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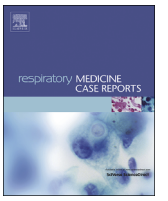

Case Report

A case of plastic bronchitis with a remarkable response to steroids

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ABSTRACT

Plastic bronchitis can cause fatal airway obstruction. An 85-year-old woman with no medical history presented to the emergency department of our hospital with progressing respiratory failure and hemoptysis. Bronchoscopy revealed a fibrin-type cast thrombus in the trachea, and plastic bronchitis was diagnosed. Initial treatment involved airway thrombus removal, and the patient survived. However, bleeding persisted for 6 days, and respiratory status showed slight improvement despite ventilatory management. Steroids were administered for concomitant acute respiratory distress syndrome, and there was marked improvement in both airway hemorrhage and respiratory failure. The patient was extubated, the steroid dose was reduced, and no rebleeding was observed. The patient was discharged from the hospital 1 month after the onset of symptoms. Blood tests were positive for the myeloperoxidase-anti-neutrophil cytoplasmic antibody; however, no biopsy was performed, and no specific symptoms were observed. A definitive diagnosis was therefore not reached. The causes of plastic bronchitis are numerous, and there are no standardized diagnostic criteria or treatment guidelines for this condition. The present case suggests that steroids may be effective in some patients with plastic bronchitis.

1. Introduction

Plastic bronchitis is a rare disease that causes respiratory symptoms due to formation of mucus plug that blocks the airway. The illness can be fatal if complicated by acute respiratory failure [1]. Plastic bronchitis can occur in all age groups, especially in children, and has numerous causes [1]. The two major causative mechanisms for plastic bronchitis are inflammatory and non-inflammatory injuries. The former includes allergic diseases (asthma, atopy, allergic bronchopulmonary aspergillosis) and infections (such as those of influenza virus, adenovirus); the latter includes postoperative cardiac complications (such as those of Fontan and Blalock–Taussig surgery), lymphatic abnormalities (lymphangiectasia, lymphangioma), acute chest syndrome due to sickle cell disease, and several other diseases associated with occupational exposure and post-transplantation complications [2].

In cases where the cause of plastic bronchitis is known, various treatment methods have been attempted. However, in many cases, the cause of plastic bronchitis remains unidentified [2]. In any event, treatments are implemented based on a trial-and-error approach, given the lack of standardized treatment options [1].

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2. Case report

An 85-year-old woman with no medical history called for emergency medical services after experiencing dyspnea, cough, and hemoptysis for >20 minutes. Upon arrival of the emergency medical services, the patient had a normal level of consciousness, SpO_2 was 88% (room air), the respiratory rate was 24 breaths/min, and other vital signs were normal. However, her vital signs worsened during transport, and upon arrival at our hospital, the patient presented with a Glasgow Coma Scale score of E1V1M4, SpO_2 of 70% (assisted ventilation, oxygen 10 L/min), blood pressure of 176/120 mmHg, and a heart rate of 130 beats/min. There was no record of collagen vascular disease based on personal medical and family history. The patient did not have a history of alcohol consumption or smoking. When the patient arrived at the hospital, there were no findings of purpura, peripheral neuropathy, otitis media, and vasculitis, or history of sinusitis or epistaxis. Breath sounds were diminished bilaterally, and the patient was intubated due to inadequate oxygenation. A computed tomography (CT) scan, which was obtained immediately after intubation, showed a continuously occupying substance located in the trachea and bronchi (Fig. 1). No abnormalities were observed in the vascular structures of the neck on three-dimensional CT. The object was successfully removed by guiding the airway obstruction into the intubation tube using a bronchoscope and extubating the substance in one piece (Figs. 2, 3A and 3B). After removal of the airway obstruction, the patient's condition improved remarkably, both in terms of consciousness and respiratory status. The patient remained on ventilatory support to prevent further airway obstruction due to hemoptysis. The blood test results at the time of admission are shown in Table 1, and the results of hematological tests performed during hospitalization are shown in Table 2. White blood cell counts of 13100/μL, C-reactive protein levels of 7.97 mg/dL, and mildly elevated pulmonary surfactant protein-A and pulmonary surfactant protein-D levels were noted. Re-

