A Multifaceted Approach to the Management of Plastic Bronchitis After Cavopulmonary Palliation

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Background. **Plastic bronchitis is a rare, potentially life-threatening complication after Fontan operation. Hemodynamic alterations (elevated central venous pressure and low cardiac output) likely contribute to the formation of tracheobronchial casts composed of inflammatory debris, mucin, and fibrin. Pathologic studies of cast composition support medical treatment with fibrinolytics such as inhaled tissue plasminogen activator (t-PA).**

Methods. **This was a retrospective case series of medical, surgical, and catheter-based treatment of patients with plastic bronchitis after cavopulmonary palliation.**

Results. **Included were 14 patients (86% male, 93% white). Median age at Fontan operation was 2.7 years (range, 1.2 to 4.1 years), with median interval to plastic bronchitis presentation of 1.5 years (range, 9 days to 15.4 years). Cast composition was available for 11 patients (79%) and included fibrin deposits in 7. All patients were treated with pulmonary vasodilators, and 13 (93%) were treated with inhaled t-PA. Hemodynamically significant lesions in the Fontan pathway were addressed by catheter-based (n = 9) and surgical (n = 3) interventions. Three patients (21%) underwent heart transplantation. Median follow-up was 2.7 years (range, 0.6 to 8.7 years). Symptoms improved, such that 6 of 13 patients (46%) were weaned off t-PA. Rare or episodic casts are successfully managed with outpatient t-PA in most of the other patients. Of the 3 patients who underwent heart transplant, 2 are asymptomatic and 1 has recurrent casts in the setting of elevated filling pressures and rejection.**

Conclusions. **A systematic step-wise algorithm that includes optimization of hemodynamics, aggressive pulmonary vasodilation, and inhaled t-PA is an effective treatment strategy for patients with plastic bronchitis after cavopulmonary connection.**

(Ann Thorac Surg 2014;■:■–■)

Plastic bronchitis is a rare, potentially life-threatening complication of the Fontan operation, the final palliative procedure for various forms of single-ventricle heart disease [1–6]. Plastic bronchitis is characterized by the formation of rubbery casts of the tracheobronchial tree that may cause cough, wheezing, dyspnea, and hypoxia; progressive airway obstruction may lead to asphyxia and death. Plastic bronchitis has been described in patients with respiratory disorders, including severe asthma, allergies, cystic fibrosis, and sickle cell acute chest syndrome [7–9], but appears to occur most commonly in patients with congenital heart disease and Fontan circulation. The true prevalence of plastic bronchitis after Fontan is unknown because the diagnosis depends on direct visualization of a cast after expectoration or on bronchoscopy. Some estimate the prevalence of the disorder to be as high as 4% to 14% in patients with Fontan circulation [10].

The pathogenesis of plastic bronchitis after Fontan is largely unknown. Hemodynamic alterations inherent in the Fontan circulation (elevated central venous and pulmonary artery pressures, relatively low cardiac output) likely contribute in some manner to a break in mucosal integrity and injury to the alveolar–capillary barrier [11]. Leakage of proteinaceous and cellular material into the airways results in cast formation. However, a disconnect often exists between a patient's Fontan hemodynamics (ie, degree of central venous hypertension) and the development of plastic bronchitis. Why a minority of patients develop plastic bronchitis and others do not is unclear.

Given the unclear pathogenesis of plastic bronchitis, treatment regimens are based on case reports and anecdotal data. Antiinflammatory agents, bronchodilators, antibiotics, and mucolytics, along with aggressive pulmonary toilet, may decrease disease severity [12]. Treatment with pulmonary vasodilators may increase cardiac output by decreasing pulmonary vascular resistance and augmenting ventricular filling [13]. Plastic bronchitis may resolve after surgical or catheter-based interventions to improve hemodynamics or after cardiac transplantation [12]. In addition, aerosolized tissue plasminogen activator (t-PA) is an important treatment option that may decrease cast burden and improve clinical symptoms in patients with plastic bronchitis after Fontan [1, 2, 14, 15].

Despite the absence of a complete understanding of the pathophysiology of plastic bronchitis after Fontan, a

Accepted for publication April 1, 2014.

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Published by Elsevier Inc

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2014.04.015

standardized protocol and management strategy may offer a pathway for a successful outcome for this life-threatening condition. How plastic bronchitis develops is unique to the specific patient with a single ventricle; however, thematic commonalities may be evident. This report describes our experience with medical, catheter-based, and surgical treatment of plastic bronchitis at our institution during the last 10 years and provides insight into the evolution of our current management scheme for this disease.

