ORIGINAL ARTICLE

Bullous lung disease due to marijuana

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Background and objective: In contrast to the well-described effects of tobacco smoking upon pulmonary emphysema, with ~15% of smokers being affected at the age of 65 years, the effects of marijuana smoking are rarely reported and poorly understood.

Methods: We report a series of 10 patients (mean age 41 ± 9 years, eight male, two female), who presented over a period of 12 months to our respiratory unit with new respiratory symptoms, and who admitted to regular chronic marijuana smoking (>1 year continuously). Symptoms on presentation were dyspnoea (n = 4), pneumothorax (n = 4) and chest infection (n = 2).

Results: High-resolution CT revealed asymmetrical, variably sized, emphysematous bullae in the upper and mid zones. However, the CXR was normal in four patients and lung function was normal in five.

Conclusions: Marijuana smoking leads to asymmetrical bullous disease, often in the setting of normal CXR and lung function. In subjects who smoke marijuana, these pathological changes occur at a younger age (approximately 20 years earlier) than in tobacco smokers.

Key words: bullous lung disease, marijuana.

INTRODUCTION

Marijuana is the dried material from the hemp plant, Cannabis sativa. The active ingredient in all forms of marijuana is delta-9-tetrahydrocannabinol, which is rapidly absorbed from the lungs and bound to endogenous cannabinoid receptors in the central nervous system,1 providing the psychoactive effects that users seek.

The commonest method of marijuana use is by smoking, either as a rolled cigarette (joint) or through a water-filled pipe (bong). The rate of marijuana use has increased significantly over the past three decades in most developed societies,2 and is currently 1–3% among adults and 10% among 21-year-olds in Australia and New Zealand.3 In contrast, ~20% of adults currently smoke tobacco.

Marijuana is inhaled as extremely hot fumes, usually to peak inspiration, and held for as long as possible before slow exhalation. This may predispose to greater damage to the lung parenchyma than is seen with standard tobacco smoking. Seven case reports of bullae (large and multiple) in predominant marijuana smokers have been published.4–6 The true prevalence and incidence of such bullae is not known, and they were not mentioned in a recent position statement on marijuana smoking.7 Indeed, it was concluded that ‘all the available evidence suggests that the risks of regular marijuana smoking are similar to those of regular tobacco smoking’.7

Clinical suspicion that marijuana smokers are more prone to bullous lung disease was prompted by a single case report.8 Over the next 12 months, data were collected on a further nine regular marijuana smoking patients, who presented to our centre over a 12-month period with respiratory ailments, and are the bases of this report.

METHODS

All patients (inpatient or outpatient) requiring admission to the Alfred Hospital, Melbourne with new respiratory symptoms, and who volunteered that they

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had smoked marijuana regularly for at least a 12-month period of their lives, were identified. The 350-bed university-based teaching hospital has a 30-bed respiratory ward, in addition to an outpatient service assessing approximately 250 patients per week. The mean age of patients admitted with tobacco smoking-related COPD is 67 years. Demographic data, details of marijuana and tobacco usage and mode of inhalation, CXR, alpha-1-antitrypsin level, high-resolution CT (HRCT) scan of the chest and details of lung function were recorded. Marijuana usage was estimated by the patient in terms of years smoked, mode of ingestion (joint or bong), number of 'smokes' per day and number of grams consumed per day. Marijuana usage was compared using an estimate of ‘joint years’ (1 joint year = 365 joints) and/or 0.75 g marijuana per smoke, based on an average of 0.5–1.0 g marijuana per joint. The study was approved by the Alfred Hospital Ethics Committee (project no.180/70) and all patients provided informed consent.

RESULTS

Ten patients who smoked marijuana regularly were identified. Three were outpatients with subacute problems and seven were inpatients with acute respiratory disorders. The diagnoses on presentation were spontaneous pneumothorax (n = 4), pulmonary abscess (n = 2), acute or chronic respiratory failure (n = 3) and subacute exertional dyspnoea (n = 1). One patient had a long history of asthma, and in recent years had become HIV seropositive and developed sleep apnoea. The mean age of the patients was 41 years, and eight were male (Table 1). HRCT generally showed asymmetrical, variably sized, emphysematous bullae mainly in the upper and mid zones, and in both the peripheral and central regions of the lungs (see Figs 1–10).

Lung function testing indicated that five patients had no evidence of airflow obstruction and three had moderate to severe airflow obstruction. One patient failed to attend for lung function testing despite numerous attempts to contact her. Age and tobacco and/or marijuana consumption (amount and mode) were similar in the groups with normal or abnormal lung function. Only three patients had abnormal CXR and lung function.

