

The Management of Influenza Virus-Induced Plastic Bronchitis in Pediatric Patients: A Case Report and Literature Review

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Abstract

Although the incidence is very rare, plastic bronchitis (PB) could be a serious comorbid disease of virus infection in children, especially in those who have a history of bronchial asthma. We have recently experienced an influenza virus-induced PB who was successfully treated by endoscopic intervention under multidisciplinary approach in our institution. The purpose of this report is to confirm the role of otolaryngologists in the management of potentially lethal pediatric PB. A 7-year-old girl visited our institution (Kyorin University Hospital) and was hospitalized to the Pediatrics Department with worsening cough and chest pain. Chest radiography and computed tomography imaging showed a complete atelectasis of the left lung. Influenza virus testing proved the infection of influenza A in this patient, and she was treated by antiviral medication (peramivir hydrate), systemic steroid therapy and respiratory rehabilitation. However, her symptoms were worsening, and she was consulted to our department. Multiple clinical information suggested PB, and bronchoscopic evaluation/treatment was performed under general anesthesia using laryngeal mask 4 days after her hospitalization. Endoscopic intervention visualized the blockage of left main bronchus with highly viscous mucous, and her symptoms were improved by endoscopic suctioning of the mucus; and it was found that the inflammatory cells were eosinophil. Her pulmonary condition got better immediately after suctioning, and she was discharged 10 days after the intervention. Our report suggested the indispensable role of otolaryngologist for successful diagnosis and treatment of the influenza virus-induced PB in pediatric patients.

Keywords: Plastic bronchitis; Influenza virus-induced PB; Atelectasis; Endoscopic suctioning; Eosinophil

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Introduction

Seasonal influenza is an acute respiratory infection caused by the influenza virus and is self-limited, and patients usually recover without complications. In Japan, an epidemic is observed every winter season, and in a typical case, symptoms suddenly develop with the upper respiratory tract, such as fever greater than 38 °C, rhinorrhea, and cough. In addition, symptoms are accompanied by muscle pain, vomiting, and diarrhea and then reach the lower respiratory tract, causing moist cough and gradual recovery. If dyspnea occurs while experiencing influenza and atelectasis is observed on chest radiography, plastic bronchitis (PB) is considered. PB is often reported during influenza pandemic [1].

In this report, a 7-year-old girl presented with respiratory distress after experiencing seasonal influenza A, and atelectasis of the left lung was observed on chest radiography and computed tomography (CT). She did not recover with conservative treatment, and we performed the suctioning of the mucous plug using flexible bronchoscopy. We described the clinical features, chest radiographic results, treatment, and role of bronchoscopy.

Case Report

A previous healthy 7-year-old girl had a severe cough 3 days previously and was provided a common cold medicine as the diagnosis for streptococcal infection in a pediatric clinic (clarithromycin 200 mg/day, L-carbocistein 750 mg/day, and ambroxol hydrochloride 45 mg/day). However, her condition did not improve, and her cough was worsened. Moreover, she developed left upper body pain, and was admitted to the Pediatric Department of our university hospital on Sunday. She lives with her parents and a younger brother, and there is no pet at home. She had no remarkable medical, family, psychosocial, birth, and developmental histories. She had no drug allergy, and no food allergy, but she had allergic rhinitis. She had received all vaccinations as scheduled in Japan Pediatric Society; however, she did not receive flu vaccination this winter.

Physical examination at hospital admission revealed respiratory distress, as indicated by tachypnea (respiratory rate,

28 breaths/min; peripheral oxygen saturation, 92% in room air). The patient's breath sounds were poor in the left lung, and wheezing was heard in the right lung. Moreover, she had shoulder breathing and mild retractive breathing. Her temperature was 37.1 °C, heart rate was 116/min, and her blood pressure was 114/72 mm Hg. Upon cardiac auscultation, the rhythm was rapid but regular, no cardiac murmur was detected. There were no other findings on physical and neurological examination. The patient's laboratory examinations were as follows: white blood cell count, 8,200/ μ L (neutrophils, 79.9%; eosinophils, 1.5%); C-reactive protein level, 0.10 mg/dL; and total immunoglobulin E, 282 IU/mL. The arterial blood gas analysis was as follows: pH, 7.399; pCO₂, 37.2 mm Hg; pO₂, 50.5 mm Hg; HCO₃, 22.5 mm Hg; base excess, -1.5; and oxygen saturation, 85.2%. The rapid nasal swab influenza antigen test was negative for influenza A and B, and the anti-mycoplasma antibody test was negative (Table 1). Chest radiography revealed low permeability in the left lung field. Chest CT revealed decreased permeability in the left lung field (Fig. 1a-c). The patient was diagnosed with atelectasis of the left lobe and was admitted to the Pediatric Department.

