Management of Pleural Empyema: Don't Miss the Point!

Marios E. Froudarakis Demosthenes Bouros

Department of Pneumology, Democritus University of Thrace Medical School, Alexandroupolis, Greece

Pleural infections are an important health problem, since mortality and costs due to prolonged hospitalization remain quite high for a 'benign' disease supposed to be accurately treated [1, 2]. The goal of the management of pleural infection is the quick relief of sepsis in order to cure the patient. This results in reduced hospital stay, avoids surgical treatment, improves morbidity and mortality, and therefore reduces the total costs of treatment [1, 2]. Published guidelines on the management of pleural infection [3] seem to be more like 'eminence-' than 'evidence'-based guidelines, since many Cs or Ds, some Bs and only two As exist.

With respect to antibiotic treatment, the cornerstone of therapy, it should be borne in mind that *Streptococcus pneumoniae* is cultured in only 10%, while the incidence of *Streptococcus milleri*, *Staphylococcus aureus* and anaerobic bacteria is increasing [3, 4]. Indeed, microbiologic tests were globally disappointing in the identification of the causal pathogen [4]. First-line antibiotic treatment must be based on the local microbiology, patient history and coexisting illnesses, and differentiate between community- and hospital-acquired infections. Positive pleural fluid culture should help to adapt antibiotic therapy accordingly. A first-line treatment may contain penicillin or β -lactamase penicillin combined with metronidazole for the community-acquired infections [3]. For the hos-

pital-acquired infection, a combination should cover methicillin-resistant *Staphylococcus aureus* and anaerobes [3].

Tube drainage is indicated in the presence of pus or positive pleural fluid culture, loculations on chest ultrasonography (U/S)/computed tomography (CT) or an effusion covering at least 50% of the hemithorax [1]. Pleural fluid pH, especially pH <7.20, may also be helpful in decision-making, provided that it has been done correctly and keeping in mind that different loculations may have different pHs [5]. Bedside chest U/S done by a respiratory physician is the gold standard (simple, fast and cheap) to detect loculations; concomitantly, the largest loculation for the insertion of the chest tube is determined [6–8]. The decision to remove the tube depends on the improvement in the patients' condition and also the findings on the chest U/S, which are necessary in the monitoring of these patients [1].

The use of fibrinolytics in pleural infection is a matter of debate. Phase II studies, a few of them randomized, were effective in improving the patients' condition, chest X-ray and pleural drainage [9–11]. Yet, the number of patients enrolled was small. A randomized trial (MIST-1) in the UK [12], enrolling 454 patients, showed no effect of streptokinase in the outcome of patients with pleural infection, which proved to have serious flaws,

since drainage was performed without imaging guidance, participating centers had little experience in treating empyema patients, no stratification according to the stage of the disease was proposed, and the primary endpoint was argued [13–16]. Of note, one A in the recent guidelines concerned the use of fibrinolytics and was based on this study [3]. Some of these flaws were repeated also in the second trial (MIST-2) [17], although this trial was positive for the combination of recombinant tissue plasminogen activator with DNase. Two meta-analyses, one in 2008 [18] and one recently published [19], showed that in patients with parapneumonic pleural effusion the use of fibrinolytics is beneficial, since surgical referral may not be indicated. Indeed, the primary endpoint in this patient population should be the control of sepsis in order to avoid surgery.

Early or late referral to surgery is still a matter of debate. It seems that early thoracoscopy is the method of choice in the fibrinopurulent stage [20, 21] as it is less invasive than open thoracotomy [1] and provides significant benefit compared to classic treatment in two randomized trials [22, 23] (although they were not blinded and included a small number of patients). Referral to surgery should be considered in case of persistent sepsis or unsuccessful drainage (late referral) [24] after additional examinations, e.g. bronchoscopy and chest CT, to exclude bronchogenic carcinoma.

In this issue of *Respiration*, Dusemund et al. [25] report results on their experience in empyema patients treated at the St. Gallen Hospital. Despite the limitation of the lack of a uniform decision-making algorithm due to the retrospective character of their study, they report on a relatively large patient population (78 empyema patients), reflecting very much the routine practice in general. According to their results, the main therapeutic interventions in empyema patients were early treatment initiation with intravenous antibiotics, chest tube drainage with routine use of intrapleural fibrinolytics (particularly in the presence of loculations) and the use of bedside chest U/S. It is also interesting to note that with this management, the empyema-related mortality rate was relatively low (5.1%; 4 of 78 patients); 2 patients died after surgical treatment, and 3 of the 4 deceased patients were aged over 90 and had severe comorbidities. An important finding in their study was the significant degree of persistent chest pain months after surgery, which may affect the quality of life in these patients.

In conclusion, treatment of a patient with pleural empyema should be restricted to experienced centers since diagnosis, assessment of severity and therapeutic management is complicated. A good understanding of the disease and of each individual case as well as rapid and successful management, as reported by Dusemund et al. [25], is not only beneficial for the patients themselves but also for the community, with a significant reduction in mortality and costs.

