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Case Report

Plastic bronchitis and a novel management approach with streptokinase inhalation therapy: a case study

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ABSTRACT

Plastic bronchitis (PB) is a rare condition of obstructive bronchial casts. The most common demographic that is affected by PB is children but adults with acute onset have also been reported. At present, there are no established guidelines for the management of PB which has led to the proposition of a variety of treatment regimens. Inhaled streptokinase (SK) can be one such treatment modality for this rare condition. An adult female patient presented to the Grodno university clinic with complaints of dyspnea, shortness of breath, and expectoration of firm, long, and branching bronchial casts. We used inhaled SK to treat this patient based on the cast composition on microscopic evaluation. Written consent was taken from the patient mentioned in the study. The study was approved by the hospital and institutional ethics committee. SK, a potent fibrinolytic agent, can be useful in lysing fibrin-rich bronchial casts. With Inhaled SK therapy, there was a gradual improvement in the overall condition of the patient. In the subsequent clinical follow-up, the patient was asymptomatic and without recurrent casts. The course of treatment and positive recovery of the patient signifies the fact that inhaled SK can be a suitable therapeutic approach in PB. Therefore, based on our novel therapeutic approach, SK inhalation may be a possible treatment for bronchial casts in PB.

Keywords: Plastic bronchitis, Streptokinase, Bronchial casts, Inhaled Streptokinase, Asthma, Case-study

INTRODUCTION

Plastic bronchitis (PB) is an uncommon and underdiagnosed disease of obstructive airway casts characterized by the formation and expectoration of bronchial casts of amorphous material, which can be potentially fatal.[1] It is probably an underdiagnosed disease; to date, less than 600 cases of PB have been reported, and its incidence is unknown.[2] The pediatric population is the most common demographic in which PB is encountered especially following corrective cardiac surgery, such as the Fontan procedure. However, it also occurs in adults[3]. PB has also been observed in patients with variants of abnormal lymphatic anastomosis.[4]

PB manifests clinically with the sudden onset of cough, wheezing, progressive dyspnea, refractory hypoxemia, chest or pleuritic pain, and occasionally fever. The most pertinent feature of PB is the formation of bronchial casts that can vary from rubbery structures filling the small airways to casts formed of amorphous material occupying the entire bronchial tree.[2] The bronchial casts have been characterized into two types. Type I casts is inflammatory with components including neutrophils, eosinophils, and Charcot Leyden crystals seen in asthma and CF along with fibrin and mucin. These casts are believed to have been formed due to decreased mucociliary clearance mechanisms. Type II casts are associated with congenital heart disease status post-Fontan procedure and are found histologically to be acellular with proteinaceous lymph

material as the major component.[5] In addition, PB sometimes presents without any known risk factors, in these cases, the casts are acellular which are often suggesting of an undetected underlying abnormality of the lymphatic drainage system.[4,6] Upon physical examination wheezing, attenuated breath sounds, and dullness to percussion can be observed. Radiological examinations such as chest X-rays and CT scans typically show partial atelectasis of the segments involved with compensatory hyperinflation of the unaffected segments. Diagnosis is confirmed by rigid and/or flexible bronchoscopy or by repeated observation of the expectorated structures.[2]

Herein, we describe a case of an adult female patient with a history of bronchial asthma (non-allergic form neutrophilic phenotype), who presented to the Grodno University clinic with expectoration of firm, long, and branching bronchial casts.

