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Emphysema and secondary pneumothorax in young adults smoking cannabis

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Abstract

Background: We observed a remarkable increase in the number of young patients who presented with lung emphysema and secondary spontaneous pneumothorax (SSP) at our institution for over a period of 30 months; most of them have a common history of marijuana abuse. **Study design:** Retrospective case series. **Methods:** Seventeen young patients presented with spontaneous pneumothorax with bullous lung emphysema were systematically evaluated over a period of 30 months. All were regular marijuana smokers. Clinical history, chest X-ray, CT-scan, lung function test, and laboratory and histological examinations were assessed. We compared the findings of this group (group I) with the findings of non-marijuana smoking patients (group II) in the same period. The findings of this series were also compared with the findings of 75 patients presented with pneumothorax in a previous period from January 2000 till March 2002 (group III). **Results:** In group I, there were 17 patients: the median age of the patients was 27 years (range 19—43 years), 16 males and 1 female. All were living in Switzerland. All but one smoked marijuana daily for a mean of 8.8 years and tobacco for 11.8 years. CT-scan showed multiple bullae at the apex or significant bullous emphysema with predominance in the upper lobes only in two patients. Only two patients had reduced forced first second expiratory volume (FEV1) and one reduced vital capacity (VC) below the predicted 50%. This correlated with the subjectively asymptomatic condition of the patients. All but two patients were treated by video-assisted thoracoscopic surgery (VATS) for prevention of relapsing pneumothorax. Histology showed severe lung emphysema, inflammation, and heavily pigmented macrophages. In group II, there were 85 patients: there were 78 males, the median age was 24 years (range 17—40 years), 74 patients smoked tobacco for 13.4 years but no marijuana. CT-scan in 72 patients showed only small bullae at the apex but no significant emphysema; other clinical, laboratory, and histopathological findings showed no significant difference in group I. In group III, there were 75 patients: there were 71 males and 4 females. Mean age was 25 years (range 16—46 years). Six smoked marijuana daily for a mean of 3.2 years, and 62 smoked tobacco for 14 years. CT-scan done in 59 patients showed few small bullae at the apex but no significant lung emphysema. The presence of lung emphysema on CT-scan in group I was significantly different than in groups II and III ($p = 0.14$). No significant difference was found among all groups in the form of clinical, laboratory, and histopathological findings. **Conclusions:** In case of emphysema in young individuals, marijuana abuse has to be considered in the differential diagnosis. The period of marijuana smoking seems to play an important role in the development of lung emphysema. This obviously quite frequent condition in young and so far asymptomatic patients will have medical, financial, and ethical impact, as some of these patients may be severely handicapped or even become lung transplant candidates in the future.

Keywords: Pneumothorax; Cannabis; Lung emphysema

1. Introduction

A surprising increase in the number of young adults with secondary pneumothorax due to lung emphysema was observed. These so far oligosymptomatic patients presented at the surgical emergency unit, as the condition manifested first with a pneumothorax.

Marijuana smoking peaked in 1979 and decreased continuously thereafter until the early 1990s. Since then, according to a recently published national survey on substance abuse in the United States, prevalence of marijuana smoking has increased continuously in high school and college students, as well as in young adults aged 19—32 years. In 1999 prevalence (use within the past month) was 23% in high school seniors, 19% in college students, and 15% in young adults. Daily use was reported by 6.0% of high school students, 4.0% of college students, and 4.4% of young adults [1]. Similarly, the number of the 14—15-year-olds who tried cannabis rose from 19% to 29% in boys and 18% to 25% in girls in

Abbreviations: SSP, secondary spontaneous pneumothorax; FEV1, first second forced expiratory volume; VC, vital capacity; VATS, video-assisted thoracic surgery; CRP, C-reactive proteins.

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the UK from 1999 to 2001 [2]. These numbers are comparable with the ones in countries like The Netherlands or Switzerland, which have a more liberal drug policy. In a large survey on health in Switzerland in 2002, 19.5% of the population between 15 and 64 years had experience with cannabis products of which 18% were between 15 and 34 years old. 4.6% declared consumption on a regular basis and one-half of them at least once a week. The overall consumption in the Swiss population increased from 16.3% of the 15–39-year-olds in 1992 to 27.7% in 2002 [3]. The annual production of cannabis in Switzerland is thought to be 200 tons. In the editorial in the *British Journal of Medicine* by Henry et al. the number of cannabis smokers in the UK was estimated to be 3.2 millions [2]. The impact of cannabis on the health of the general population is most probably underestimated.

