CASE REPORT

Resolution of Empyema Thoracis after Patient Refusal of Surgical Intervention: A Case Series and Review of the Literature

John H. Ferguson[1,*]

[1]*Rocky Mountain Pulmonary and Critical Care. 8550 W. 38th Avenue, Suite 202. Wheat Ridge, CO 80033*

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Abstract: Parapneumonic effusions occur commonly in patients hospitalised with pneumonia. Both complicated parapneumonic effusions and empyema are often managed initially with tube thoracostomy and intrapleural t-PA and DNase. If complete expansion of the lung is not achieved, surgical intervention is considered. We present three cases of patients with complicated parapneumonic effusions who experienced complete recovery despite declining surgical intervention and discuss the pitfalls in management. While very few patients have complete radiological resolution at the time of discharge, medical therapy is successful in at least 90% of cases. At 3-6 months from presentation, the radiological findings may improve significantly with antibiotic therapy. Surgery should be considered for patients with non-resolving sepsis markers including elevated temperature, C-reactive protein, and white blood cell count, in addition to non-improving imaging. Incomplete resolution of the parapneumonic effusion should not be considered a treatment failure, and attempts to normalise CT imaging may result in prolonged hospitalisation and unnecessary surgical intervention.

Keywords: Complicated parapneumonic effusion, decortication, empyema, pneumonia, VATS.

1. INTRODUCTION

Parapneumonic effusion (PPE) occurs in up to 40% of hospitalised patients with pneumonia [1]. When high-risk pleural features are present, including a glucose less than 40 mg/dL, LDH > 1000 U/L, LDH 3x upper limit of normal if loculated, pH < 7.2, pleural fluid gram stain positive or culture positive, or purulent return of the fluid, then tube thoracostomy is often recommended [2]. Despite the frequency of occurrence, there is a lack of consensus regarding a definition of treatment success and the indication for surgery in patients with a parapneumonic effusion [1]. Prevention of death or disability and reducing hospital length of stay are frequently regarded to be the primary endpoint, however, physicians often consider complete radiographic resolution on CT imaging to be a treatment success [3, 4]. In a survey of physicians' opinions regarding a successful PPE treatment, 60% of responders considered patient defervescence to be a successful outcome, whereas the remaining 40% would pursue further pleural drainage strategies [5].

A protocol studied in the MIST2 trial is commonly used to improve drainage from loculations in a PPE. This trial randomised 210 patients into four groups: placebo, t-PA, DNase, or t-PA and DNase in combination. Only 5.7% of these patients experienced complete resolution of the effusion by chest x-ray at one week, while only one hundred and six patients (50.4%) had as much as a 50% improvement in the pleural opacity in that time. The MIST2 study concluded that the chest x-ray pleural opacity in parapneumonic effusion was improved to a greater extent in patients treated with the combination of t-PA and DNase when compared to placebo. Its efficacy was modest, with an absolute change in the pleural opacity by -29.5% in the t-PA/DNase group and by -17.2% in the placebo group [6].

Antibiotics penetrate the pleura with excellent concentration and may be effective in the treatment of complicated parapneumonic effusions or empyema despite a lack of complete drainage [7, 8]. We present three cases of resolution of parapneumonic effusion despite a recommendation for surgery and review the literature to answer the following questions.

1. What criterion constitutes a treatment success in the management of pleural space infection?
2. Is resolution by chest imaging necessary to be considered a treatment success?

2. CASE REPORTS

2.1. Patient #1

A 69-year-old malnourished man was admitted with complaints of choking, chest pain, and poor oral intake. His

*Address correspondence to this author at the Rocky Mountain Pulmonary and Critical Care. 8550 W. 38th Avenue, Suite 202. Wheat Ridge, CO 80033; Tel: 303-940-1661; E-mail: jferguson@rockymtnpulmonary.com

