# E-Cigarette or Vaping-Associated Pneumomediastinum: A Case Report and Pathophysiological Explanation

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## Keywords
Spontaneous pneumomediastinum ; e-cigarette ; vaping ; pathophysiology ; adolescent health.

## Abstract

We report the case of a 16-year-old male who presented to the emergency room with chest pain, fever and shortness of breath. Upon physical examination Hamman's sign was positive. The patient was diagnosed with spontaneous pneumomediastinum, most probably caused by e-cigarette use and/or asthma exacerbation. He was treated with nebulizations with salbutamol, corticosteroids and antibiotics and made a full recovery.

This case adds to the evidence of e-cigarette or vaping-associated pneumomediastinum in adolescents. We identified three mechanisms by which vaping can cause pneumomediastinum: the act of smoking itself, through alveolar damage as part of e-cigarette or vaping product use-associated lung injury or, in a secondary way, by triggering an asthma exacerbation.

This case highlights the importance for pediatricians to ask about the use of e-cigarettes in adolescents presenting with chest pain, gastro-intestinal, constitutional and/or respiratory complaints. It also shows that we must educate our patients about the risks of e-cigarette use whenever the opportunity is there. Spontaneous pneumomediastinum should be considered in the differential diagnosis of adolescents with chest pain who use e-cigarettes.

## Introduction

Pneumomediastinum is a pathological condition characterized by free air in the mediastinal space. It can be categorized as spontaneous or traumatic. Spontaneous pneumomediastinum (SPM) is a rare condition, particularly in children and adolescents. The reported incidence in this population (under 18 years old, excluding newborns with SPM) presenting to the emergency department ranges from 1 in 8.000 to 1 in 15.000 in retrospective studies (1). However, one study found an incidence of 1 in 368 when routine screening was performed on young adults (14-29 years old) admitted for unexplained chest pain or dyspnea (2). This suggests that SPM may often go undiagnosed in children and adolescents presenting with chest pain.

In adolescents, SPM is most commonly triggered by an asthma exacerbation (3). However, recent case reports suggest a potential risk of SPM in otherwise healthy adolescents who use e-cigarettes (4-11). This case adds to the evidence of e-cigarette or vaping-associated pneumomediastinum in adolescents.

A recent survey conducted in 2023 among adolescents living in Curaçao, found that 16% of teenagers on the island owned an e-cigarette, with 41% of them having used the device in the past six months. The youngest users were just 10 years old, highlighting the urgency of this issue in pediatric care (12).

In Belgium, a similar survey conducted in 2018 showed that 7.4% of adolescents had used an e-cigarette in the 30 days preceding the survey. When the survey was repeated in 2022 within the Flemish community, the percentage had risen to 11.9% (13). These findings indicate a growing trend in e-cigarette use among adolescents, emphasizing the need for clinicians to be aware of its dangers and the importance of educating young people about the associated health risks.