2. Patients and methods

2.1. Study design

Among the 102 patients who presented with spontaneous pneumothorax at the emergency unit of our institution within a 2.5-year period (April 2002–October 2004), 17 patients who had relevant pulmonary emphysema and history of marijuana and nicotine abuse were retrospectively systematically evaluated. Two female patients who met the criteria of the study were excluded as no surgical treatment was needed. Retrospectively, we compared the findings of this group with the findings of non-marijuana smoker pneumothorax patients in the same period. The findings of this series were also compared with the findings of all pneumothorax patients who were operated upon in a previous period from January 2000 until March 2002. The patients were divided into three groups: group I, 17 patients (marijuana smoking patients, April 2002–October 2004); group II, 85 patients (non-marijuana smoking patients in the same period); and group III, 75 patients (all pneumothorax patients operated on from January 2000 to March 2002). Age, sex, nicotine abuse, laboratory, radiological findings, histopathological findings, operative procedures, and outcome were compared. *p*-value was significant under 0.05%.

2.2. Diagnosis and management

After admission, all patients underwent clinical examination and standard laboratory examinations. Not all examinations could be performed on all patients due to suboptimal compliance. A chest X-ray was performed and a 24F chest drain was inserted under local anesthesia. Serum α1-antitrypsin levels were measured in 16 patients in group I, 5 patients in group II, and 7 patients in group III. CT-scan of the chest could be performed in 15 patients in group I, 74 patients in group II, and 59 patients in group III. Lung function was done in 12 patients in group I, 70 patients in group II, and 62 patients in group III.

2.3. Surgical treatment

In group I, surgical treatment for the prevention of recurrent pneumothorax by VATS was done in 15 patients. Two refused surgery and were treated with chest tube insertion only. In group II, VATS was done in 65 patients (5 patients had the first episode, 58 patients had the second episode, and 2 patients had recurrence after previous VATS). In group III, VATS was done in 50 patients (3 patients had pneumothorax for the first time, 46 patients had the second episode, and 1 patient had recurrence after previous VATS). In all groups, the surgical procedures using VATS for bullectomy and/or resection of the apex (Endo GIA 45, Ethicon Endosurgery, Cincinnati OH) in addition to pleural abrasion were performed. For bullectomy done mostly in group I, 4–6 cartridges have been used. In case of apex resection 1–3 cartridges were needed. Pleura abrasion over the upper five ribs was done in all first or second episode of pneumothorax. In case of recurrence after VATS, pleurectomy was performed.

3. Results

3.1. Medical history

The main complaints at the time of admission were shortness of breath (n = 12 in group I, n = 68 in group II, and n = 61 in group III), pleuritic chest pain (n = 5 in group I, n = 12 in group II, and n = 9 in group III), and/or cough (n = 9 in group I, n = 18 in group II, and n = 14 in group III). Onset of these symptoms varied between a few hours and several days before admission.

In group I, all but one patient had an uneventful medical history. This patient had been previously diagnosed with emphysema on a routine chest X-ray by his family doctor, but no treatment was necessary. No patient was on any regular medication. The median BMI was 19.2 kg/m^2 (range 16.5–28 kg/m^2).

Marijuana consumption on a daily basis was noted in 16 patients (median 6 joints/day), 1 patient smoked marijuana only three times per week and did not smoke cigarettes. All other patients had additional nicotine abuse (mean 7 pack years, range 3–25 pack years). The mean duration of marijuana smoking was 8.8 years (range 3–20 years). In all patients it was shorter than the duration of tobacco smoking (11.6 years, range 4–23 years). Four patients reported a sporadic cocaine use, one LSD over 3 years, and one had sporadic heroin abuse. In group II, 3 patients had known allergic reaction, 1 patient had bronchial asthma, and 74 patients smoked tobacco for 13.4 years. In group III, no medical history was known; 6 smoked marijuana daily for a mean of 3.2 years, and 62 smoked tobacco for 14 years.

3.2. Physical examination

Physical examination and review of systems did not reveal any particular findings except the typical signs of pneumothorax and/or emphysema with no significant difference in all groups.

3.3. Laboratory findings

Routine laboratory did not show any pathological findings, except in one patient who had elevated leucocytes and CRP

values due to an infected bulla. The measurements of α1-antitrypsin serum levels were in the normal range with a median of 1.5 g/l (normal values 0.83—1.99 g/l). One patient had a borderline value in group I, two patients in group II, and one patient in group III.