DISCUSSION

We report the details of 10 patients who regularly used marijuana, and who developed new respiratory symptoms. Nine of these patients showed severe asymmetrical and variably sized bullae on HRCT. The novel messages from this case series are the young age at presentation and the lack of abnormality on CXR or lung function testing in nearly half of these patients, despite the abnormal HRCT findings.

The mean age at presentation of our group of patients was 41 years, which contrasts significantly with the 62–67 years mean age of patients with smoking-related COPD. The findings in marijuana smokers also contrast with those on cigarette smokers, among whom <15% show changes in lung function and HRCT findings are often normal, or ~50% reveal only subtle airway wall thickening. Wu et al. reported that marijuana smokers have a 70% larger inspiratory volume and hold their breath four times longer, indicating markedly different breathing manoeuvres compared with cigarette smokers. The concentration and pulmonary deposition of inhaled particulate matter, and the rise in carboxyhaemoglobin saturation, are estimated to be two- to threefold greater with marijuana compared with tobacco smoking. Histopathological studies have shown airway inflammation even after limited exposure to marijuana smoke.

The upper lobe predominance of smoking-related emphysema due to high V/Q units is well recognized, compared with basal bullae in alpha-1 antitrypsin deficiency due to low V/Q units. All the patients in this study had normal alpha-1 antitrypsin levels. However, the manoeuvre used by marijuana smokers usually involves a larger inspiratory effort and a longer period of breath holding, thereby affecting more apical and mid zones of the lung. This manoeuvre could also result in barotrauma to the lung. Of
<table>
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<th>Patient no.</th>
<th>1</th>
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<th>Mean ± SD</th>
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| Age (years) | 40  | 49  | 34  | 27  | 42  | 47  | 52  | 28  | 49  | 45  | 40.8 ± 9.4 |
| Gender      | M   | F   | M   | M   | F   | M   | M   | M   | M   | M   |           |
| Presentation| Abscess | Abscess | pneumTx | pneumTx | pneumTx | pneumTx | Dyspnoea | Dyspnoea | Dyspnoea | Dyspnoea | pneumTx |
| Tobacco smoking history | Current | Current | Current | Current | Current | Current | Current | Current | Current | Current | Current |
| Tobacco consumption (pack-years) | 27  | 20  | 1   | 9   | 2   | 20  | 30  | 2   | 10  | 27  | 14.3 ± 10.4 |
| Cannabis consumption (years) | 3 g J & B | 2–3 J/day | 3–4 J/day | 1 g/day J & B | NA | 3–4 g B/day | ~3 g B/day | 7 g J & B/day | 12 B/week | 252 g J & B |           |
| Marijuana consumption (joint-years) | 80  | 11  | 35  | 13  | NA | 163 | 132 | 149 | 17  | 67  | 74 ± 61 |
| Alpha-1-antitrypsin (g/L) | 3.42 | 3.71 | 1.56 | 1.36 | NA | 1.86 | 1.86 | 1.6  | 1.7  | 1.5  | 2.13 ± 0.9 |
| FEV₁, L (% predicted) | 3.8 (105) | 3.2 (104) | 4.2 (87) | 4.5 (91) | NA | 4.3 (109) | 2.2 (66) | 1.4 (40) | 0.9 (24) | 1.0 (42%) | 3.04 ± 1.4 |
| FVC, L (% predicted) | 5.2 (114) | 4.6 (122) | 5.6 (96) | 5.9 (99) | NA | 6.1 (126) | 4.4 (105) | 3.6 (89) | 2.1 (48) | 2.3 (79%) | 4.71 ± 1.4 |
| FEV₁/FVC (%) predicted | 77 (93) | 70 (84) | 74 (83) | 76 (88) | NA | 70 | 51 (65) | 40 (47) | 41 (50) | 44 (52%) | 62.5 ± 15.7 |
| DLCO, mL/min/mm Hg (%) | 28.4 (85) | 19.3 (76) | 32.5 (82) | 34.3 (84) | NA | 19.6 (57) | 12.5 (40) | 18.2 (50) | NA | 22.8 (87%) | 23.5 ± 8.2 |
| KCO, mL/min/mm Hg/L (%) | 4.1 (75) | 3.6 (77) | 4.9 (91) | 4.6 (82) | NA | 2.4 (47) | 2.0 (43) | 3.3 (53) | NA | 5.3 (88%) | 3.56 ± 1.08 |
| FRC, L (% predicted) | 3.8 (105) | 4.3 (124) | 3.8 (89) | 5.2 (123) | NA | 4.2 (106) | 4.0 (111) | 4.9 (134) | NA | 2.8 (195%) | 4.31 ± 0.6 |
| TLC, L (% predicted) | 7.2 (111) | 6.6 (109) | 6.8 (87) | 8.0 (103) | NA | 6.3 (121) | 7.2 (114) | 7.5 (111) | NA | 3.8 (145%) | 7.34 ± 0.63 |
| RV, L (% predicted) | 1.8 (95) | 2.1 (98) | 1.5 (70) | 2.4 (119) | NA | 2.4 (109) | 2.6 (124) | 3.6 (209) | NA | 5.7 (123%) | 2.35 ± 0.8 |
| RV/TLC percentage | 25  | 32  | 22  | 30  | NA | 29 | 36  | 48  | NA | 48  | 31.7 ± 8.5 |
| CXR          | Abnormal | Abnormal | Normal | Normal | Normal | Normal | Normal | Abnormal | Abnormal | Normal |           |

