CASE REPORT

Bronchiolitis obliterans complicating a pneumothorax after Stevens-Johnson syndrome induced by lamotrigine

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Bronchiolitis obliterans (BO) was defined as a nonreversible obstructive lung disease in which the bronchioles are always compressed and narrowed by fibrosis or inflammation. In the severe event of lung collapse after BO, surgical intervention is often recommended, and conservative therapy is thought to be ineffective. Here, we report the case of a 9-year old girl clinically diagnosed as having bronchiolitis obliterans with abrupt occlusion of the right B4b bronchus. After a lamotrigine-induced Stevens-Johnson syndrome (SJS) occurred, she presented with total collapse of the right lung on admission, which was subsequently complicated by a pneumothorax during conservative treatment, but with the re-expansion of the right upper lobe after intervention. The case indicates the possibility of reversing pulmonary atelectasis in BO. Thus, surgery may not be necessary.

Introduction

Bronchiolitis obliterans (BO) initiates a chronic scarring process affecting small airways of the lung, which results in the progressive obliteration of small airways with resulting obstructive lung disease. The possible primary reasons include adenovirus infection, mycoplasma pneumoniae infection, rejection after lung or bone marrow transplant, and Stevens-Johnson syndrome.1–4 The sequelae was
irreversible, with no standard or effective treatment available, especially in the event of proximal bronchial obstruction.\textsuperscript{4,5}

When severe obliteration occurs, the BO presents with lung collapse, and surgical resection of the collapsed lung is performed.\textsuperscript{4-6} Here we report the case of a 9-year-old girl diagnosed on clinical grounds as having BO associated with Stevens-Johnson syndrome (SJS). For her, total collapse of the right lung occurred with partial lung re-expansion (right upper) after conservative therapies. Histologically, only one similar case has been documented.\textsuperscript{6}

**Case report**

A 9-year-old girl with a 3-year history of epilepsy was admitted to the emergency room at our hospital on July 26, 2010, with a widespread, rapidly progressive eruption of the skin and mucosa, as well as a fever over 39°C, after taking a double oral dose of lamotrigine, an oral medicine used for epilepsy control.

Approximately 10% of her body surface area was involved, and she was diagnosed as having SJS induced by lamotrigine (Fig. 1). Routine blood tests showed a white blood cell count of $12.31 \times 10^9/L$, lymphocytes of 41.3%, mononuclear leukocyte rate of 9.3%, and neutrophil rate of 41.20%. On the second day after admission, no infiltrative or organizing change was found on chest radiography, and she was discharged 12 days later after treatment with antibiotics and steroids, with resolution of her skin symptoms, and no respiratory symptoms or fever.

However, 1 week later, the patient re-presented to our hospital with symptoms of shortness of breath, wheeze, and cough, but with no sputum or fever. Respiratory rate was 25 breaths per minute. Collapse of the right chest was noted in visual examination and there was a unilateral diffused wheeze on auscultation. Chest radiography revealed the complete collapse of the right lung, proximal bronchial extension on the right side, and an overinflated left lung (Fig. 2A). A computed tomography (CT) scan demonstrated total collapse of the right lung with dilatation of the larger central airway, together with over-inflation of the left lung (Fig. 2B). Bronchoscopy revealed no neoplasm or foreign body in the airways, but it did show an abrupt occlusion of the right B4b bronchus (Fig. 3). Biopsy under bronchoscopy showed only chronic inflammatory changes in the occluded airway. Pulmonary function tests showed a forced expiratory volume in one second (FEV\textsubscript{1}) of 1.02 L/min, a baseline FEV\textsubscript{1} expressed as percent of predicted (pre-FEV\textsubscript{1}) of 54%, a forced vital capacity (FVC) of 1.02 L, a baseline FVC expressed as percent of predicted (pre-FVC) of 47%, a maximal voluntary ventilation (MVV) of 34.8 L, and a baseline MVV expressed as percent of predicted (pre-MVV) of 48%.

Arterial blood gas measurements showed a partial pressure of oxygen (pO\textsubscript{2}) of 57 millimeters of mercury (mmHg), a partial pressure of carbon dioxide (pCO\textsubscript{2}) of 28 mmHg, a potential of hydrogen (pH) of 7.43, and bicarbonate of 18.3 mmol/L. Routine blood tests showed a white blood cell count of $4.90 \times 10^9/L$, lymphocytes of 49.2%, mononuclear leukocyte rate of 11.3%, and neutrophil rate of 38.40%. Erythrocyte sedimentation rate was 6 mm/hour. A tuberculin test was negative. An examination for microorganisms was also negative.

![Figure 1](image-url) Severe mucocutaneous reaction involving the lips, ears, hands, and legs.
With the exclusions of tuberculosis, microorganisms infection, bronchial asthma (BA), as well as bronchiolitis obliterans with organizing pneumonia (BOOP), a diagnosis of BO associated with SJS was considered. Treatment was started with a combination of antibiotics (Cefaclor), a mucolytic agent (ambroxol hydrochloride), a steroid (dexamethasone), a bronchodilator (salbutamol sulphate aerosol), bronchoalveolar lavage, and chest physiotherapy.