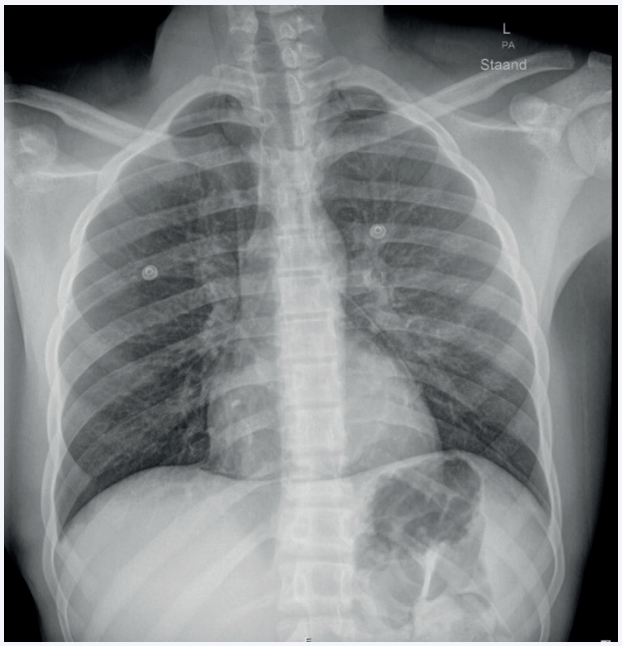
## Case

A 16-year-old male presented to the emergency department with chest pain, fever, and shortness of breath. The pain began the night before, predominantly on the left side of his chest, spreading to his left arm. He attributed the pain to muscle strain sustained from lifting a goat earlier that day. The following morning, he developed shortness of breath and a fever, which led him to seek medical attention. The pain intensified with respiration. Additionally, he reported abdominal discomfort and a loss of appetite in de days prior to his presentation. His medical history is notable for bronchial hyperreactivity at four years of age and amphetamine intoxication at ten years of age.

His vitals upon arrival: temperature of 38.3 degrees Celsius, respiratory rate 36/min with a saturation of 91% in room air, heart rate 109/min and blood pressure 136/79 mmHg.

Significant physical assessment findings: in- and expiratory wheezing over all lung fields with crepitations over the right lower lung field as well as crepitations synchronous with the heart beat (Hamman's sign).

**FIGURE 1:** Thoracic X-ray at moment of presentation




Thoracic X-ray was obtained (Figure 1) and showed pneumomediastinum with suspicion of pneumopericardium. Computed tomography (CT) of the thorax (Figure 2, 3) confirmed the presence of pneumomediastinum with associated emphysema in the neck. Pneumopericardium and pneumothorax were ruled out. There was also bronchial wall thickening visible, especially in the lower lobes, which was attributed to the use of e-cigarettes and/or underlying asthma.

Laboratory results showed leukocytosis (white blood cell count of 13.2 x10⁹/L [reference range 3.5 - 11.0] with neutrophilia and a CRP of 26 mg/L [normal <10]. D-dimer was negative. Blood cultures were obtained and remained negative.

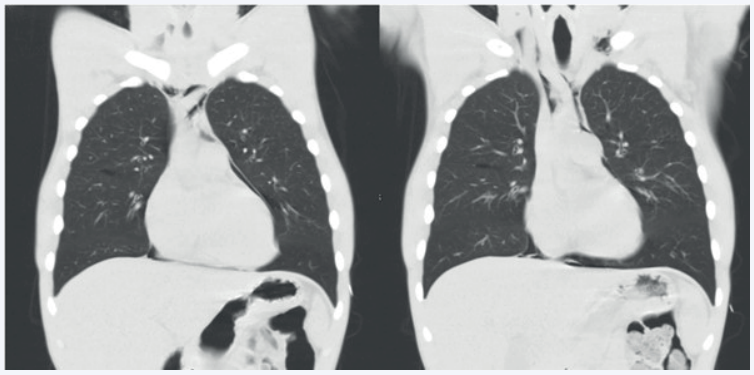
Electrocardiogram, performed to look for signs of cardiac ischemia or arrhythmias, was normal.

Given the patient's medical history and presenting symptoms, asthma exacerbation was our primary differential diagnosis.

The patient was treated with non-steroidal anti-inflammatory drugs and acetaminophen, frequent nebulizations with salbutamol and oxygen suppletion through a venturi mask. Given the severity of his presentation, the treatment regimen was intensified with the addition of oral prednisone (20mg twice daily) to manage an asthma exacerbation and intravenous amoxicillin/clavulanic acid (1000/200mg four times daily) to address a possible underlying lung infection.

During his admission, we learned that he used e-cigarettes with nicotine on a regular basis. He denied smoking combustible cigarettes or using other drugs. E-cigarette associated lung injury was considered as a potential cause of his pneumomediastinum (see discussion). No further investigations were conducted.