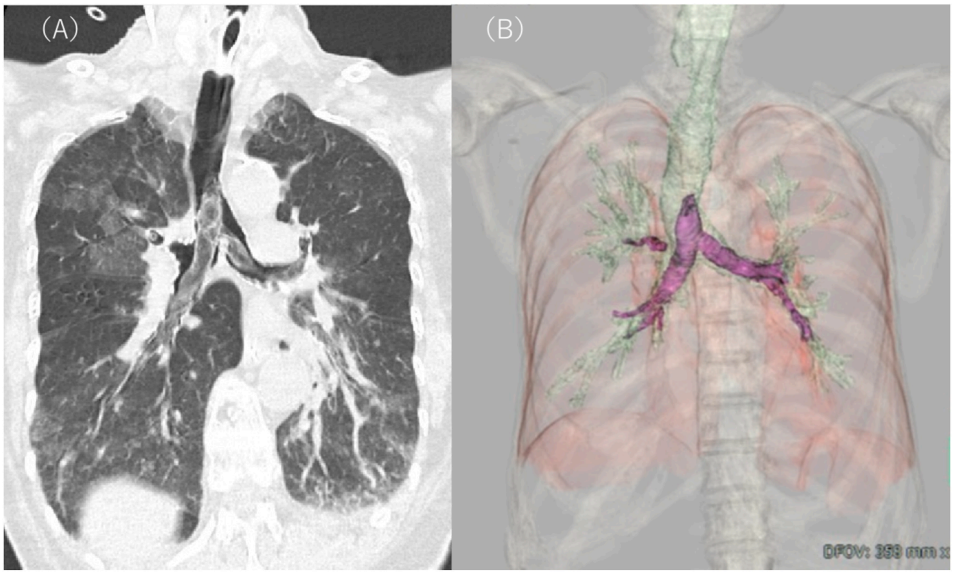

Fig. 1. Chest CT findings (A) Plain CT (coronal section). (B) Three-dimensional reconstructed multi-masked bronchial CT. Continuous occupying material is observed from the main bronchi to the bronchioles. Diffuse frosted shadows are observed in both lung fields.
CT, computed tomography

Fig. 2. Removed intratracheal substance.
Dendritic red mucus thrombus with a clear visualization of the bronchial tree in detail.

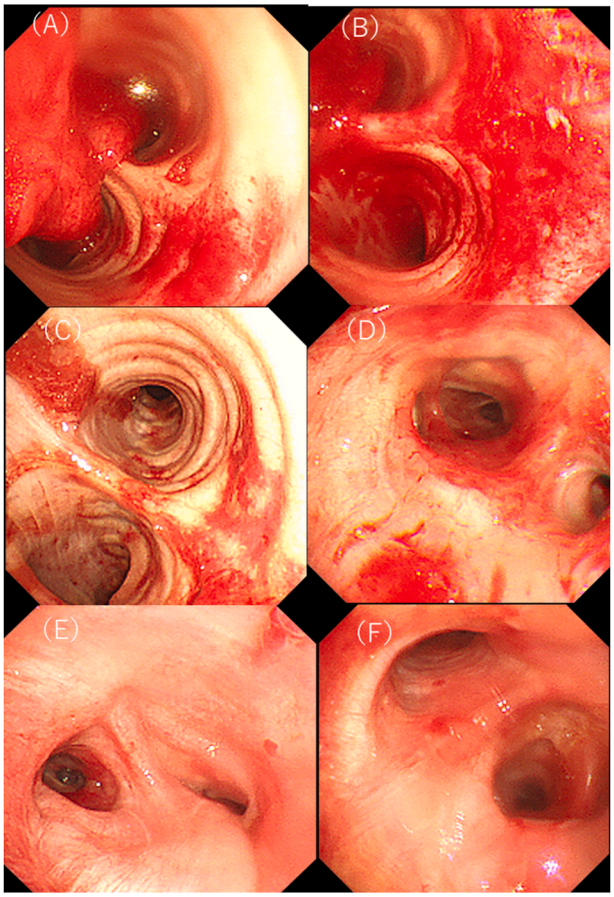

Fig. 3. Endoscopic view of the bronchial tube
(A, B) Bronchoscopic findings upon arrival at the hospital.
Material occupying the tracheal lumen and bleeding in the tracheal mucosa. (C, D) Bronchoscopy findings on day 4 after hospitalization. No new cast thrombus appeared, although intratracheal bleeding persists. (E, F) Bronchoscopy findings on day 7 of hospitalization. Intratracheal bleeding almost disappeared after steroid administration.