Patients and Methods

All patients with a clinical or pathologic diagnosis of plastic bronchitis managed through the Single Ventricle Survivorship Program at the Children's Hospital of Philadelphia between January 1, 2003, and August 22, 2013, were eligible for inclusion in this retrospective case series. Hospital records were reviewed for demographic information and pertinent clinical characteristics. Demographic and anatomic characteristics were summarized by standard descriptive summaries and are expressed as means ± standard deviations and percentages. The study protocol was approved by the Children's Hospital of Philadelphia Institutional Review Board (IRB No. 13-010445).

Results

Fourteen patients met the inclusion criteria. Demographic characteristics are summarized in Table 1. Patients were 86% male and 93% white. Hypoplastic left heart syndrome was present in 6 patients (43%). Thirteen patients underwent Fontan completion at median age of 2.7 years (range, 1.2 to 4.1 years), with an extracardiac conduit in 6 patients (46%), lateral tunnel in 6 (46%), and a catheter-based covered stent baffle (performed at an another institution) in 1 (8%). One patient was not deemed a Fontan candidate given a limited pulmonary vascular bed and a history of venous thrombosis and remains with a superior cavopulmonary connection. Twelve Fontan patients (92%) were fenestrated at the time of initial operation.

Four patients had persistent pleural effusions for more than 2 weeks after the Fontan operation. One of these patients required brief extracorporal membrane oxygenation support in the immediate postoperative period and then had persistent pleural drainage for more than 3 weeks. The patient expectorated casts on postoperative day 22 and was subsequently converted back to a Glenn circulation given the early development of plastic bronchitis in the setting of persistent pleural drainage and elevated Fontan pressures. Conversion to a Glenn circulation was achieved through catheter techniques. Late-onset pleural effusions developed in 2 patients at 3 and 5 months after Fontan operation. The patient whose effusions occurred at 5 months was found to have a thrombotic Fontan occlusion requiring revision.

Median time from Fontan to plastic bronchitis presentation was 1.5 years (range, 9 days to 15.4 years). Symptoms developed in 2 patients within 1 month (postoperative days 9 and 22) of the Fontan procedure. All patients had a history of cast expectoration at diagnosis (Fig 1). Two patients had life-threatening airway obstruction and cardiorespiratory failure; one required extracorporal membrane oxygenation, and the other required emergency intubation and multisystem organ dysfunction developed. Five patients had a history of prolonged cough, repeated respiratory infections, or chronic dyspnea several months to years before cast expectoration.

Echocardiograms from plastic bronchitis presentation were available in 12 patients (86%). Most patients had normal or low normal ventricular function, with little or no atrioventricular valve regurgitation (Table 1).

Thirteen patients underwent cardiac catheterization at most 6 months from plastic bronchitis presentation. Median pressures were 15.5 mm Hg (range, 10 to 28 mm Hg) in the Fontan baffle and 8 mm Hg (range, 4 to 16 mm Hg) in the ventricle at end-diastole. Pulmonary vascular resistance indexed to body surface area was 1.6 Wood units (range, 1.1 to 4.4 Wood units), and the cardiac index was 3.3 L/min/m^2 (range, 2.5 to 4 L/min/m^2). Hemodynamic data for individual patients are presented in Table 1.

Pathologic reports from bronchoscopy specimens or expectorated casts were available for 11 patients (79%). Cast composition in 7 patients included fibrin deposits, whereas the casts of 4 patients showed evidence of inflammatory infiltrate only.

Table 2 details treatment strategies for the included patients. Medical management included some combination of bronchodilators, mucolytics, and inhaled steroids in all patients. Many patients received vest physiotherapy to provide aggressive pulmonary toilet. One patient was receiving chronic oral steroid treatment upon presentation to our institution. All patients were treated with the pulmonary vasodilator sildenafil, the most common dose being 20 mg, 3 times daily. Bosentan was used as an additional pulmonary vasodilator in 3 patients. Carvedilol was used in 5 patients to slow the heart rate and to potentially encourage ventricular filling. Digoxin was used when plastic bronchitis symptoms recurred in the setting of congestive heart failure.

Thirteen patients were treated with inhaled t-PA at a dose of 4 mg (4 mL) inhaled 2 to 4 times daily. One patient experienced significant epistaxis due to an elevated international normalized ratio while receiving t-PA, warfarin, and aspirin. A few months later, this patient experienced epistaxis, purpura, and coagulopathy due to an accidental warfarin overdose. Anticoagulants and t-PA were held until the error was discovered. The patient recovered without incident.

Nine patients underwent catheter-based interventions to relieve hemodynamically significant residual or recurrent lesions at the time of plastic bronchitis diagnosis (Table 2). A catheter-based strategy was used to convert 1 previously mentioned patient from a Fontan to a Glenn circulation. A vascular device was placed in the superior aspect of the Fontan baffle to occlude inferior vena cava