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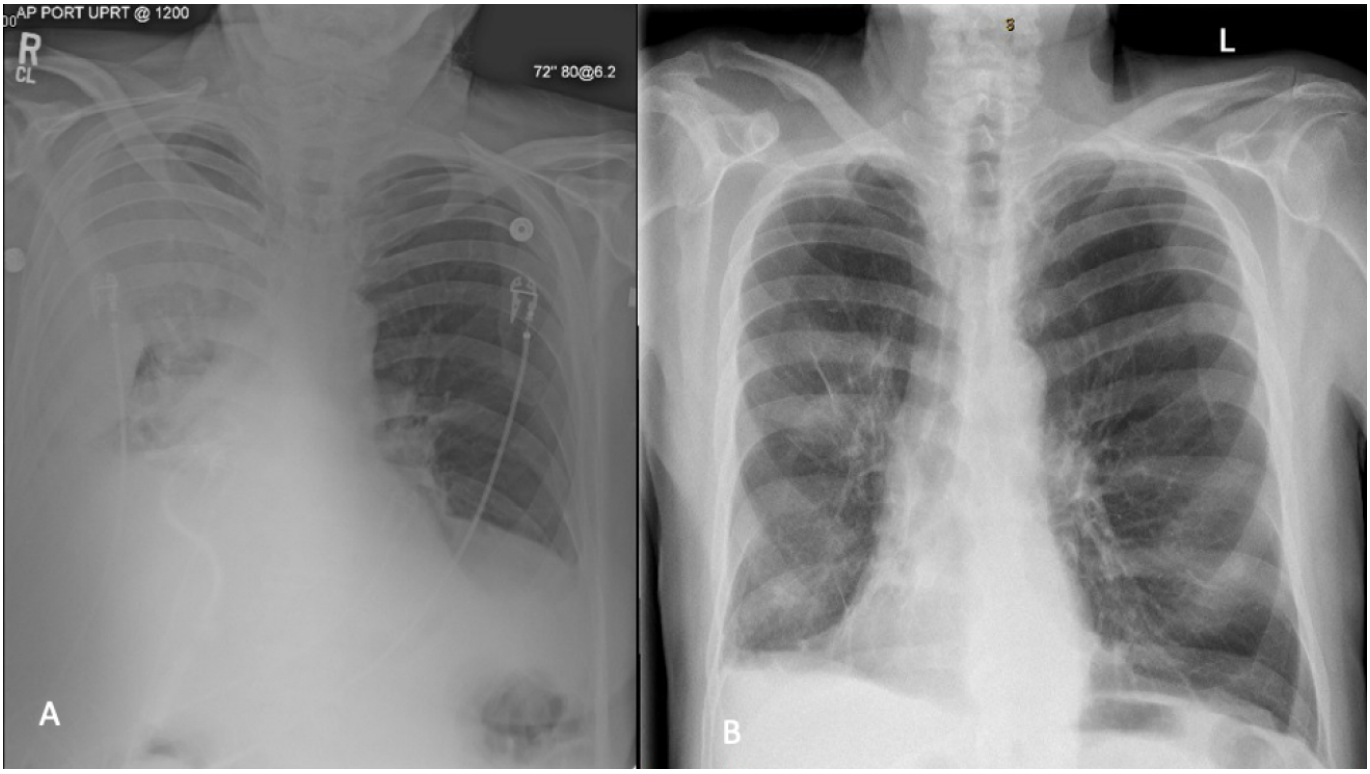

Fig. (1). Patient #1 chest x-ray prior to discharge (**A**) and one-month after discharge following treatment with oral amoxicillin-clavulanate (**B**).

