

Plastic Bronchitis Associated With Influenza a Virus in a Child With Nephrotic Syndrome

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Case report

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Abstract

Background

Plastic bronchitis (PB) combined with nephrotic syndrome (NS) is rare, and the pathophysiological relationship between PB and NS has not been elucidated. We report a case of an 8-year-old boy with life-threatening PB caused by an influenza infection during a relapse of NS.

Case presentation

The patient was on immunosuppressive drugs for NS. He developed fever due to an influenza A virus infection, followed by respiratory distress and frequent vomiting. Prednisolone was administered for possible bronchial asthma and NS. His respiratory status deteriorated rapidly, which required ventilator management. A large mucus plug was aspirated using bronchoscopy. He was then diagnosed with PB caused by the influenza A virus. Increased lower airway secretion and fluid leakage into the airways by relapse of NS were considered the causes of mucus plug formation. Besides, the decreased circulating blood volume might have made the bronchial secretions viscous with cast formation.

Conclusions

Pediatric patients with NS may be at a higher risk of developing PB. As PB is a life-threatening condition, patients with NS should be closely monitored when simultaneously infected with influenza virus.

Background

Plastic bronchitis (PB) is a potentially life-threatening acute respiratory disease that can cause bronchial obstruction due to a cast-like mucus plug. The following causes of PB have been reported: atopy, bronchial asthma, airway diseases such as cystic fibrosis, and postoperative congenital heart disease [1–3]. Although few cases associated with nephrotic syndrome (NS) have been reported, these studies did not elucidate the association between the pathophysiology of NS and PB. The combination of NS and PB is a rare condition, and such cases should be evaluated because NS may be a risk factor for PB. Here, we present a case of pediatric PB during a relapse of NS.

Case Presentation

An 8-year-old boy experienced frequently relapsing NS since the age of 2 years despite being on immunosuppressive drugs (tacrolimus and mizoribine) for approximately 1 year prior to the current hospitalization. One month before admission, he experienced an episode of relapse and his prednisolone (PSL) dose was tapered off. He developed proteinuria and eyelid edema few days before admission, indicative of yet another relapse episode.

One day before admission, he developed fever, followed by respiratory distress and frequent vomiting. Physical examination on the day of admission revealed a body temperature of 39.5 °C, blood pressure of

122/71 mmHg. He had tachycardia (182 beats/min), tachypnea (48 breaths/min), and hypoxemia (88%). He appeared pale, with cold extremities, and dry lips and skin. He had hyperventilation, see-saw breathing, and decreased breath sounds in the right lung. His hemoglobin level (18.3 g/dL), and urine protein level (6,933 mg/dL) and specific gravity (1.050) were elevated, whereas the serum albumin level was reduced (2.5 g/dL). Chest radiography showed reduced permeability of the lower lobe of the right lung with no air bronchograms. The rapid influenza antigen test was positive for influenza A virus; however, viral isolation did not detect H1N1. The patient had not been vaccinated against influenza.

The patient was in hypovolemic shock, which was thought to be indicative of decreased circulating blood volume due to reduced oncotic pressure from NS-induced hypoproteinemia. We administered 12.5 g of albumin at frequent intervals, in addition to massive infusions of isotonic solution to increase extracellular fluid, 20 mL/kg rapid administration, and catecholamine support with adrenaline and dobutamine. Fluid infusion was closely monitored to avoid overhydration. To treat the infection, we used a combination of meropenem and vancomycin and peramivir, an anti-influenza drug. In addition, because of his atopy, PSL (60 mg/day; 2 mg/kg/day) was administered for possible bronchial asthma and NS. However, his respiratory status worsened, and a few hours after admission, ventilatory management was initiated. Bronchoscopy revealed a large mucus plug embolizing the right bronchus, which was aspirated (Fig. 1). Based on these findings, he was diagnosed with PB caused by the influenza A virus. His respiratory status gradually improved, and he was extubated on the 5th day of admission.

On the 10th day of admission, the patient developed pulmonary arterial thromboembolism caused by a thrombus in the right internal jugular vein, where a central venous catheter had been placed, and he underwent anticoagulation therapy with heparin and warfarin. The intrapulmonary arterial thrombus decreased in size and resolved on the 25th day, leading to an increase in blood flow to the right internal jugular vein.

