Tissue plasminogen activator and pulmozyme for postoperative-retained hemothorax: A safe alternative to postoperative re-exploration

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ABSTRACT

Successful treatment of traumatic hemothoraces is imperative to reduce morbidity and mortality among patients. Treatment modalities range from more conservative to invasive measures, including antibiotic therapy, thoracostomy tube placement, video-assisted thoracoscopic surgery, or thoracotomy. Various studies have documented success in using fibrinolytics such as tissue plasminogen activator (tPA) in conjunction with deoxyribonuclease administered through a chest tube to resolve a hemothorax. The optimal dose and frequency of fibrinolytic therapy have not yet been determined although most studies report administering therapy two times a day for 3 days. We report a successful case of a one-time dose of fibrinolytic therapy through thoracostomy tube which could support that a single dose may be ideal and sufficient enough to resolve a hemothorax. We also performed this in the acute postoperative period, which has not been well studied, and believe fibrinolytic therapy can be safe to use in this setting.

Key Words: Deoxyribonuclease, postoperative, tissue plasminogen activator, traumatic hemothorax

INTRODUCTION

Pleural infections are associated with a significant morbidity and mortality and can lead to traumatic hemothoraces secondary to surgical interventions. Treatment is aimed at draining the infected fluid, which can require thoracostomy tubes, video-assisted thoracoscopic surgery (VATS), or a thoracotomy to fully evacuate the infected fluid or subsequent blood that accumulates in the thoracic space. More conservative measures include antibiotic therapy and intrapleural fibrinolytic therapy to avoid surgery.[1] Treatment with fibrinolytics such as tissue plasminogen activator (tPA) in conjunction with deoxyribonuclease (DNase) has been well studied and documented in the literature. Recent studies have suggested using tPA along with a DNase two times a day for 3 days to provide optimal treatment and resolution of the pleural effusion.[2] However, the use of these drugs has not been studied in patients who have recently undergone surgery, and its safety in the immediate postoperative period has been questioned. We report a case of a 28-year-old male with a resolved hemothorax after a one-time dose of tPA and pulmozyme (DNase) 3 days following a thoracotomy and decortication for a complex pleural effusion.

CASE REPORT

The patient is a 28-year-old male with a history of intravenous heroin abuse and untreated hepatitis C. He presented with worsening shortness of breath—requiring
mechanical ventilation—a hemorrhagic stroke, methicillin-sensitive *Staphylococcus aureus* bacteremia, and large bilateral pleural effusions. Computed tomography (CT) scan of the chest revealed extensive pulmonary infiltration of the lungs with large loculated complex pleural effusions bilaterally. There was no evidence of pulmonary embolism. Transesophageal echocardiography revealed mitral and tricuspid valve endocarditis. Mainly due to his hemorrhagic stroke, it was decided that his endocarditis would be treated medically. However, due to his complex loculated pleural effusions and significant concern for empyema, it was felt that he would benefit from pulmonary decortication and drainage of his pleural abscesses.

He was taken to the operating room for right thoracotomy with decortication, lysis of adhesions, and drainage of intrapleural empyema. He tolerated this procedure well, and his initial postoperative chest X-ray showed a significant improvement in his right-sided effusions [Figure 1]. However, on postoperative day 2, despite two appropriately placed chest tubes, he demonstrated what appeared to be a new hemothorax [Figure 2]. Its etiology was unclear. Due to reluctance to return him to the operating room to evacuate his hemothorax, it was decided to attempt instillation of tPA and pulmozyme, through the chest tube, into his pulmonary space on postoperative day 3. At the bedside, 10 mg of tPA in 50 cc of 0.9% normal saline was combined with 5 mg of pulmozyme inhalation solution for a total of 60 cc, and this was administered into the chest tube through an 18-gauge needle into the self-sealing portion of the chest tube connection system [Figure 3]. The chest tube was then clamped for 1 h to allow the drug to accumulate in the pleural space. Upon unclamping of the chest tube, 730 cc of dark sanguinous fluid immediately drained from the chest tube. Follow-up chest X-ray showed a right pleural effusion that was diminished in size compared to the morning’s chest X-ray [Figure 4]. Follow-up hemoglobin remained stable at 7.1 g/dL down from 7.5 g/dL. However, the following morning, his hemoglobin dropped to 6.4 g/dL and he was transfused two units of packed red blood cells.

A surveillance CT scan of his head was performed to monitor the progression of his stroke which did not show any evidence of progression or new pathology after administration of the tPA.

He subsequently required left-sided decortication, tracheostomy, and placement of a percutaneous feeding tube—all of which were performed in an uncomplicated manner. Over the next couple of days, his chest tubes and drains were removed without difficulty, his neurologic status improved to the point in which he was awake, following commands, and moving all extremities, and his ventilator requirements improved to the point where he was transferred to a long-term care facility for further rehabilitation and recovery. Two months postoperatively, he was discharged home with his tracheostomy and feeding tube having both been removed.

**DISCUSSION**

Given the significant morbidity associated with complicated pleural effusions, it is essential that these cases be treated appropriately and successfully. Conventional treatment includes antibiotics and thoracostomy tube placement. However, this is only successful in approximately 70% of patients. Patients who fail conservative therapy ultimately require surgical interventions such as a VATS or thoracotomy with decortication for definitive management and resolution. Many studies have reported success in resolving complicated pleural effusions by using tPA and DNase and have demonstrated a decrease in the number of patients requiring surgery in addition to shortened hospital stays. A recent retrospective observational study by Piccolo et al. looked at a large cohort of patients from various centers across three different countries to determine the pragmatic use of fibrinolytics for patients inadequately responding to conventional therapy. Their primary outcome was treatment success defined by survival at the time of discharge and no surgical intervention within 30 days of the first treatment dose. They found that of the 107 patients included in their study, 92.3% of the patients did not require surgery. In this study, patients were given intrapleural treatment with 10 mg of tPA and 5 mg of DNase two times a day for a total of up to six doses. In our case, we used one dose of 10 mg of tPA and 5 mg of DNase for evacuation of a presumed hemothorax. We opted to perform a thoracotomy instead of initially placing a chest tube and giving tPA because he was septic, his overall clinical picture was poor, and definitive management for his condition in a timely fashion was essential.