1Normal alpha-1 antitrypsin = 0.88–1.74 g/L.
B, bong; F, female; J, joint; KCO, Krogh constant for Dlco/Va; pneumTx, pneumothorax; M, male; NA, not available; joint year, 365 joints; 1 joint, 0.5–1.0 g cannabis.
note, four of 10 patients presented with spontaneous pneumothorax, raising the question of whether these lung bullae contributed to the development of pneumothorax, or the barotrauma caused by marijuana inhalation.

The extensive injurious effect of marijuana on the respiratory tract has been documented in numerous studies. Regular marijuana use leads to alveolar macrophage dysfunction\textsuperscript{15,20} and possible depression of the immune system,\textsuperscript{21} resulting in increased incidence of pulmonary infection. In addition, endoscopic findings of erythema, oedema and increased secretions, histopathological alterations in bronchial biopsies and dysregulated growth of the bronchial epithelium have been noted.\textsuperscript{20} These processes may well contribute to the greater frequency of upper airway cancer observed in this population.

Two patients presented with culture-negative upper lobe abscesses. One of these patients had fungal elements in his sputum and improved with conventional antibacterial and antifungal treatment, whereas the other responded to conventional antibiotics. They were both active marijuana smokers at presentation and both used joints and water pipes. There are reports of atypical aspergillosis infections in immunocompromised marijuana smokers,\textsuperscript{22,23} tuberculosis among users sharing a bong,\textsuperscript{24} and histoplasmosis in a marijuana plant gatherer.\textsuperscript{25}

In addition to bullous disease, marijuana smoking is associated with interstitial fibrosis,\textsuperscript{5} byssinosis\textsuperscript{26} and necrotizing pulmonary granuloma.\textsuperscript{27} However, none of the patients in this study had obvious occupational exposure or peripheral signs of connective tissue disease suggestive of underlying causes of the disease process. A recent report from New Zealand suggested that early and long-term marijuana consumption is associated with a greater incidence of lung cancer than use of tobacco alone.\textsuperscript{28}
Unlike tobacco-related COPD, there is a paucity of good longitudinal studies on marijuana smoking and its effects on lung function and carbon monoxide transfer factor.\textsuperscript{27,29–32} The largest of these studies\textsuperscript{27} compared annual spirometry over an 8-year period in 394 subjects (131 heavy marijuana smokers, 112 marijuana and tobacco, 65 tobacco alone, 86 non-smokers). Of the 66% who completed the study, the rate of decline in $FEV_1$ was not different in the marijuana smokers compared with similarly aged (~32 years) non-smokers.\textsuperscript{27} The present findings are consistent with that study, in that spirometry was often normal despite significant bullous disease being detected by HCRT.

The limitations of this study are that it was a case series, without a formal control group. Estimates of tobacco and marijuana use were based upon patient recollection. Finally, the population screened were those presenting with respiratory complaints to a large teaching hospital. Accordingly, there is a need to confirm these findings with larger prospective community-based studies that are controlled for tobacco use.\textsuperscript{28}

In summary, atypical bullous disease was present in all patients with respiratory symptoms who volunteered that they were regular users of marijuana. Surprisingly, CXR were normal and lung function was mildly reduced in ~45% of the patient group. Given that 1–2% of the mature adult population is estimated to use marijuana regularly, a prospective epidemiological study of marijuana smokers is required to assess the prevalence and incidence of lung disease and, in particular, so that comparisons can be made with purely tobacco-related pulmonary damage.

REFERENCES

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