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Review of the Effectiveness of Tissue Plasminogen Activator for the Treatment of Plastic Bronchitis in Patients with Fontan Physiology

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Introduction

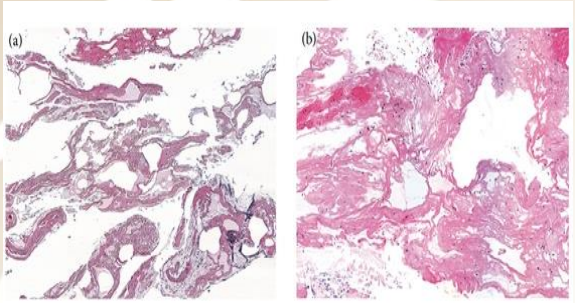
Plastic bronchitis is a condition characterized by the formation of bronchial casts ranging from small to large obstructions of the pulmonary airways. Cast formation is intricate and resembles a plastic, rubbery model of the airway it obstructs. Its form was first described by Galen (A.D. 131-200). One of the patient populations at risk for developing this rare complication are those with single ventricle disease who are surgically corrected to Fontan physiology. It is a very abnormal type of circulation that is suspect in the development of plastic bronchitis. The cellular composition of plastic bronchitis differs from the casts seen in patients with chronic respiratory diseases such as asthma or lymphatic disorders of the lung and, as a result, complete airway obstruction may occur more quickly with a resultant life-threatening and possibly fatal event.

Bronchial casts may also be seen in other disease states such as sickle cell disease, metastatic lung tumors, bronchopulmonary aspergillosis, thalassemia alpha, and inhalation injuries (Do, Randhawa, Chin, Parsapour, & Nussbaum, 2012). Tissue plasminogen activator in an aerosolized form has shown to be effective therapy in most cases. The following information is an update on the adaptation of this therapy in the last 5 years.

Pathophysiology

Fontan physiology (or circulation) involves hooking up systemic venous return directly to the branch pulmonary artery(s) thus bypassing the right side of the heart. This is also referred to as "passive circulation" and forward blood flow through the lungs is accomplished by pressure gradients between the central venous circulation and the pulmonary vascular bed. The etiology is unclear, however increased pulmonary venous pressures may contribute to affecting the respiratory epithelium and interruption of the bronchial mucosa causing proteinaceous material to leak and hypersecretion of mucus with resultant cast formation. Histology samples of patients with congenital heart disease reveal acellular casts with mucin and fibrin and the absence of Charcot –Leyden crystals . Patients with primary pulmonary diseases reveal a combination of inflammatory casts, eosinophils, Charcot –Leyden crystals and mucin thought t o be due to chronic bronchial inflammation (Do, 2009; Goldberg, 2010; Singhal, 2013). See figure 1.

Figure 1

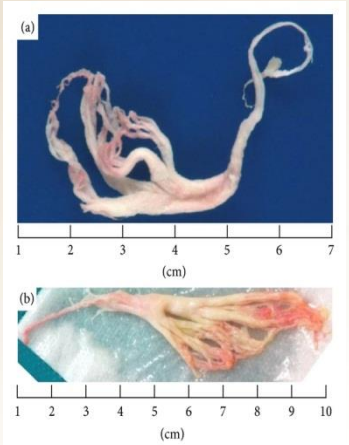


Slide (a) reveals hypocellular fibrinous casts. Slide (b) reveals inflammatory casts with eosinophils, Charcot-Leyden crystals and mucin.

Signs and Symptoms

The most common presenting symptoms are cough and intermittent dyspnea (Goldberg, Rychik, & Dodds, 2010). The cough may be productive or non-productive depending on the patient's ability to expectorate casts. Frequently, thick mucus is expectorated with a mucus plug consistency which can be deceiving as the mucus plugs may actually be fragments breaking away from the cast. Chest pain and fever are also reported but occurs more frequently in patients with pulmonary parenchymal disease. Cardiac patients rarely exhibit a fever, and blood and sputum cultures are usually negative (Heath et al., 2011). Breath sounds may be diminished, coarse, and wheezing may be present. Chest x-ray reveals opacity and consolidated lung fields similar to pneumonia and, bronchoscopy or expectoration of a cast is the only reliable determinant of the diagnosis. See figure 2.

