

# **Cannabis-induced bullous lung disease leading** to pneumothorax

# Case report and literature review

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### Abstract

**Rationale:** Marijuana use has been increasing in the United States among college students and young adults. Marijuana use has been associated with bullous lung disease which can lead to pneumothorax. There are other recreational drugs like methylphenidate, cocaine and heroin which have been associated with pneumothorax.

**Patient concerns:** We present a case of a 30-year-old man with spontaneous pneumothorax associated with marijuana use. The patient had no medical conditions and presented to the emergency room with chest pain. The physical examination revealed decreased breath sound on the right side of the chest.

**Diagnoses:** Bed side ultrasound of chest showed stratosphere sign, absent lung sliding; consistent with right-sided pneumothorax. **Interventions and outcomes:** The patient underwent placement of a chest tube. Computed tomography chest scans

performed on day two also showed bullous lung disease in the right lung. Serial x-rays of the chest showed re-expansion of the lung.

**Lessons:** Despite the beneficial effects of Marijuana there are deleterious effects which are emphasized here. This case highlights the need for further studies to establish the relationship between marijuana use and lung diseases in the absence of nicotine use.

**Abbreviations:** CT = computed tomography, CXR = chest roentgenogram.

Keywords: bullous lung disease, marijuana, pneumothorax

# 1. Introduction

Marijuana is the most prevalently used illegal drug worldwide.<sup>[1]</sup> Marijuana, now ubiquitous, is derived from the Cannabis sativa plant, which is native to Asia. Because cannabis is highly lipid soluble, it is quickly absorbed by the respiratory and gastroin-

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testinal mucosa. Smoking marijuana produces effects within a few minutes of inhalation, whereas ingested marijuana takes about 1 to 3 hours to produce effects.<sup>[2]</sup>

In 2015, the prevalence of daily marijuana use among students in the 8th, 10th, and 12th grades was reported as 1.1%, 3%, and 6%, respectively. The perceived risks of marijuana smoking have declined in the 2000s.<sup>[3]</sup>

Use of marijuana is associated with deleterious consequences such as impaired short-term memory, impaired motor coordination, altered judgement, paranoia, psychosis, altered brain development, poor educational outcome, and symptoms of chronic bronchitis. Pneumomediastinum, pneumothorax, and subcutaneous emphysema have been reported with deep inhalation of marijuana involving breath holding. Risk for head, neck, lung, and testicular cancer has also been reported. Other rare adverse effects such as hemoptysis and myocardial infarction have been reported. This case report presents a young man with a history of smoking marijuana who presented with pneumothorax.<sup>[4,5]</sup>

# 2. Case presentation

A 30-year-old African American man presented to the emergency room with sudden onset of severe, right-sided chest pain. He had no medical comorbidities, reported no history of trauma, and did not have a history of any surgeries or medication use. He reported that he smoked marijuana daily for 5 years but did not report performing valsalva maneuvers. He did not have a history of nicotine use. The physical examination revealed clubbing of the fingers and decreased breath sounds on the right side of the chest. Bed side ultrasound of chest showed absence of lung sliding (Fig. 1). Chest roentgenogram (CXR) (Fig. 2) findings were consistent with those of right-sided pneumothorax. The patient underwent chest tube drainage of the lung. Repeat ultrasound after chest tube showed lung sliding (Fig. 3). A computed

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Patient's informed consent is available with corresponding author and can be produced when required.



Figure 1. M mode showing absent lung sliding, stratosphere sign.



Figure 3. M mode showing sea shore sign.

tomography scan (CT) of the patient's chest showed a few apical bullae in the right lung (Fig. 4). Urine toxicology results were positive for cannabinoids. Laboratory analysis results showed normal homocysteine levels (7.6 umol/L), normal rheumatoid factor levels, and a negative human immunodeficiency virus test result.

The chest tube was removed after 4 days, and the patient's CXR showed continued reexpansion (Fig. 5). The patient was discharged from the hospital with scheduled pulmonary and thoracic outpatient follow-up.

# 3. Discussion

Marijuana was used for multiple therapeutic purposes in the past, including as an antiemetic, analgesic, muscle relaxant, and appetite stimulant. Marijuana has also been widely used in various clinical settings for its anti-inflammatory, anxiolytic, hypnotic, and antidepressant effects.<sup>[6,7]</sup> Marijuana is currently a Schedule I controlled substance in the United States.

Some respiratory consequences of daily marijuana smoking have been well documented, including a high incidence of chronic cough, sputum production, and wheezing.<sup>[8]</sup> Clubbing indicates chronic inhalation of marijuana abuse. The pathophysiology of marijuana-induced finger clubbing may be due to increase in the expression of vascular endothelial growth factor-alpha or of its receptors.<sup>[9,10]</sup>

Smoking marijuana is associated with a 66% larger puff volume and a 33% increase in breathing depth and inhalation time compared with smoking tobacco. Marijuana smokers also hold their breath 4 times longer than tobacco smokers do.