3.4. Lung function

The overall pulmonary function of the 12 patients who agreed to undergo lung function testing was normal with a median FEV1 of 4.5 l (mean 3.8 l, range 2.2—5.0 l) and a median FVC of 5.7 l (mean 4.9 l, range 3.9—6.5 l). Only two of these patients had reduced FEV1 of the predicted 31% and 33% (1.2 and 1.7 l) and only one of them had FVC of 2.5 l (59%). In all other patients the values were above the predicted 89%. The overall pulmonary function performed in 70 patients in group II and in 62 patients in group III showed no significant difference to group I ($p = 0.062$).

3.5. Radiological findings

Chest X-ray was done in all patients; CT-scan performed in 88% ($n = 15$) in group I, in 85% ($n = 72$) in group II, and in 79% ($n = 59$) in group III has been examined by our radiologist. Similar findings with different severity of peripheral emphysema and apical bullae were noted in all patients in group I (Fig. 1A and B, Fig. 2A and B). The distribution of the emphysema was homogenous in two patients with predominance in the upper fields. The bullae varied in size from 0.3 cm to 12 cm. In one patient a fluid level in a bulla was noted, indicating infection. In three patients the upper lobes were almost completely replaced by large bullae. On the other hand, there was no lung emphysema reported in the other two groups ($p = 0.014$), apart from very small bullae $\leq$1 cm in diameter at the apex of the lung in 84% in group II and 89% in group III. These small bullae were more on the right side ($p = 0.12$).

3.6. Histopathological examination

The histopathological examination showed the presence of bullae with destruction of the acinar wall and the respiratory bronchioles with focal alveolar edema. In addition, the alveolar and bronchiolar lumina were focally filled with heavily pigmented macrophages. The alveolar septa were markedly thickened by a fibrotic stroma. The same pigment as in the macrophages could be found in the fibrotic stroma and the thickened pleura. A moderate inflammatory infiltrate and fibrinous exudate was present (Fig. 2A and B). In all other patients there was no significant difference in the histological findings apart from the obvious smaller bullae at the apex of the lung (Fig. 3).

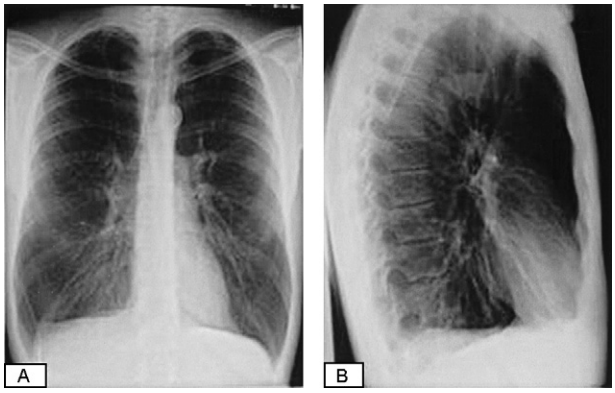

Fig. 1. (A, B) Chest X-ray showing signs of emphysema (32-year-old male). Pleural drain is on the right side.

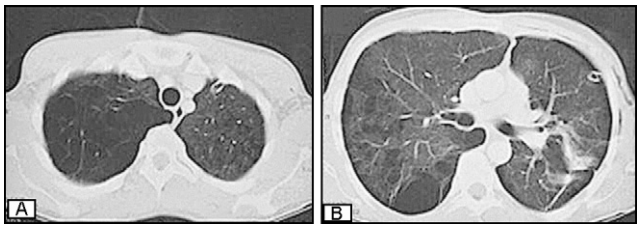

Fig. 2. (A, B) Chest CT-scan showing bilateral peripheral bullous emphysema. The pleural drain is in situ on the left side.

3.7. Recurrence after VATS

The overall recurrence rate after VATS was 3% and there was no significant difference in all groups.

4. Discussion

Over a period of 30 months we observed a remarkable increase in secondary spontaneous pneumothorax in otherwise healthy young adults. All patients were in good general condition, which was in contrast to the radiological findings.

The risk of developing pneumothorax after tobacco smoking or alkaloid cocaine consumption is described [4,5]. A few reports of pneumothorax or pneumomediastinum following combined use of marijuana, heroine, or cocaine have been published [6—9]. Recently, a bilateral spontaneous pneumothorax was, however, reported in a 23-year-old cannabis smoker with normal lung parenchyma in the CT-scan [10]. But these reports describe single and supposedly rare cases.