The proteinuria gradually decreased and completely cleared on the 14th day of admission. Treatment with a combination of tacrolimus and mizoribine was resumed, and rituximab was restarted from the 23rd day. The patient was discharged at 30 days after admission. He remained in remission for 6 months after discharge from our hospital.

Discussion And Conclusions

The present case suggests that patients with NS may have a higher risk of developing PB, which is a life-threatening disease. Therefore, the respiratory status of a patient with simultaneous NS and influenza should be monitored closely.

In airway diseases that are risk factors for PB, bronchial narrowing due to bronchospasm and post-inflammatory fibrosis, increased secretions, and acute and chronic inflammation of the airway mucosa contribute to mucus formation. After cardiac surgery for congenital heart lesions, damage to the peribronchial lymphatic channels, pleural adhesions, and increased venous pressure are thought to be

involved in the formation of mucus plugs. It has been surmised that PB and protein-losing enteropathy (PLE) after Fontan surgery have similar mechanisms of lymphatic leakage to the bronchi and intestinal tract, and the activation of the immune and inflammatory systems may trigger the development of PB [4,5]. During relapse of NS, the lung interstitium might be edematous due to hypoproteinemia, and the exudate is likely to easily leak into the bronchi. In the present case, no wheezing was heard, although the patient had a history of atopy. PSL (60 mg/day; 2 mg/kg) was administered for possible bronchial asthma. The dose was reduced to 30 mg/day (1 mg/kg) after improvement of hypoproteinemia to lower the risk of steroid psychosis.

Several cases of pediatric PB and underlying NS have been reported [6-10]. A Japanese boy who developed PB during relapse of NS was reported to be infected with the influenza B virus. He was unvaccinated [7]. The patient developed oliguria during the course of the illness and required renal replacement therapy. In a report of 14 cases of PB due to influenza A and B at a single center in China, one patient had NS and developed renal dysfunction that required renal replacement therapy during the course of the disease [8]. In a report of pediatric cases of severe influenza A from another center in China, two of the 15 patients had NS, one of whom died after development of PB [9].

Seear et al. classified the pathological findings of mucus plugs into two categories [10]. Type I is an inflammatory type formed by inflammatory cells, mainly eosinophils, and fibrin. Type II is an acellular type formed by mucin and mononuclear cells, which often occurs after Fontan surgery. The mucus plug in our case showed numerous neutrophils and eosinophils and was classified as type I. The mucus plugs in the cases of Oonoki et al. and in the Chinese patients also displayed a type I pathology [6,9]. In contrast, in a study comprising 21 children with PB at a single center, one child had NS and presented with a type II mucus plug [11]. Therefore, we speculated that patients with NS can have either types of mucous plugs.

Further, children with NS have often been reported to have allergic disease [12]. Our patient had atopy and possibly the complication of bronchial asthma. We hypothesized that the pathophysiology of PB was as follows: a lower airway viral influenza infection caused increased secretion and infiltration of inflammatory cells into the airway. Relapse of NS led to hypoproteinemia and leakage of fluid into the subcutaneous tissue and airways. Subsequently, the decrease in circulating blood volume caused the bronchial secretions to become viscous causing cast formation. The infection in our patient might have been more severe due to oral immunosuppressive medications; nevertheless, we found no case report of PB in post-transplant or immunocompromised pediatric patients caused by an influenza virus. Additionally, hypoglobulinemia associated with NS may contribute to disease severity. Children with frequently relapsing NS who developed PB while not experiencing relapse of NS, although they had a low level of immunoglobulin G (IgG; 311 mg/dL) at the time of onset [6]. In addition, in the case of PLE and PB after Fontan surgery, regular supplementation of albumin and IgG was provided because of low IgG level (342 mg/dL) at onset [13]. At onset, our patient's IgG level (775 mg/dL) was in the lower normal range. Children with NS may be at a higher risk of developing PB with the potential for severe disease due

to the following two factors: the patient's predisposition to complications of allergic diseases and the pathophysiology of protein loss during a relapse.

Patients with NS are known to have a higher risk of thrombus formation from intravascular condensation due to hypoproteinemia and leakage of anticlotting factors [14]. Furthermore, the patient in the present case might have been prone to thrombus formation from hypercytokinemia associated with infection and catheter placement. However, details of the pathophysiology have not yet been proven.

In summary, PB may be life-threatening; therefore, pediatric patients with NS should be followed-up more carefully, especially during the influenza epidemic period, as protein leakage may be exacerbated by an infection.

