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José Miguel Durán Alama,* Manel Vilá Justribó, and Ferran Barbe Illa

[a] *Servicio de Neumología, Hospital Universitario Arnau de Vilanova, Lleida, Spain*

*Corresponding author.
E-mail addresses: jomidual@telefonica.net (J.M. Durán Alama). mvilaj@gmail.com (M.Vilá Justribó).

Bullous Emphysema in a Smoker of Marijuana and Tobacco

Enfisema ampolloso en fumadora de marihuana y tabaco

To the Editor:

The relationship between tobacco smoking and chronic obstructive pulmonary disease (COPD) is well known, but the idea that smoking cannabis in its various forms is innocuous has led to habitual consumption and, consequently, to the appearance of associated diseases with the passage of time.

We describe the case of a 30-year-old woman who was a regular smoker of marijuana (34 cigarette-years) and tobacco (17 pack-years). Allergic to penicillin but with no other relevant history, she complained of dyspnea on exertion. Physical examination revealed no abnormalities. A chest radiograph revealed bullae of various sizes in both lung fields. Computed tomography (Figure) showed emphysematous bullae in both pulmonary apices and significant centrilobular and panlobular emphysematous changes with multiple pseudocystic formations ranging in diameter from a few millimeters to 2 cm. The standard workup was normal. The α_1-antitrypsin in blood level was 167 mg/dL. A sweat test showed a value of 40 mmol/L. Spirometry revealed a forced vital capacity (FVC) of 5.08 L (108%), a forced expiratory volume in 1 second (FEV_1) of 3.53 L (95%), and FVC/FEV_1 of 0.69. A bronchodilator test was negative. Lung volume measurements showed a total lung capacity of 6.80 L (113%), a functional residual capacity of 3.79 L (124%), and a residual volume of 1.68 L (97%). Lung diffusion tests showed a carbon monoxide diffusing capacity of 79% and a ratio of carbon monoxide diffusing capacity to alveolar volume of 110%.

The association between marijuana smoking and COPD has been demonstrated.[1] In the short term smoking marijuana leads to bronchodilation,[1] and in the long term it is associated with airflow limitation, chronic cough, bronchitis, and reduced exercise tolerance.[2] Regular smokers of 3 or 4 marijuana cigarettes per day present histologic abnormalities similar to those observed in smokers of approximately 20 tobacco cigarettes per day.[3,4] This difference is partly explained by the distinct ways in which marijuana and tobacco are smoked. Since smokers of marijuana inhale more deeply and retain the smoke for a longer period, the volume is equivalent to 4 times what a smoker of tobacco takes in.[5] Additionally, carboxyhemoglobin and tar levels that result from smoking a marijuana cigarette are from 3 to 5 times greater than the levels produced by a tobacco cigarette. A recent review noted that marijuana smoking is associated with premalignant changes in the lungs, and benzopyrene, an aromatic polycyclic hydrocarbon present in both tobacco and marijuana, has been associated with mutations related with lung cancer.[6]

Furthermore, both marijuana and tobacco seem to be addictive and physicians should not only advise patients against smoking tobacco but also inform them about the harmful effects of marijuana use. This is particularly important when counseling young people.

