Pulmonary vasodilation therapy with sildenafil citrate in a patient with plastic bronchitis after the Fontan procedure for hypoplastic left heart syndrome

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Plastic bronchitis is a rare disease intractable to medical treatment, including steroids. It is characterized by recurrent expectoration of peculiar bronchial casts. Plastic bronchitis may be caused by primary bronchopulmonary disease but may occur in children after surgery for cyanotic congenital heart disease, especially after the Fontan procedure. Although the etiology of this rare disease remains unknown, the elevations of central venous pressure (CVP) and disorders of the lymphatic system are suggested as probable pathogenetic mechanisms for plastic bronchitis, the same as for protein losing enteropathy. We report here a case of plastic bronchitis after the Fontan procedure with successful treatment by combined use of epoprostenol and sildenafil citrate.

Clinical Summary
A 4-year-old boy with hypoplastic left heart syndrome and bilateral superior venae cavae was admitted to our hospital for recurrent pneumonia and chronic coughing. He underwent a Norwood procedure at 14 days old, a bilateral bidirectional Glenn procedure at 3 months old, and a Fontan procedure at 3 years old. After the Fontan procedure, he had severe pneumonia, atelectasis, and chylothorax, which necessitated mechanical assisted ventilation for 3 weeks. Two months after the Fontan procedure, a productive cough, wheezing, and dyspnea developed. A chest x-ray film revealed diffuse infiltration in the right middle and lower lobes. Despite treatment with antibiotics, he started to expectorate peculiar bronchial casts (Figure 1), which led to the diagnosis of plastic bronchitis. Echocardiography demonstrated normal right ventricular systolic and diastolic function with trivial tricuspid regurgitation. There was neither stenosis of the Fontan route nor pleural effusion. Oral prednisolone (2 mg/kg/d) was given for his plastic bronchitis, but he resumed expectorating the bronchial casts. Cardiac catheterization 132 days after the Fontan procedure showed increased mean CVP and pulmonary arterial pressure up to 16 mm Hg. The pulmonary arterial resistance (PAR) was 8.1 Wood units/m². Cardiac index calculated by the Fick method was 2.8 L/min/m². To reduce mean CVP with a pulmonary vasodilator, we started a continuous intravenous infusion of epoprostenol at a starting dose of 2 ng/kg/min, which was gradually increased to 16 ng/kg/min over 8 weeks. Although he had no bronchial casts for the initial 3 weeks after administration of epoprostenol, he started to expectorate the bronchial casts again. A repeated cardiac catheterization 3 months after the start of epoprostenol therapy showed improvement in hemodynamic parameters: mean CVP was decreased to 12 mm Hg and PAR to 4.5 Wood units/m². However, he continued to produce bronchial casts. Bronchoscopic examination revealed that the bronchial casts were produced from the right bronchus. After informed consent had been obtained from his parents, sildenafil citrate, a selective phosphodiesterase-5 inhibitor, known to be a very potent pulmonary arterial vasodilator, was added to reduce PAR further. The initial dosage of sildenafil citrate was 0.5 mg/kg/d, and dosage increased to 1.0 mg/kg/d. After the addition of sildenafil citrate to epoprostenol, no bronchial casts were expectorated. He was able to be weaned from epoprostenol 6 months after starting sildenafil citrate. No recurrence of the bronchial casts has been found since then.

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Discussion
Bronchial casts have been reported in association with a number of childhood diseases, including cyanotic congenital heart diseases, and may cause life-threatening airway obstruction. Seear and associates\(^5\) reported two types of bronchial casts, inflammatory and acellular, on the basis of histologic findings. In the acellular type, the casts are composed more of mucin than of fibrin and lack infiltration of inflammatory cells. This condition is mainly observed in patients who have been operated on for cyanotic heart disease. On the other hand, inflammatory cellular infiltration, with neutrophils, lymphocytes, and macrophages, is prominent in the inflammatory type and may be the result of acute or chronic inflammation or an allergic reaction in the airway.

The histologic findings of the bronchial casts in our patient revealed fibrin clusters including monocytes and macrophages, which suggest the inflammatory type of bronchial cast even though he had no history of allergic airway disease such as bronchial asthma \(\text{Figure 2}\). The one explanation for this is that his bronchial casts appeared only during respiratory infections. Aside from this, the presence of inflammatory plastic bronchitis in our patient is very unusual, because most patients with plastic bronchitis after cardiac surgery have acellular casts.

Treatment of plastic bronchitis is reported to be difficult. Inhaled or oral prednisolone is usually effective for the inflammatory type of plastic bronchitis. Although oral prednisolone was commenced in our case, expectoration of bronchial casts continued and was resistant to steroid therapy. Then we started continuous intravenous infusion of epoprostenol to reduce mean pulmonary arterial pressure, since high CVP and PAR were considered as probable causes of plastic bronchitis, especially after the Fontan procedure. After administration of epoprostenol, expectoration of bronchial casts stopped once, but then recurred. Therefore, we added sildenafil citrate as an additional potent pulmonary vasodilator to further reduce CVP and PAR. After the addition of sildenafil citrate, he stopped expectorating bronchial casts and finally could be weaned from epoprostenol 6 months after starting sildenafil citrate.

In summary, pulmonary vasodilatation therapy with sildenafil citrate and epoprostenol effectively treated steroid-resistant plastic bronchitis after the Fontan procedure. The exact mechanism of this successful pulmonary vasodilation therapy remains unknown, but from a practical point of view, this combination therapy of sildenafil citrate and epoprostenol was clinically very effective for a patient with plastic bronchitis involving high CVP and PAR after the Fontan procedure.

References