**FIGURE 2:** Chest CT, frontal plane

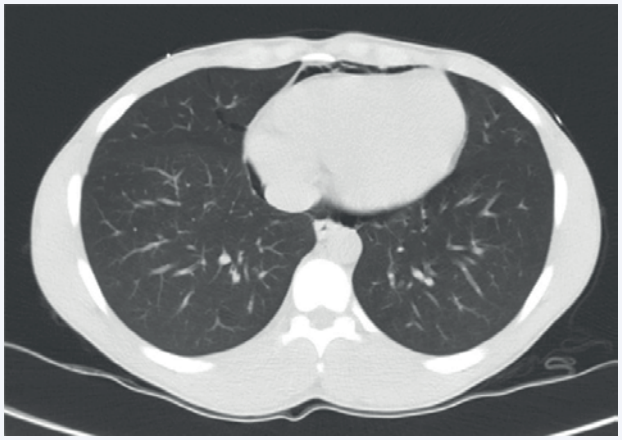


His clinical condition gradually improved. On the fifth day, a follow-up thoracic X-ray showed normalization of the mediastinum. The course of amoxicillin/clavulanic acid was completed over five days, while prednisone was continued for seven days. Oxygen therapy was discontinued after six days.

After eight days, the patient was discharged with a tapering schedule for salbutamol puffs and maintenance therapy with formoterol/beclomethasone. He also received counseling on the potential impact of vaping on his lung health.

Although follow-up was arranged, the patient did not attend his scheduled appointments.

**FIGURE 1:** Chest CT, transverse plane



## Discussion

### Causes of spontaneous pneumomediastinum linked to e-cigarette use

SPM is most commonly caused by alveolar rupture that allows air to enter the surrounding bronchovascular sheath and flow down a pressure gradient from the alveolus to the mediastinum as demonstrated by Macklin and Macklin in 1939. Alveolar rupture occurs when the pressure gradient between the alveoli and the surrounding structures reaches a critical level and can therefor occur by increased intra alveolar pressure and/or by decreased pressure in the interstitial space (14). Abnormalities of the alveolocapillary membrane can contribute to the occurrence of alveolar rupture (15).

This mechanism explains how asthma exacerbation and Valsalva maneuver when lifting heavy objects can cause SPM. As previously stated, the use of e-cigarettes has also been associated with the occurrence of SPM in adolescents and young adults.

We propose two mechanisms by which e-cigarette use may directly result in alveolar rupture.

**TABLE 1:** Results from retrospective cohort study of 44 adolescents by Kopsombut G et al. (22)

| | |
|---|---|
| Content of vape | 90% delta-9-tetrahydrocannabinol containing products |
| Presenting symptoms at time of admission | Most common: vomiting, fever, cough<br>84% constitutional symptoms (fever, weight loss, fatigue, chills, headache)<br>81% gastro intestinal symptoms (nausea or vomiting, diarrhea, abdominal pain)<br>74% respiratory symptoms (cough, shortness of breath, chest pain or tightness, congestion, hemoptysis) |
| Laboratory findings (average and CI) | Elevated white blood cell count of 14.300/µL (CI, 13.7–15.0) with neutrophilic predominance<br>CRP of 25.2 mg/dL (CI, 22.1–28.2)<br>Erythrocyte sedimentation rate of 66.7 mm/hour (CI 26.9–76.4)<br>Abnormal coagulation studies were observed in all 21 patients who underwent such testing: PT of 17.7 seconds (CI, 16.4–19.1), INR of 1.54 (CI,1.43–1.66) |
| Imaging studies | Chest radiograph:<br>- 20% normal<br>- 26% abnormal with hyperinflation, pneumomediastinum or pneumothorax<br>- 54% lung field haziness or multifocal opacities<br>Chest CT scan:<br>- 100% lung parenchymal pathology: bilateral ground glass opacification with sub pleural sparing. The lower lobes were more affected than the upper lobes |
| Pulmonary function testing | 21% of tested individuals (n=14) had signs of airway obstruction (forced expiratory volume in 1 second/forced vital capacity <85% of predicted value)<br>This normalized after hospitalization (within 6 weeks) |
| BAL | 3 out of the 4 BAL samples exhibited the presence of red blood cells, while all 4 demonstrated the presence of lipid-laden macrophages |