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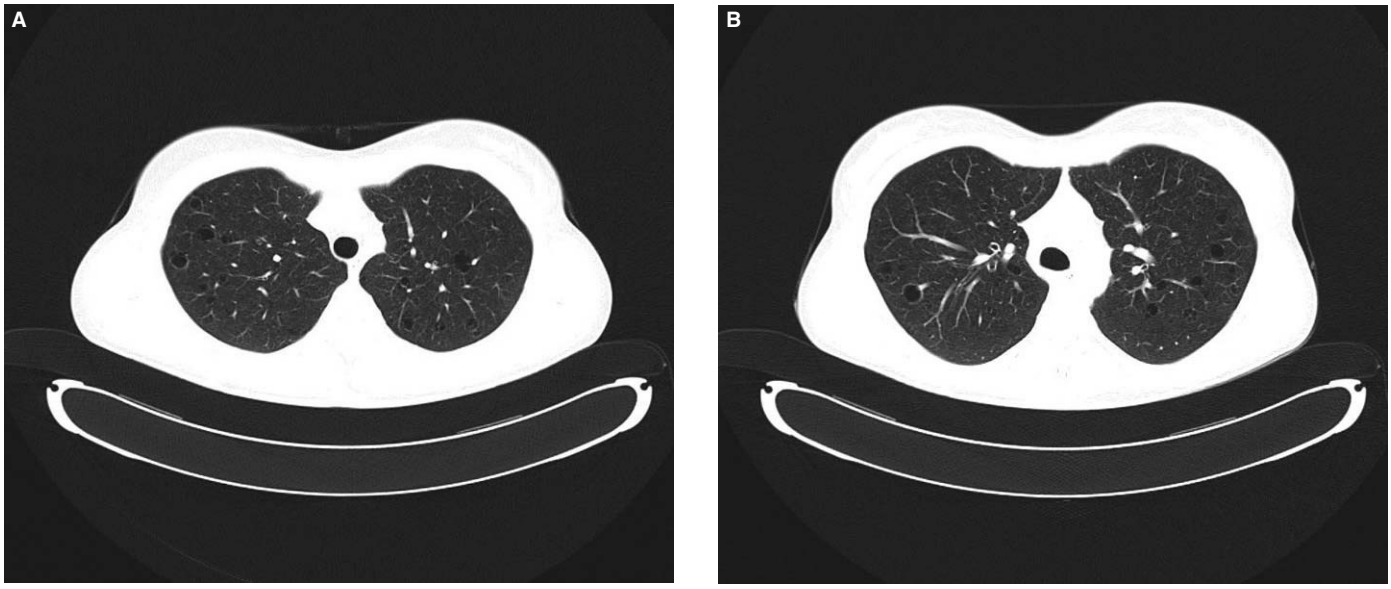

Figure (A and B). Computed tomography showing emphysematous bullae in both lungs and marked centrilobular and panlobular emphysematous changes with multiple pseudocystic formations ranging in diameter from a few millimeters to 2 cm in both lungs.

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Rosa Irigaray Canals,[a,*] Enrique Villar Redondo,[b] and María Antonia Campins Verger[b]

[a] *Servicio de Neumología, Clínica Rotger, Palma de Mallorca, Baleares, Spain*
[b] *Servicio de Medicina Interna, Clínica Rotger, Palma de Mallorca, Baleares, Spain*

*Corresponding author.
E-mail address: rosairigaray@yahoo.es (R. Irigaray Canals).

Air Leak Syndrome Due to Graft Versus Host Disease

Síndrome de fuga aérea por enfermedad del injerto contra huésped

To the Editor:

Chronic graft versus host disease (GVHD) is a serious late complication of allogenic bone marrow transplantation, occurring in 60% to 80% of transplanted patients.[1] Bronchiolitis obliterans is a pulmonary manifestation of GVHD, and the appearance of air leak syndrome is very rare.[1,2] We report the case of a patient with air leak syndrome as the first sign of lung disease associated with GVHD.

A 30-year-old female patient was admitted to our service with dyspnea, subcutaneous emphysema, and pneumomediastinum. Two years earlier the patient had been diagnosed with a type of myelodysplastic syndrome (refractory anemia with excess blasts-1) and paroxysmal nocturnal hemoglobinuria. Initial treatment with implantation of umbilical cord stem cells failed and was followed by allogenic bone marrow transplantation, resulting in complete recovery and no side effects. A year later, the patient experienced a relapse and developed acute myeloblastic leukemia, requiring another stem cell transplant using umbilical cord blood. Chronic immunosuppressive therapy was given with cyclosporin and prednisone.