past medical history was notable only for asthma and a remote stroke. He was not immunocompromised, had no significant alcohol or tobacco use, and had excellent dentition. Vital signs included a temperature of 38.8 C, pulse 130, BP 110/66, respiration rate 20, and oxygen saturation of 92% on room air. Pertinent laboratory investigations included a white blood cell count of 25.8/microlitre (normal 4-11/microlitre), hemoglobin 13.4 g/dL (normal 14-17 g/dL), and platelets 568/microlitre (normal 150-450/microlitre). Blood urea nitrogen was 29 mg/dL (normal 7-18 mg/dL), creatinine 1.3 mg/dL (normal 0.6-1.3 mg/dL), and albumin 2.2 g/dL (normal 3.5-5 g/dL). Liver function values were within normal limits. A CT of the chest was performed which demonstrated a right lower lobe cavitary lung abscess and an associated large pleural effusion. Tube thoracostomy was performed on the first day of hospitalization with fluid analysis consisting of a complicated parapneumonic effusion with non-purulent fluid, pleural pH < 6.82, glucose 62 mg/dL, and culture positivity for *Streptococcus anginosus*, *Veillonella species*, *Fusobacterium nucleatum*, and *Escherichia coli*. The patient was treated with intravenous piperacillin/tazobactam and six doses of intrapleural t-PA/DNase were administered through the chest tube. Thoracic surgery was consulted on day 4 for the persistence of an extensive multiloculated pleural effusion (Fig. **1A**). The consensus was achieved regarding the need for surgery, but the risk was felt to be exceedingly high due to his frail appearance and lethargy. The patient was considered to have a poor prognosis for a meaningful recovery due to the severity of loculations on CT, his functional status, persistent leukocytosis of 22.2/microlitre, and temperature of 37.4 C. Hospice was recommended and the chest tube was removed after the patient agreed to end-of-life care. He was discharged to an inpatient hospice but remained on oral antibiotics. The patient continued oral amoxicillin-clavulanate with gradual clinical improvement in fevers and reduction in cough. He was discharged to home from hospice one-month later to complete a total of 3 months of oral antibiotics. Repeat chest x-ray in the outpatient setting demonstrated a near-complete resolution of the pleural opacity (Fig. **1B**). The patient suffered no residual respiratory impairment and returned to his baseline weight and functional status.

2.2. Patient #2

A 48-year-old poorly nourished man was admitted with increasing shortness of breath, yellow sputum, and abdominal pain over a three-week interval. He had been treated with an oral antibiotic two weeks prior to his admission for acute bronchitis. His past medical history was notable for dysphagia secondary to an oesophageal stricture. He was not immunocompromised and had no significant alcohol or tobacco use. Vital signs included a temperature of 37.7 C, pulse 102, BP 110/78, respiration rate of 18, and arterial saturation of 89% on 2lpm oxygen. Admission laboratory investigations were pertinent for a white blood cell count of 13.9/microlitre with a neutrophil predominance, haemoglobin 9 g/dL, and platelet count of 655/microlitre, urea nitrogen of 17 mg/dL, creatinine 0.67 mg/dL, and serum albumin of 1.3 g/dL. Liver function values were found to be within the normal limits. A CT chest and abdomen on admission demonstrated a multiloculated pleural effusion (Fig. **2A**). Tube thoracostomy was performed and six doses of t-PA and DNase were initiated per the MIST2 protocol, along with administration of intravenous piperacillin-

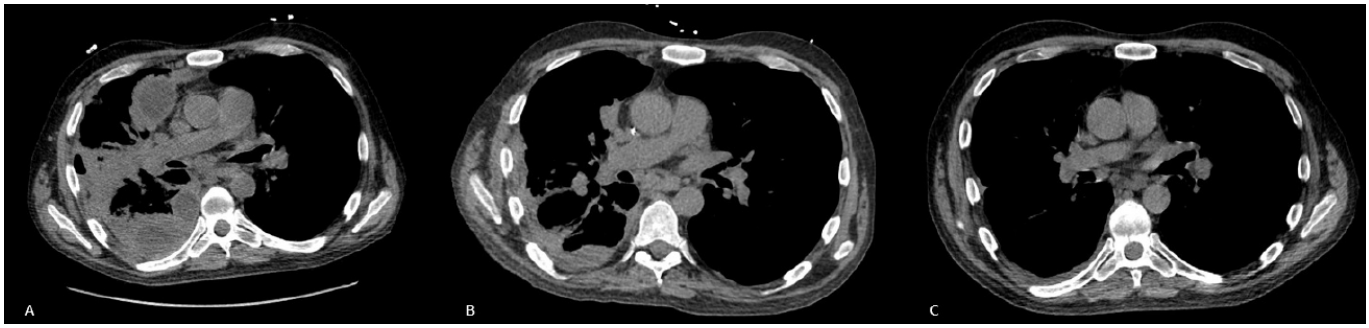

Fig. (2). Patient #2 CT chest at admission (**A**), discharge (**B**), and one-month after discharge following treatment with intravenous piperacillin-tazobactam (**C**).

