Plastic Bronchitis in a Post-Fontan Pediatric Patient with Normal Hemodynamics: A Case Report

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ABSTRACT

Plastic bronchitis (PB) is a relatively unknown condition where mucin or fibrin casts develop in the bronchial tree resulting in airway obstruction. It is commonly seen within the realms of pediatric cardiology and pulmonology. Some common etiologies include sickle cell disease, asthma, cystic fibrosis, and congenital heart disease. Mortalities of PB cases associated with congenital heart disease range from 29% to 60%.

A five-year-old patient with single ventricle physiology underwent the Fontan procedure and presented with PB after two months, earlier than the reported mean of 2.2 years to 2.8 years.¹² He had normal hemodynamics on cardiac catheterization and casts with an unusual histology. Our case is unique because a majority of post-Fontan PB had acellular mucinous casts, but our patient’s casts consisted of mucin, fibrin, and inflammatory cells. Secondly, our patient had normal extra-cardiac Fontan mean pressure of 11 mmHg, which is lower than the average Fontan mean pressure described in the literature.

INTRODUCTION

Plastic bronchitis (PB) is a relatively unknown condition where mucin or fibrin casts develop in the bronchial tree resulting in airway obstruction. It is commonly seen within the realms of pediatric cardiology and pulmonology and some common etiologies include sickle cell disease, asthma, cystic fibrosis, and congenital heart disease. Long-term mortalities of PB cases associated with congenital heart disease range from 29% reported by Brogan et al.⁴ to 33% reported by Madsen et al.,⁵ and acute mortalities are as high as 60% (3 out of 5 patients reported by Sear et al.).³ Median time to death from PB diagnosis is 0.4 years.² This case presentation is an opportunity to educate the medical community on early recognition of PB as early diagnosis and treatment are key to reducing its high mortality rate. Prior to diagnosis, patients with PB present
with non-specific signs of physical distress on physical examination. Rarely, the sound of a flag snapping, or a mucus plug hitting an airway surface, may be heard. Radiologic findings are also typically non-specific. Currently, PB is diagnosed definitively only when a bronchial cast in an easily recognizable branching tree pattern is expectorated or visualized by bronchoscopy. PB is thought to be under-diagnosed due to the fact that the patient presents with a wide range of non-specific symptoms. The patient may be misdiagnosed as having asthma, chronic bronchitis, or pneumonia.

The pathophysiology of PB is still not completely understood, as evidenced by the wide range of diseases in which it arises, including sickle cell disease, asthma, cystic fibrosis, and congenital heart disease. Several classification schemes have been proposed to categorize similar etiologies in an attempt to elucidate the underlying etiology. Before 2005, the most widely used classification system was created by Seear et al., where casts are classified as either inflammatory casts (Type 1), or acellular non-inflammatory casts (Type 2). It was originally thought that patients with congenital heart surgeries have acellular Type 2 casts. However, patients with congenital heart surgeries do develop Type 1 casts. Furthermore, this oversimplified division is problematic because even if no inflammatory casts are seen in the casts, thus falling into the non-inflammatory cast category by the Seear et al. classification, inflammation may in fact have been the trigger for forming these casts. Thus, it was later recognized that there are more than two clear-cut categories than that of Seear et al.’s classification. The classification system by Madsen et al., who classified PB cases found in the literature from 1965 to 2005, is more comprehensive because it is classified primarily by clinical disease association and secondarily by cast histology. The three types of histologies found in structural heart diseases are casts with mucin only, casts with mostly mucin and inflammatory cells, and casts with mucin, chyle, and fibrin. The casts found in lymphatic disorders are chylous casts. The casts found in allergic diseases and asthma have predominantly eosinophils (“inflammatory casts” per Seear et al.). The casts found in acute chest syndrome in sickle cell disease are, as one would expect, fibrinious casts. In a review of 15 cases of post-Fontan PB, 9 (60%) had mucinous casts (called “acellular casts” in Seear et al.’s classification scheme), 4 (27%) had mucinous casts with inflammatory cells, and 2 (13%) had chylous casts with mucin and fibrin.