CASE REPORT

A 39-year-old female, with a history of Bronchial asthma (non-allergic form neutrophilic phenotype), started suffering from paroxysmal coughing and mild expectoration of sputum from the onset of the spring season, in 2022. She did not seek any medical or professional consultation at the beginning of the disease course, disregarding the condition as a normal cough associated with seasonal shifts. There was a progression of cough and a gradual increase in sputum expectoration. Roughly four months after the onset of the symptoms, the patient sought professional help leading to hospitalization based on the presenting features. On hospitalization, a chest CT examination showed an interstitial (inflammatory) type of pneumonia most likely due to viral etiology (Likely COVID-19 infection). A bronchoscopy done a week later showed focal hyperemia observed in the bronchi on the right and left upper lobe branches. The lumen of the bronchus of the middle lobe was obstructed by a thick clot. A grey-green color clot was extracted using an endoscope. Clot size 8.0×2.0 cm. One week later, on a subsequent bronchoscopy, there was a visible obstruction of a few bronchi on the right by thick whitish-yellow-colored clots, segments S4 to 7 were partially obstructed. The patient's condition worsened after a few days with an increase in sputum expectoration and a gradual increase in the size of clots. It was further complicated, showing a risk of developing type 2 respiratory failure. The patient was treated symptomatically and after stabilization, the patient was discharged with continuous high-dose combined anti-inflammatory therapy: Tiotropium bromide (2.5 mcg) inhaler, beclomethasone (100 mg) and formoterol fumarate (6 mg) inhaler, methylprednisolone, azithromycin (500 mg q.d.), mucolytics-long-term (ambroxol 30 mg 1 tab 3 times a day or inhalation through a nebulizer). This initial therapeutic approach did not relieve the patient's symptoms and the standard mucolytic therapy did not prove to be very effective.

Six months after the initial presentation of symptoms and after seeking the initial therapeutic approach the patient now presented to us at the outpatient department of Grodno university clinic with complaints of cough with sputum discharge in the form of firm, long, and bronchi-shaped casts (Figure 1). There was noticeable shortness of breath at rest and even with slight exertion. A provisional diagnosis of PB was placed. The patient was questioned for relevant history while also examining her past medical record and treatment regimens. While gathering the anamnesis, there were bouts of a sudden and steep decline in oxygen Saturation (SpO_2) (from 99% to mid-80s and even as low as 70s in a very short duration) which led to immediate hospitalization of the patient. Although the SpO_2 would immediately return to normal after the expectoration of sputum. A full body check-up was ordered, revealing some peculiar findings. Ultrasound of the left adrenal gland showed an adenoma of unspecified hormonal activities along with a nodular knot-like structure with calcification. Ultrasound of the Right kidney revealed heterogeneous thickening of renal parenchyma of the kidney and an angiomyolipoma-like formation. Ultrasound of the left kidney revealed a similar homogenous thickening of parenchyma. Ultrasound of the thyroid showed an isoechoic nodule located in the right lobe.

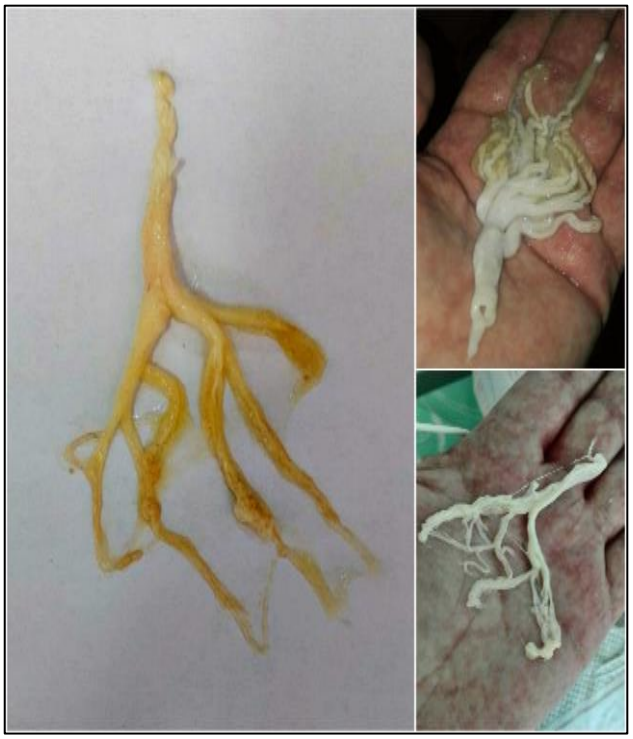

Figure 1: Bronchial casts of the patient with PB.

Common blood tests and biochemical analysis showed MCV (Mean red blood cell volume) 103.4 Fl. (82-92) Fl; MCH (Mean corpuscular hemoglobin) 33.6 pg (28-32) pg; neutrophils, 43.4% (45-70%); lymphocytes, 43% (18-40%); monocytes, 9.7% (3-8%); segmented neutrophils, 71% (45-70%); total protein 56 gm/l (65-85) gm/l.