nal failure was absent. Urinalysis was negative for occult blood, and 1 + for protein. Blood, sputum, and urine cultures yielded negative results. To prevent pneumonia, sulbactam + ampicillin was administered, and daily bronchoscopy was performed to evaluate the airway; however, exudative bleeding persisted in the trachea (Fig. 3C and D). Follow-up CT performed on day 6 after hospitalization showed an extensive ground-glass appearance in both lung fields. Since the P/F ratio was 120, acute respiratory distress syndrome was diagnosed, and prednisolone 62.5 mg/day was started, resulting in improved respiratory status and intratracheal bleeding (Fig. 3E and F). On day 9 after hospitalization, the patient showed improvement in her inflammatory response, and since there was no symptom relapse, the dose of prednisolone was reduced to 40 mg/day, antibiotic therapy was terminated, and the patient was extubated on the same day. No findings of interstitial pneumonia were noted. Pathological examination revealed that the main components occupying the airway were blood clots and fibrin. Other mucus components and an infiltration of inflammatory cells were also present, including macrophages and neutrophils (Fig. 4). There was no evidence of malignancy or infection. Although the blood test results on day 4 revealed myeloperoxidase-anti-neutrophil cytoplasmic antibody (MPO-ANCA) positivity (Table 1), a diagnosis of microscopic polyangiitis was not made, since a biopsy was not performed due to the risk/benefit considerations. Steroid treatment was continued based on a favorable response and the possibility of microscopic polyangiitis. On day 27 after hospitalization, the prednisolone dose was reduced to 35 mg/day, and the patient was discharged on day 31. The patient is currently being monitored in the outpatient care department and has been prescribed a reduced prednisolone dose of 25 mg/day.

3. Discussion

We encountered a case of airway obstruction caused by an intra-tracheal cast thrombus formed in an older adult with no medical history. In cases of plastic bronchitis reported to date, the main component of the extracted cast embolic material has been characterized according to the cause of the disease [2]. For example, predominating fibrin, or fibrin and mucin, without inflammatory cells is characteristic of congenital heart disease [2]. Lymphatic abnormalities are often dominated by chyle, whereas allergic diseases often precipitate fibrin, eosinophils, and Charcot–Leyden crystals [3]. Cases of infection show inflammatory cell infiltration and the presence of pathogens, whereas acute chest syndrome cases are dominated by fibrin, macrophages, and lipids [2,3]. In this case, the em-

Table 1
Clinical parameters at the time of admission/baseline.

White blood cell	13.11 (3.3–8.6)	×10^3/μL	Alanine aminotranseferase	15 (7–23)	U/L
Red blood cell	4.34 (3.86–4.92)	×10^6/μL	Lactate dehydrogenase	188 (124–222)	U/L
Hemoglobin	13.0 (11.6–14.8)	g/dl	Albumin	3.2 (4.1–5.1)	g/dL
Hematocrit	41.5 (35.1–44.4)	%	Troponin T	0.044 (≦0.014)	ng/mL
Platelet	253 (158.0–348.0)	×10^3/μL	NT-proBNP[a]	234 (≦125)	pg/mL
			Sialylated carbohydrate KL-6	126 (105–401)	U/mL
C-reactive protein	7.97 (0.00–0.14)	mg/dL	SP-A[a]	52 (<43.8)	ng/mL
Procalcitonin	0.04 (<0.5)	ng/mL	SP-D[a]	119 (<15)	ng/mL
(1 → 3)-β-D-glucan	negative				
			Prothrombin time	9.9 (0.8–1.2)	sec
Sodium	142 (138–145)	mEq/L	APTT[a]	35 (25–35)	sec
Potassium	3.9 (3.6–4.8)	mEq/L	Fibrinogen	664 (220–400)	mg/dL
Chloride	104 (101–108)	mEq/L	D-dimer	4.9 (<1.0)	μg/mL
Calcium	8.9 (8.8–10.1)	mg/dL	Antithrombin	75 (80–130)	%
Blood urea nitrogen	24.4 (8.0–20.0)	mg/dL			
Creatinine	0.64 (0.46–0.79)	mg/dL	Antinuclear antibody	negative	
Uric acid	4.9 (2.6–5.5)	mg/dL	Anti-GBM antibody	<2.0 (<3)	U/mL
Total bilirubin	0.4 (0.4–1.5)	mg/dL	PR3-ANCA	<1.0 (<3.5)	U/mL
γ-glitamyl transpeptidase	5 (9–32)	U/L	MPO-ANCA	13.9 (<3.5)	U/mL
Aspartate aminotransferase	19 (13–30)	U/L	Aspergillus antibody	negative	