There are many post-Fontan PB patients with PAP that is not elevated as well as post-Fontan patients with elevated PAP who do not develop PB, suggesting that the etiology of PB is multifactorial. A seminal case-control study by Schumacher et al. of 25 PB patients found these statistically significant risk factors: elevated post-Fontan PAP, chylothorax, chest tube drainage > 13 days, postoperative ascites, and post-Fontan aorto-pulmonary collateral coil placement. All of these factors involve an abnormality in the production or drainage of pulmonary fluid. These additional risk factors suggest that the pathophysiology of PB is multi-factorial and includes hyper-secretion of mucus stimulated by inflammatory insult such as Fontan surgery or respiratory infection in addition to decreased drainage due to either increased PAP or lymph blockage. Madsen et al. proposed that there is first a genetic predisposition which is brought to effect by inflammation, such as a Fontan surgery that triggers mucus hyper-secretion or a lower respiratory tract infection. In a 2013 review of 654 Fontan patients from 1992 to 2007, Caruthers et al. noted 2 diagnosed cases of plastic bronchitis in post-Fontan patients and described 51 cases of possible PB based on patients’ self-reported expectoration of mucin casts. The wide range of these numbers suggest that PB may be underdiagnosed. In the literature, the time from Fontan to PB diagnosis was
found to have a mean of 2.2 years to 2.8 years.\textsuperscript{1,2} Caruthers et al.\textsuperscript{1} described possible causes as increased pulmonary vascular pressures or valve dysfunction, which injure the alveolar-capillary barrier, or lymphatic dysfunction due to injury during surgery.

There is currently no consensus about the relative importance of the above factors. In particular, there is no consensus regarding the importance of high PAP post-Fontan to the risk of PB. Schumacher et al.’s 25 cases\textsuperscript{2} of PB had an average post-Fontan PAP of 16.5 mmHg (range 12 to 22) compared to 43 non-PB Fontan patients with average PAP of 13 mmHg (range 12 to 15), but 39% of the non-FB patients did not have available PAP information. Costello et al.\textsuperscript{5} also reported a post-Fontan PB with lateral tunnel mean pressure of 10 mmHg, where the cast was found to consist of fibrin, mucin, and inflammatory cells. Tzifa et al.\textsuperscript{9} reported a case of post-Fontan PB where Fontan mean pressure was 13 mm Hg, the cast consisted of fibrin and neutrophils, and the cast culture grew Staphylococcus aureus.

Our case is unique in several aspects: a review of 15 patients who developed PB after undergoing Fontan surgery showed that a majority of post-Fontan PB had mucinous casts, but our patient’s casts consisted of mucin, fibrin, and inflammatory cells, similar to those described by Costello et al.\textsuperscript{5} Secondly, our patient had normal extracardiac Fontan mean pressure of 11 mmHg, which is lower than the mean pressure of patients described in the literature\textsuperscript{2,5} Our case did not have any of the risk factors as reported by Schumacher et al.\textsuperscript{2} that could have triggered an earlier therapeutic response.

**CASE PRESENTATION**

A 5-year-old boy, born early term via spontaneous vaginal delivery at estimated gestational age of 37 weeks 4 days, presented with prenatally diagnosed double-inlet left ventricle (DILV) and hypoplastic aorta with ventriculoarterial (VA) discordance with aorta anterior and rightward to his pulmonary artery. The mother was 32 years old, gravida 5, para 5. Prenatal ultrasound at 22 weeks was significant for single ventricle heart anatomy, two vessel cord, posterior placenta, and a cephalic presentation. In double
inlet left ventricle, mixed oxygenated and de-oxygenated blood flows from both atria into the left ventricle, and then to the pulmonary trunk, as the aorta and pulmonary trunk are transposed. The aorta receives this mixed blood for systemic circulation via the ductus arteriosus. The right ventricle is hypoplastic or non-existent, and connected to a hypoplastic aortic arch. A subsequent ultrasound at 34 weeks was notable for hypoplasia of the inferior vermis, which is consistent with Dandy-Walker syndrome. At delivery, his Apgar scores were 9 and 9 at 1 and 5 minutes respectively. He breathed spontaneously with oxygen saturation at 90%. He was given prostaglandins to maintain a patent ductus arteriosus to keep it patent prior to corrective surgery. His other medical history included CHARGE syndrome, Dandy-Walker syndrome, bilateral optic nerve colobomas, gastric tube feeds, and developmental delays. Family history was unremarkable.

