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"Tree-in-Bloom": Severe Acute Lung Injury Induced by Vaping Cannabis Oil

To the Editor:

"Marijuana" is defined by the United States Food and Drug Administration as the original parts (dried flowers and leaves) or forms of derivatives of the plant *Cannabis sativa L.* (1). In 2009, because of the high potential for abuse from its psychoactive ingredients (mainly δ-9-tetrahydrocannabinol [THC]), marijuana was categorized as a hallucinogen and was assigned to controlled substance Schedule 1, which also includes opioids and derivatives (1). This remains effective to date despite marijuana legalization in many states and emerging petitions for rescheduling (2).

Marijuana may affect respiratory health differently depending on differences in formulation and in methods and intensity of use. We report a case of acute respiratory failure that developed shortly after an individual inhaled vaporized cannabis oil. To the best of our knowledge, this adverse effect has not been reported previously.

Case Summary

A relatively healthy 54-year-old man was admitted to the hospital through the emergency department (ED) for acute onset of dyspnea and hemoptysis. He had never smoked cigarettes but had been vaping cannabis oil approximately once weekly for several years.

One day before presentation and 6 hours after vaping cannabis oil, the man developed dyspnea. His wife noticed that his breathing was rapid and shallow. He remained dyspneic the next day and started to expectorate blood-tinged sputum, which progressed to small quantities of "pure blood." This prompted a visit to a physician who advised him to go to an ED after he noted resting oxygen saturation (Sp_{O_2}) of 82%.

In the ED, the patient's Sp_{O_2} was 91% at rest while breathing supplemental oxygen at 6 liters per minute via nasal cannula. Physical examination was unremarkable except for tachypnea. A computed tomographic angiogram of the chest did not reveal pulmonary embolism, but instead showed extensive airspace opacification in a centrilobular nodular pattern roughly resembling a "tree in bloom" (Figure 1).

Antibiotic therapy was initiated after blood and sputum samples were sent for culture. Urine toxicity screening was positive

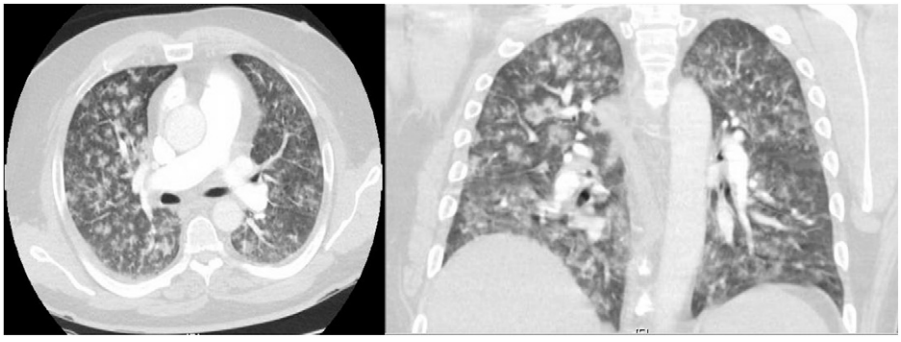

Figure 1. Chest computed tomographic scan showed extensive focal airspace opacities and the centrilobular nodular pattern giving an overall appearance not of "tree in bud" but of "tree in bloom." (*Left panel*) Transverse plane. (*Right panel)* Coronal plane.

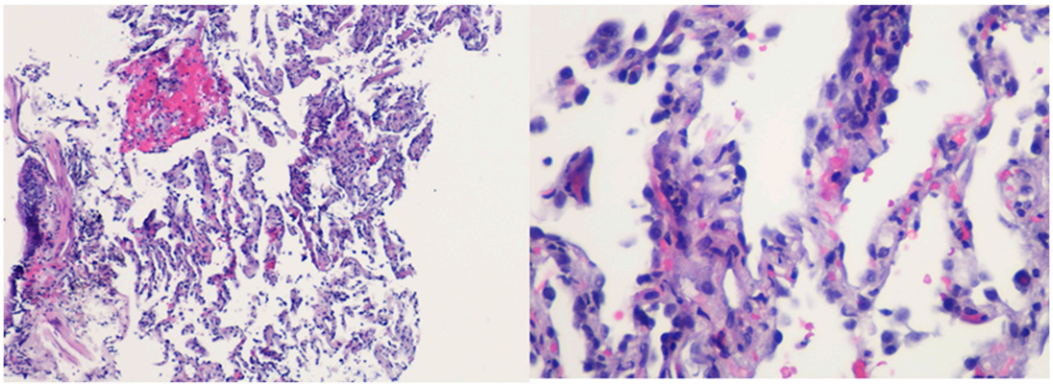

Figure 2. Focal hemorrhage, organizing pneumonia, and type 2 pneumocyte reactive hyperplasia. (*Left panel*) Hematoxylin and eosin staining, original magnification × 110. (*Right panel*) Hematoxylin and eosin staining, original magnification × 400.

for cannabinoids only. The patient was admitted to the intensive care unit on 50% oxygen via nasal cannula at a high flow rate to maintain Sp_{O_2} ⩾92%.

Flexible bronchoscopy yielded bloody lavage fluid suspicious for diffuse alveolar hemorrhage, with 61% neutrophils, 8% lymphocytes, and 2% eosinophils. Flow cytometry of the fluid showed a CD4/CD8 ratio of 0.46. Histopathology of alveolar tissue obtained via transbronchial biopsy showed organizing pneumonia (Figure 2). Urine antigens for legionella and histoplasmosis were negative. An upper respiratory viral panel was negative and HIV serology and rheumatologic tests were all negative. Microbiologic culture was negative for all samples.