tazobactam. The pleural fluid consisted of frank pus with glucose < 3 mg/dL, and LDH 2923 U/L. Pleural fluid culture was positive for both *Pseudomonas aeruginosa* and *Streptococcus anginosus*. Thoracic surgery was consulted on day 3 for consideration of decortication but felt his surgical risk was excessive due to his malnourishment and poor functional status. A repeat chest CT on day 3 to reassess for effusion resolution showed a marked improvement in the parapneumonic effusion but with persistent moderate loculations. On day 4, the patient's temperature had improved to 36.3 C, the white blood cell count improved to 10.91/microlitre and platelets had improved to 568/microlitre. Despite the clinical improvement, two additional chest tubes were inserted into the remaining loculations. On day 10, a third CT chest was performed to assess the progress, which once again demonstrated incomplete resolution (Fig. **2B**). Despite the clinical improvement the patient was again recommended for decortication of persistent pleural space opacities, but he elected to be discharged on antibiotics. At one-month follow-up he remained afebrile and back to his baseline functional status. A final CT chest demonstrated a near- complete resolution of the pleural opacity (Fig. **2C**).

2.3. Patient #3

A 78-year-old woman with a past medical history of a hiatus hernia was admitted with one-month of increasing cough and dyspnoea. She experienced oesophageal reflux related to her hiatus hernia, but had good dentition and no significant alcohol or tobacco use. She was treated as an outpatient with levofloxacin for the cough but due to progressive dyspnoea she was admitted through the emergency room. Vital signs included a temperature of 36.1 C, pulse 107, BP 160/97, respiration rate of 28, and arterial saturation of 92% on a non-rebreathing oxygen mask. Admission laboratory investigations were pertinent for a white blood cell count of 19.6/microlitre, haemoglobin 12.2 g/dL, platelet count 426/microlitre, blood urea nitrogen 14 mg/dL, creatinine 0.73 mg/dL, and serum albumin of 1.8 g/dL. Liver function values were within normal limits. Chest x-ray and CT of the chest demonstrated a hiatus hernia and a large loculated left pleural effusion. Thoracocentesis was performed with pleural fluid consisting of non-purulent fluid, glucose 109 mg/dL, LDH 1047 U/L, and pH 7.31. Oral clindamycin was initiated. On day 2, a CT was performed demonstrating a persistent pleural effusion. Pleural fluid culture was positive for *Streptococcus intermedius* and tube thoracostomy was performed on day 8. Despite her clinical improvement, thoracic surgery was consulted as a repeat CT chest demonstrated a persistent moderate loculated effusion. A final CT chest on day 13 demonstrated a loculated hydropneumothorax and decortication was again recommended, although her white blood cell count remained only mildly elevated at 11.54/microlitre with a temperature of 36.9 C. Chest x-ray on day 15 demonstrated a persistent effusion (Fig. **3A**), however the patient declined any further treatment and was discharged to home against physician advice on oral amoxicillin-clavulanate. She was seen in the outpatient clinic 3 weeks after discharge at which time a repeat chest x-ray demonstrated complete resolution of the pleural opacity (Fig. **3B**). She experienced no further symptoms such as dyspnoea or cough and returned to her normal functional status.

3. DISCUSSION

It has long been thought that drainage of complicated parapneumonic effusions and empyema leads to improved patient outcomes [1]. Ten percent of parapneumonic effusions develop into empyema and if left untreated or undrained may lead to chronic fibrosis, lung entrapment, and death [2]. Early drainage can identify high-risk patients and improve the volume of the effusion [9]. The rapid availability and high sensitivity of CT and ultrasound have led to increased recognition of loculations not visible on chest x-ray. In the organising stage of a parapneumonic effusion, bacterial and macrophage migration lead to fibrin deposition and loculation formation. The presence of loculations indicates intense inflammation in this stage, but does not indicate an inability to resolve with antibiotics. Lysis of these adhesions can be performed with either surgery or with tube thoracostomy and intrapleural medical therapy.