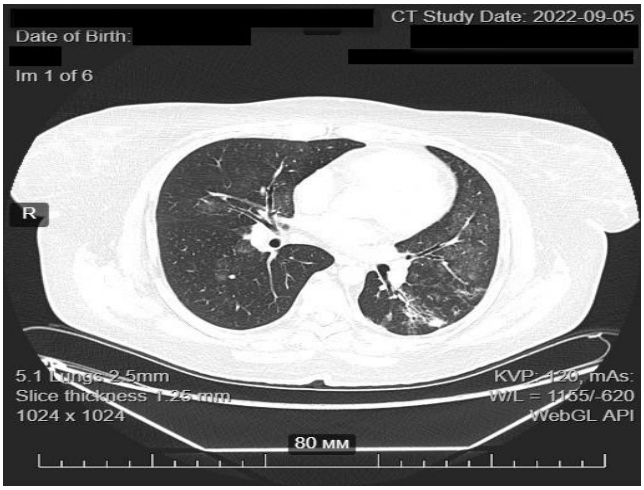

Figure 2: Primary chest computerized tomography, of the patient of PB, showing left lung lower lobe consolidation.

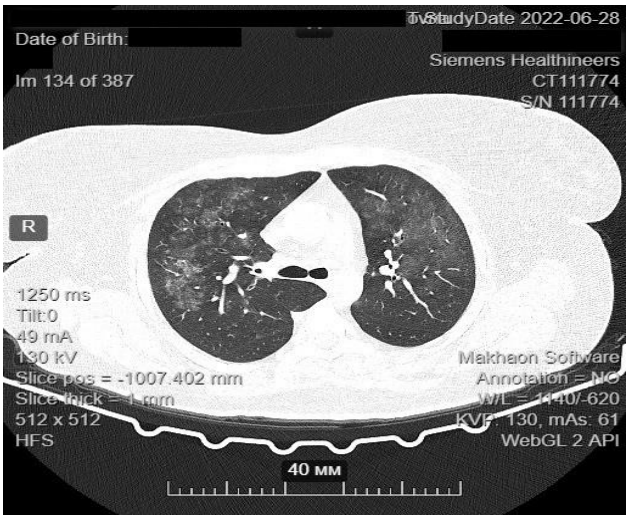

Figure 3: CT scan of the patient with COVID-19 infection in anamnesis, the scan shows ground glass opacification of both lungs with 35-40% lung involvement.

CT examination (Figure 2) of the patient was performed where the lower lobe of left lung tissue appeared consolidated in the S10 segment. The right lung was found to have an additional lobe with an abnormally located azygous vein. A zone of inflammatory consolidation appeared in the left lower lobe and was compared to the previous CT results performed during the past COVID-19 infection (Figure 3). On comparison, both scans showed areas of compaction of the lung tissue with a "Ground-glass opacification" appearance, but they are less intense now with the appearance of reticular changes, especially in the upper lobe of the left lung.

Video-assisted thoracoscopy was performed for a biopsy of S4 and S9 of the left lung. The procedure was conducted under general anesthesia. In the lower lobe, cyanotic areas with lattice structures were seen. An atypical tissue resection of S4 and S9 was performed. Histopathological examination showed lung tissue with focal carnification, mild inflammatory infiltration, fragments of lung tissue with small dystelectases, and sclerotic changes in blood vessels. Bronchoscopy was performed for the removal of the bronchial cast. On removal of the cast, the SpO_2 of the patient was immediately restored to normal.

Microscopic examination of bronchial casts showed expectoration rich in fibrin, inflammatory cells, and necrotic lung tissue. Sputum showed negative serological and microbiological studies. The patient was found to have expectorated the casts for three days after the bronchoscopy. Confirm diagnosis of PB was placed based on the radiological dynamics of the course of the disease in this patient.