The number in () indicates the reference value for each parameter.
[a] NT-Pro BNP: N-terminal prohormone of brain natriuretic peptide, SP-A: Pulmonary Surfactant Protein-A, SP-D: Pulmonary Surfactant Protein-D, APTT: Activated partial thromboplastin time, Anti-GBM antibody: Anti-glomerular basement membrane antibody, PR3-ANCA: proteinase-3-anti-neutrophil cytoplasmic antibodies, MPO-ANCA: myeloperoxidase-anti-neutrophil cytoplasmic antibodies.

Table 2
Changes in main clinical parameters during hospitalization.

	Reference values	Day 1	Day 4	Day 6	Day 7	Day 9	Day 26
White blood cell (×10^3/μL)	3.3–8.6	13.1	9.5	9.7	10.5	9.9	12.4
C-reactive protein (mg/dL)	0.00–0.14	7.97	24.51	22.85	14.93	4.28	0.06
Creatinine (mg/dL)	0.46–0.79	0.64	0.53	0.48	0.45	0.49	0.51
Estimated GFR (mL/min/1.73m^2)	>60	75.8	80.2	89.4	96.0	87.4	83.7

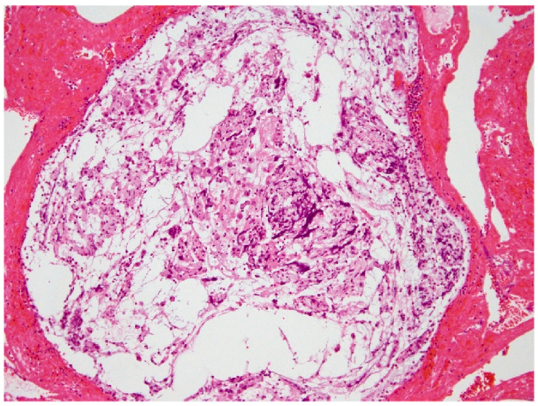

Fig. 4. Pathological findings of dendritic red mucus thrombus.
Hematoma is composed of coagulum and fibrin, with no epithelial components. Mucus and inflammatory cell infiltrates, including macrophages and neutrophils, are present. No neoplastic changes or malignant findings are observed. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

bolic material extracted consisted mainly of fibrin thrombus, with small amounts of mucus components and inflammatory cells, including macrophages and neutrophils. According to the gross findings and pathological results of fibrin thrombus in this case, hemorrhage was considered the main cause of plastic bronchitis. Microscopic polyangiitis is also a causative disease to consider, since inflammatory cell infiltration was observed and blood tests were positive for MPO-ANCA. As of date, there are no reports on the frequency of plastic bronchitis caused by ANCA-associated vasculitis or its pathogenesis. However, ANCA-associated vasculitis is thought to cause not only inflammation but also airway hemorrhage, which may predispose to the development of plastic bronchitis. In this case, the bronchoscopy and pathology findings strongly suggested the involvement of airway hemorrhage and inflammation. The usefulness of ANCA measurement in ANCA-associated vasculitis is very high, with a specificity of >90% [4], and microscopic

polyangiitis was suspected as a cause of hemoptysis, although it could not be confirmed as such using Japanese diagnostic guidelines [5,6].