Figure 2.



(a) Expectorated cast. (b) Cast extracted during flexible bronchoscopy.

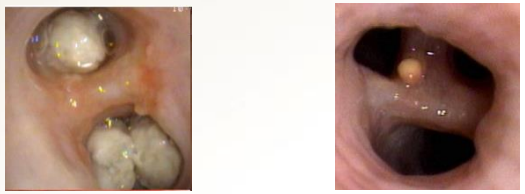
Treatment

Once the airway is stabilized, patients with congenital heart disease suffering from the rare complication of plastic bronchitis are first evaluated for circulatory efficiency. A cardiac catheterization is performed to determine venous systemic and pulmonary pressures, development of collateral circulation in the lungs, narrow pulmonary vessels and evaluation of the Fontan circuit. The Fontan conduit may be fenestrated to reduce systemic venous pressure; narrowed blood vessels may be stented open, collaterals closed with obstructive devices and the functioning cardiac valve and ventricle assessed for optimum performance. Fontan physiology, at its best outcome mimics chronic, low grade congestive heart failure. Every effort is made to decrease systemic venous pressures and optimize cardiac output (Goldberg, et al.,2010). However, there is no guarantee of successful prevention of a recurrence of plastic bronchitis. If histology shows dilated lymphatics, thoracic duct ligation is also considered especially if the patient exhibits problems with pleural effusions. (Colanari, Quarti, Pozzi, Gasparini, Carloni, & de Benedictis, 2014)

Pharmacological therapy interventions include systemic and inhaled corticosteroids, mucolytics such as acetylcysteine and dornase alpha, and fibrinolytics namely Urokinase and Alteplase.

Tissue plasminogen activator (tPA) or Alteplase, is a serine protease that leads to localized fibrinolysis by converting plasminogen to plasmin. According to the literature topical application and nebulized tPA has been the most successful treatment without adverse effects in several case reports of children with congenital heart disease complicated by cast bronchitis. Brogan et al. (as cited by Do et al., 2012) isolated and incubated a bronchial cast from a Fontan patient and topically applied saline, Urokinase and Alteplase. The saline produced no effect, the Urokinase made the cast softer and, the sample treated with Alteplase, completely dissolved. See figure 3.

Figure 3.



The left picture shows cast fragments wedged in the upper and lower lobes. The picture on the right shows the effect of tPA application after 15 minutes.

Nursing Care

The acute phase of illness requires care to be focused on protecting and maintaining a patent airway and preventing acute deterioration due to sudden obstruction. Extreme occlusion may require high frequency ventilation with intermittent bronchoscopies performed to treat casts topically and safely remove them. Once the airways are cleared, emphasis is placed on long term supportive care, and determining a medication regime that effectively prevents recurrence if possible.

Patient and caregiver teaching are vitally important for patient safety and quality of life. Common upper respiratory illnesses or worsening congestive heart failure symptoms may confound the signs and symptoms of plastic bronchitis especially if the cough is non-productive.

Education regarding chest physiotherapy techniques, maintaining a consistent medication schedule and prompt notification of their physician and healthcare team cannot be over- emphasized since there has been no established pattern to the recurrence of cast formation. Its onset may be sudden or develop over time. Coordination with emergency medical services in the patient's community promotes prompt transfer to a tertiary center familiar with the disease process and capable of treating acute airway issues. Family caregivers must comprehend the need to intervene quickly when a cough and dyspnea develops by notifying their cardiologist as soon as the symptoms appear and information taught needs to be return demonstrated by the "teach back" method to the nurse. Close monitoring of a recurrence is essential. Journals are helpful to parents and caregivers for tracking signs, symptoms, medication dosing and frequency, and the patient's general state of health. Important contact numbers should be listed in the front of the journal for easy access.

Conclusion

Kunder et al. (2013) report one of the largest case studies of plastic bronchitis retrospectively reviewed which included eight patients with Fontan physiology in the cohort and state that:

"the mechanism of cast formation remains unclear both for the inflammatory casts associated with lung disease and the hypocellular casts associated with congenital heart disease. Currently, data are limited regarding optimal treatment of plastic bronchitis, so the clinician must rely on individual anecdotal case reports to guide therapy. " The occurrence rate is estimated to be from 4 to 14% with a poor prognosis .