The first mechanism pertains to the act of smoking itself and is also the proposed mechanism by which inhalation of smoking related drugs can cause SPM. In individuals who smoke cocaine or marijuana, a specific breathing pattern has been observed that may result in alveolar trauma. This pattern involves a forced exhalation, followed by inhalation against a closed airway (Muller's maneuver) which creates a negative intrapleural pressure. It is hypothesized that the narrow lumen of the e-cigarette may cause the user to inhale even more strongly, thereby enhancing the effect of Muller's maneuver (11). Additionally, exhalation against a closed glottis (Valsalva maneuver) is a common occurrence during smoking, representing another way by which smoking may lead to SPM (16-19).

The second mechanism is through alveolar damage as part of the acute lung injury seen in e-cigarette or vaping product use-associated lung injury (EVALI). The first large case series covering 98 cases of EVALI was published in 2019 by Layden et al. as a result of a public health investigation initiated by the Wisconsin Department of Health Services and the Illinois Department of Public Health (20).

Subsequently, a case definition of EVALI was proposed by the Centers for Disease Control and Prevention (CDC) in America. A case must meet three criteria: a history of vaping within 90 days prior to symptom onset, pulmonary infiltrate on imaging and the absence of an alternative diagnosis such as infection (i.e., diagnosis of exclusion). Presenting symptoms may be respiratory, gastrointestinal or constitutional (21).

Table 1 summarizes the clinical characteristics of EVALI in adolescents (12 to 18 years of age) based on a retrospective cohort study performed by Kopsombut et al (n=44) (22).

Although the coagulopathy observed in this patient group does not align with the clinical presentation defined by the American Thoracic Society—which is based on literature review and expert opinions from both adult and pediatric specialists—all other findings described above are consistent (23). The authors could not identify the exact causation for the observed coagulopathy in their cohort and suggest further studies on this subject (22). In our patient, no coagulation studies were performed apart from D-dimers, which were within normal limits.

The exact pathophysiology of EVALI is not yet fully understood, but it is thought that inhaled chemicals cause direct cell damage and disrupt immune responses, leading to lung inflammation. E-cigarettes can contain various harmful substances, but vitamin E acetate has been strongly implicated as a key factor in the 2019 outbreak. A pivotal study by Blount et al. found vitamin E acetate in 94% of bronchoalveolar lavage (BAL) fluid samples from EVALI patients, while none was detected in healthy controls, including smokers and e-cigarette users without lung injury (24). This additive, used as a thickening or diluting agent in delta-9-tetrahydrocannabinol (THC)-containing vaping liquids, became common on the illicit market in late 2018 and gained popularity in 2019, coinciding with the surge in EVALI cases.

Vitamin E acetate can alter surfactant properties, making it less effective at maintaining normal surface tension in the lungs (24). It also causes cytotoxic effects in various lung cells and activates macrophages that cannot break it down, leading to cell death and an exaggerated inflammatory response (25). This explains the frequent finding of lipid-laden macrophages in BAL fluid from EVALI patients (22). Animal studies have since confirmed that inhaled vitamin E acetate can reproduce lung damage similar to that seen in human EVALI cases (26, 27).

These findings led the CDC to issue a warning against using vitamin E acetate in vaping products in 2020 (28). Following increased public awareness, removal of vitamin E acetate from many THC e-liquids, and enforcement against illicit products, EVALI cases peaked in September 2019 and declined sharply afterwards, prompting the CDC to end national surveillance in February 2020. However, isolated cases still occur (29).

While vitamin E acetate accounts for most THC vaping–associated cases, approximately 14% of EVALI patients during the CDC's national surveillance period reported using only nicotine-containing e-cigarettes (28). This indicates that additional causative agents may contribute to EVALI, including flavoring additives, solvents such as propylene glycol and glycerol, manufacturing contaminants, or nicotine itself. Notably, nicotine vapor exposure directly increases pulmonary endothelial permeability, disrupts endothelial barrier integrity, and promotes inflammation and oxidative stress in a dose-dependent manner (27, 30-32).