The patient was admitted with subcutaneous cervical emphysema and spontaneous pneumomediastinum in the upper hemithorax, with no signs of pleuropulmonary involvement or mediastinal abnormalities on the chest radiograph. A high-resolution computed tomographic scan (HRCT) showed extensive subcutaneous emphysema and pneumomediastinum without pneumothorax or tracheobronchial lesions, in addition to significant bronchiectasis with marked thickening of the bronchial walls and an alveolar-interstitial pattern with centrilobular nodules of tree-in-bud appearance suggestive of pulmonary involvement due to GVHD (Figure). A flexible fiberoptic bronchoscopy and a transbronchial biopsy showed no abnormalities. *Pseudomonas aeruginosa* was isolated from the bronchial aspirate and the infection was treated. The patient showed clear clinical improvement with resolution of subcutaneous emphysema and pneumomediastinum.

One month after discharge, forced spirometry showed deterioration in lung function with a forced vital capacity (FVC) of 72% (previous result, 102%); forced expiratory volume in 1 second (FEV_1) of 41% (previous, 107%); FEV_1/FVC of 54% (previous, 89%); midexpiratory flow rate of 12% (previous, 121%); residual volume of 178% (previous, 75%); and carbon monoxide diffusing capacity of 48% (previous, 70%). This severe obstruction with rapid-onset air trapping in a patient with the history described here suggested a diagnosis of bronchiolitis obliterans due to GVHD according to international criteria.

Subcutaneous emphysema and spontaneous pneumomediastinum have been linked to asthma, addiction to inhaled drugs, occult pneumothorax, and forced Valsalva maneuvers.[3] Allogenic bone marrow transplantation represents a risk for recipients due to systemic immune cross-reactivity caused by the graft. GVHD follows a bimodal pattern with an early and late peak.[1,4,5] GVHD-bronchiolitis obliterans is rare[1,2] and diagnosis is based on the following clinical findings: *a)* inexplicable chronic airflow obstruction (FEV_1, <80% in the absence of respiratory infection), *b)* flow-volume curves suggestive of small-airway disease, and *c)* residual volume greater than 115% of predicted.[4] Radiographic images and lung biopsy are nonspecific. Treatment consists of corticosteroids and clinical outcome is generally unfavorable. Overall mortality is 50% to 55%.

The true incidence of air leak syndrome is unknown. It has been described as the presence of extra-alveolar gas and includes pneumothorax, pneumomediastinum, pneumopericardium, subcutaneous emphysema, and interstitial emphysema. The pathogenesis tends to be alveolar rupture that causes interstitial emphysema, which then dissects along bronchovascular sheaths to the hilum and into the mediastinum (Macklin effect).[6] Rupture occurs in the presence of increased intraalveolar pressure (bronchial obstruction with coughing or vomiting) or damage to the alveolar walls (infectious causes, such as invasive aspergillosis, or noninfectious causes, such as pulmonary emphysema and bronchiolitis obliterans). The appearance of air leak syndrome in our case is linked to poor prognosis due to the presence of bronchiolitis obliterans in association with invasive aspergillosis. A wait-and-see surgical approach is therefore advisable, and conservative treatment is usually enough.

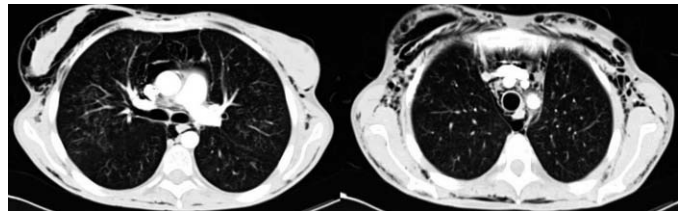

Figure. Computed tomographic scan showing extensive subcutaneous emphysema and pneumomediastinum without pneumothorax, in addition to significant bronchiectasias with marked thickening of the bronchial walls and an alveolar-interstitial pattern with a patchy ground-glass appearance.