ORIGINAL ARTICLE

COMMUNITY-ACQUIRED THORACIC EMPYEMA – DOES MICROBIOLOGICAL IDENTIFICATION MATTER?

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Abstract

Objectives: *To describe the clinical characteristics, comorbidities and clinical outcome of hospitalized patients with the diagnosis of community acquired thoracic empyema in our hospital, with particular emphasis on the impact of identification of the causative agent.*

Methods: *We performed a retrospective review of the clinical files of hospitalized adult patients diagnosed with community acquired thoracic empyema between 2012 and 2016.*

Results: *A total of 81 patients (64 men and 17 women), with a mean age of 54.6+-17.3 years, were included in this study. It was possible to identify the microbiological agent in 59.3% (n=48) of the patients. The median length of hospital stay was 29 days (P25=20 and P75=44.5) and a tendency to longer duration was seen in patients with a microbiological isolation (32 days vs 23 days; p=0.056). No significant difference was observed between patients with and without microbiological isolation, regarding the mortality.*

Conclusion: *In this group of patients a positive pleural fluid culture tends to be associated with longer lengths of hospital stay, which may lead to speculation that they were more advanced infectious processes at the time of diagnosis.*

INTRODUCTION

Thoracic empyema refers to an infected purulent and often loculated pleural effusion, usually a complication of pneumonia. It is a potentially life-threatening condition, that is associated with high morbidity, mortality and need for invasive treatments and its incidence seems to be increasing globally[1]. It was described by Mikkola et al[2] an overall survival at 5 years of 80.6%. Common empyema associated comorbidities are known, such as smoking, Chronic Obstructive Pulmonary Disease (COPD), diabetes mellitus and arterial hypertension[3].

The treatment is challenging. Antibiotic therapy is the hallmark of therapy, and usually chest tube drainage, surgical debridement or even thoracotomy is necessary[4]. As soon as the empyema is identified, a chest tube drainage is recommended for all patients and they should receive antibiotics based on bacterial results of pleural fluid or blood culture and their antibiotic susceptibility tests; empirical antibiotic therapy should be started in case of sterile cultures or if the patient's clinical condition does not allow waiting for the result of the cultures. It must be based on local hospital protocol and antibiotic resistance patterns[4].

Little is known about the impact of the microbiological agent identification on the outcome of the patient with thoracic empyema, and what is found in the literature is controversial. For example, although the study of Jimenez et al[5] suggests that microbiological investigation of pleural fluid adds very little to the standard

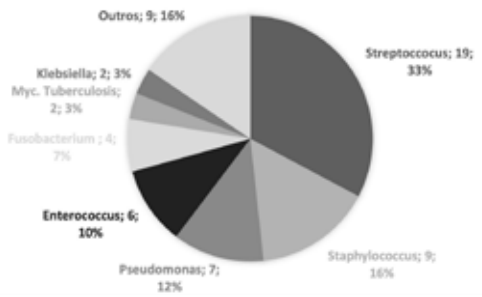

Figure 1 *Microbiological isolation*

management of parapneumonic effusions, in the study conducted by Okiror L et al[6], it seems that culture-positive empyema was associated with worse outcomes in patients submitted to debridement or decortication.

Our aim is, then, to describe the clinical characteristics, comorbidities and clinical outcome of hospitalized patients with the diagnosis of community acquired thoracic empyema in our hospital, with emphasis on the impact of identification of the etiologic agent.

METHODS

The clinical files of hospitalized adult patients diagnosed with community acquired thoracic empyema between 2012 and 2016 were reviewed. Hospital-acquired empyemas were excluded. We analyzed the medical records of each patient regarding age, sex, comorbidities, microbiological identification, clinical evolution and outcome. Continuous variables are expressed as mean/median and standard deviation/interquartile range, using Mann-Whitney U Test. A p-value of <0.05 was considered statistically significant and all analyses were conducted using the SPSS software package (IBM SPSS Statistics 23).