On the next day following admission, the patient was diagnosed using a rapid antigen test for influenza (influenza A). She was diagnosed with influenza virus-induced PB and was treated with antibiotics (clarithromycin), expectant (L-carbocistein, ambroxol hydrochloride, acetylcystein inhalation), bronchodilators (procaterol hydrochloride hydrate), and antiviral drug (peramivir hydrate, 240 mg) and received intravenous infusion of steroids (methylprednisolone) (Fig. 2). The pediatric doctors explained to her parents about the bronchoscopic removal on hospital day 2. She became increasingly dyspneic, and her SpO₂ was 87% (room air) despite conservative treatment via nasal oxygen (5 L/min). After supplying O₂ via an oxygen mask, dyspnea was not relieved. On day 4 following admission, the patient underwent flexible bronchoscopy because of worsening dyspnea. Chest radiography and CT revealed atelectasis in the left lung field and a mucous plug in the left bronchus (Fig. 3a, b).

We believed that we needed to perform flexible bronchoscopy. Flexible bronchoscopic removal of the mucosal plug was performed under general anesthesia using laryngeal mask ventilation by an anesthesiologist. A laryngeal flexible endoscope with a forceps channel was inserted, and viscous white secretions were observed in the left bronchial region. Suction was repeatedly performed (Fig. 4a-f), and the mucus plugs were removed due to cast friability and fragmentation (Fig. 5). A chest radiograph obtained after bronchoscopy and partial removal of the cast revealed marked improvement of the atelectasis finding in the left upper lung (Fig. 6a). Histopathology of the bronchial cast showed eosinophilic infiltration (Fig. 7). The patient's left upper body pain disappeared, and shoulder breathing and mild retractive breathing improved after the bronchoscopic removal of the mucosal plug. Conservative treatment (sulbactam/ampicillin, predonine, L-carbocistein, ambroxol hydrochloride, acetylcystein inhalation, procaterol hydrochloride hydrate) was continued; she was relieved from all symptoms of the PB and atelectasis finding in her left lung on chest radiograph (Fig. 6b). She was discharged from our hospital 10 days after bronchoscopic treatment. The patient was prescribed inhaled corticoster-

Table 1. Laboratory Data on Admission

WBC	8.2 × 10 ³ / μ L
Neutrophils	79.9%
Eosinophils	1.5%
Basophils	1.2%
Lymphocytes	11.0%
RBC	491 × 10 ⁴ / μ L
Hb	13.3 g/dL
Ht	40.0%
Plt	25.8 × 10 ⁴ / μ L
Na	139 mmol/L
K	4.3 mmol/L
Cl	105 mmol/L
UN	8.0 mg/dL
Cr	0.23 mg/dL
TP	7.2 g/dL
Alb	4.7 g/dL
TB	0.5 mg/dL
AST	23 IU/L
ALT	11 IU/L
IgG	985 mg/dL
IgA	52 mg/dL
IgM	175 mg/dL
CRP	0.10 mg/dL
Non-specific IgE	209 IU/dL
Ferritin	30 ng/dL
RSV	(-)
Flu (A/B)	(-/-)
Mycoplasma	(-)
Cryptococcus	(-)
Blood culture	Negative
Tuberculosis specific IFN- γ	(-)
Urinalysis	
Protein	(-)
Blood	(-)
Sugar	(-)
β_2 -MG ^a	260 μ g/L
NAG ^a	46 IU/L

