Outcomes of Empyema Management with Intrapleural tPA and DNase

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ABSTRACT

BACKGROUND: Parapneumonic effusions and empyema are side effects of pneumonia that cause significant morbidity and mortality. Current guidelines recommend drainage of these effusions with tube thoracostomy or surgical debridement in addition to systemic antibiotics. This case series examines the technique to maximize drainage of complicated parapneumonic effusions (cPPE) through tube thoracostomy by instilling tissue plasminogen activator (tPA)/ deoxyribonuclease (DNase) tPA and DNase into the pleural cavity in a community hospital setting.

METHODS: We retrospectively reviewed all patients admitted to Erlanger hospital in Chattanooga from Jan 2010 to April 2015 who presented with cPPE and were treated with intrapleural medications to increase drainage. Data was collected, tabulated, and summarized with mean (standard deviation) or frequencies as appropriate.

RESULTS: We reviewed 9 cases; 6 women and 3 men (age range: 44 to 86 years). In total, there were 6 patients with empyema and 3 patients with cPPE. The decrease in size of the pleural effusion was seen qualitatively on chest X-ray, and quantitatively, the output from the chest tube after the tPA and DNase treatment. The decrease in chest tube output ranged from 2-4 L. Of the 6 patients who had empyema, 4 required surgical lung decortication. The 3 patients with cPPE were managed with medical therapy and had adequate clinical improvement. The average hospital stay was 16.1 days.

CONCLUSION: In this small series, the intrapleural tPA and DNase was effective in reducing the size of pleural effusion as well as reducing the rate of surgical consultation.

Keywords: Parapneumonic Effusions; Empyema; Pneumonia; Tissue Plasminogen Activator; Deoxyribonuclease

INTRODUCTION

Parapneumonic effusions and empyema are side effects of pneumonia that cause significant morbidity and mortality. Over half of patients with bacterial pneumonia will develop a parapneumonic effusion that can lead to greater than tripling of mortality [1]. Poor outcomes are increased with complicated parapneumonic effusions (cPPE) defined as a pH of <7.2, positive Gram stain, culture of pleural fluid for bacteria, or frank pus in the pleural cavity. Current guidelines recommend drainage of these effusions with tube thoracostomy or surgical debridement in addition to systemic antibiotics [2]. Tube thoracostomy is less invasive than video-assisted thoracoscopic surgery (VATS) or thoracotomy but may not be able to drain effusions with multiple loculations and septations. Further medical therapy has previously included intrapleural fibrinolysis with streptokinase. In 2005, Multicenter Intrapleural Sepsis Trial (MIST) 1 showed that there was no significant improvement in mortality when intrapleural fibrinolytics alone were used [3]. In 2011, a follow up study, MIST2, showed that adding fibrinolytics such as tissue plasminogen activator (tPA) and deoxyribonuclease (DNase) to the pleural space demonstrated decreased mortality and lower surgical referrals and reduced hospital length of stay [4]. This case series examines the results of using this technique in a community hospital setting.

METHODS

We retrospectively reviewed all patients admitted to Erlanger hospital in Chattanooga, Tennessee, USA from January 2010 to April 2015 who presented with cPPE and were treated with intrapleural medications to increase drainage. The intrapleural medication was administered according to the protocol in the MIST2 study. Only patients with exudative pleural effusions on lab testing and associated loculations on imaging were included. Data was collected, tabulated, and summarized with mean (standard deviation) or frequencies as appropriate.

RESULTS

We reviewed 9 cases; 6 women and 3 men ranging in age from 44 to 86 years. All patients presented with dyspnea and pleuritic chest pain and had signs of systemic infection. All but one presented with fever greater than 100.5 F and leukocytosis. The patient's clinical, pleural fluid characteristics with interventions done and outcome are shown in table 1.

Pleural Fluid Examination: The pH of the pleural fluid was less than 7.2 to be classified as cPPE. There were 3 patients included who did not have pH measured. These exceptions were made for high clinical likelihood of cPPE. Patient 1 had significantly elevated White Blood Cells (WBC) with abundant Polymorphonuclears (PMN) in the pleural fluid. Patient 5 had frank pus in the pleural cavity, and patient 8 had glucose of less than 5 mg/dL in the pleural fluid. Of the 9 patients, 4 had positive cultures, and 2 were culture negative but had frank pus seen in the pleural cavity. In total there were 6 patients with empyema and 3 patients with cPPE.

Intervention: The patients were started on antibiotics and then had the pleural fluid drained. About half of the patients had an initial diagnostic thoracentesis followed by chest tube placement, and the other half had the chest tube placed directly at the same time that diagnostic samples were taken. The intrapleural medication was administered according to the protocol in the MIST2 study. First 10mg of tPA was administered through the chest tube which was then clamped for one hour. Then 5mg of DNase was administered through the chest tube which was again clamped for 1 hour. Then the chest tube was opened to wall suction. This regimen was to be administered twice daily for 3 days for a total of 6 doses. However, in practice, the total number of doses varied ranging from 3 to 12.

