

Case Report

Bronchiolitis Obliterans Organizing Pneumonia Following Consumption of *Sauropus androgynus*

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Abstract: Bronchiolitis obliterans organizing pneumonia (BOOP) is a rare disorder affecting the small airways, alveoli and the walls of small bronchi. This form of lung injury involves inflammation and stiffening of lung areas with organized tissue. There are several known causes of BOOP, and several systemic disorders have BOOP as an associated primary pulmonary lesion. An outbreak of BOOP among young women has been publicly reported in Taiwan from late 1994 and onward. The source of the illness was traced to the consumption of *Sauropus androgynus*. Herein, we describe a case of a 28-year-old woman who developed a rapid pulmonary toxicity after drinking fresh *S. androgynus* purée daily for a period of two months, as an alleged regimen for weight reduction. Ga-67 citrate imaging portrayed the inflammatory status in her eyes, parotids and lungs. Pathological pattern of open-lung biopsy specimens was characteristic of BOOP. The toxicity is believed related to alkaloid papaverine contained in the plant. Bioactive principles of *S. androgynus* and pathogenetic mechanism underlying BOOP remain unidentified.

Keywords: Bronchiolitis Obliterans Organizing Pneumonia, Papaverine, *Sauropus androgynus*, Weight Reduction

1. Introduction

Bronchiolitis obliterans organizing pneumonia (BOOP) is a rare disorder affecting the small airways, alveolar ducts and alveoli. The term bronchiolitis obliterans refers to swirls or plugs of myxoid fibroblastic tissue filling the small bronchiolar lumens. Organizing pneumonia refers to organized swirls of inflammatory tissue filling the alveoli and the alveolar ducts. Causes of BOOP include radiation therapy, certain fumes or chemicals, respiratory infections, immunological dysfunctions; and a variety of medications [1]. In late 1994, *Sauropus androgynus* had been introduced to young and middle-aged women in Taiwan, and been alleging to lose weight and to cure various diseases. The plant was enthusiastically consumed. However, an outbreak of lung toxicity was made public a few months later. Respiratory disorders, including flu-like illness, dyspnea and organizing pneumonia, affected hundreds of Taiwanese women, with several reported deaths [2, 3]. Since the sole common factor

was consumption of the botanical purée, *S. androgynus* was then the culprit responsible for BOOP outbreak in Taiwan. There is no common consensus on the pathogenetic mechanism of BOOP yet. Further botanical and pharmacognostical studies of *S. androgynus* are necessary to set safe levels for its application [4].

2. Case Report

A 28-year-old Taiwanese woman with no history of cardiopulmonary disease presented with progressive respiratory distress over the past 4 days. One week earlier, she had experienced fever, headache, malaise and exertional dyspnea. Anti-cold remedy gave no appreciable improvement. The patient reported taking *Sauropus androgynus*, 150 grams (4 taels) of the raw plant daily for 2 months, in attempt to lose her weight. Leaves and green stems of the sapling were blended to form a purée and flavored with pineapple or guava. The patient achieved a 10-kg weight reduction after

consuming the regimen. However, she experienced glossitis, paresthesia, palpitation and fatigue, and stopped drinking *S. androgynus* purée in the last two weeks.

On admission, she was an obese adult (75 kg-158 cm) in extreme respiratory distress and asthenia. Examination was notable for tachycardia of 120 beats/min, tachypnea of 36 breaths/min, blood pressure of 150/90 mmHg, and temperature of 38.3°C. Bilateral crackles were audible. Chest radiograph demonstrated negative results. Arterial blood gas analysis showed severe hypoxemia, as evidence by pH 7.38 (7.38 – 7.42), pCO₂ 39 (38 – 42 mmHg), and pO₂ 35 (80 – 100 mmHg). WBC count was $14.7 \times 10^3/\mu\text{L}$, with a differential of 66% segmented neutrophils and 21% lymphocytes. Hemoglobin level was 14 g/dl. Biochemical analysis revealed mild liver function impairment, ALT 58 U/L and AST 53 U/L. There was no electrolyte disturbance. Tc-99m MAA lung perfusion scan excluded the presence of pulmonary embolism. She was put on inhaled aerosol therapy due to difficulty in breathing.

Subsequently, high resolution CT disclosed ground-glass opacities in LUL, RUL, and RML. Gallium citrate scintigraphy to look for infection or cancer in the body revealed abnormal accretion of Ga-67 in the lacrimal and salivary glands, and patchy uptake in bilateral lungs (Figure 1), consistent with a systemic involvement of the inflammatory process. On the fifth hospital day, an open-lung biopsy was performed. Pathology showed peribronchial mononuclear infiltrations, submucosal fibrosis and obliteration of the bronchiolar lumens, characteristics of BOOP. Serologic tests and lung tissue processing for histopathologic cultures and stains were not diagnostic of any concomitant infection. The results for cytomegalovirus study were negative. Steroid treatment was then commenced. Gradually over 30 days as arterial blood gas parameters normalized, her ventilator support was removed. The patient enrolled in pulmonary rehabilitation to reduce some of the residual effects of BOOP and to improve exercise tolerance. She gained her weight back later.

