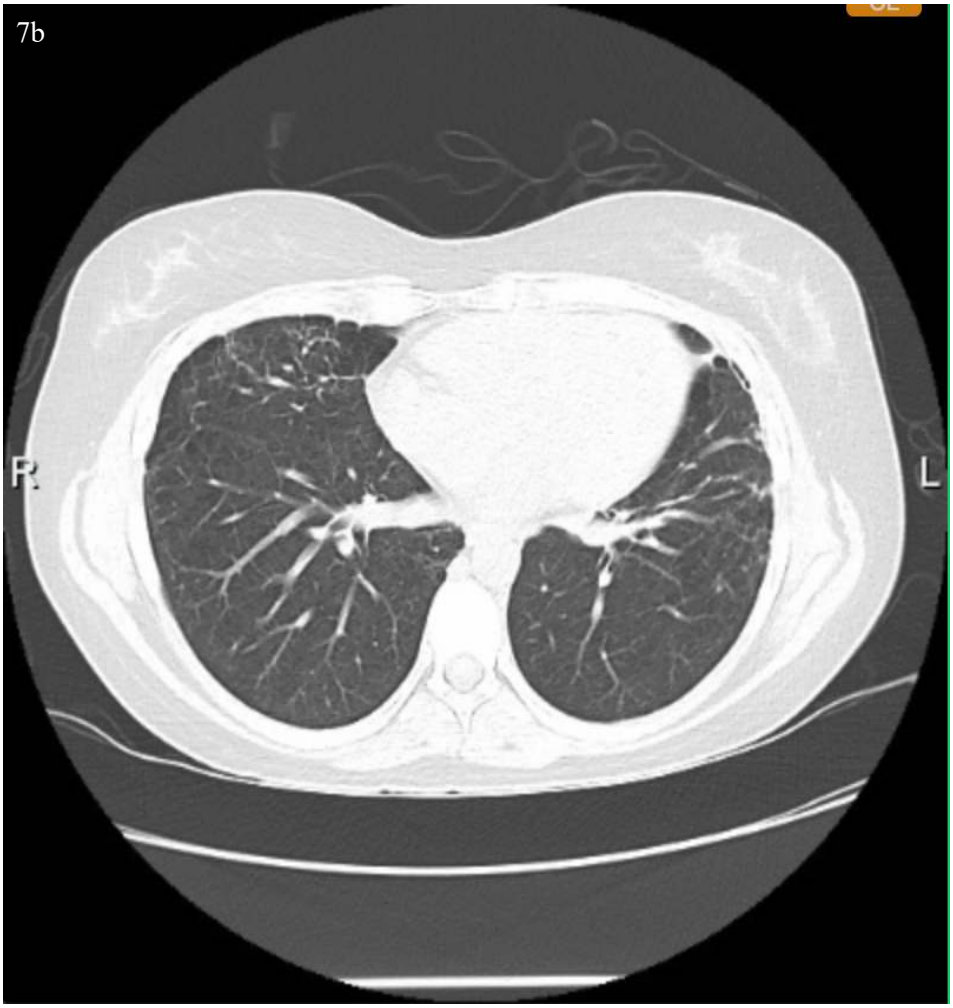
Figures 7a-c. Chest computed tomography scans without contrast show that the left apex's conspicuous bullous have almost completely resolved - remaining reticular densities in the lung apices and bases are seen.

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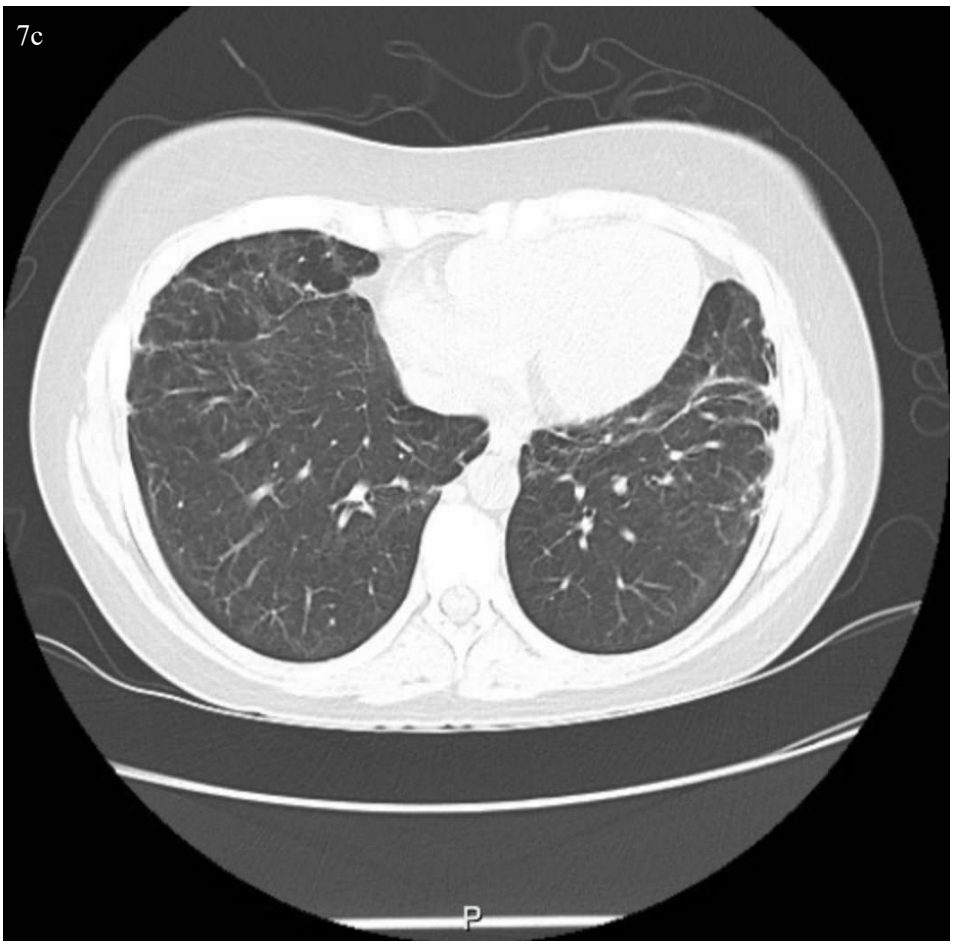
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