Outcome: Following the initial administration of intrapleural tPA and DNase, all patients had improved drainage and reduction in size of the pleural effusion on follow up chest X-ray. The decrease in size of the pleural effusion was seen qualitatively on chest X-ray, and the visual examination showed decrease in all cases. For more quantitative measurement, the output from the chest tube after the tPA/DNase treatment was found to be from 2-4 L. There was an increase in drainage of about 0.5-1L on the day following the first dose of tPA/DNase.

Of the six patients who had empyema, 4 required surgical lung decortication. The 3 patients with cPPE were managed with medical therapy and had adequate clinical improvement. The average hospital stay was 16.1 days. For the 4 patients who underwent surgery the average length of stay was 19 days. For the patients who improved with medical management, the average length of stay was 13.8 days. One patient, who improved with the intrapleural therapy, had reaccumulation of pleural effusion after the removal of the chest tube. This patient was taken for surgery and was found to have both empyema and hematoma in the pleural cavity. One patient, who died, had an exudative effusion that was refractory to tPA and DNase and subsequently went for surgical decortication. Her post-operative course was tenuous, and she did not regain respiratory function. Her family changed her code status to 'comfort measures only' and soon afterwards she passed away.

DISCUSSION

In this series, we examined whether the intrapleural therapy studied in the MIST2 trial had reproducible results in a community hospital setting with improvement in the size of loculated effusions that were not drainable by simple tube thoracostomy. We found that after using the therapy regimen in the MIST2 trial, each patient had improvement in the size of pleural effusion as detected by imaging and increased drainage through the chest tubes. The interventions were well-tolerated by patients and 2 of the 6 patients did not require surgical decortication, which would have been indicated otherwise in these patients.

The length of hospital stay for empyema can be quite long, and averages from 17-22 days in various studies [5]. Patients who are post-thoracotomy, require an average stay of 18 days

Table 1: Clinical, Pleural fluid characteristics of Patients with interventions done and outcome

ID	Age/ Sex	Temp (°F)	WBC (10^3/mL)	pH	LDH (U/L)	Glucose (mg/dL)	Protein (mg/dL)	Fluid WBC (10^3/mL)	Gram stain	Culture	Dx	tPA/ Dnase (# of doses)	Pleural Fluid Drained (mL)	Surgery	LOS (days)
1	62M	100.8	17.3	NA	1476	156	5100	15,641	Neg	Neg	cPPE	5	1866	No	7
2	52M	99.7	18.5	7.2	1189	86	5500	4599	NA	NA	cPPE	6	3940	No	21
3	60F	98	9.2	7.2	1472	66	3100	253	GPC	MSSA	Emp	4	3919	Yes	25
4	50M	97.5	14.2	6.6	NA	<5	3000	44,303	GPC	Strep B	Emp	5	3937	No	13
5	44F	102.3	4.2	7.31	451	37	2300	693	Neg	Neg	Emp	4	3795	Yes	25
6	47M	96.2	18.3	7.07	684	50	4800	125	Neg	Neg	Emp	4	1990	Yes	12
7	71M	96.4	13.9	NA	NA	NA	NA	NA	GPC	MSSA	Emp	6	3200	Yes	14
8	86M	98.8	38.8	NA	2970	<5	4100	3197	Neg	Neg	cPPE	3	3100	No	15
9	70F	99.9	31.8	6.99	2436	70	4600	1871	Neg	Strep A	Emp	12	2010	No	13

M=Male, F=Female, LDH: Lactate Dehydrogenase; WBC: White Blood Cell; cPPE: Complicated Parapneumonic Effusion; F: Fahrenheit; NA: Not available, LOS = Length of Stay, Cory= Corynebacterium, Emp = Empyema, Neg = Negative, GPC = Gram Positive Cocci, MSSA = Methicillin Sensitive Staphylococcus Aureus, Strep B = Streptococcus Group B, Strep A = Streptococcus Group A

[6]. Length of stay in our series of patients is on par with these time frames. The average stay for all 9 patients was 16.1 and the average stay for post-operative patients was 19. Patients who responded to the intrapleural therapy had admission length of 13.8 days; this is 2 days less than the total average and a full 5 days less than thoracotomy patients. These findings were also noticed in one random controlled study with a decrease in the length of hospital stay with use of intrapleural fibrinolysis [7].

Further studies are needed to determine the most effective time course that will improve outcomes in patients with cPPE without causing adverse events with treatment. Furthermore, given the risk for adverse events with the use of fibrinolytics, it will be essential to have a standardized method to effectively give this treatment while minimizing risk for bleeding into the pleural space.

CONCLUSION

In this small series, the intrapleural tPA - DNase appears to be effective in reducing the size of pleural effusion as well as reducing the rate of surgical consultation and the length of hospital admission.

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