^aThese are results of October 3 (hospital day 3). WBC: white blood cell; RBC: red blood cell; Hb: hemoglobin; Ht: hematocrit; Plt: platelet; UN: urea nitrogen; Cr: creatinine; TP: total protein; Alb: albumin; TB: total bilirubin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; Ig: immunoglobulin; CRP: C-reactive protein; RSV: respiratory syncytial virus; Flu: influenza virus; IFN: interferon; MG: microglobulin; NAG: N-acetyl- β -D-glucosaminidase.

oid (fluticasone propionate 100 μ g, two times/day, for 2 years), bronchodilators (L-carbocistein 750 mg/day, and ambroxol hydrochloride 45 mg/day) and antileukotriene (pranlukast hydrate

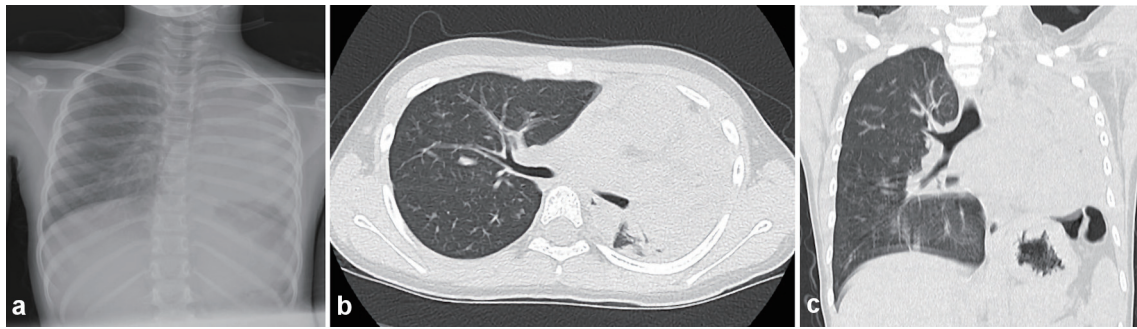


Figure 1. Chest radiography and computed tomography on admission day. (a) Chest radiography on admission revealed the low permeability in the left lung field. (b, c) Chest computed tomography (axial and coronal) revealed the decreasing permeability in the left lung field.