The patient was started on SK inhalations (1.5 million diluted in 10 ml solution. Inhalations of 1.5 ml per 2 ml of physical solution through a nebulizer 2 times a day), tiotropium bromide (2.5 mcg) inhaler, Beclomethasone (100 mg) and formoterol fumarate (6 mg) inhaler, methylprednisolone, azithromycin (500 mg q.d.), acetylcysteine effervescent tablet (600 mg b.i.d.), omeprazole (20 mg q.d.), inhalations with acetylcysteine (2 to 4 mL of a 10% solution), lisinopril (20 mg q.d.), indapamide (2.5 PO q.d.), aspirin (75 mg), cefixime (400 mg q.d.), and metronidazole (400 mg t.i.d).

The patient showed a gradual recovery with a reduction in cast formation and expectoration. There was a concrete improvement in levels of SpO_2, with normalization of oxygen saturation, maintained at a stable and constant level without any additional interventions. Lymphangiography was beyond the scope of the clinic to which the patient was admitted, due to which she was referred for Lymphangiography to an established center. The patient was recommended to undergo Lymphangiography to investigate for any possible lymphatic malformations.

DISCUSSION

PB, also known as cast bronchitis, is a rare pulmonology condition consisting of branching intrabronchial cast formation that leads to obstruction of intermediate and distal airways. Patients often present with signs of fever, dyspnea, refractory hypoxemia, productive cough, or pleuritic chest pain.[2] PB has a variety of causes in adult and pediatric populations. Ranging from anatomic (thoracic duct stenosis, lymph flow variation, thoracic duct duplication); infectious (H1N1 influenza, AIDS/Kaposi sarcoma, adenovirus, adenovirus serotype 7, mycoplasma pneumonia, influenza B14); surgical (Coronary artery bypass graft, bilateral lung transplantation, Fontan procedure, Glenn shunt, tetralogy of Fallot repair, arterial switch operation); inflammatory processes (Atopy or asthma, idiopathic chronic eosinophilic pneumonia) to idiopathic causes.[7]

Our patient was found to have many concomitant anomalies like a left adrenal gland adenoma of unspecified hormonal activities with a nodular knot-like structure with calcification; heterogeneous thickening of renal parenchyma of kidneys, and an angiomyolipoma-like formation in the right kidney. Isoechoic nodules in the right lobe of the thyroid gland. An additional lobe in the right lung and an abnormally located azygous vein. History of lymphangiectasia of the duodenum. The patient also had syndactyly of second and third phalanges of the foot. This might hint towards an underlying genetic association of unknown origin and might predispose certain populations with these defects to PB.

The onset of the disease occurred at the beginning of the spring season with a gradual increase in sputum expectoration with rising temperature. Although no associations of PB with seasonal exacerbations have been described in the past, there might be an element of atmospheric temperature and seasonal allergies. The symptoms gradually declined on the season transition towards autumn, with a drop in temperature. The patient upon discharge was recommended a low lipid and protein diet. She followed the diet rigorously for a few days and reported significant improvement in symptoms. On one of the subsequent follow-ups, the patient described that when she resumed consumption of diets high in lipid and fat contents, although even occasionally, there was an exacerbation of cast formation. Thus, patients can be recommended to alter their lipid and protein intake.

Studies have reported bronchoscopy to be the most effective method for cast removal.[8,9] However, casts can sometimes be brittle and sticky, potentially impeding their extraction. Under such circumstances, adjuvant therapies in combination with bronchoscopy, are administered for cast removal.[7,10] Corticosteroids, α-chymotrypsin, macrolide antibiotics, sirolimus, N-acetylcysteine, unfractionated heparin, and tissue plasminogen activators (tPA) are common selections for adjuvant therapies in anecdotal cases.[7,11] However, there have been no reported cases of treatment of PB with SK. Therefore, the use of SK as an adjuvant treatment, of which this is the first reported case, might be a novel schema for therapeutic cast removal, and a new avenue in treating fibrinogenous bronchial casts.