Abbreviations

IgG, Immunoglobulin G

NS, Nephrotic syndrome

PB, Plastic bronchitis

PLE, Protein-losing enteropathy

PSI, Prednisolone

Declarations

Funding: No support/funding was received for this report.

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Ethics approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Consent to participate: This is not an experimental case report. Therefore, consent to participate was not required.

Consent for publication: Informed consent was obtained from the patient's guardian for the publication of this case report.

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Figures

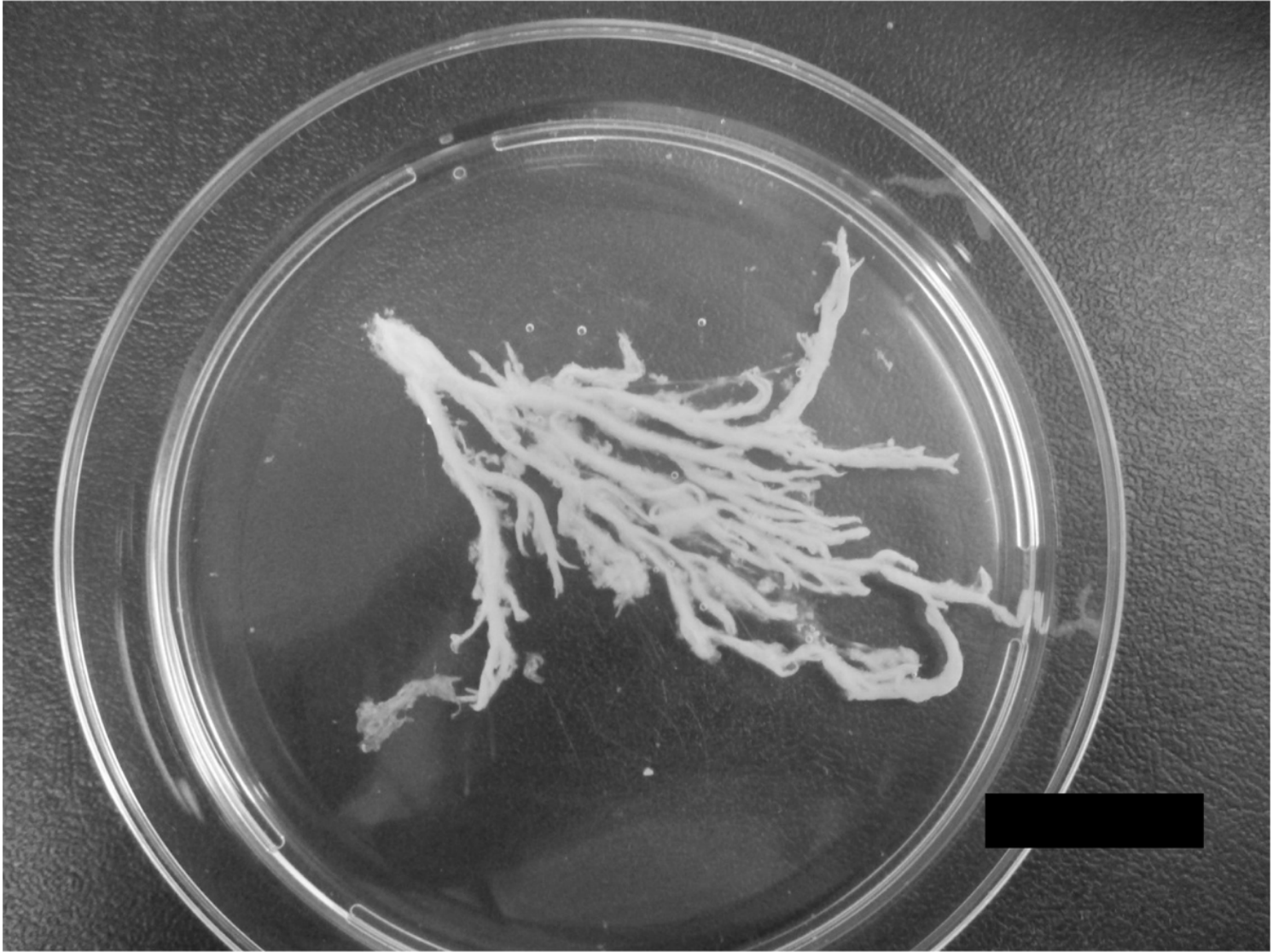


Figure 1

Mucus plug from the right bronchus