The patient underwent Norwood and Sano operations at the age of 7 days. In the Norwood procedure, the pulmonary trunk was disconnected from the pulmonary arteries and then reconnected to the aorta, so that blood could flow from the single ventricle to the pulmonary trunk and then to the aorta, thus relieving the need for a patent ductus arteriosus. In the Sano procedure, which is a temporary measure to provide blood supply to the disconnected pulmonary arteries, a shunt was placed between the single ventricle and the pulmonary arteries. He then received a bidirectional Glenn procedure, Sano takedown, and resection of a left ventricle pseudoaneurysm at 4 months old, and an extracardiac non-fenestrated Fontan at 4 years old. The Sano was replaced by the bidirectional Glenn where the superior vena cava is directly connected to the right pulmonary artery so that the right atrium is bypassed. In the Fontan procedure, the inferior vena cava was connected to the right pulmonary artery so that the right atrium is bypassed, allowing deoxygenated blood to flow from the body directly to the lungs without being pumped by the heart.

The patient’s postoperative course was complicated by chydous effusion from the left chest tube on post-operative day 6 and transaminitis which resolved by his discharge on day 17. His chest tubes were in place for 16 days.

Figure 2. A) Hematoxylin and eosin staining of bronchial cast shows fibrin (pink) and mucin (blue/grey). (original magnification 20x). B) Higher magnification shows mucin, fibrin, and mixed inflammatory cells, including monocytes, lymphocytes, neutrophils, and rare eosinophils. (Hematoxylin and eosin stain, original magnification 400x).
Two months after his Fontan surgery, he developed fever and a productive cough and presented to the emergency department with respiratory distress and oxygen desaturation to 70% compared to a post-Fontan oxygen saturation of 93%. A collected respiratory viral panel was positive for Rhinovirus and Enterovirus. He had multifocal infiltrates on the chest x-ray and was diagnosed with pneumonia.

Five months after his Fontan surgery, he again presented with respiratory distress after 5 days of upper respiratory symptoms. Chest x-ray showed hazy opacities in the right upper and mid-lung zones as well as the retro-cardiac region. The impression was multifocal pneumonia. Viral panel was again positive for Rhinovirus and Enterovirus, suggesting that his PB episodes occurred secondary to inflammation as a result of viral infection. This was the first time his mother reported that he coughed up a bronchial cast at home, leading to his diagnosis of plastic bronchitis upon admission. He improved with saline and albuterol, and was subsequently discharged with albuterol inhalation solution every 4 hours as needed, and budesonide inhaled 2 times a day, with outpatient pulmonology follow-up.

Twelve months post-Fontan surgery, he again presented to the ED after coughing out bronchial casts at home. He was afebrile, tachypneic, and had an oxygen saturation of 85% on room air. Coarse breath sounds were heard bilaterally on auscultation, with decreased sounds on the right side. Chest x-ray showed prominent lung markings and bilateral patchy opacities (Figure 3). There was no pleural fluid. He received rigid and flexible bronchoscopy, which removed casts from his right middle lobe.

Pathology described the bronchial casts as consisting of mucus and fibrin with inflammatory cells (Figure 2). His laboratory data were notable for: nasal swab polymerase chain reaction (PCR) positive for methicillin-resistant Staphylococcus aureus (MRSA), respiratory viral panel positive for Rhinovirus and Enterovirus, and blood cultures positive for Corynebacterium pseudodiphtheriticum. At the hospital, he was started on sodium chloride inhalation, albuterol inhalation, dornase alfa inhalation, and budesonide inhalation.

Catheterization at 16 months post-Fontan showed left ventricle end diastolic pressure of 6 mmHg, compared to the normal range of less than 12 mmHg. The mean pressure in the extracardiac Fontan was 11 mmHg, compared to the normal range of a mean of 10 to 17 mmHg. The mean pressures of the left and right pulmonary artery were 11 and 10 mmHg respectively, compared to the normal range of a mean of 10 to 17 mmHg. Transpulmonary gradient was 6 mmHg, compared to a normal level of 6 mmHg, and pulmonary vascular resistance-index (PVRI) was less than 2 WU x m2, compared to a normal range of 1 to 3 WU x m2. After the patient was placed on 100% FiO2, the Fontan pressures decreased from 10-11 mmHg to 9-10 mmHg. His cardiologist and pulmonologist agreed that in light of his normal Fontan pressures and good hemodynamics, he would not benefit from a fenestration creation, as his PB episodes were manageable medically.