Cannabis has been used over five millennia for the treatment of many conditions including pain, inflammation, neuralgia, migraine, and dysmenorrhea. It has also been used as an anticonvulsant, muscle relaxant, and for restlessness

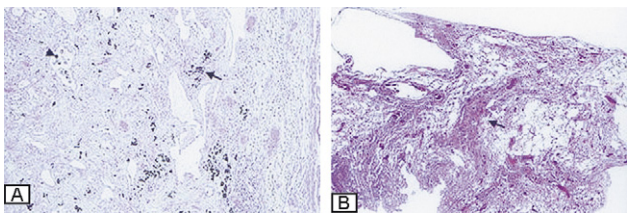

Fig. 3. (A) Histological sample of an apical pulmonary resection showing subpleural bullae, the focal alveolar edema (arrow), and the focal consolidation (arrowhead) (hemalaun and eosin, bar 1000 μm). (B) Subpleural interstitial fibrotic area. Note the heavily pigmented alveolar macrophages (arrowhead), the same pigment deposited in the fibrotic stroma (arrow) and the thickened pleura with a moderate inflammatory infiltrate and fibrinous exudation (hemalaun and eosin, bar 100 μm).

and anxiety in terminal illness [11,12]. In the early 1970s it was deemed to be of little medical use and was removed from most medication lists. Thereafter, studies have demonstrated a bronchodilator response as a physiological short-term effect of inhaled marijuana. This may be attributed to the pharmacologic effect of γ9-tetrahydrocannabinol [13,14] and the stimulation of the cannabinoid-1 receptor on postganglionic parasympathetic nerve endings on airway smooth muscle, leading to inhibition of acetylcholine release [15]. Some known consequences of habitual marijuana smoking include an increased prevalence of chronic cough, sputum production, and wheeze, as well as a higher frequency of acute bronchitis [16–18]. In addition, the risk for myocardial infarction seems to be increased by 4.2 times within an hour after smoking cannabis [2] and the risk for psychosis is increased especially in young adults with a predisposition [19].

Interestingly enough the CT-scan performed in 72 patients in group II and in 59 patients in group III showed only small bullae (under 1 cm in diameter) at the apex with no signs of emphysema of the lung, even in patients who smoked marijuana over a period of 3 years in group III. We oppose that the period of marijuana smoking is an important factor in the development of lung emphysema in these patients. There was no significant difference in the length of the thoracic drainage or in the length of hospital stay between all groups. The rate of recurrence after VATS was not significantly higher in patients with secondary pneumothorax who smoked marijuana.

In a small case series of four patients, three of them from West India with significant exposure to marijuana, the authors describe multiple bullae in the upper lung fields and little parenchymal lung disease elsewhere. As three of these patients had limited tobacco use, those authors concluded that marijuana smoking is the reason for the parenchymal changes, possibly accelerated by tobacco smoking [20]. In contrast, we observed a significant lung change in patients who smoked marijuana for a longer period than 3 years, as well as a homogeneous distribution of emphysema in this series, unlikely to be tobacco emphysema, the so far largest single-center series from a western country, but a predominant upper lobe emphysema was noticed in two patients, which may confirm the findings by other authors as well.

In western countries, the condition seems to be much more frequent. Based on our observations and the prevalence of cannabis smoking in developed countries, we propose to introduce the term 'joint years' (joints/day times years of abuse) to assess the severity of the exposure, as it seems that one joint per day is equivalent to at least to one packet of cigarettes per day.

Subjectively, these young patients were asymptomatic and most of them still had normal lung volumes. Therefore, they only consulted a doctor when the pneumothorax occurred.

The increase of young patients with emphysema, associated with an increase in cannabis smoking in young adults in many countries, may create major health problems in future with a strong medical, financial, and ethical impact, as a number of these patients may be severely handicapped or even end up as lung transplant candidates. The public awareness of the health hazards by cannabis smoking has to be increased (Table 1).