The MIST2 trial reported treatment success of tube thoracostomy with twice daily t-PA/DNase in 95.8% of patients [6]. Treatment failure defined as the need for surgical referral by 3 months was reduced in patients treated with t-PA/DNase when compared to placebo, but not in patients treated with t-PA alone [6]. Based on the findings of this trial, a cohort of 107 patients was treated with the same

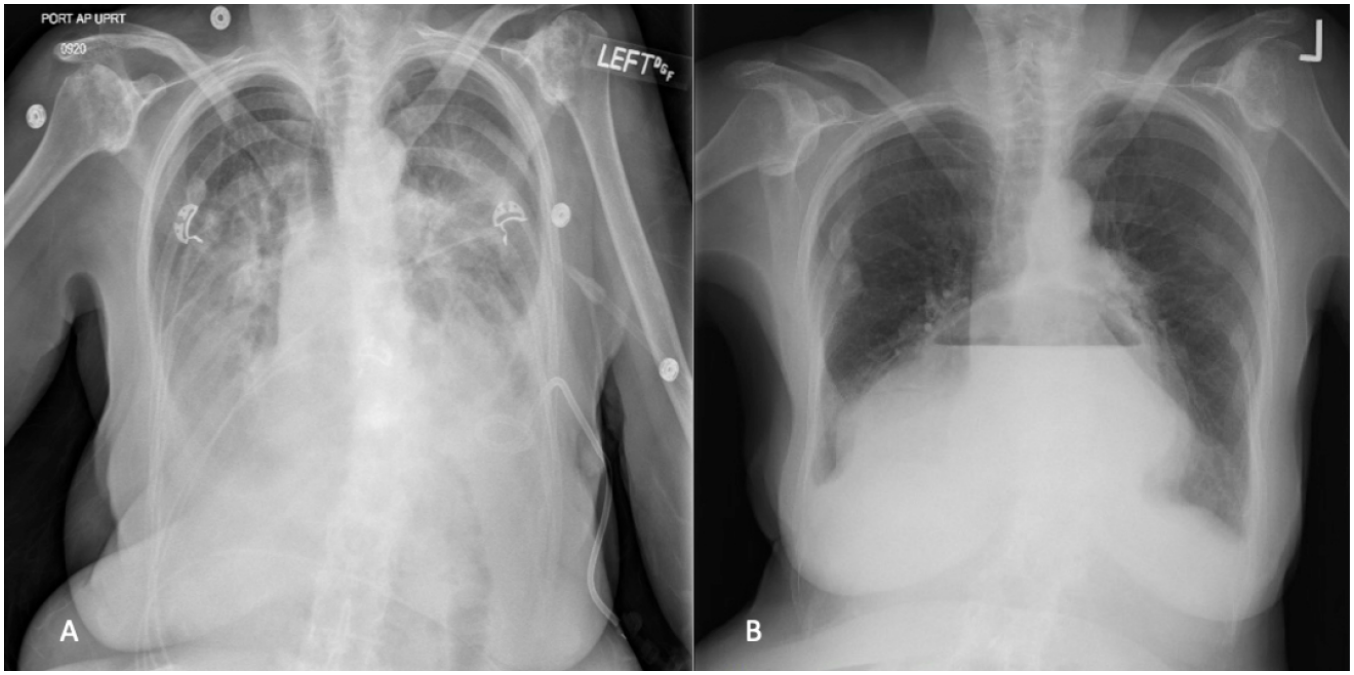

Fig. (3). Patient #3 chest x-ray prior to discharge (**A**) and one-month after discharge following treatment with oral amoxicillin-clavulanate (**B**). A large hiatus hernia projects onto the mediastinum.

t-PA/DNase regimen [10]. Treatment success, defined as the combination of survival and avoidance of surgical intervention, was shown to be 92.3% [10]. A third study to assess the effectiveness of t-PA/DNase in complicated PPE led to normalisation of the white blood cell count, patient defervescence, radiological improvement, and avoidance of surgery in 90.4% of patients [11]. A trial of once-daily t-PA/DNase was successful in 87.3% of patients; success being defined as survival to discharge with avoidance of surgical intervention at 30 days [12]. In a reduced dose trial of t-PA/DNase, 91.8% of patients were alive without the need for surgery at 30 days [13]. Lastly, a retrospective study of concurrent t-PA and DNase administration demonstrated a success of 85%, defined as clinical and radiological improvement without the need for surgery, in which every death appeared to be related to significant comorbidities [14]. These trials establish the first observation.

