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The Outcome and Safety of a Long Course of Inhaled Tissue Plasminogen Activator in The Management of Plastic Bronchitis: A Case Report

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ABSTRACT

Background: Plastic bronchitis (PB) is a rare disease that is characterized by formation of rubber-like tracheobronchial casts that occlude the airway, occurring secondary to several conditions, most commonly as a complication of single-ventricle palliative cardiac surgery. Inhaled tissue plasminogen activator (t-PA) was reported to be effective in treating PB. **Aim of the work:** To show the outcome and safety of a long course of inhaled tissue plasminogen activator in the management of plastic bronchitis. **Methodology:** this was a case report**,** we report the case of a teen with PB treated with a prolonged course of t-PA with no adverse effects. **Results:** we reported the case of an 11-year-old boy with trisomy 21 who had a Fontan procedure for his complex congenital heart disease, complicated by PB that was treated with a prolonged course of t-PA. Our patient was an 11-year-old boy with trisomy 21 who was diagnosed with an unbalanced AV canal defect with a small right ventricle and bilateral superior vena cava. His surgical cardiac course consisted of a pulmonary artery banding at 2 months of age and bilateral bidirectional Glenn with tightening of the pulmonary artery banding at 24 months of age. He had pulmonary artery debanding and ligation of both right and left Glenn shunts at the age of 6 years. Since the age of 3 years, he was admitted many times to the hospital with various diagnoses, including bronchial asthma, bronchopneumonia and pulmonary hypertension, all of which were treated accordingly. He was admitted at the age of 9 years with a history of fever and cough productive of plastic-like material that took the form of the bronchial tree. The diagnosis of PB was confirmed. Subsequently, he was admitted frequently with the diagnosis of PB and was treated with aggressive airway clearance including hypertonic saline, dornase alpha and t-PA. The longest t-PA duration was 82 days, which clinically proved to be effective and safe. **Conclusion:** PB is a rare and serious disease. The long-term use of inhaled t-PA was effective and safe.

Keywords: plastic bronchitis, t-PA, Fontan surgery.

INTRODUCTION

Plastic bronchitis (PB), previously known as fibrinous bronchitis, pseudo membranous bronchitis, mucoid impaction, Hoffman bronchitis or cast bronchitis, is a rare and fatal disease characterized by the formation of rubber-like tracheobronchial casts that occlude the airway [(1)].

Although the exact pathogenesis of cast formation remains poorly understood, many investigators have tried to explain the cast formation as defects in lymphatic drainage into the bronchial tree; to date, this remains the accepted explanation [(2)].

Plastic bronchitis can occur secondary to pulmonary disease (Asthma and chronic suppurative lung disease), cardiac disease (post-cardiac surgery secondary to congenital cyanotic heart disease; post-Fontan connecting systemic venous return to pulmonary circulation); hematological disorders (Sickle cell anemia, thalassemia alpha and lymphoma), immunodeficiency (infectious causes such as TB, viral infection and bronchopulmonary aspergillosis) and the use of pegylated interferon [(3)].

Systemic lymphatic disease or conditions such as Turner's and Noonan's syndrome are also associated with plastic bronchitis, even though the predisposing factors have not yet been determined [(4)].

Plastic bronchitis is classified into 2 main types: inflammatory (Type 1), with high infiltration of eosinophilic inflammatory cells and casts composed mainly of fibrin and acellular (Type 2) with little or a cellular infiltrates composed mainly of mucin, occurring predominantly in patients with congenital cyanotic heart disease. Plastic bronchitis was diagnosed by the expectoration of branching bronchial casts, atelectasis seen on chest X-ray and performance of rigid bronchoscopy [(5)].

Management of PB includes various strategies, including removal of casts by rigid bronchoscopy, controlling the underlying disease, use of anti-inflammatory drugs such as steroids or nonsteroidal drugs (ibuprofen, corticosteroid), azithromycin or inhaled lytic agents (acetylcysteine, DNAse, heparin, and tissue-plasminogen activator) and surgical management [(6)].