The rationale behind using SK inhalation instead of heparin or tPA inhalation was based on an *in vitro* study done by Samama et al in their study they described the relative thrombolytic and fibrinogenolytic properties for multiple thrombolytic agents. For similar thrombolytic activities, fibrinogenolysis provoked by single-chain urokinase plasminogen (scu-PA) activator was less marked than with tissue plasminogen activator (tPA) and high and low molecular weight urokinase (HMW UK, LMW UK), while SK showed the highest activity.[12] Based on the rich fibrin composition of the bronchial casts it was decided to use SK in inhalation form, owing to the highest fibrinolytic activity of SK amongst all the fibrinolytic agents.

A major disadvantage of SK is related to its antigenicity, and complications secondary to it.[13] SK is a single-chain protein of molecular weight 48,000 which contains no carbohydrates and is isolated from filtrates of beta-hemolytic *Streptococcus*. In common with other foreign proteins, SK infusion induces antibody production in humans. Acute and immediate reactions associated with SK infusions have been commonly reported. Bronchospasm, chills, hypotension, and urticaria have all been described. Other non-specific malaise, headache, nausea, and vomiting occasionally complicate SK therapy. Pyrexia occurs later in the course of SK therapy.[14] Callan et al in their study described delayed hypersensitivity reactions after SK therapy.[15] The illness in such patients features diffuse vasculitis with rash, fever, arthralgia, proteinuria, haematuria, and sometimes impaired renal function.[14,15]

Abdelaal Ahmed Mahmoud et al. in their study demonstrated the use of SK inhalation in the treatment of acute respiratory distress syndrome (ARDS), SK dramatically improved oxygenation, lung mechanics, and other parameters with a resultant higher extubation rate, shorter ICU stay, as well as a higher survival rate compared to unfractionated heparin or conventional management in patients with severe ARDS.[16] Although, it seems that changes in the method of administration of SK might not elicit similar immune reactions; theoretically, slow systemic absorption of SK through the alveoli can take place (by either intracellular or paracellular mechanisms).[17] Therefore, a possibility of an exaggerated immune reaction should be kept in mind and necessary interventions according to protocols must be followed.[18] In the case of our patient bedside arrangements for an anticipated anaphylactic reaction were made to mitigate any uncertain life-threatening emergency.

Although PB is rarely seen in clinical practice, clinicians should be aware that PB can be possible under the following circumstances. (a) Respiratory tract obstruction, ventilation defects, and refractory hypoxemia occur in a short time in absence of inhalation of a foreign body. (b) Reduced respiratory sounds unilaterally or bilaterally on pulmonary auscultation. (c) Radiological chest examination shows pneumothorax, compensatory emphysema, or atelectasis. (d) No signs of improvement in the condition of the patient on administering routine treatment, with unexplained acute respiratory distress syndrome and acute lung injury. (e) Patients expectorating casts in the shape of a bronchial tree before. In such cases, aggressive treatment, including bronchoscopy and adjuvant therapies, such as inhaled SK, is the key to saving lives and reducing sequelae.

We propose a few hypotheses for PB based on our case study.

Due to its high fibrinogenolytic properties, inhaled SK can be a novel therapeutic approach in the management of PB, especially in patients who have bronchial casts with rich fibrin composition. Previously, PB has been noted in patients with asthma after viral infections like Influenza A.[19,20] This-hints towards a possible correlation between COVID-19 and PB. PB can potentially be a long-term complication in asthmatic patients who were affected by COVID-19. Non-specific midline/ congenital anomalies might hint towards an underlying genetic association of unknown origin and might predispose certain populations with these defects to PB. Exacerbation of PB episodes with a seasonal rise in temperature.

Limitations

While this scientific paper was being prepared the patient still did not undergo lymphangiography, this did not allow us to rule out existing lymphatic malformations, if any completely.