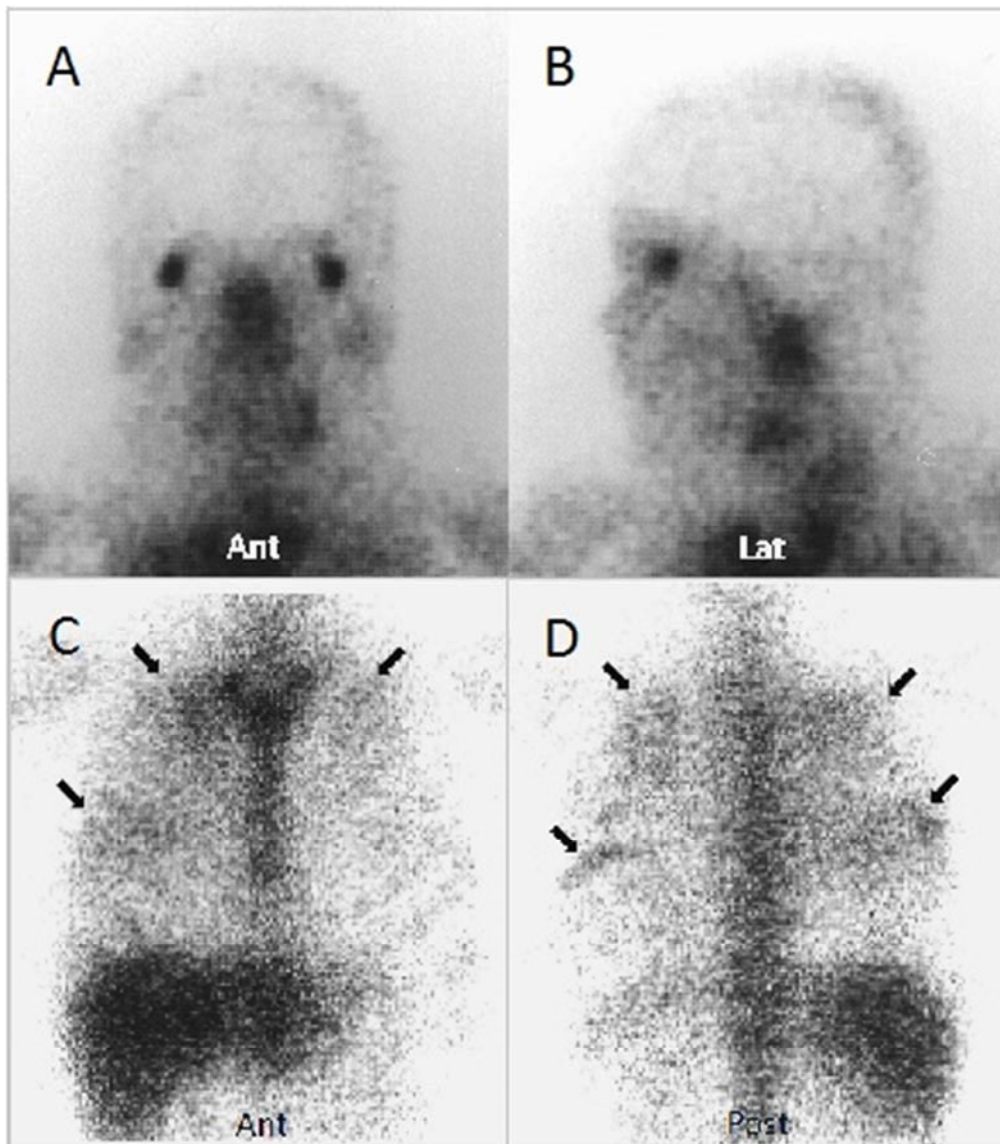


Figure 1. Ga-67 citrate scan revealed pathological accretion of Ga-67 in the eyes and salivary glands and patchy uptake in bilateral lungs (arrows), consistent with an active process of systemic inflammation. Homogenous activity in the liver and bone marrow was considered as normal physiologic uptake.

3. Discussion

Sauropus androgynus is a leafy plant widely distributed in wasteland at low altitudes throughout southwest mainland China, Vietnam, Malay Peninsula, Indonesia and India. *S. androgynus* leaf has been used in cooking and is considered to be a nutritive vegetable in the tropic countries [4, 5]. Ethnobotanical uses for wound healing, promoting lactation, reducing blood sugar and lowering fever are likewise applied. Around the mid of 1990s, *S. androgynus* was introduced to Taiwan and was popularly called “slimming vegetable” or “Indian sapling”. Since its herbal properties had been over-boasted of, *S. androgynus* was enthusiastically consumed as a natural regimen for weight reduction, blood pressure control, laxative and many other medical purposes. Commercial cultivation of the plant had been extended in Southern Taiwan for eager demands. However, pharmacognostical researches related to the plant are sparse. Its propensity of poisoning had been ignored, and hundreds cases of pulmonary toxicity were resulted in.