In addition to the aforementioned mechanisms, e-cigarettes can also indirectly contribute to SPM by precipitating an asthma exacerbation. As e-cigarette use is a known risk factor for developing asthma and increases the frequency of exacerbations in asthma patients, this provides a secondary pathway through which e-cigarettes may lead to SPM (33).

## Literature cases of spontaneous pneumomediastinum attributed to e-cigarette use

A literature search yielded eight case-reports describing in total nine cases of SPM attributed to e-cigarette use in adolescents aged 18 years or younger (4-11). Of those nine cases, five were reported as part of EVALI (4, 8-10) and two were believed to be due to forceful inhalation (act of smoking) and/or secondary to coughing (7, 11). In two of the cases, no suspected causative mechanism was mentioned (5, 6). It is our hypothesis that both of these cases were due to the act of smoking.

Table 2 provides an overview of the characteristics of these nine cases.

All of the listed cases attributed to EVALI, were users of THC containing e-cigarettes, adding to the evidence of the strong link between THC containing e-cigarettes and EVALI. These cases were published/occurred in the years 2019-2020, when vitamin E acetate was still used as additive to THC containing e-liquids. Unfortunately, in only one case was the patient's e-liquid analyzed, revealing a vitamin E acetate concentration of 66%.

Cases that were attributed to the act of smoking used nicotine containing e-cigarettes or did not specify which specific product was used nor investigated what substances it contained.

## Application and integration of the above information into the case

In this case, e-cigarette use and asthma exacerbation are likely contributors to the patient's spontaneous pneumomediastinum (SPM). While non-vape-related causes such as heavy lifting, respiratory infection, or an asthma flare from another trigger were considered, none fully explain the full symptom profile.

The patient presented with the typical EVALI triad—gastrointestinal, respiratory, and constitutional symptoms—and lab findings aligned with previous adolescent EVALI cases, including bronchial wall thickening on CT (22, 34). However, failure to meet CDC criteria (no pulmonary infiltrate on chest imaging, infectious causes could not be ruled out) argue against a definitive EVALI diagnosis (21).

Given the patient's history of childhood bronchial hyperreactivity, undiagnosed or reactivated asthma remains a plausible cause, possibly triggered by regular e-cigarette use, which is known to exacerbate asthma (33).

Lifting a goat, potentially involving a Valsalva maneuver, may have contributed by increasing the intrathoracic pressure, but this does not explain the systemic symptoms. Similarly, while lower respiratory infections can cause SPM, the lack of radiographic evidence makes pneumonia unlikely.

In conclusion the SPM diagnosed in our patient is most likely caused by e-cigarette use and/or asthma exacerbation.

**TABLE 2:** Characteristics of nine reported cases of SPM directly related to e-cigarette use in adolescents

| | Age | Sex | Nicotine or THC containing vape | Vit E acetate containing liquid | Reported mechanism | | | Mechanism based on our interpretation |
|---|---|---|---|---|---|---|---|---|
| | | | | | EVALI | Act of smoking | No mechanism reported | |
| ***Case 1 (4)*** | 18 | Male | Both | Not specified | x | | | EVALI |
| ***Case 2 (4)*** | 17 | Female | Both | Not specified | x | | | EVALI |
| ***Case 3 (5)*** | 17 | Male | Not specified | Not specified | | | x | Smoking |
| ***Case 4 (6)*** | 17 | Male | Nicotine and flavoring additives | Not specified | | | x | Smoking |
| ***Case 5 (7)*** | 18 | Male | Not specified | Not specified | | x | | Smoking |
| ***Case 6 (8)*** | 15 | Male | THC | Not specified | x | | | EVALI |
| ***Case 7 (9)*** | 16 | Female | Both | Not specified | x | | | EVALI |
| ***Case 8 (10)*** | Teenage | Male | Both, "off-brand", mint-flavored nicotine product | The most recently vaped THC cartridge contained 66% tocopheryl acetate (Vitamin E) | x | | | EVALI |
| ***Case 9 (11)*** | 18 | Male | Not specified | Not specified | | x | | Smoking |