The basic treatment for plastic bronchitis is removal of embolic material and the prevention of new embolic material formation [1]. In many cases, the embolic substance can be removed using the bronchoscope during intubation [1]. Reports suggest that instant cooling of the embolic material during removal, respiratory exercise therapy, and induction of high-frequency vibration to loosen adhesions are effective treatments [1,7,8]. In addition, N-acetylcysteine, urokinase, and tissue plasminogen activator can be nebulized to assist lysis before bronchoscopy is performed, effectively assisting in the removal of embolic material [9,10]. Treatment of the underlying disease is effective in preventing new embolic material formation; for example, lymphangiography and selective embolization of abnormal lymphatics are effective in cases of primary lymphatic abnormalities [11]. Lymphatic flow obstruction after cardiac surgery (secondary lymphatic abnormalities) is a common cause of plastic bronchitis, especially in children; thus, management of cardiac insufficiency also plays a vital role in treatment [2]. Extracorporeal membrane oxygenation is also considered when heart failure is uncontrolled [2,12]; however, it was not considered in this case given the patient's age and the prompt removal of embolic material. In plastic bronchitis cases caused by other diseases, including inflammatory conditions such as allergic diseases, patients were effectively treated with bronchodilators, steroid inhalants, expectorants, and low-dose long-term administration of macrolides [12]. In non-inflammatory settings, oral sirolimus, a treatment for lymphangioleiomyomatosis, and dornase alfa have been reported to be effective in acute chest syndrome cases; to the best of our knowledge, no studies have shown the consistent efficacy of a single agent, regardless of whether plastic bronchitis has an inflammatory or non-inflammatory cause. In this case, the use of a nebulizer during bronchoscopy was considered; however, the cast thrombus was successfully removed by performing bronchoscopy with tracheal intubation and extubation with a suction tube connected to the intubation tube. Steroid administration for suspected acute respiratory distress syndrome and microscopic polyangiitis was significantly effective in preventing the return of embolic material.

Wang et al. reported the efficacy of steroid therapy in 32 cases of cast bronchitis with hemoptysis [13]. The 32 patients were divided into steroid (n = 18) and non-steroid (n = 14) groups. The causative diseases were bronchitis in 17 cases, tuberculosis in 5 cases, pneumonia in 5 cases, and unknown in 5 cases. Pathologically, fibrin was deposited from airway cast emboli observed in these 32 cases, and immune cells such as eosinophils, neutrophils, lymphocytes, and macrophages, were deposited in others, which was consistent with inflammatory cast findings in all cases. The authors noted that the steroid-treated group showed more rapid symptomatic improvement with no mortality events when compared to the non-treated group [13]. Other reports have shown that steroids are markedly effective in treating cast bronchiolitis with a background of pneumonia and heart failure [14]. Although the mechanism whereby steroid administration suppresses the formation of cast embolic material is unclear, steroids may suppress bronchial inflammation by inhibiting the expression of inflammatory cytokines [13]. In the present case, although the causative disease could not be identified, the main components of the embolic material were fibrin and inflammatory cells, suggesting that an inflammatory disease was the underlying cause; hence, steroids were remarkably effective.

From the reported cases, steroids may be effective in the treatment of cases of cast bronchiolitis, particularly those caused by inflammatory disease. However, the subtype of patients for whom steroids are effective and the mechanisms through which the medications work are yet to be determined.

4. Conclusion

- Steroids may be effective in the treatment of plastic bronchiolitis with suspected ANCA-associated vasculitis.
- Further studies are needed to validate the efficacy of steroid administration in the treatment of plastic bronchitis and identify the subtypes of patients for whom steroid administration is particularly effective.

Statement of ethics

All procedures were performed in accordance with the Declaration of Helsinki of the World Medical Association. Written informed consent was obtained from the patient prior to the study. Ethical approval was obtained from the Ethics Committee of Sapporo City General Hospital. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Author contributions

Mone Murashita and Takumi Tsuchida drafted the manuscript and collected patient information. Takayoshi Oyasu, Yoshihiro Sadamoto, and Akira Kodate participated in the treatment of the patient and collected patient information. Yuki Matsuura, Akio Endo and Keisuke Bando contributed substantially to the revision of the manuscript drafts. Hisako Sageshima interpreted data and edited the manuscript. All authors have read and approved the final manuscript.

Data availability statement

All data generated and analyzed during this study were included in this article. Further inquiries can be directed to the corresponding author.

Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Not applicable.

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