

Cryptococcal empyema treated with tube thoracostomy and intrapleural fibrinolysis

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Abstract

A 55-year old woman with a history of relapsed T-cell ALL presented with right pleuritic chest pain and decreased breath sounds over the right hemithorax. Imaging of the chest showed loculated effusions. Tube thoracostomy was performed with intrapleural application of alteplase and dornase alpha over a 3-day period. Repeat imaging demonstrated a marked decrease in the volume of the effusion. In most prior published cases of pleural cryptococcosis, surgical drainage was required in addition to prolonged antifungal agents. More than 50% of patients with cryp-

tococcal infection have severe underlying disease or immunodeficiency state making them high risk for surgery. This is the first case to our knowledge of cryptococcal empyema successfully treated with tube thoracostomy and intrapleural fibrinolysis.

Introduction

Empyema and complicated parapneumonic effusion usually result from bacterial invasion of the pleural space [1]. Although often associated with pneumonia, it can also develop after thoracic surgery or trauma. Complicated pleural effusion is objectively defined when pleural fluid pH drops to below 7.20 in addition to other less sensitive markers such as glucose below 60 mg/dL and Lactate dehydrogenase (LDH) more than three times the upper limit of normal [2]. Usually, an invasive procedure such as tube thoracostomy, is necessary for its resolution [3]. Mortality can be as high as 47% in hospital acquired infections [4]. Recent studies have noted a change in the bacteriology of empyema, possibly due to the widespread use of antibiotics as well as an increase in the incidence of fungal empyema [5,6]. Moreover, mortality in fungal empyema has been reported to be as high as 70% [5].

Although most patients previously have been treated with a combination of surgical drainage and antifungal therapy, the treatment of fungal empyema has not been protocolized and there is no consensus or guidelines for therapy [3,5,7].

We present a case of fungal empyema in a woman previously diagnosed with T-cell acute lymphocytic leukemia (ALL) successfully treated with tube thoracostomy and intrapleural fibrinolytic therapy in addition to antifungal antibiotics.

Case Report

A 55-year old woman with a history of relapsed T-cell ALL presented with several days of fever, cough and right sided pleuritic chest pain. Computed tomography (CT) of the chest showed a small loculated right pleural effusion with adjacent consolidation of the right lower lobe. Broad spectrum antibiotics including meropenem were initiated. Ultrasound-guided thoracentesis yielded serous, slightly cloudy pleural fluid. Analysis of the fluid revealed a neutrophil-predominant exudative process with a pH of 7.0, glucose of 109 mg/dL and LDH of 260 IU/l. The patient remained febrile with worsening pleuritic chest pain and a repeat CT revealed recurrence of the effusion with significant loculations (Figure 1). Due to the posterior location of dominant loculation as well as to guide optimal placement, ultrasound-guided tube thora-

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costomy via the Seldinger technique with a 14 French pigtail catheter was performed. Intrapleural instillation of alteplase (t-PA) 10 mg and dornase alpha (DNase) 5 mg concurrently twice daily over a 3-day period was initiated. For each instillation, the chest tube was clamped for 1 h. Meanwhile, pleural fluid culture yielded *C. neoformans* and amphotericin B was initiated. Repeat imaging 24 h after the last fibrinolytic dose demonstrated a 76% decrease in the size of the effusion, measured volumetrically, with small residual loculation (Figure 2). Another attempt to drain the fluid was unsuccessful as the loculation was quite small and located para-scapular. Since the patient continued to improve clinically, no further pleural drainage was attempted. She was discharged approximately 3 weeks following her initial presentation on oral fluconazole. Repeat chest CT obtained 1-week post discharge showed complete resolution of the pleural effusion (Figure 3).

Discussion

Pleural infections are associated with high morbidity and mortality [4]. As noted above, complex pleural effusions and empyema can be fatal in as much as half of the patients who develop them. Early drainage of the pleural fluid and appropriate antibiotic therapy is fundamental to treatment. Prior to the MIST 2 trial, complex parapneumonic effusions and empyema often required surgical intervention for complete evacuation of the pleural space and control of infection [3]. Less invasive options such as antibiotics and drainage with tube thoracostomy fails in about a third of the patients [8,9].

The use of intrapleural fibrinolytic therapy in the treatment of complex pleural effusions dates back to the 1950s when Tillet et al reported that intrapleural injection of streptokinase and streptodornase facilitated pleural drainage in patients with empyema [10]. Widespread use of these agents did not start until the 1990s when several observational studies reported the usefulness of fibrinolytics in the management of patients with loculated parapneumonic effusions [11,12]. Although this potential benefit of intrapleural

fibrinolytics was not supported by the large First Multicenter Intrapleural Sepsis Trial (MIST1) and a subsequent meta-analysis [13,14], Rahman and colleagues were able to show the benefits of intrapleural fibrinolytics (t-PA-DNase) in terms of fewer referrals for thoracic surgery and shorter hospital stay [8]. Subsequent studies have also shown successful management of complicated pleural space infections with t-PA and DNase [9,15].

A recently published meta-analysis comparing surgical *versus* non-surgical (tube thoracostomy with or without intrapleural fibrinolysis) management for pleural empyema concluded that there was no difference in mortality between the groups. Video-assisted



Figure 2. Repeat CT showing marked decrease in pleural fluid with some residual loculations.



Figure 1. Sagittal CT showing loculated effusion before chest tube placement.



Figure 3. Follow-up CT-post 3 weeks showing complete resolution of the effusion.

thoroscopic surgery (VATS), however, was found to reduce the length of hospital stay compared to thoracostomy drainage only [16]. However, in this study, not all patients who underwent tube thoracostomy were treated with intrapleural fibrinolytics.

Although rare, the incidence of fungal empyema is increasing, and a significant number of cases have been reported in patients with underlying malignancy and severe immunocompromised state [5]. Most cases are due to *Candida* species.

Cryptococcus neoformans is a ubiquitous fungus found in soil. Humans are exposed to it by inhalation resulting in pulmonary infection which can range from asymptomatic to disseminated infection. Involvement of the pleural space is extremely rare [17-19]. Most cases of fungal empyema have required surgical management with prolonged antifungal agents and there is a paucity of literature supporting intrapleural fibrinolytics [5,7]. Even in the MIST 2 trial, none of the reported cases involved documented fungal infections. Although recent advances in surgical management have reduced postoperative morbidity, surgical management has risk for complications and can often be limited by co-morbidities [20]. Moreover, patients at risk of and especially those who develop fungal pleural infections often have significant comorbidities including cancer, diabetes mellitus, long-term steroid treatment, hepatic cirrhosis, solid organ transplant, alcoholism, human immunodeficiency virus infection or recent surgery [5,7]. In circumstances such as this, when surgical management might be associated with high perioperative risks, tube thoracostomy and intrapleural fibrinolytics is a promising alternative. Close monitoring to assess for failure of therapy such as inadequate drainage and ongoing sepsis should still warrant surgical intervention after weighing the risks and benefits.

Our patient with a cryptococcal empyema and underlying T-cell ALL was treated successfully with tube thoracostomy and intrapleural fibrinolytic therapy.

Conclusions

Our case illustrates that this is a viable treatment option and should be considered in patients with high risk for perioperative morbidity.

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