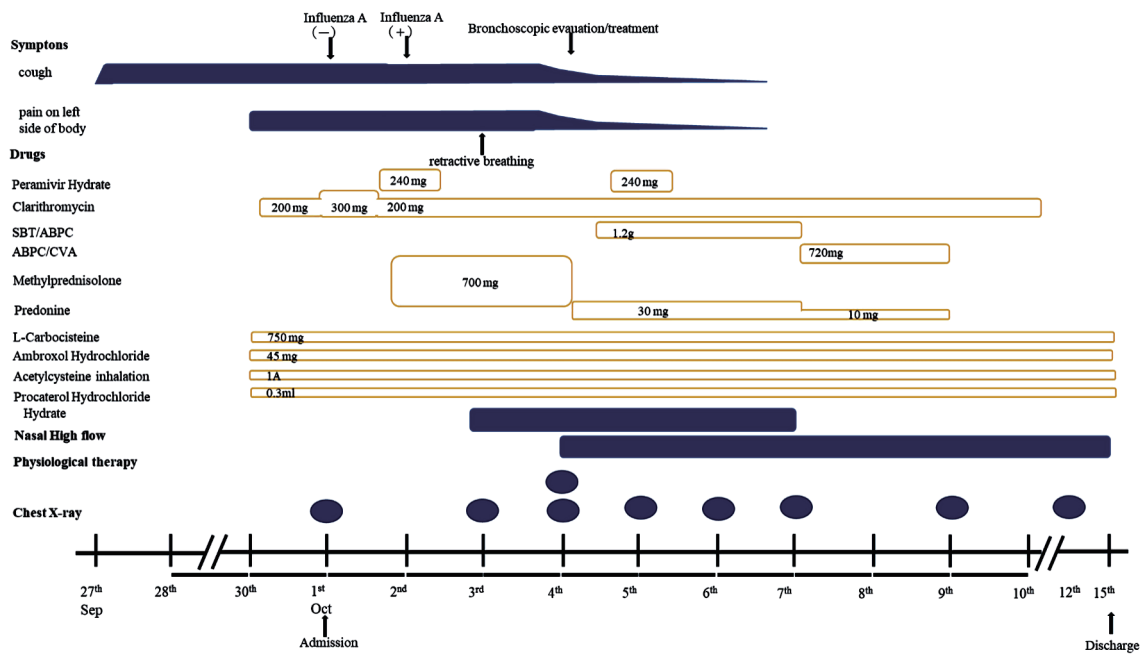


Figure 2. Clinical course after admission. This figure showed time course of applied medicine and chest radiography. SBT/AMPC: sulbactam/ampicillin; AMPC/CVA: amoxicillin-clavulanate.

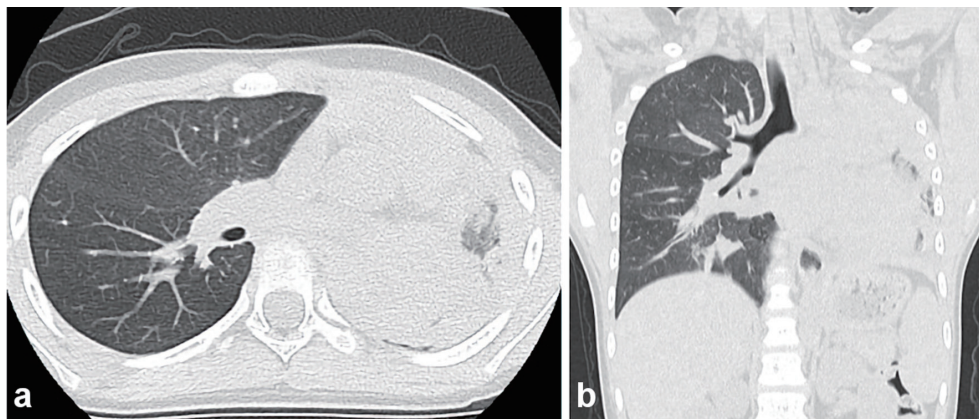


Figure 3. Chest computed tomography on day 4 following admission (axial and coronal) revealing the total atelectasis in the left lung field and a mucous plug in the left bronchus.