The use of inhaled tissue-plasminogen activator (t-PA) is theoretically associated with bleeding tendency [(7)].

METHODOLOGY

Here, we report the case of a teen with PB treated with a prolonged course of t-PA with no adverse effects.

The report of the case:

Our patient was an 11-year-old boy with trisomy 21 who was diagnosed with an unbalanced AV canal

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defect and a small right ventricle and bilateral superior vena cava. His surgical cardiac course consisted of pulmonary artery banding at 2 months of age and bilateral bidirectional Glenn with tightening of the pulmonary artery banding at 24 months of age. He had pulmonary artery debanding and ligation of both right and left Glenn shunts at the age of 6 years. Since age of 3 years, the patient had a history of recurrent cough, shortness of breath and fever associated with hypoxia and wheezing. He needed 3 admissions where he was treated for bronchial asthma and pneumonia and was discharged on prophylactic fluticasone inhaler, singulair and salbutamol. At the age of 6 years, he was diagnosed with pulmonary hypertension based on echocardiography findings and clinical assessment; nevertheless, cardiac catheterization was not performed at that time because he was unfit. Therefore, the patient was started on sildenafil, and he responded to the medication. His accepted oxygen saturation was above 75%. The patient was admitted at age of 9 years with a history of fever and coughs for 4 days, followed by dyspnea and cough productive of mucus that was large in amount, yellowish and thick in consistency. The next day, he expectorated plastic-like material that took the form of the bronchial tree [Figure 1].

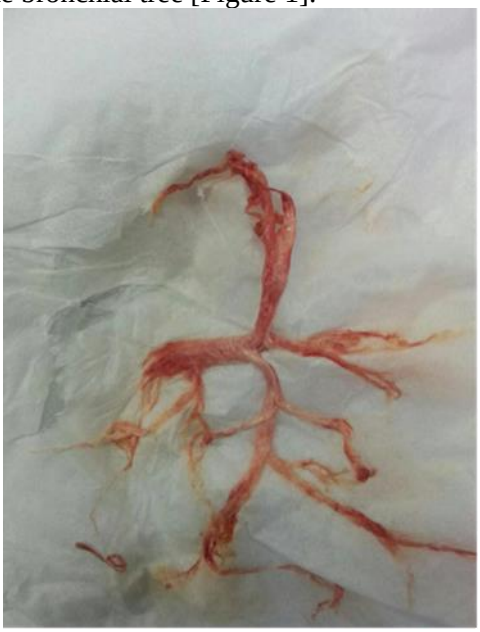

Figure 1: expectorated plastic-like material that took the form of the bronchial tree

He was clinically in respiratory distress with hypoxemia. Auscultation revealed bilateral crackles and wheezing. His blood gas revealed respiratory acidosis and the chest X-ray revealed right-sided upper lobe collapse [Figure 2]. Therefore, he was admitted to Prince Sultan Military Medical City/Riyadh/KSA.

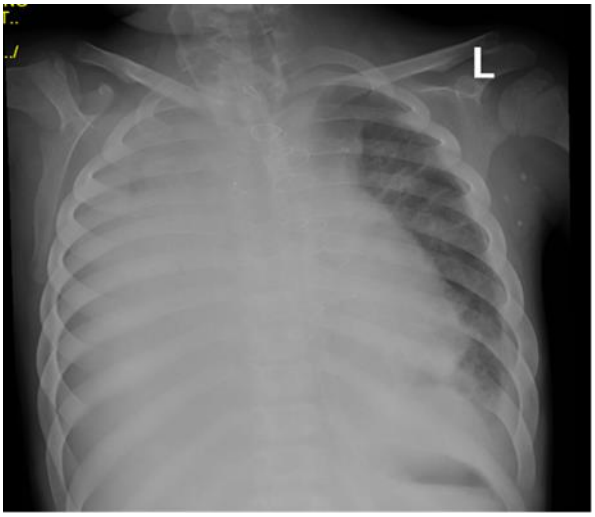

Figure 2: Chest X-ray revealed right-sided upper lobe collapse

As part of the treatment plan, he received a course of t-PA nebulization 5 mg every 4 hours with tapering doses over 5 days. The patient improved and was discharged on the 14th day of admission.