1. The success of medical therapy for parapneumonic effusions is > 90% [6, 10-14]

Despite its critical importance, the MIST2 trial was effective in halving the size of the effusion on chest x-ray at day 7 in only 26 of 55 (47.2%) patients and led to complete resolution in only 6 (10.9%) patients treated with this regimen. The authors expected this modest change in pleural opacity as the MIST2 enrollment power was based on previous data that assumed a 50% improvement in the pleural opacity at 1 week in placebo-treated patients [6]. In the cohort described by Piccolo *et al*, the percentage of parapneumonic pleural opacity on chest x-ray improved only from a median of 35% to 14% at hospital discharge [10]. The trial of once-daily t-PA/DNase decreased the degree of pleural opacity in 55 patients from only a mean of 51.5% to a mean of 22.6% at day 7 [12]. The study of concurrent t-PA and DNase was more significant, reducing the CT pleural fluid volume from a median of 361 mL to 80 mL [11]. Lastly, the reduced dose t-PA/DNase trial reduced the hemithorax pleural opacity from 42% to 16% with only 2 of 55 patients (3.6%) experiencing complete resolution at hospital discharge [13]. This leads to the second observation.

2. Only half of the medically treated parapneumonic effusions have at least a 50% improvement in chest x-ray opacity at 1 week, and only 3-10% experience complete resolution by this time [6, 10-13]

In contrast to the short interval assessments in the aforementioned trials, the MIST1 trial evaluated imaging at 3 months. The MIST1 trial randomised 454 patients with pleural infection to six doses of either placebo or streptokinase. There was no difference in mortality or the rate of surgery in the two groups [15]. Despite the negative endpoint, at 3 months there was at least a 90% improvement of the chest x-ray in 75% of patients who received streptokinase [15]. A subsequent trial of streptokinase for complicated parapneumonic effusions reduced the mean area of shadowing from 54% on admission to 24.5% at the time of discharge; however, at the 6-month interval follow-up the mean area of pleural shadowing had been reduced even further to 4.7% [16]. Similarly, in the trial of a reduced dose t-PA/DNase, the pleural opacity was reduced from 16% at discharge to 3.8% at 30 days [13]. The discrepancy of the pleural opacity improvement at day 7 or discharge compared to that at 1-6 months supports that complicated parapneumonic effusions and empyema can improve with time and antibiotic therapy. The fact that antibiotics can achieve excellent concentrations within the pleural space further supports this notion (7). This is the third observation.

3. Most patients with a parapneumonic effusion treated medically have a near-complete resolution at 3 and 6 months [13, 15-16]

Thus, if treatment success is considered to be a live patient who does not require surgery, then a complete resolution of the effusion on imaging during hospitalisation cannot serve as a surrogate marker.

Each patient described in the case series was initially considered medical treatment failures in need of surgical intervention, but in retrospect was in fact, a treatment success. There were several pitfalls in the management of these patients. The first patient was thought to be such a considerable treatment failure to be discharged to a hospice, only to make a complete recovery. The treating physicians failed to recognise the first observation, that with adequate medical therapy the team might have prevented death, and a decision for hospice care was premature for a disease that can often resolve with conservative therapy. In the second patient, physician perception of the need for complete drainage led to two additional chest tubes, a prolonged stay, and nearly missed surgical intervention. This belief disregarded the second observation, that a non-resolving opacity on imaging was not indicative of treatment failure and that persistent pleural opacities should be expected at discharge. The third patient was hospitalised for 2 weeks with multiple interventions and a recommendation for surgery due to persistent radiological opacities, only to recover completely. The treating physicians failed to recognise the final observation that pleural space opacities can improve with time and antibiotics.