The patient's oxygen requirement declined rapidly after the first day. He was discharged to home on Day 5 with ambulatory Sp_{O_2} >95% while breathing ambient air. Because of the rapid improvement, he was not treated with a corticosteroid. A repeat computed tomographic scan of the chest obtained 2 weeks after discharge showed complete resolution of lung opacities (Figure 3).

Discussion

We believe that vaping a product sold as cannabis oil was the cause of our patient's respiratory failure, given the temporal relationship between inhalation and the onset of symptoms, his rapid improvement without further exposure, and the fact that no other plausible cause was identified. The findings of pulmonary alveolar hemorrhage, neutrophil-predominant lavage, a reverse CD4/CD8 ratio (3), and organizing pneumonia in lung tissue biopsy specimens further support acute inhalational lung injury as the cause of respiratory failure.

Detrimental respiratory effects have been associated with the inhalation of combustion products of marijuana, including smoking hand-rolled leaves (joints) or water pipes (bong). Acute use can cause pneumothorax (4) and bronchodilation, which was exploited to treat asthma in the 19th century (5). Habitual use increases the prevalence of respiratory symptoms such as chronic cough and dyspnea (6). Chronic bronchitis is likely caused by products of combustion, which include pyrolytics such as tar and irritants such as ammonia and nitrogen oxides (7). Whether inhalation of marijuana smoke can cause emphysema or lung cancer is controversial (6, 8, 9). Marijuana smoke inhalation, which may be associated with damage to the pulmonary epithelial barrier (10), has rarely been reported to cause severe lung injury (11–13).

Vaporizing systems were developed with the goal of reducing the adverse respiratory effects of inhaling tobacco and cannabis derivatives. Ideally, cannabis vaporizers should have high efficiency for delivering THC and should minimize the generation of deleterious byproducts. Currently available products are designed to achieve those goals by heating dried marijuana parts to a temperature above 180°C (to vaporize cannabinoids) and below 230°C (to avoid combustion)

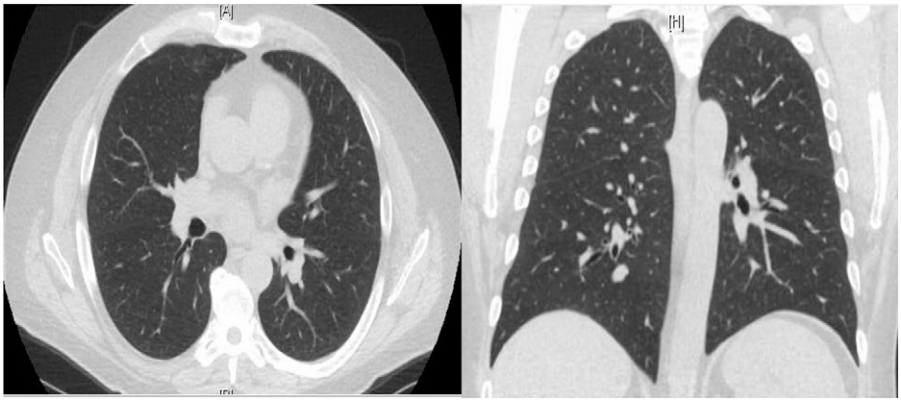

Figure 3. Repeated computed tomographic chest scan 2 weeks after the initial one, showing complete resolution of the airspace opacities.

(14, 15). Cannabis oil vaping is a newer method of use; a prefilled cartridge of cannabinoid concentrated oil is loaded into a hand-held vaporizer, which has a battery-operated heating system. This method avoids vaporizing crude marijuana parts and is thought to be safer.

However, some oil products are extracted from marijuana using additives such as propylene glycol which, although classified as "generally recognized as safe" by the Food and Drug Administration when ingested orally, can potentially cause lung injury when inhaled at a high temperature (16). Heating can also transform propylene glycol into carbonyls such as formaldehyde, a carcinogen and respiratory irritant (17). Flavoring ingredients, including diacetyl, may also pose risks to respiratory health (18); although it is more recognized in e-cigarette use, it can be present in cannabis oil vaping.

Our patient reported using "pure cannabis oil" containing 32–40% of THC extracted with CO_2 with no additives. Although we found only cannabinoids on toxicological screening of his urine, we cannot exclude the possibility that lung injury was caused by some contaminant. Other possible contributors to his severe adverse lung reaction include the method used to extract the oil, the combustion temperature, and barotrauma from a forceful Valsalva maneuver during or after vaping. Further studies are needed to confirm our observation and to identify risk factors.

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Concomitant Diffuse Alveolar Hemorrhage and Pulmonary Embolism in a Child with Isolated Pulmonary Capillaritis

To the Editor:

Isolated pulmonary capillaritis (IPC) is a small-vessel vasculitis of the lung that is classically described as pauciimmune. There is a well-documented increased risk of venous thromboembolism in antineutrophil cytoplasmic antibody (ANCA)–associated vasculitides; however, thrombosis has never been described as a complication of IPC. Here we describe a young child with IPC who presented with life-threatening diffuse alveolar hemorrhage and concomitant bilateral pulmonary emboli.

Case Presentation

A 2.5-year-old girl with trisomy 21 and a repaired atrioventricular septal defect was admitted to a community hospital with a 3-day history of progressive respiratory distress. She was anemic (hemoglobin, 39 g/L [~24 mmol/L]) and thrombocytopenic (platelets, 118×10^9/L). A chest radiograph revealed bilateral diffuse parenchymal infiltrates with no focal consolidation (Figure 1).

She was treated for community-acquired pneumonia, but her respiratory status continued to deteriorate. On Day 8 of illness, she was transferred to our pediatric intensive care unit. On Day 10, she developed respiratory failure. She was intubated, and a right internal jugular central venous line was placed. On intubation, copious fresh blood was suctioned from the endotracheal tube. An echocardiogram showed intact cardiac repair with no evidence