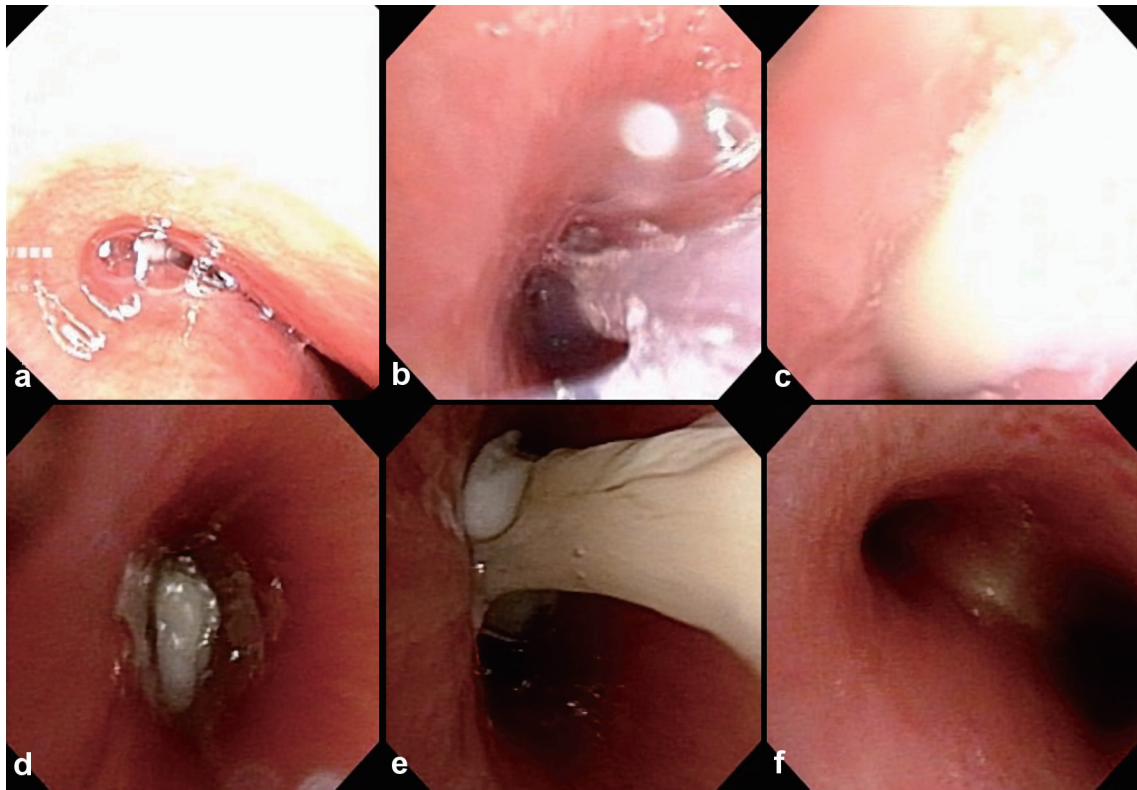


Figure 4. (a-f) Bronchoscopic visualization of secretions in the bronchus with patent left lobe orifice. The author (presenter, otolaryngologist) performed flexible bronchoscopy, which revealed a whitish rubbery material occluding the left lower lobe bronchus, and plastic casts were removed. The casts fragmented were removed by extraction via suctioning during fiberoptic bronchoscopy.

225 mg/day, for 1 month). The patient underwent the respiratory functional test 1 month after discharge; the forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio were 1.31 L, 1.38 L, and 94.9%, respectively. The patient has been in a good condition with no respiratory infection, bronchial asthma, and recurrence of influenza virus-induced PB for 2 years after discharge.

This study was approved by the Faculty of Medicine Research Ethics Committee of Kyorin University (approval number, 1318).



Figure 5. Gross findings demonstrate the fragmentation of casts.

Discussion

In this case report, we described the clinical features, chest radiographic results, and treatment for the patient with influenza virus-induced PB. A role of bronchoscopy was very important for the treatment of PB.

PB is a disease characterized by bronchial obstruction and respiratory failure due to the formation of a highly mucous plug. The earliest description of PB appeared more than 100 years previously [2]. The chief symptoms for patients with PB were dyspnea, wheezing, pleuritic chest pain, and fever [3, 4]. The typical findings of breath sounds showed poor or absent sounds in the affected lung. PB might occur more frequently in all age groups epidemiologically, and PB in children is usually associated with congenital heart disease with the Fontan procedure [5]. However, some clinicians have reported on pediatric patients with influenza virus infection. The first cases of influenza virus-induced PB were reported in an influenza A (H1N1) pdm09 pandemic that occurred in 2009. Pediatric patients with influenza virus-induced PB in the previous English language literature were reported in a total 35 cases (28 cases of influenza A [1, 6-10] and seven cases of influenza B [11-14]) (Table 2). In pediatric patients with PB-induced influenza A and influenza B, the median ages were 4 years (age, 1 year and 10 months to 11 years) and 6 years (age, 5 to 8 years), with male predominance (the ratio was 6:1 to 8:1). PB was predominantly common in women [15]; however, these