Alteplase has been proven to effectively dissolve bronchial casts yet optimal dosing strategy and length of maintenance therapy remain unknown. Some patients have responded with just one dose during the acute phase while others require home nebulization every 6 hours for months after the initial hospitalization. There have been no observed side effects with tPA yet the volume of patients reported in the literature is statistically too low to prove best outcomes or how to achieve best outcomes with a specific dosing regimen. There is also a major concern regarding the expense of tPA therapy and the reluctance of third party payers to cover the cost so determining the amount required for minimal efficient dosing facilitates better insurance coverage of the treatment options for these patients.

An international plastic bronchitis registry to collect data on patients has been established to hopefully resolve questions about the pathophysiology of the disease and the most effective treatment. (www.clinicaltrials.gov, NCT0166398)

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"References Cited"

Colanari, M., Quarti, A., Pozzi, M., Gasparini, S., Carloni, I., & de Benedictis, F.M. (2014). Management of plastic bronchitis with nebulized tissue plasminogen activator: Another brick in the wall. *Italian Journal of Pediatrics, 4,* 18-24. Retrieved from: http://ijponline,nte/content/40/1/18

Do, P., Randhawa, I., Chin, T., Parsapour, K., & Nussbaum, E. (2012). Successful management of plastic bronchitis in a child post Fontan: Case report and literature review. *Lung, 190,* 463-468. DOI: 10.1007/s00408-012-9384-x

Goldberg, D. J., Dodds, K., & Rychik, J. (2010). Rare problems associated with the Fontan circulation. *Cardiology of the Young. 20,*(Suppl. 3), 113-119. doi: 10.1017/S1047951110001162

Heath, L., Ling, S., Bacz, J., Mane, G., Schmidt, L., Myers, J.L., Tsai, W. C., Caruthers, R. L., Hirsch, J., C., & Stringer, K. A. (2011). Prospective, longitudinal study of plastic bronchitis cast pathology and responsiveness to tissue plasminogen activator. *Pediatric Cardiology, 32,* 1192-1189. doi: 10.1007/s00246-011-0058-x

Kunder, R., Kunder, C., Sun, H.Y., Berry, G., Messner, A., Frankovich, J., Roth, S., & Mark, J. (2013). Pediatric plastic bronchitis: Case report and retrospective comparative analysis of epidemiology and pathology. *Case Reports in Pulmonology.* Retrieved from http://dx.doi.org/10.1155/2013/649365

Singhal, N.R., Da Cruz, E.M., Nicolarsen, J., Schwartz, L.I., Merritt, G.R., Barrett, C., Twite, M.D., & Ing, R.J. (2013). Perioperative management of shock in two Fontan patients with plastic bronchitis. *Seminars in Cardiothoracic and Vascular Anesthesia,17*(1), 55-60. doi: 10.1177/1089253213475879

Additional Resources

Caruthers, R.L., Kempa, M. Loo, A., Gulbransen, E., Kelly, E., Erickson, S.R., Hirsch, J.C., Schumacher, Stringer, K.A. (2013). Demographic characteristics and estimated prevalence of Fontan- associated plastic bronchitis. *Pediatric Cardiology,34* 256-261.

Do, T.B., Chu, J.M., Berdjis, F., & Anas, N.G. (2009). Fontan patient with plastic bronchitis treated successfully using aerosolized tissue plasminogen activator: A case report and review of the literature. *Pediatric Cardiology, 30,* 352-355. DOI: 10.1007/s00246-008-9312-2

Gibb, E., Blount, R., Lewis, N., Nielson, D., Church, G., Jones, K., & Ly, N. (2012). Management of plastic bronchitis with topical tissue-type plasminogen activator. *Pediatrics, 130*(2), 446-451. DOI: 10.1542/peds.2011-2883

Zaccagni, H.J., Kirchner, L., Brownlee, J., Bloom, K. (2008). A case of plastic bronchitis presenting 9 years after Fontan. *Pediatric Cardiology,29,* 157-159. doi: 10.1007/s00246-007-9127-6