The outcomes of the patients described are consistent with a case report of a pediatric patient with persistent pleural opacity resolving completely with appropriate antibiotic therapy [17]. In a retrospective analysis of 64 pediatric patients with empyema treated with antibiotics alone, only 2 (3.1%) required readmission for surgery [18]. In another retrospective cohort of patients diagnosed with complicated parapneumonic effusions, 14 of 16 were successfully treated with antibiotics alone [8]. Treatment failure, defined as the need for surgical intervention in case control studies, may occur through outcome differential misclassification bias due to investigator driven measures of success [19]. When comparing clinical characteristics of medical failures or success in one retrospective study of 85 patients, the only meaningful characteristic for progressing to surgery was purulence, rather than relevant clinical markers: persistent leukocytosis, C-reactive protein elevation, or fever [20]. This supports the notion that physician bias may contribute to perceived treatment failure.

Careful selection of patients for early surgical intervention should be in collaboration with thoracic surgery, infectious disease, and pulmonary medicine and attempt to achieve consensus. Early decortication might be beneficial for patients with a significant risk of death, including an elevated RAPID score or those with extensive multiloculated effusion and sepsis syndrome in an attempt to shorten the duration of the hospitalisation [9]. Questions remain regarding the indications and the optimal timing of surgical intervention. Further investigation is needed to understand which variables predict failure of medical therapy and at what point in the disease process should surgery be considered.

The median inpatient stay with parapneumonic effusions is 15 days, with 20% remaining hospitalised for over one month. If medical therapy is selected, attention should be given to signs of resolving sepsis including normalising temperature, leukocytosis, and C-reactive protein in addition to improvement, but not resolution, of the effusion. Patients who demonstrate clinical improvement should be administered 2-4 weeks of outpatient antibiotics with close follow up. In our case series of three patients, a total of 11 CTs were performed. Multiple CTs may increase recognition of insignificant pleural fluid collections that would otherwise resolve with antibiotics alone, and one CT during hospitalisation is generally sufficient if there is clinical improvement.

CONCLUSION

Successful treatment of patients with parapneumonic effusion should be considered to be resolution of sepsis markers and radiographic improvement. Complete resolution of pleural opacities on chest imaging at discharge may not be necessary when there is clinical improvement. If outpatient patient adherence to antibiotics and follow up is expected, then further inpatient attempts at complete radiographic resolution may prolong hospital stay, lead to more invasive procedures, and lead to unnecessary surgery.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are base of this research.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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None.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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Declared none.

REFERENCES

[1] Light RW. Pleural Diseases. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins 2013.

[2] Light RW, Girard WM, Jenkinson SG, George RB. Parapneumonic effusions. Am J Med 1980; 69(4): 507-12. [http://dx.doi.org/10.1016/0002-9343(80)90460-X] [PMID: 7424940]

[3] Biswas A, Jantz MA, Barnes MD, Mehta HJ. Management of noncommunicating multiloculated pleural space infection with fibrinolytic augmented multiple chest tube drainage. J Bronchology Interv Pulmonol 2016; 23(2): e14-7. [http://dx.doi.org/10.1097/LBR.0000000000000263] [PMID: 27058724]

[4] Misthos P, Sepsas E, Konstantinou M, Athanassiadi K, Skottis I, Lioulias A. Early use of intrapleural fibrinolytics in the management of postpneumonic empyema. A prospective study. Eur J Cardiothorac Surg 2005; 28(4): 599-603. [http://dx.doi.org/10.1016/j.ejcts.2005.07.005] [PMID: 16129614]

[5] Strange C, Sahn SA. The clinician's perspective on parapneumonic effusions and empyema. Chest 1993; 103(1): 259-61. [http://dx.doi.org/10.1378/chest.103.1.259] [PMID: 8417890]

[6] Rahman NM, Maskell NA, West A, *et al.* Intrapleural use of tissue plasminogen activator and DNase in pleural infection. N Engl J Med 2011; 365(6): 518-26. [http://dx.doi.org/10.1056/NEJMoa1012740] [PMID: 21830966]

[7] Teixeira LR, Sasse SA, Villarino MA, Nguyen T, Mulligan ME, Light RW. Antibiotic levels in empyemic pleural fluid. Chest 2000; 117(6): 1734-9. [http://dx.doi.org/10.1378/chest.117.6.1734] [PMID: 10858410]