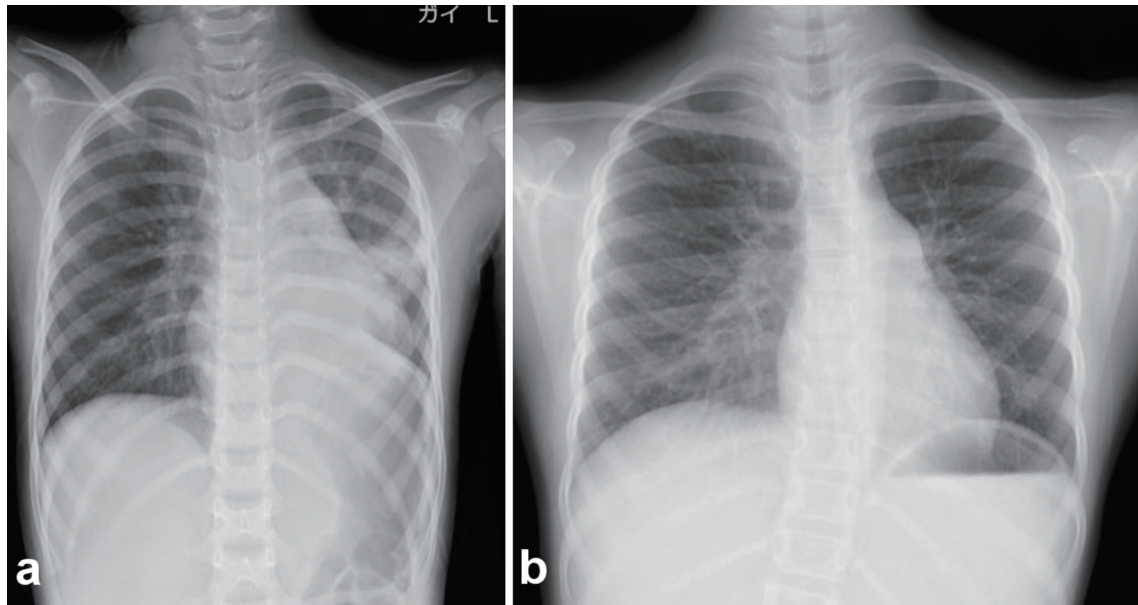


Figure 6. Chest radiography after bronchoscopic suctioning. (a) Finding immediately after bronchoscopic suctioning. After bronchoscopic removal of casts, the atelectasis finding in the left upper lung on chest radiography was improved. (b) Chest radiography revealed a marked improvement in the left lung.

differences are unknown. Interestingly, most of the patients were Asian, Japanese, Chinese, and Korean (32/35 cases, 91.4%) [1, 6-14]. Cough, wheezing, and fever, such as a common cold, were the most initial symptoms. The dyspnea was worsened, and breath sounds decreased in the affected lung.

The most common radiographic finding was atelectasis in the affected lung, and these findings were significantly more frequent in the left lung than in the right lung [9]. However, the affected side was nonspecific (influenza A, right lung 7/28, left lung 9/28, bilateral lung 6/28, unknown side 6/28; influenza B, right lung 4/7, left lung 3/7). The underlying disease was allergy (influenza A, 11/28; influenza B, 3/7). It is likely that the underlying allergic mechanism might be a high-risk factor regardless of the type of influenza, similar with previous reports [1, 6-14].

The treatment for PB is based on the treatment of the pa-

thologies that cause the symptoms. Common therapies include removal of mucus plugs using bronchoscopy, bronchial lavage, humidification, prescribing expectorant, and pulmonary physical therapy by a physiotherapist [11]. The treatments, including oxygen therapy, antiviral drugs (influenza A, 21/28; influenza B, 6/7), systematic steroids (influenza A, 19/28; influenza B, 5/7), and antibiotics (influenza A, 8/28; influenza B, 6/7), were dependent on the attending physician. Antiviral drugs and systemic steroids have been administered in almost all patients, but these drugs have been used based on experience. Terano et al reported that anti-influenza virus agents may not be effective for the treatment of PB [8], and Uda et al reported that antiviral drugs may improve the outcome of severe respiratory failure due to influenza A [1]. We believed that an antibiotic should be administered if the condition is pneumonia. Of the 35 patients with PB, 31 were in-