## Treatment and outcome of spontaneous pneumomediastinum

Spontaneous pneumomediastinum (SPM) is generally a benign and self-limiting condition that typically resolves within 3 to 15 days. Management usually consists of analgesia, rest, avoidance of activities that increase intrathoracic pressure and treatment of any identified underlying condition (35). Although high-concentration oxygen therapy is frequently employed—based on the proposed "nitrogen washout" effect, which may accelerate resorption of free air into surrounding blood vessels — the supporting evidence is limited (36). A recent review by Grasmuk-Siegl et al. highlighted the absence of adequately randomized controlled trials validating oxygen therapy in normoxemic patients with pneumothorax (37). For the treatment of SPM, evidence is even more limited. Consequently, routine oxygen administration in children and adolescents with SPM is not universally recommended and should be individualized.

Our patient was managed in line with these general principles, receiving analgesics, bed rest, and treatment for an asthma exacerbation—presumed to be the underlying cause—as previously described. Empirical antibiotics were initiated to cover potential pneumonia. Following admission, the patient disclosed a history of e-cigarette use, prompting consideration of EVALI as a differential diagnosis. According to CDC guidelines, EVALI management includes corticosteroids and cessation of e-cigarette use (21). However, there are no randomized clinical trials establishing the efficacy of specific therapeutic interventions for EVALI. Reported treatment is largely supportive and comprises oxygen therapy, (non-) invasive ventilation, corticosteroids and empiric antibiotics. Dose and duration of corticosteroid therapy vary considerably across cases (23).

In practice, the management of EVALI overlaps substantially with that of asthma exacerbation, particularly in the use of supportive care, oxygen supplementation, and corticosteroids to reduce inflammation—whether due to inhaled toxins in EVALI or allergic airway hyperresponsiveness in asthma. Key differences include the routine use of bronchodilators in asthma, which are not commonly indicated in EVALI unless bronchospasm is present. Moreover, while antibiotics are often empirically prescribed in suspected EVALI until infection is excluded, they are generally reserved for asthma exacerbations only when bacterial infection is suspected. Importantly, while smoking and vaping cessation is advisable in both conditions, it is of primary importance in the treatment of EVALI.

In this case, the initial treatment effectively addressed both possible diagnoses. Given the patient's steady clinical improvement and the substantial overlap in treatment approaches, no additional diagnostic investigations or changes to the management plan were deemed necessary.

## Long-term health effects of e-cigarette use on previously non-smokers

Given the growing prevalence of e-cigarette use among adolescents, understanding potential long-term health effects is essential for counseling and follow-up. In this section, we provide a brief overview of what is currently known about these long-term effects. Because e-cigarettes were only introduced about 20 years ago, and widespread use has emerged mainly in the past decade, there is still limited clinical and experimental evidence regarding their long-term impact (27). Nevertheless, several worrisome findings have already been reported in the short and medium term, indicating negative effects of e-cigarette use on the cardiovascular and respiratory systems.

A recent review by Izquierdo-Condoy et al. on the health implications of e-cigarette use indicates that while switching to e-cigarettes may offer some health benefits for smokers, their use in a non-smoking, healthy population is associated with several adverse effects (38). These include increased heart rate, elevated mean arterial blood pressure, greater arterial stiffness and various changes in the respiratory system such as altered transcriptomes of small airway epithelium cells and alveolar macrophages, as well as signs of airway obstruction on lung function tests. Many of these effects are linked to the harmful impact of nicotine, although current evidence is conflicting, and further research is needed to determine whether nicotine is solely responsible.