At the age of 11 years, he had a similar episode, and during the admission, he required mechanical ventilation. Flexible bronchoscopies revealed plastic bronchitis. The patient was maintained on aggressive airway clearance medications with 7% hypertonic saline, Pulmozyme (Dornase alpha), antibiotics, and 2 courses of t-PA nebulization 5 mg every 4 hours, the first one for 7 days and the second for 30 days, separated by 19 days.

Five months later, he presented in respiratory failure and was admitted to the cardiac ICU because of his pre-existing condition that was complicated by a valvular insufficiency and because he required mechanical ventilation. He had fluctuating symptoms of thick plastic secretions causing segmental collapses. During this admission, he received 3 courses of t-PA nebulization 5 mg every 4 hours, the longest one being 82 days in duration.

DISCUSSION

Plastic bronchitis symptoms are attributed to plastic materials that obstruct the airway, causing respiratory symptoms, with the chest X-ray findings of atelectasis associated with areas of compensatory hyperinflation. The diagnosis is made by expectoration of these casts or by bronchoscopy [8]. Cast formation can occur secondary to various conditions; the most common predisposing factor for cast formation is having a Fontan procedure for congenital cyanotic heart disease, as was the case with our patient [9,10].The exact etiology of why these casts form is not completely understood;

nevertheless, it has been attributed to hemodynamic alterations (elevation of pulmonary artery pressure and relatively low cardiac output) leading to third-space fluid loss, abnormalities in lymphatic drainage and hyper-secretion of airway mucus. Another theory involves an association between PB and protein-losing enteropathy [9,11,12]. As our patient had elevated pulmonary artery pressure responding to sildenafil, the most likely explanation of cast formation in our case is PB secondary to pulmonary hypertension. The management of PB includes targeting the underlying condition and therapy to aid in the removal and expectoration of the casts [8]. Optimizing the cardiac output and hemodynamic circulation is achieved by medical therapy, cardiac catheterization, pacing and surgical intervention. Failure to improve cardiac function exposes the patient to the risk of recurrence and plastic cast formation [13].

This explains the recurrence of symptoms in our patient, who had a complicated cardiac history further worsened by his valvular involvement. Other modalities of treatment that target the removal of casts include anti-inflammatories, mucolytics and fibrinolytics, in addition to performing bronchoscopy for cast removal [14]. Part of our management was fibrinolytic therapy. Nebulized tissue plasminogen activator (t-PA) is the most frequently used, though the efficacy of t-PA remains unknown and there are no comparative randomized studies of its safety and effectiveness. It has been reported to be effective in reducing cast burden and improving symptoms [8,11,13,15]. Our patient responded very well on the initial course of nebulized t-PA 5 mg every 4 hours; however, once the patient developed Fontan failure, his plastic bronchitis recurred, and he became dependent on t-PA with symptoms recurring after discontinuation of the medication. There are no reported side effects of nebulized t-PA except for one case of reported epistaxis; however, that patient was on warfarin and aspirin [13].

Our case demonstrated that the use of nebulized t-PA was not associated with bleeding tendency, even with a prolonged course of treatment (194 days).

CONCLUSION

PB is a rare and serious disease. The long-term use of inhaled t-PA appeared to be effective and safe.

Authors' contributions:

Alenazi A. was responsible for the case. **Alenazi A. and Alzaid M**. wrote and edited the case, collected and checked the references and made critical changes. Both authors read and approved the final report.

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