RESULTS

The analyzed sample consisted of 81 patients, of which 64 (79.0%) were men and 17 (21.0%) were women. The mean age was 54.6 +/- 17.3 years. Empyemas were on the right side in 41 patients (50.6%) and bilateral in 3 patients (4.9%). The most frequent comorbidities were smoking (51.9%, n=42), alcoholism (35.8%, n=29), arterial hypertension (30.9%; n=25), chronic obstructive pulmonary disease (COPD) (17.3%; n=14) and diabetes mellitus (14.8%; n=12) (Table 1). Almost one third of the patients (32,7%) needed intervention by Stomatology during hospital stay.

The pleural fluid of each patient was collected by thoracentesis, chest tube drainage or intraoperatively and it was possible to identify the causative agent of the

Table 1 **Patients data**

	n	%
Patients (n=81)		
Male	64	79
Female	17	21
Mean Age, years (SD)	54.6 (17.3)	
Empyemas (side)		
Right	41	50.6
Left side	37	44.5
Bilateral	3	4.9
Comorbidities		
Smoking	42	51.9
Alcoholism	29	35.8
Arterial Hypertension	25	30.9
COPD	14	17.3
Diabetes mellitus	12	14.8
Active neoplasms	9	11.1
Drug addiction	8	9.9
Cardiac failure	8	9.9
Hepatitis B and/or C	6	7.4
HIV	3	3.7
Hemodialysis	2	2.5

Table 2 **Microbiological identification rate**

Microbiological identification	n	%
Yes	48	59.3
No	33	40.7

thoracic empyemas in 59.3% of the cases (n=48) (Table 2).Regarding the 33 cases with negative pleural fluid, only one (3%) showed positive blood culture; for the remaining 48 cases with positive pleural fluid, 10 positive blood cultures (20.8%) were observed, with the same agent.

The most common genera of microorganisms were Streptococcus (39.5%, n=19), followed by Staphylococcus (18.8%, n=9), Pseudomonas (14.6%, n=7), Enterococcus (8.3%, n=4), Fusobacterium (6.2%, n=3), Mycobacterium tuberculosis (4.2%, n=2), Klebsiella (4.2%, n=2) and only

one reported case of each of the following species of microorganisms: Acinetobacter baumanii, Escherichia coli, Lactobacillus, Morganella morganii sabonii, Nocardia otitidiscavarium, Pneumocystis jirovecii, Prevotella denticola, Proteus mirabilis and Salmonella typhimurium (Fig. 1). In 16.6% of positive results (n=8), the culture was polymicrobial.

Considering the targeted antibiotic treatment of patients with positive pleural fluid culture, 37 patients (77%) were submitted to first-line antibiotics only, while the remaining 23% (n=11) needed, at least, second-line targeted treatment. Regarding patients without microbiological isolation (n = 33), only one third (n=11) needed the escalation of the antibiotic regimen.

Fifty-eight patients (71.6%) underwent surgery, of which 31 (38.3%) in the form of video-assisted thoracoscopic debridement (VATS-d) and 27 (33.3%) of thoracotomy and decortication (T-D).The remaining 23 patients (28.4%) received standard treatment with chest tube drainage and respiratory physiotherapy, as we can see in Table 3. All patients were treated with antibiotics.

In the description of complications, for each type of surgical intervention (VATS-d or T-D) patients were divided into three groups: patients without complications, patients with minor complications (Clavien-Dindo I -II) and patients with major complications (Clavien-Dindo III - IV) – Table 3. Regarding patients submitted to VATS-d, 24 patients (77.4%) had no complications, 3 patients (9.7%) experienced minor complications (2 prolonged air leaks - >3days; 1 hemothorax with conservative management) and 4 (12.9%) had major ones (2 patients with persistent infection after debridement underwent thoracotomy with decortication; 1 re-operation due to hemothorax; 1 refractory respiratory failure needing mechanical ventilation). Considering patients submitted to T/D, 13 (48.1%) did not have complications, 6 (22.2%) had minor complications (6 prolonged air leaks) and 8 had major complications needing reoperation (3 prolonged air leaks; 2 hemothorax; 2 empyema recurrence; 1lobar necrosis) – Table 3.