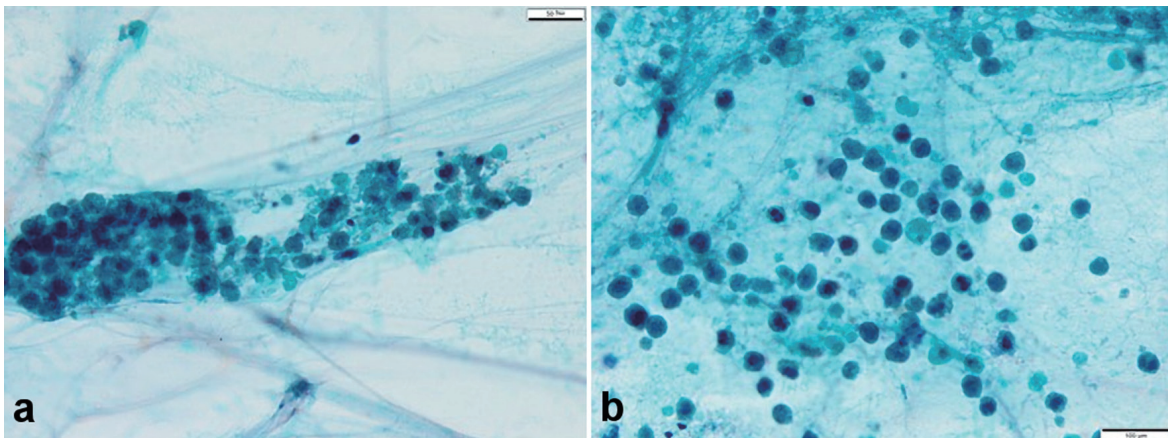


Figure 7. (a, b) Sputum cytopathology (hematoxylin and eosin stain, $\times 40$). Numerous eosinophils were found; however, an evident malignant finding was not found. Eosinophils were considered the inflammatory cells. Charcot-Leyden crystals were not observed.

Table 2. A Total 35 Cases of Pediatric Patients With Influenza Virus-Induced Plastic Bronchitis in Previous English Reports

	Influenza type A	Influenza type B
Case	N = 28	N = 7
Sex (boy/girl)	25:3	6:1
Age	1 year and 10 months to 11 years	5 years to 8 years
Average age	4.4 years	6.9 years
Median age	4 years	6 years
National	Japanese: 10 Korean: 1 Chinese 17	Japanese: 4 American: 3
Underlying disease (allergy)	11/28	3/7
Affected side on chest X-ray or CT		
Right	7/28	4/7
Left	9/28	3/7
Bilateral	6/28	-
Unknown	6/28	-
Therapy		
Antiviral drug	21/28	6/7
Steroid	19/28	5/7
Antibacterial drug	8/28	4/7
Bronchoscopic removal	28/28	7/7
Mechanical ventilation	25/28	6/7
Outcome	26/28 improve including: 2/28 recurrence (the second attack was infected with influenza type B) improve, 2/28 death	7/7 improve including: 1/7 recurrence (the second attack was infected with influenza type A) improve

CT: computed tomography.

tubated and mechanically ventilated; however, in this case report, the patient did not require intubation and mechanical ventilation. All pediatric patients underwent bronchoscopic mucosal plug removal. Bronchoscopic removal of casts was more effective when their symptoms and radiographic findings were not recovered by conservative treatment [1, 6-14]. In our case, the patient was relieved off dyspnea, shoulder breathing, and chest pain immediately after bronchoscopic intervention. However, two cases of death have been reported [10]. For a more careful point, the recurrence of the influenza virus-induced PB was reported in three patients (influenza A, two patients; influenza B, one patient) [9, 10, 14]. Interestingly, a second PB occurred due to different types of influenza virus. Recently, *Mycoplasma pneumoniae* infection and adenovirus-induced PB have been reported [16, 17].

We believed that the best treatment of PB was bronchoscopic removal of casts, not conservative treatment (antiviral drug, antibiotic drug, expectant, and steroid).

Conclusions

In conclusion, the possible diagnosis of PB should be considered in children with severe respiratory failure during the influenza season. In particular, allergic condition is considered a

risk factor for developing PB. Bronchoscopic examination and treatment might immediately be performed after the diagnosis with PB is established.

Moreover, it is necessary to perform bronchoscopy for the differential diagnosis from an airway foreign body. We, otolaryngologists, are accustomed to using flexible endoscopes in our daily practice; therefore, we can play a role in actively performing bronchoscopic treatment, which is a treatment for PB.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Written informed consent was obtained from the patient's mother for publication of this case report and accompanying images.

Author Contributions

M. Miyamoto contributed to conceptualization, formal analysis, writing-original draft, and writing-review and editing. Y. Yanagishita, A. Kure, S. Hashimoto and T. Takiura provided medical care. A. Hosaki provided diagnosis and medical care. K. Yan provided supervision, and K. Saito provided conceptual advice and supervision. All authors read and approved the final manuscript.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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