Figure 2. Chest roentgenogram on admission consistent with right pneumothorax. Arrows showing the pleural line.



Figure 4. CT scan of chest showing pneumothorax and small bullae in right upper lobe (arrows pointing to bullae). CT = computed tomography.



Figure 5. Chest roentgenogram on discharge showing reexpanded lung.

Marijuana smoking deposits 3 times more tar in the lungs than cigarette smoking. The above findings from study done by Wu et al showed 3 times as much material is delivered to the mouth during single marijuana smoking than the tobacco smoking and also one third of the material inhaled from the smoke of marijuana stayed in the lungs. As a result, carboxyhemoglobin levels increase leading to decrease oxygen carrying capacity of blood. With the above findings it implies that smoking only a few marijuana cigarettes has the similar effect on symptoms and lung histopathology, as smoking more than 20 tobacco cigarettes a day.<sup>[11]</sup>

In 1972, Miller et al<sup>[12]</sup> were the first to report a case of pneumomediastinum resulting from performing high-pressure valsalva maneuvers during marijuana smoking. Barotraumas in the form of pneumomediastinum, pneumothorax, and subcutaneous emphysema may occur with deep inhalation of marijuana involving breath holding or valsalva maneuvers.<sup>[13]</sup>

The other recreational drugs that have been associated with pneumothorax are cocaine, heroin, and methylphenidate. There are several medications like pentamidine, nitric oxide, bleomycin, vinblastine, carboplatin, gemcitabine, bevacizumab, paclitaxel, doxorubicin, amiodarone, cisplatin, cyclophosphamide and tacrolimus have been associated with pneumothorax.<sup>[14]</sup>

The common etiologies for primary spontaneous pneumothorax are smoking, family history, marfans syndrome, homocystinuria, thoracic endometriosis. Secondary spontaneous pneumothorax can be caused by underlying emphysema, necrotizing pneumonia, Langerhans cell histiocytosis, lymphangioleiomyomatosis, pneumocystis, catamenial, and interstitial lung disease.<sup>[15,16]</sup>

Beshay et al reported the largest case series of spontaneous pneumothorax in patients who frequently smoked marijuana and found severe bullous lung disease in the upper lobes of the lungs among marijuana smokers and hence recommended considering marijuana abuse as a cause of emphysema in young patients.<sup>[17]</sup> Johnson et al<sup>[18]</sup> showed that 3 of 4 patients with very limited tobacco use had multiple bullae in the upper lung fields and small parenchymal lung disease in other areas caused by marijuana use. Furthermore, Thompson and White<sup>[19]</sup> reported 3 cases of marijuana users with large bullae in the upper lobe of the lungs on computed tomography scans.

However, Fiorelli et al compared 13 habitual marijuana smokers with nonsmokers and did not find a causal role of marijuana in the development of emphysema. The mechanism for bullae formation in marijuana users is not well known, combination of direct toxic components in marijuana, prolonged breath holding which can generate high inspiratory pressure leading to barotrauma. Inflammatory cells in marijuana smokers cause pulmonary toxicity causing loss of lung elastic recoil leading to bulla formation.<sup>[20]</sup>

Spontaneous pneumothorax can be caused by valsalva, Muller maneuver, barotrauma and extreme breath holding while smoking marijuana. Although mechanism of bullae formation in marijuana users in not well known. Other mechanism is coughing while breath holding in inspiration, which can cause increased intra-alveolar pressure, creating disruptive shearing force in alveoli close to vascular structure causing pneumothorax.<sup>[21]</sup>

Also, in an analysis of bronchial biopsy samples from marijuana and tobacco smokers, Gong et al<sup>[22]</sup> showed that marijuana smokers had multiple histologic abnormalities such as basal cell hyperplasia, squamous metaplasia, thickened basement membrane, and submucosal inflammation with eosinophil's and lymphocytes. Although marijuana and tobacco smoker exhibit similar abnormalities. A study done by Fligiel et al<sup>[23]</sup> showed marijuana smokers exhibit more histological abnormalities than tobacco smokers.

Bedside ultrasound of chest can help detect pneumothorax and decrease need of computed tomography.<sup>[24]</sup> Absent lung sliding on M-mode suggests pneumothorax, which is stratosphere sign. The lung point is an ultrasound sign with 100% specificity for pneumothorax.<sup>[25]</sup>

Our patient did not have family history of pneumothorax. There were no clinical findings suggestive of marfans syndrome or ankylosing spondylosis. CT chest did not have cyst or nodules or traction bronchiectasis or honey comb findings, which excludes Langerhans cell histiocytosis, lymphangioleiomyomatosis and interstitial lung disease. Our patient did not have hamartomas of skin which makes Birt-Hogg-Dube syndrome unlikely. He did not have central line, thoracentesis, trans bronchial biopsy, or intubation which can cause nonspontaneous pneumothorax. Only etiology in our case was marijuana abuse.

Our patient was a young patient, who denied any history of nicotine use, making the bullous lung disease likely secondary to the marijuana smoking. He denied performing breath holding or valsalva maneuvers that have been associated with barotraumas due to marijuana use.