[8] Berger HA, Morganroth ML. Immediate drainage is not required for all patients with complicated parapneumonic effusions. Chest 1990; 97(3): 731-5. [http://dx.doi.org/10.1378/chest.97.3.731] [PMID: 2306975]

[9] Rahman NM, Kahan BC, Miller RF, Gleeson FV, Nunn AJ, Maskell NA. A clinical score (RAPID) to identify those at risk for poor outcome at presentation in patients with pleural infection. Chest 2014; 145(4): 848-55. [http://dx.doi.org/10.1378/chest.13-1558] [PMID: 24264558]

[10] Piccolo F, Pitman N, Bhatnagar R, *et al.* Intrapleural tissue plasminogen activator and deoxyribonuclease for pleural infection. An effective and safe alternative to surgery. Ann Am Thorac Soc 2014; 11(9): 1419-25. [http://dx.doi.org/10.1513/AnnalsATS.201407-329OC] [PMID: 25296241]

[11] Majid A, Kheir F. Concurrent intrapleural installation of tissue plasminogen activator and DNase for pleural infection. Ann Am Thorac Soc 2016; 13(9): 1512-8. [http://dx.doi.org/10.1513/AnnalsATS.201602-127OC] [PMID: 27333122]

[12] Mehta HJ, Biswas A, Penley AM, Cope J, Barnes M, Jantz MA. Management of intrapleural sepsis with once daily use of tissue plasminogen activator and deoxyribonuclease. Respiration 2016; 91(2): 101-6. [http://dx.doi.org/10.1159/000443334] [PMID: 26761711]

[13] Popowicz N, Bintcliffe O, De Fonseka D, *et al.* Dose de-escalation of intrapleural tissue plasminogen activator therapy for pleural infection. The alteplase dose assessment for pleural infection therapy project. Ann Am Thorac Soc 2017; 14(6): 929-36. [http://dx.doi.org/10.1513/AnnalsATS.201609-673OC] [PMID: 28324671]

[14] Bishwakarma R, Shah S, Frank L, Zhang W, Sharma G, Nishi SP. Mixing it up: coadministration of tPA/DNase in complicated parapneumonic pleural effusions and empyema. J Bronchology Interv Pulmonol 2017; 24(1): 40-7. [http://dx.doi.org/10.1097/LBR.0000000000000334] [PMID: 27984384]

[15] Maskell NA, Davies CWH, Nunn AJ, *et al.* U.K. Controlled trial of intrapleural streptokinase for pleural infection. N Engl J Med 2005; 352(9): 865-74. [http://dx.doi.org/10.1056/NEJMoa042473] [PMID: 15745977]

[16] Diacon AH, Theron J, Schuurmans MM, Van de Wal BW, Bolliger CT. Intrapleural streptokinase for empyema and complicated parapneumonic effusions. Am J Respir Crit Care Med 2004; 170(1): 49-53. [http://dx.doi.org/10.1164/rccm.200312-1740OC] [PMID: 15044206]

[17] Cremonesini D, Thomson AH. How should we manage empyema: antibiotics alone, fibrinolytics, or primary video-assisted thoracoscopic surgery (VATS)? Semin Respir Crit Care Med 2007; 28(3): 322-32. [http://dx.doi.org/10.1055/s-2007-981653] [PMID: 17562502]

[18] Long AM, Smith-Williams J, Mayell S, Couriel J, Jones MO, Losty PD. 'Less may be best'-Pediatric parapneumonic effusion and empyema management: Lessons from a UK center. J Pediatr Surg 2016; 51(4): 588-91. [http://dx.doi.org/10.1016/j.jpedsurg.2015.07.022] [PMID: 26382287]

[19] Wait MA, Sharma S, Hohn J, Dal Nogare A. A randomized trial of empyema therapy. Chest 1997; 111(6): 1548-51. [http://dx.doi.org/10.1378/chest.111.6.1548] [PMID: 9187172]

[20] Davies CW, Kearney SE, Gleeson FV, Davies RJ. Predictors of outcome and long-term survival in patients with pleural infection. Am J Respir Crit Care Med 1999; 160(5 Pt 1): 1682-7. [http://dx.doi.org/10.1164/ajrccm.160.5.9903002] [PMID: 10556140]