Our patient’s extracardiac Fontan and LV pressures are comparable to those reported by Costello et al. A patient at the age of 48 months had lateral tunnel mean pressure of 10 mmHg, and LV end diastolic pressure of 4 mmHg; she subsequentially presented with PB at age 53 months, or 21 months after the fenestration closure. In comparison, our patient presented with PB only 2 months after his Fontan procedure. A notable difference between our patient’s case and the one reported by Costello et al. is that our patient had a nonfenestrated extracardiac Fontan as compared to a fenestrated Fontan operation at age 26 months with a subsequent clo
sure of the fenestration using subcutaneous snare 6 months later. So it remains unknown whether the fenestration closure contributed to her development of PB, though she did have normal Fontan pressures after the fenestration closure.

Our patient continues to be managed on an outpatient basis by his primary cardiologist and pulmonologist. At 21-month follow-up since his Fontan surgery, he is doing well on a regimen of albuterol nebulizers, 7% saline spray, dornase alfa, atenolol, and a percussion vest. He attends school, though his oxygen saturation drops to around 70% when walking several blocks. He continues to desaturate while coughing out casts but recovers quickly. Known triggers for his episodes of casts are upper respiratory tract infections.

The treatment of PB depends on an assessment of etiology and trials of less invasive procedures first. In our patient, since Fontan pressures were found to be normal, his PB likely was triggered by respiratory tract infections, so the appropriate treatment is not Fontan fenestration, but rather bronchoscopic removal of bronchial casts followed by daily airway clearance regimens. Aerosolized urokinase and tissue plasminogen activator (t-PA) are used to treat PB with high fibrin concentration. When aerosolized t-PA is used, it is administered every one or two hours, and dosed based on the patient’s weight. Because of the rarity of this disease and its treatment, the dosing and schedule is done on a trial basis according to other published case reports. 

Mucoylitics (dornase alfa and acetylcysteine) are useful in those with high mucin composition. Bronchoscopic cast removals, chest physiotherapy, inhaled corticosteroids, low dose antibiotics, budesonide, levalbuterol or albuterol, inhaled mucoylitics dornase alfa and acetylcysteine, topical dornase alfa applied during bronchoscopy, direct and inhaled t-PA, inhaled hypertonic saline (3%), oral azithromycin, and oral spironolactone are usual treatments. Manna et al. describe a case of cystic fibrosis PB where initial treatments of physiotherapy, intratracheal 0.9% saline, and negative pressure suction by bronchoscopy failed, but success was achieved using intratracheal nebulized recombinant human DNase (rhDNase). The rhDNase was introduced into the bronchi followed by chest physiotherapy to fragment the bronchial casts; the disintegrated mucus plugs were then removed by bronchoscopic suction. Rarer treatments used are high-frequency jet ventilation and thoracic duct repairs in chylous casts.

**DISCUSSION**

Our patient presented to the hospital on three occasions with respiratory distress and was diagnosed with PB at the second visit. It is possible that he had bronchial casts that were not coughed up at his first visit at 2 months post-Fontan. He had fever on the first two visits, and elevated white blood cell count on only the first visit. At all three presentations, he had a respiratory viral panel positive for *Rhinovirus* and *Enterovirus*, suggesting that inflammation as a result of viral infection triggered his PB episodes. This theory is supported by the finding of inflammatory cells in his casts. In future studies, it would be beneficial to see if PB with normal PAP has predominance of the mucin and inflammatory cells type of casts rather than the mucin only type, and if PB with high PAP has mostly mucin only casts. If so, the utility of prophylactic antimicrobials in preventing PB episodes for patients with normal PAP should be investigated.
LEARNING POINTS

1. It is important to consider other risk factors for post-Fontan plastic bronchitis (PB) despite normal pulmonary artery pressure (PAP) so that early bronchoscopy is performed, and therapies can be started early.

2. Parents of patients with congenital heart disease, especially those who are post-Fontan surgery, should be counseled to report if their child has thick mucus expectoration with coughing.

3. The utility of prophylactic antimicrobials to prevent PB episodes for patients with normal PAP should be investigated.

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REFERENCES