Further studies to evaluate the incidence of bullous lung disease in patients with marijuana use are required. Although some research exists, further studies to elucidate the mechanism of development of bullous lung disease in the absence of breath holding and valsalva maneuvers need to be done.

# 4. Conclusions

The prevalence of bullous lung disease among marijuana smokers, both in relation to the general population and to cigarette smokers, warrants further research. It is imperative that physicians educate patients and colleagues about the potential dangers of marijuana, which is often used recreationally. This case report highlights the risk of bullous lung disease leading to pneumothorax following marijuana smoking.

#### References

- Jouanjus E, Leymarie F, Tubery M, et al. Cannabis-related hospitalizations: unexpected serious events identified through hospital databases. Br J Clin Pharmacol 2011;71:758–65.
- [2] Benson MK, Bentley AM. Lung disease induced by drug addiction. Thorax 1995;50:1125-7.
- [3] Johnston LD, O'Malley PM, Miech RA, et al. Monitoring the Future national survey results on drug use, 1975–2015: Overview, key findings on adolescent drug use. 2016. The university of Michigan institute for Social Research.
- [4] Volkow ND, Baler RD, Compton WM, et al. Adverse health effects of marijuana use. N Engl J Med 2014;370:2219–27.
- [5] Hashmi HR, Duncalf R, Khaja M. A case report of cannabis induced hemoptysis. Medicine (Baltimore) 2016;95:e3232.
- [6] Ashton CH. Adverse effects of cannabis and cannabinoids. Br J Anaesth 1999;83:637–649.
- [7] Taylor DR, Poulton R, Moffitt TE, et al. The respiratory effects of cannabis dependence in young adults. Addiction 2000;95:1669–1677.
- [8] Bloom JW, Kaltenborn WT, Paoletti P, et al. Respiratory effects of nontobacco cigarettes. Br Med J (Clin Res Ed) 1987;295:1516–8.
- [9] Atkinson S, Fox SB. Vascular endothelial growth factor (VEGF)-A and platelet-derived growth factor (PDGF) play a central role in the pathogenesis of digital clubbing. J Pathol 2004;203:721–8.
- [10] Schuller A, Cottin V, Hot A, et al. Finger clubbing and altered carbon monoxide transfer capacity in cannabis smokers. Eur Respir J 2008;31: 473–4.
- [11] Wu TC, Tashkin DP, Djahed B, et al. Pulmonary hazards of smoking marijuana as compared with tobacco. N Engl J Med 1988;318: 347–51.
- [12] Miller WE, Spiekerman RE, Hepper NG. Pneumomediastinum resulting from performing Valsalva maneuvers during marijuana smoking. Chest 1972;62:233–4.

- [13] Birrer RB, Calderon J. Pneumothorax, pneumomediastinum, and pneumopericardium following Valsalva's maneuver during marijuana smoking. N Y State J Med 1984;84:619–20.
- [14] Hauben M, Hung EY. Pneumothorax as an adverse drug event: an exploratory aggregate analysis of the US FDA AERS database including a confounding by Indication analysis inspired by Cornfield's condition. Int J Med Sci 2013;10:965–73.
- [15] Bintcliffe O, Maskell N. Spontaneous pneumothorax. BMJ 2014;348: g2928.
- [16] Noppen M, De Keukeleire T. Pneumothorax Respiration 2008;76:121-7.
- [17] Beshay M, Kaiser H, Niedhart D, et al. Emphysema and secondary pneumothorax in young adults smoking cannabis. Eur J Cardiothorac Surg 2007;32:834–8.
- [18] Johnson MK, Smith RP, Morrison D, et al. Large lung bullae in marijuana smokers. Thorax 2000;55:340-2.
- [19] Thompson CS, White RJ. Lung bullae and marijuana. Thorax 2002;57:563.
- [20] Fiorelli A, Accardo M, Vicidomini G, et al. Does cannabis smoking predispose to lung bulla formation? Asian Cardiovasc Thorac Ann 2014;22:6571.
- [21] Aujayeb A, Donald C, Doe S. Breath-holding in a marijuana smoker. Respir Med Case Rep 2012;5:69–72.
- [22] Gong HJr, Fligiel S, Tashkin DP, et al. Tracheobronchial changes in habitual, heavy smokers of marijuana with and without tobacco. Am Rev Respir Dis 1987;136:142–9.
- [23] Fligiel SE, Roth MD, Kleerup EC, et al. Tracheobronchial histopathology in habitual smokers of cocaine, marijuana, and/or tobacco. Chest 1997;112:319–26.
- [24] Lichtenstein DA, Mezière G, Lascols N, et al. Ultrasound diagnosis of occult pneumothorax. Crit Care Med 2005;33:1231–8.
- [25] Lichtenstein D, Mezière G, Biderman P, et al. The "lung point": an ultrasound sign specific to pneumothorax. Intensive Care Med 2000; 26:1434–40.