Studies investigating the long-term effects of e-cigarette use in healthy populations remain limited. Regarding cardiovascular risks, e-cigarette use has been associated with higher odds of myocardial infarction compared to non-users (39, 40). Concerning respiratory health, a longitudinal analysis of the adult PATH (Population Assessment of Tobacco and Health) study found a statistically significant link between former or current e-cigarette use at baseline and the development of respiratory diseases—such as COPD, chronic bronchitis, emphysema or asthma—about two years later (41). Additionally, in vitro experiments and animal studies indicate that e-cigarette exposure increases oxidative stress, protease activity, inflammation, and DNA damage, suggesting a potential elevated risk for COPD and lung cancer (42). Although these findings point toward possible long-term harm, more robust research is essential to clarify the overall long-term health effects of e-cigarette use.

Beyond these direct health impacts, it is important to highlight the additional risks for young people due to the so-called gateway effect: evidence suggests an association between e-cigarette use and subsequent combustible cigarette smoking (43). Children and adolescents, often attracted by the appealing designs and flavors, may develop nicotine addiction and transition to other tobacco products. Furthermore, youth e-cigarette use has been linked to increased use of other substances, such as alcohol, marijuana and other illicit drugs (44).

## Strengths and weaknesses of this case report

This case served as a foundation for generating hypotheses regarding the pathophysiology of e-cigarette-associated SPM in adolescents. It provided an opportunity to explore the various potential triggers for SPM in this instance and reflects the diagnostic reasoning clinicians regularly navigate.

However, the diagnostic limitations of this case should be addressed. In future cases, it would be valuable to perform microbiological analyses to rule out infectious causes of SPM and to support the diagnostic workup for EVALI.

Furthermore lung function testing might be useful. There is no place for lung function testing in the acute diagnostic workup of SPM since forceful in-and exhalation could aggravate the condition. In follow-up however it might be useful for two reasons: first, to identify underlying asthma, which requires appropriate treatment and monitoring; and second, in case of EVALI, to monitor the residual lung damage. Lung function abnormalities have been described in pediatric EVALI patients, which may persist despite clinical improvement. It is on the other hand not useful as a retrospective diagnostic measure for EVALI since there is no clear lung function signature of EVALI. Reported abnormalities include both airflow obstruction as restriction or a combination of both, with our without impaired diffusion capacity (34, 45, 46).

The lack of follow-up in this case is suboptimal because of the suggested adverse health effects of vaping and the long-term respiratory, cognitive and vaping behavior outcomes patients with EVALI face, as described by Blagev et al. (47). In their cohort of seventy-three adult patients diagnosed with EVALI they found that 39% of them had cognitive impairment, 48% reported respiratory limitations, 59% had mood disorders (anxiety and/or depression) and 62% had post-traumatic stress symptoms after 1 year of follow-up.

Unfortunately most of them continued vaping, with only 38% quitting all vaping and smoking behaviors with younger age being associated with reduced vaping behavior after EVALI.

In future cases, we recommend a structured, multidisciplinary follow-up in accordance with the guidelines of the CDC and the American Thoracic Society. An initial follow-up visit should take place within 48–72 hours after discharge to assess clinical stability, reinforce abstinence from e-cigarette use, ensure medication adherence and address any comorbidities as well as social or behavioral health needs. A second follow-up visit approximately two months after discharge is advisable to evaluate for persistent abnormalities on pulmonary function tests and imaging. Additionally, the CDC recommends an interim follow-up within 2–4 weeks—often coinciding with completion of corticosteroid tapering—to assess pulmonary function and radiographic resolution. Further long-term follow-up is equally important to monitor for the aforementioned long-term effects (23, 48).

## Conclusion

By outlining the various pathophysiological pathways through which vaping can lead to pneumomediastinum, this case underscores that vaping should be considered a potential cause of SPM in adolescents. It adds to the growing evidence linking e-cigarette use to adverse respiratory outcomes in this age group. Given the rising prevalence of e-cigarette use, the unclear long-term health risks, and its potential role as a gateway to other substance use, there is an urgent need for increased awareness and preventive education targeting this vulnerable population.

## Statements

The author(s) have no conflicts of interest to declare.

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent for publication of this case was obtained orally and written down in the file of the patient.

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