CONCLUSION

A 39-year-old female presents to the outpatient clinic with complaints of sudden and progressive dyspnea and was found to have expectoration of casts in the shape of the bronchus. The casts obstructed the airways causing a drop in SpO_2 levels down to critical values. No established management guidelines exist for the management of PB, and this has led to the rise of a variety of treatment regimens. One such novel therapeutic approach has been described by us in our case study. Based on the expectoration of fibrin rich bronchial casts the patient was treated with Inhaled SK, this therapeutic approach showed positive results in our patient and proved its efficacy as a potential treatment option for PB. Due to its high fibrinogenolytic properties, it was decided to use Inhaled SK instead of other inhaled thrombolytic agents. The treatment was successful as the patient was asymptomatic by the end of the treatment and on the follow-up, the visit showed no signs and symptoms of recurrence of casts. We suggest an additional hypothesis that PB can be a sequela of long-term post-COVID-19 complications in patients with Asthma. In patients having non-specific midline/ congenital anomalies suggesting an underlying genetic association of unknown origin. A seasonal element, probably immunogenicity or a temperature rise can be a possible association.

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REFERENCES

1. Grizales CL. Plastic bronchitis: A case report. Respir Med Case Rep. 2019;28:100876.
2. Brogan TV. Plastic bronchitis in children: A case series and review of the medical literature. Pediatr Pulmonol. 2002;34:482-7.
3. Ntiamoah P, Mukhopadhyay S, Ghosh S, Mehta AC. Recycling plastic: diagnosis and management of plastic bronchitis among adults. Europ Respiratory Rev. 2021;30:210096.
4. Smith CL. Liver lymphatic anatomy and role in systemic lymphatic disease. Eur Radiol. 2022;32:112-21.
5. Verghese S, Jackson M, Vaughns J, Preciado D. Plastic Bronchitis in a Child with Fontan's Physiology Presenting for Urgent Rigid Bronchoscopy. Anesth Analg. 2008;107:1446-7.
6. Rubin BK. Plastic Bronchitis. Clin Chest Med. 2016;37:405-8.
7. Patel N, Patel M, Inja R, Krvavac A, Lechner AJ. Plastic Bronchitis in Adult and Pediatric Patients: A Review of its Presentation, Diagnosis, and Treatment. Mo Med. 2015;118:363-73.
8. Nakamoto H. Airway emergency during general anesthesia in a child with plastic bronchitis following Fontan surgery: a case report. JA Clin Rep. 2020;6:6.
9. Grizales CL. Plastic bronchitis: A case report. Respir Med Case Rep. 2019;28:100876.
10. Shimura S. Effect of expectorants on relaxation behavior of sputum viscoelasticity *in vivo*. Biorheology. 1983;20:677-83.
11. Xiong L, Rao X, Peng X, Zhang G, Liu H. Management of Plastic Bronchitis Using α-Chymotrypsin: A Novel Treatment Modality. Cureus. 2021;13551.
12. Samama M. Comparison of thrombolytic, fibrinolytic, and fibrinogenolytic properties of tissue plasminogen activator, streptokinase, single-chain urokinase, high molecular weight and low molecular weight urokinase in human plasma *in vitro*. Fundam Clin Pharmacol. 1988;2:509-23.
13. Barnham M. Hypersensitivity and streptokinase. The Lancet. 1900;335:535.
14. Chesterman CN. Late adverse effects of streptokinase. Aust N Z J Med. 1992;22:106-8.
15. Argent N. Proteinuria and thrombolytic agents. The Lancet. 1990;335:106-7.
16. Abdelaal Ahmed Mahmoud A, Mahmoud HE, Mahran MA, Khaled M. Streptokinase Versus Unfractionated Heparin Nebulization in Patients with Severe Acute Respiratory Distress Syndrome (ARDS): A Randomized Controlled Trial with Observational Controls. J Cardiothorac Vasc Anesth. 2020;34:436-43.
17. Von Wichert P. Absorption of higher-molecular-weight substances via the lung. Pol Arch Med Wewn. 2012;122(1):78-83.
18. Shaker MS. Anaphylaxis-a 2020 practice parameter update, systematic review, and Grading of

Recommendations, Assessment, Development and Evaluation (GRADE) analysis. J Allergy Clin Immunol. 2020;145:1082-23.
19. Wang Y, An S. Plastic bronchitis associated with influenza A virus in children with asthma. J Int Med Res. 2021;49:030006052110653.
20. Murata Y, Ishihara S, Sato Y, Ohta T. Plastic Bronchitis Associated with Influenza: An Adult Case. Internal Med. 2021;60:1647-8.

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