The bioactive principles of *S. androgynus* have not fully been known. Excessive consumption of the leaves was previously reported to cause dizziness, drowsiness and constipation [4]. As a matter of fact, 100 gm fresh leaf contains about 580 mg of alkaloid papaverine [5]. The aforementioned dose of papaverine is equivalent to 4 capsules prescribed for treating cardiovascular diseases (each capsule contains papaverine hydrochloride USP 150 mg). Papaverine, as a vasodilator and smooth muscle relaxant, in high doses and prolonged using might permanently damage pulmonary microcirculation. A thorough inquiry of collected BOOP cases disclosed that most of patient consumed the plant purée continuously more than one month preceding the onset of dyspnea. In contrast to ethnic use of the plant in general cooking uneventfully, the toxic substance of *S. androgynus* might be thermolabile and dose-dependent [3]. Besides some were imported from abroad, *S. androgynus* consumed in Taiwan market were mostly cultivated species. Recent phytochemical studies described that the plant contains a wide range of biomolecules constituents that might contribute to its medicinal, toxic, and antioxidant properties [6]. A hospital-based case-control study of 54 victims observed that an excessive intake, uncooked regimen, and consuming vendor's preparation were the risk factors of the event [7]. Patients who consumed *S. androgynus* juice made by vendors have a greater chance of developing lung toxicity than those who consumed homemade juice. Possibly unethical vendors might have added supplements to the juice causing a synergistic effect to promote intoxication [7]. Further pharmaco-botanical and taxonomic studies of the plant to set safe levels for its medicinal application and public consumption are needed [4].

BOOP is a subacute or chronic respiratory disorder, characterized by the proliferation of granulation tissue in bronchiolar lumen, associated with a variable degree of interstitial and airspace infiltration by mononuclear cells and foamy macrophages [1, 8]. Clinically, BOOP lacks specific clinical and radiological features, manifesting by a flu-like

illness, dry cough, exertional dyspnea and bilateral patchy (alveolar) infiltrates [1]. The ESR is usually elevated, and pulmonary function tests show a restrictive pattern [8]. Neither conventional radiographs nor CT findings are specific to BOOP and are seen in a variety of lung-infective, inflammatory and neoplastic processes. Conventional chest radiographs may reveal patchy infiltrates, small linear opacities, or reticulonodular opacities [9]. CT features of BOOP vary. Common findings are airspace consolidation, ground-glass attenuation, parenchymal nodules, reticular and linear opacities, and architectural distortion [8]. Lung biopsy continues to be the preferred method for establishing a diagnosis. Histological findings show connective tissue masses composed of myxoid fibroblastic tissue resembling granulation tissue filling the lumens of terminal and respiratory bronchioles and extending in a continuous fashion into alveolar ducts and alveoli, representing an organizing pneumonia [1]. Diagnosis can be established only after exclusion of other entities that may show similar pattern.

The pathogenetic mechanism underlying BOOP is still unclear in most cases. The association with respiratory infections, various lung disorders [10], immunological dysfunctions [11, 12], following chest irradiation [13], and exposure to certain fumes, chemicals and various stimuli [1, 8, 14] has been described in the literatures. An overactive immune response to certain stimuli has been proposed as the initiation of the inflammatory process. Clinically, elevated tumor necrosis factor (TNF)- α [2], predominant T-cells in peribronchiolar infiltrate [2], and increased interleukin (IL)-5 and IL-10 transcription in bronchial cells [3] suggest a likelihood of T-cell-mediated autoimmunity. In addition to fever and glossitis, the pathologic accretion of Ga-67 in the eyes, salivary glands and lungs seen in our patient are presumed to be a systemic inflammation with lung predominance. In the process of BOOP, it is assumed that an inflammatory reaction leads to tissue organization. Steroid, with its anti-inflammatory potency, is recommended as first-line treatment for symptomatic patients and progressive disease [8]. Reasons for the response to corticosteroid in BOOP remain unknown. This might be related to vascular growth factors in BOOP that will cause normal apoptosis, and that apoptosis has an important role in the resolution process of the newly formed connective tissue in BOOP [15]. There is no consensus regarding the optimal doses of prednisone and optimal treatment duration. The dosage is generally 0.75 mg/kg/day for 1 to 3 months, then 0.50 mg/kg mg/day for 3 months, then 10 to 20 mg/day or every other day for a total of 1 year [8]. Severe cases, stuffed up with organized lesions in distant airways, are fatal and usually not responding to steroid or bronchodilators. Lung transplantation may be needed as the last resort [2].

4. Conclusion

BOOP is a subacute or chronic form of respiratory inflammation with a good response to steroid therapy. Although most cases are idiopathic, it can also be seen in

association with connective tissue diseases, a variety of stimuli, malignancy, and immunodeficiency syndrome. Clinicians must be aware of this disorder, as it may present as non-resolving pneumonia related to the consumption of certain purée and herbs.

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