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Case Report

# *Sauropus androgynus*-associated bronchiolitis obliterans of mother and daughter – autopsy report

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ABSTRACT

*Sauropus androgynus* (SA) is a vegetable that causes constrictive bronchiolitis obliterans (BO) with consequent findings classified into injury, inflammation and fibrosis, according to clinical factors including amount of SA exposure, period of SA exposure, and individual predisposition. We reported mother and daughter SABO autopsy cases with similar clinical course, including 11 month SA exposure and Aspergillosis infection after high dose prednisolone therapy. Their major differences were in the amount of SA exposure (mother: 1440 g, daughter: 2190 g) and the survival period post exposure (mother: 21 months, daughter: 32 months). The histopathological comparison between them showed a statistical difference in the density of foamy macrophage accumulation of moderately obstructed airways, but not in the extent of fibrosis, elastic lamina destruction, or smooth muscle hyperplasia. Foamy macrophages tend to accumulate relatively early in the course of SABO at the site with severe damage, accelerating BO formation for as long as the patient survives.



## 1. Introduction

*Sauropus androgynus* (SA) is a vegetable consumed as a slimming agent from 1994 in Taiwan, and approximately 300 patients with SA-associated bronchiolitis obliterans (BO) have been identified. In Japan, at least 8 cases have been reported, including 2 familial occurrences.

Previous literature based upon open lung biopsy and pneumonectomy specimens of SABO[1–4] demonstrated various phases including injury, inflammation, and fibrosis, and a component of SA is thought to cause an initial epithelial injury in airways. We reported herein mother and daughter autopsy cases with SABO, analyzing semiquantitatively to see what clinical factors determine the histologic differences.

## 2. Case reports (Table 1)

The mother and daughter cases visited our department with dyspnea (mother: November 2002, daughter: February 2003), showing bilateral lung hyperinflation and severe obstructive impairment. They were treated as severe asthma, however, in July 2003, giving the SA intake history since August 2002, both were diagnosed with SABO. The total amount ingested as raw SA was estimated to be 1440 g for mother, and 2190 g for daughter.

### 2.1. Mother case

In August 2003, she started oral prednisolone (0.5 mg/kg/day) for worsening hypoxemia. After weaning off prednisolone with no improvement, she was diagnosed with Chronic Necrotizing Pulmonary Aspergillosis in May 2004 and treated with Micafungin and Itraconazole. Despite symptomatic and imaging improvements, the obstructive impairment gradually progressed and she died in April 2005.

### 2.2. Daughter case

In September 2003, oral prednisolone (0.5 mg/kg/day) was started for worsening hypoxemia, and decreased to 0.25 mg/kg/day

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**Table 1**
characteristics and pulmonary function tests on admission.

| | Mother | Daughter |
|---|---|---|
| Age | 55 | 29 |
| Period from: | | |
| Onset of SA ingestion to death | 32month | 43month |
| Onset of SA ingestion to onset of SABO | 3month | 6month |
| Onset of SA ingestion to cessation | 11month | 11month |
| Cessation of SA ingestion to death | 21month | 32month |
| Amount of SA ingestion | 1440 g | 2190 g |
| Past medical history | Not significant | Bronchial asthma |
| Duration of steroid therapy | 0.5–0 mg/kg × 3 mos | 0.5–0.25 mg/kg × 4 mos |
| Improvement with steroids and bronchodilators | No | No |
| Complications | CNPA | IPA |
| Initial evaluation on admission | | |
| $FEV_1$, liters | 0.62 | 1.0 |
| $FEV_1$/FVC, % | 40.3 | 51.3 |

$FEV_1$ = Forced expiratory volume in 1 s; FVC = forced vital capacity. CNPA = Chronic Necrotizing Pulmonary Aspergillosis, IPA = Invasive Pulmonary Aspergillosis.

three months later. In December 2003, she was diagnosed with Invasive Pulmonary Aspergillosis, and managed with Micafungin, Itraconazole, Amphotericin B, and Voriconazole. However, the condition was resistant, deteriorating into death in March 2006.