The use of intrapleural fibrinolytics for postoperative-retained hemothorax has not been well studied in large prospective randomized trials. Many studies have been retrospective and studied the results of traumatic-retained hemothoraces. There have been studies retrospectively comparing VATS to intrapleural streptokinase alone for traumatic-retained hemothoraces which showed VATS to be more effective. Other studies looked at a combination of streptokinase and urokinase in the treatment of traumatic hemothorax, showing a 92% response rate in cases that were not successfully treated with tube thoracostomy alone. Two other small retrospective studies looked at the use of tPA alone for patients who had retained hemothorax or hemothorax in patients who were not good surgical candidates, and they showed that their patients required an average dose
Pastoressa, et al.: tPA and pulmozyme for postoperative-retained hemothorax

of 24–40 mg of tPA.\(^6,7\) Our case is unique in the fact that we safely administered tPA and DNase postoperatively by extrapolating from the conservative management therapies of complicated pleural effusions to successfully treat our patient. We were able to avoid the morbidity associated with a reoperative intervention for a retained hemothorax with one intrapleural dose of tPA and DNase. Nonetheless, the risks of hemorrhage from intrapleural tPA administration after surgery must be weighed with the risks of reoperative intervention.

The manufacturer of alteplase recommends weighing the risk versus benefit of intravenous tPA administration in patients with recent intracranial hemorrhage, recent major surgery, and bacterial endocarditis.\(^8\) These comorbidities are uncommon in other studies of intrapleural tPA use and are sometimes found as exclusion criteria in certain studies. These relative contraindications, however, are based on intravenous administration, not intrapleural administration.

Contraindications to intrapleural administration are not well established, but a majority of the current literature about the morbidity of intrapleural administration of tPA for hemothorax has ranged from occasional blood transfusions to thoracotomy.\(^2,9\) Despite our patient having multiple concerning comorbidities, he tolerated intrapleural tPA without difficulty and only required transfusion of two units of blood. The blood loss was attributed to the initial postoperative hemothorax and unrelated to the use of tPA since the hematocrit did not change further after its use.

Given the significance of morbidity associated with complicated pleural effusions, it is imperative that successful treatment must be provided to these patients while limiting the compound morbidity of surgical therapy. In many instances, patients will require surgical intervention for complete resolution after they have failed conservative management. As such, new data have supported the use of tPA and DNase as a safe and effective alternative to surgery for complicated pleural effusions. Despite the vast
amount of case reports and studies demonstrating its efficacy in complicated pleural effusions, the optimal dose and frequency have yet to be determined in cases of postoperative retained hemothoraces. While more extensive studies need to be conducted on this matter, we believe that this case supports the use of a single dose of tPA and DNase as an effective means of treating postoperative-retained hemothorax and will hopefully lay the groundwork for future studies. Few studies have determined a safety profile for this treatment modality, and many may be hesitant to use it during the postoperative period due to the increased risk of bleeding. While this was successful in our case, a limitation of our report is that it included only one patient; larger experiences and series are needed to further establish the safety and efficacy of this approach to this problem; nevertheless, this intervention can be an option in patients in whom reoperative surgery is not desired. Our patient had a successful outcome with no major complications after administration of the drug which indicates tPA and DNase have the potential to play a larger role in the postoperative period and can be safely used; however, this still warrants further investigation.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Boersma WG, Stigt JA, Smit HJ. Treatment of haemothorax. Respir Med 2010;104:1583-7.
2. Rahman NM, Maskell NA, West A, Teoh R, Arnold A, Mackinlay C, et al. Intrapleural use of tissue plasminogen activator and DNase in pleural infection. N Engl J Med 2011;365:518-26.
3. Piccolo F, Pitman N, Bhatnagar R, Popowicz N, Smith NA, Brockway B, et al. Intrapleural tissue plasminogen activator and deoxyribonuclease for pleural infection. An effective and safe alternative to surgery. Ann Am Thorac Soc 2014;11:1419-25.
4. Oguzkaya F, Akçali Y, Bilgin M. Videothoracoscopy versus intrapleural streptokinase for management of post traumatic retained haemothorax: A retrospective study of 65 cases. Injury 2005;36:526-9.
5. Kimbrell BJ, Yaman J, Petrone P, Asensio JA, Velmahos GC. Intrapleural thrombolysis for the management of undrained traumatic hemothorax: A prospective observational study. J Trauma 2007;62:1175-8.
6. Thommi G, Nair CK, Aronow WS, Shehan C, Meyers P, McLeay M. Efficacy and safety of intrapleural instillation of alteplase in the management of complicated pleural effusion or empyema. Am J Ther 2007;14:341-5.
7. Stiles PJ, Drake RM, Helmer SD, Bjordahl PM, Haan JM. Evaluation of chest tube administration of tissue plasminogen activator to treat retained hemothorax. Am J Surg 2014;207:960-3.
8. Activase (Alteplase) Full Prescribing Information. Activase (Alteplase) Full Prescribing Information. 2015.https://www.gene.com/download/pdf/activase_prescribing.pdf
9. Skeete DA, Rutherford EJ, Sclidt SA, Abrams JE, Parker LA, Rich PB. Intrapleural tissue plasminogen activator for complicated pleural effusions. J Trauma 2004;57:1178-83.