Table 1
Summary of history and findings of group I with secondary spontaneous pneumothorax and lung emphysema

	Median	25th/75th percentile
Age	27	23.3/31.8
BMI	19.2	18.4/20
Smoking history		
Marijuana (joints/day)	6	3/10
Duration (years)	7	5.3/11.8
Tobacco (packs/day × years)	7	3/10
Duration (years)	12.5	9/15.8
Lab		
Alpha1-antitrypsin (g/l) (NR 1.1–2.1)	1.5	1.3/1.6
Lung function tests		
FVC (l) (% predicted)	5.5 (98)	4.2/5.7
FEV1 (l) (% predicted)	4.2 (90)	2.7/4.5
FEV1/FVC (%)	77.8	70/82

References

[1] Johnston LD, O'Malley PM, Bachman JG. Monitoring the future national results on adolescent drug use: overview of key findings, 2001. Bethesda, Maryland: National Institute on Drug Abuse; 2002 [NIH Publication no. 02-5105].

[2] Henry JA, Oldfield WL, Kon OM. Comparing cannabis with tobacco. Br Med J 2003;326:942–3.

[3] Rigter H, van Laar M. Cannabis 2002 report: a joint international effort at the initiative of the Ministers of Public Health of Belgium, France, Germany, The Netherlands, Switzerland. Brussels, Belgium: Ministry of Public Health; 2002. p. 11–37.

[4] Bense L, Eklund G, Wiman LG. Smoking and the increased risk of contracting spontaneous pneumothorax. Chest 1987;92(6):1009–12.

[5] Shesser R, Davis C, Edelstein S. Pneumomediastinum and pneumothorax after inhaling alkaloidal cocaine. Ann Emerg Med 1981;10(4):213–5.

[6] Luque 3rd MA, Cavallaro DL, Torres M, Emmanual P, Hillman JV. Pneumomediastinum, pneumothorax, and subcutaneous emphysema after alternate cocaine inhalation and marijuana smoking. Pediatr Emerg Care 1987;3(2):107–9.

[7] Herrejon Silvestre A, Blanquer Olivas J, Simo Mompo M, Ruiz Montalt F, Nunez Sanchez C, Chiner Vives E. Pneumothorax due to drug inhalation. Ann Med Interne 1992;9(3):137–9.

[8] Mattox KL. Pneumomediastinum in heroin and marijuana users. JACEP 1976;5(1):26–8.

[9] Miller WE, Spiekerman RE, Hepper NG. Pneumomediastinum resulting from performing Valsalva maneuvers during marihuana smoking. Chest 1972;62(2):233–4.

[10] Goodyear K, Laws D, Turner J. Bilateral spontaneous pneumothorax in a cannabis smoker. J R Soc Med 2004;97(9):435–6.

[11] Iversen L, Snyder SH. The science of marijuana. Oxford: Oxford University Press; 2000.

[12] Morgan DR. Therapeutic uses of cannabis. London: Harwood Academic; 1997.

[13] Vachon L, FitzGerald MX, Solliday NH, Gould IA, Gaensler EA. Single-dose effects of marihuana smoke. Bronchial dynamics and respiratory-center sensitivity in normal subjects. N Engl J Med 1973;288(19):985–9.

[14] Tashkin DP, Shapiro BJ, Frank IM. Acute pulmonary physiologic effects of smoked marijuana and oral 9 -tetrahydrocannabinol in healthy young men. N Engl J Med 1973;289(7):336–41.

[15] Coutts AA, Pertwee RG. Inhibition by cannabinoid receptor agonists of acetylcholine release from the guinea-pig myenteric plexus. Br J Pharmacol 1997;121(8):1557–66.

[16] Taylor DR, Poulton R, Moffitt TE, Ramankutty P, Sears MR. The respiratory effects of cannabis dependence in young adults. Addiction 2000;95(11):1669–77.

[17] Bloom JW, Kaltenborn WT, Paoletti P, Camilli A, Lebowitz MD. Respiratory effects of non-tobacco cigarettes. Br Med J (Clin Res Ed) 1987; 295(6612):1516–8.

[18] Tashkin DP, Coulson AH, Clark VA, Simmons M, Bourque LB, Daunn S, Spivey GH, Gong H. Respiratory symptoms and lung function in habitual heavy smokers of marijuana alone, smokers of marijuana and tobacco, smokers of tobacco alone, and nonsmokers. Am Rev Respir Dis 1987;135(1):209—16.

[19] Nehquet C, Krabbendam L, Spauwen J, Kaplan C, Lieb R, Wittchen HU, van Os J. Prospective cohort study of cannabis use, predisposition for psychotic symptoms in young people. Br Med J 2005;330:11.

[20] Johnson MK, Smith RP, Morrison D, Laszlo G, White RJ. Large lung bullae in marijuana smokers. Thorax 2000;55(4):340—2.