## 3. Methods & results

### 3.1. Identification of affected airways (Fig. 1)

We obtained 11 and 19 continuous sections of right lower lobe in the mother and daughter autopsy specimens respectively, all 3 mm in thickness from the segmental bronchus to the distal portion. Both showed the affected portions extended from the 3rd, 4th or 5th branches with cartilage, numbered from segmental bronchus, up to the membranous bronchioles, especially severe in the latter. Some obstruction occurred segmentally with proximal airway enlargement, showing beadlike appearance.

### 3.2. Semiquantitative analysis of pathological findings (Fig. 2)

We obtained 46 and 39 paraffin-embedded sections from all lobes in the mother and daughter respectively. We examined 88 bronchi and 293 membranous bronchioles (mother: 185, daughter: 108) semiquantitatively, and correlations were found between the severity of bronchiolar obstruction and the degree of luminal fibrosis, elastic lamina destruction, and mural fibrosis (mother: $r =$ 0.829, 0.481, 0.295, $P < 0.001$, $<0.001$, $<0.001$, respectively)(-daughter: $r = 0.874$, 0.585, 0.233, $P < 0.001$, $<0.001$, 0.008, respectively). Foamy macrophage accumulation was observed especially in moderately obstructed bronchioles (Table 2). There was an equal level of lymphocyte infiltration regardless of degree of obstruction.

### 3.3. Histopathological comparison between mother and daughter

With Fisher's exact test, there was a statistical difference between their density of foamy macrophage accumulation ($P <$ 0.001), but not in the extent of luminal fibrosis, lamina destruction, mural fibrosis, or smooth muscle hyperplasia ($P = 0.825$, 0.195, 0.352, 0.131, respectively). With one-sided Wilcoxon's rank sum test (Table 2), we found the daughter had greater density of foamy macrophages than the mother only in moderately obstructed airways ($P = 0.048$).

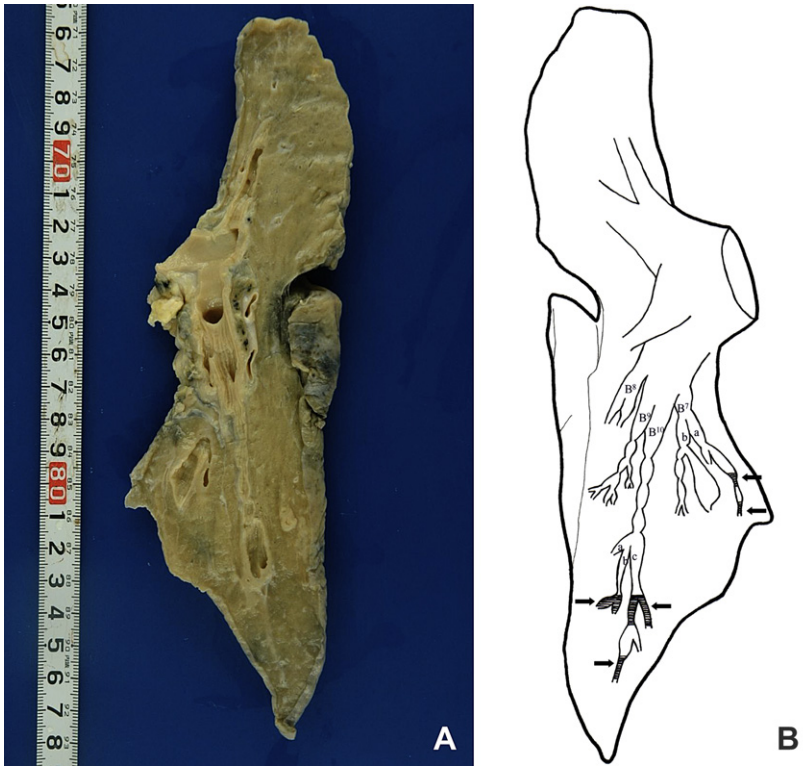


**Fig. 1.** A. Macroscopical finding of the right lower lobe of the daughter. Prominent saccular dilatation of bronchi just above the segmental narrowing. B. Reconstructed $B^{10}$ to $B^7$ configuration of the daughter's right lung. The obstruction sites are corresponding to the 3rd, 4th, or 5th order of bronchi with cartilage up to the membranous bronchioles. The obstructed areas were segmentally distributed as shown by the arrows in "B", and sometimes beadlike in appearance.