On August 18, 2010, on Day 3 following a second bronchoalveolar lavage, chest radiography confirmed a right-sided pneumothorax, with the lung compressed to nearly 20% of its normal volume (Fig. 4A). Tube thoracotomy was performed immediately. To our surprise, the right upper lobe reinflated 3 days later, with almost complete resolution of the pneumothorax, but the other lobe was still collapsed (Fig. 4B). A CT scan confirmed re-expansion of the right upper lobe, but also revealed bronchial wall thickening, an area of air-trapping, mosaic patterns, ground-glass appearances, and attenuated vessels in the lung window (Fig. 4C and D). A second pulmonary function test showed that FEV1 was 1.49 L/min and pre-FEV1 was 68%. However, from then on, conservative therapy did not achieve further reinflation of the other lobes. A 10-month follow-up was performed, and no further deterioration of the respiratory system was found.

Discussion

SJS is a rare (one to two cases per million population per year) but life-threatening mucocutaneous reaction characterized by detachment of the epidermis, acute skin blisters, and mucous membrane erosions.\(^1,7\) Drugs are the most common caustic agents of the syndrome.\(^7\) Lamotrigine, a medication used for epilepsy control, has already been confirmed as a high and independent risk factor for SJS in children.\(^7\) In this case, massive skin injury appeared rapidly after the patient took a double-dose of the medicine, with nearly 10% of her body surface involved. There was no difficulty in the diagnosis of lamotrigine-induced SJS.

BO has been found to be the main pathological change in the airways associated with SJS, and this has been confirmed in many studies.\(^3,10\) It is characterized by obliteration of the small airways lumen due to chronic inflammation and fibrosis of the airway wall and surrounding tissue, causing irreversible airway obstruction.\(^4,10\) However, the larger airways are also a target for impairment in SJS.\(^5,11\)

An early report by Tsunoda et al. described an obstruction of the cartilaginous bronchi in a patient with BO after SJS, which worsened the prognosis.\(^3\) A subsequent report by Yatsunami et al. described a patient with abrupt occlusion of the right B9a bronchus confirmed by bronchography and fiberoptic bronchoscopy.\(^11\) In our case, bronchoscopy revealed an abrupt occlusion of the right B4b bronchus. In the past, BO was diagnosed by lung biopsy, but the positive rate was limited.\(^10\)

Today in children, this diagnosis can be made with confidence based on clinical presentation, medical history, fixed obstructive lung disease on pulmonary function testing, and characteristic changes of mosaic perfusion, vascular attenuation, and central bronchiectasis on chest high-resolution CT, thus avoiding the need for lung biopsy in most patients.\(^10\)
The patient we report here presented with wheezing and an obstructive lung ventilation disorder that was not relieved by bronchodilators. With the exception of the right B4b bronchus, the large airway was unobstructed. CT scans showed small airway disease, with air-trapping, mosaic patterns, bronchial wall thickening, ground-glass changes, and attenuated vessels, all of which are indicative of BO, justifying a clinical diagnosis in our patient.

Pneumothorax is a very rare complication of SJS. To our knowledge, only four case reports of this syndrome mentioned pneumothorax. From them, we learned that the pneumothorax is a mainly adverse event, which causes the thoracotomy, or aggravates the respiratory failure. In our case, the pneumothorax appeared during conservative therapy, and it is unclear whether it was a side effect of therapy, i.e., bronchoalveolar lavage, or if it was a characteristic feature of SJS. Nevertheless, the upper lobe of the right lung reinflated soon after tube thoracotomy. The pneumothorax may have been indicative of a good prognosis, and it suggested that the small airways had not been completely obliterated before that critical moment, or the lumen obliteration could be reversed through conservative therapies. Although there was no significant sputum of the patient in our case, we must mention that the bronchoalveolar lavage was used to clear the sputum or other dirty materials of the airways, which may accelerate the re-expansion of a collapsed lung.

Compared with other characteristic high-resolution CT features of BO, lung collapse is rare, especially unilateral lung collapse. Given the high risk of infection and severe perfusion-ventilation mismatch, surgical resection of the collapsed lung is often recommended, and conservative therapy is thought to be ineffective for irreversible airway obstruction. However, to our knowledge, pulmonary atelectasis occurs when there is bronchial obstruction with absorption of the intra-alveolar gas, which indicates that the involved proximal airway has been obliterated totally before the collapse.

In view of the obliteration caused by scarring or fibrosis of the bronchiole wall, re-inflation of the collapsed lung becomes impossible in small airway recanalization. This theory is not in line with the evolution documented in our case, which was presented with the re-expansion of the right upper lobe followed by improved pulmonary function. So it would improve the function of airway ventilation after conservative therapies. There may be other factors unknown to us that play a role in airway obliteration, but with a reversible characteristic.

As we know, there is presently only one case report in the literature of re-expansion of a collapsed lung associated with bronchobronchiolitis obliterans. Govaere et al.

Figure 4  (A) Pneumothorax of the right chest, showing the right lung compressed to nearly 20% of its volume. (B) The right upper lobe reinflated, but the other lobes of the right lung remained collapsed. (C) Lobular air trapped in the left lung. (D) Diffuse air trapped with mosaic patterns, as well as vascular attenuation, ground-glass changes, and dilated and thickened airway walls.
first documented a partial lung re-expansion in an infant with bronchobronchiolitis obliterans treated conservatively, but the collapse had occurred 5 years before the re-expansion. When compared with that report, our case confirms that re-expansion of a collapsed lung is also possible in the early course of the disease if conservative therapy is given. Therefore, surgical intervention may not be necessary. However, because bronchoscopy revealed no central airways occlusion in the upper lobe, and we found no progression in the right middle lobe after therapy, we are not sure if this possibility may also exist in conditions of large central airways occlusions.

References