References

- 1 Koegelenberg CF, Diacon AH, Bolliger CT: Parapneumonic pleural effusion and empyema. *Respiration* 2008;75:241–250.
- 2 Froudarakis ME: Diagnostic work-up of pleural effusions. *Respiration* 2008;75:4–13.
- 3 Davies HE, Davies RJ, Davies CW: Management of pleural infection in adults: British thoracic society pleural disease guideline 2010. *Thorax* 2010;65(suppl 2):ii41–ii53.
- 4 Maskell NA, Batt S, Hedley EL, Davies CW, Gillespie SH, Davies RJ: The bacteriology of pleural infection by genetic and standard methods and its mortality significance. *Am J Respir Crit Care Med* 2006;174:817–823.
- 5 Rahman NM, Mishra EK, Davies HE, Davies RJ, Lee YC: Clinically important factors influencing the diagnostic measurement of pleural fluid pH and glucose. *Am J Respir Crit Care Med* 2008;178:483–490.
- 6 Koegelenberg CF, von Groote-Bidlingmaier F, Bolliger CT: Transthoracic ultrasonography for the respiratory physician. *Respiration* 2012;84:337–350.
- 7 Chen KY, Liaw YS, Wang HC, Luh KT, Yang PC: Sonographic septation: a useful prognostic indicator of acute thoracic empyema. *J Ultrasound Med* 2000;19:837–843.
- 8 Diacon AH, Brutsche MH, Soler M: Accuracy of pleural puncture sites: a prospective comparison of clinical examination with ultrasound. *Chest* 2003;123:436–441.
- 9 Bouros D, Schiza S, Tzanakis N, Chalkiadakis G, Drositis J, Siafakas N: Intrapleural urokinase versus normal saline in the treatment of complicated parapneumonic effusions and empyema. A randomized, double-blind study. *Am J Respir Crit Care Med* 1999;159:37–42.
- 10 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;170:49–53.
- 11 Froudarakis ME, Kouliatsis G, Steiropoulos P, Anevlavis S, Pataka A, Popidou M, Mikroulis D, Pneumatikos I, Bouros D: Recombinant tissue plasminogen activator in the treatment of pleural infections in adults. *Respir Med* 2008;102:1694–1700.
- 12 Maskell NA, Davies CW, Nunn AJ, Hedley EL, Gleeson FV, Miller R, Gabe R, Rees GL, Peto TE, Woodhead MA, Lane DJ, Darbyshire JH, Davies RJ: UK controlled trial of intrapleural streptokinase for pleural infection. *N Engl J Med* 2005;352:865–874.
- 13 Diacon AH, Koegelenberg CF, Bolliger CT: A trial of intrapleural streptokinase. *N Engl J Med* 2005;352:2243–2245, author reply 2243–2245.
- 14 Bouros D: A trial of intrapleural streptokinase. *N Engl J Med* 2005;352:2243–2245, author reply 2243–2245.
- 15 Rosa UW: A trial of intrapleural streptokinase. *N Engl J Med* 2005;352:2243–2245, author reply 2243–2245.

- 16 Bouros D, Antoniou KM, Light RW: Intrapleural streptokinase for pleural infection. *BMJ* 2006;332:133–134.
- 17 Rahman NM, Maskell NA, West A, Teoh R, Arnold A, Mackinlay C, Peckham D, Davies CW, Ali N, Kinnear W, Bentley A, Kahan BC, Wrightson JM, Davies HE, Hooper CE, Lee YC, Hedley EL, Crosthwaite N, Choo L, Helm EJ, Gleeson FV, Nunn AJ, Davies RJ: Intrapleural use of tissue plasminogen activator and DNase in pleural infection. *N Engl J Med* 2011;365:518–526.
- 18 Cameron RJ, Davies HR: Intra-pleural fibrinolytic therapy versus conservative management in the treatment of adult parapneumonic effusions and empyema. *Cochrane Database Syst Rev* 2008;2:CD002312.
- 19 Janda S, Swiston J: Intrapleural fibrinolytic therapy for treatment of adult parapneumonic effusions and empyemas: a systematic review and meta-analysis. *Chest* 2012;142:401–411.
- 20 Light RW: A new classification of parapneumonic effusions and empyema. *Chest* 1995;108:299–301.
- 21 Petrakis IE, Kogerakis NE, Drositis IE, Lasithiotakis KG, Bouros D, Chalkiadakis GE: Video-assisted thoracoscopic surgery for thoracic empyema: primarily, or after fibrinolytic therapy failure? *Am J Surg* 2004;187:471–474.
- 22 Wait MA, Sharma S, Hohn J, Dal Nogare A: A randomized trial of empyema therapy. *Chest* 1997;111:1548–1551.
- 23 Bilgin M, Akcali Y, Oguzkaya F: Benefits of early aggressive management of empyema thoracis. *ANZ J Surg* 2006;76:120–122.
- 24 Bouros D, Antoniou KM, Chalkiadakis G, Drositis J, Petrakis I, Siafakas N: The role of video-assisted thoracoscopic surgery in the treatment of parapneumonic empyema after the failure of fibrinolytics. *Surg Endosc* 2002;16:151–154.
- 25 Dusemund F, Weber MD, Nagel W, Schneider T, Brutsche MH, Schoch OD: Characteristics of medically and surgically treated empyema patients: a retrospective cohort study. *Respiration* 2013;86:288–294.