The authors noticed that 26.1% (n=6) of patients submitted to standard treatment needed Intensive Care, mainly for septic shock; two of them needed to be mechanically ventilated. Regarding the 31 patient's group that underwent VATS-d, a quarter (n=8) needed Intensive Care, but only 1 of them after surgery. Finally, 4 patients (14.8%) were admitted in ICU after thoracotomy and 7 (25.9%) needed this kind of care before thoracotomy was held.

The overall mortality was 6.2% (n=5), in which 2 patients underwent thoracotomy, 1 underwent VATS-d and 2 were submitted to standard treatment. The three post-operative deaths occurred in patients with several comorbidities (2 terminal hemodialysis and multiple cardiovascular risk factors, and 1 primary immunodeficiency). The remaining 2 patients that were treated with standard chest tube insertion were not fit enough for surgery.

The global median of hospital stay was 29 days (P25=20 and P75=44.5) and a tendency to longer dura-

Table 3 **Treatment and outcome. Variables are presented as n (%).**

	Standard-treatment	VATS-d	*T-D*	*Total*
Number of patients	23 (28.4)	31 (38.3)	27 (33.3)	81 (100)
Positive pleural culture	14/23 (61.0)	13/31 (41.9)	21/27 (77.7)	81 (100)
Post-surgical complications (n=58)				
No complications		24/31 (77.4)	13/27 (48.1)	37 (63.8)
Clavien-Dindo I and II		3/31 (9.7)	6/27 (22.2)	9 (15.5)
ClavienDindo III and IV		4/31 (12.9)	8/27 (29.6)	12(20.1)
ICU admission				
Yes	6/23 (26.1)	8/31 (25.8)	11/27 (40.7)	25 (30.9)
No	17/23 (73.9)	23/31 (74.2)	16/27 (59.3)	56 (69.1)
Outcomes				
Discharged home	19/23 (82.6)	26/31 (83.9)	21/27 (77.8)	66 (81.5)
Transferred to other Hospitals	2/23 (8.7)	4/31 (12.9)	4/27 (14.8)	10 (12.2)
Deaths	2/23 (8.7)	1/31 (3.2)	2/27 (7.4)	5 (6.2)

Table 4 **Length of hospital stay considering treatment and microbiological identification**

	Standard-treatment n=23	VATS-d n=31	T-D n=27
Positive culture	28.5+/-5.2 days	31.1+/-5.1 days	34.0+/-5.2 days
Negative culture	22.3+/-4.2 days	23.5+/-6.2 days	25.5+/-4.7 days
p-value	0.09	0.048	0.065

Table 5 **Complication cases considering treatment and microbiological identification***

	VATS-d n=31	Thoracotomy n=27	Total
Positive culture	5	10	15
Negative culture	2	4	6
p-value	0.049	0.01	0.03

**Notice that just 26 patients had post-operative complications*

tion was seen in patients with a microbial isolation (32 days vs 23 days; p=0.056). As we can see in Table 4, it was found that patients with positive cultural empyema submitted to VATS-d had longer hospitalizations than negative ones (31.1+/-5.1 days vs 23.5+/-6.2 days), with a statistically significant difference (p = 0.048). A trend towards longer hospital stays in positive culture patients undergoing thoracotomy or standard treatment was also observed (34.0+/-5.2 day svs 25.5+/-4.7 days and 28.5+/-5.2 days vs 22.3+/-4.2 days, respectively), however statistical significance difference was not achieved (p = 0.065 and p = 0.09). The median length of hospital stay after surgery was also longer in positive empyema patients (17days vs 8.5days;p<0.01). Another significative statistical difference was observed in terms of surgical complications rate: there were noticed complications in 5 cases in the positive empyema group and 2 cases in the negative empyema group submitted to VATS-d (p=0.049), and 10 cases in the positive empyema group and 4 cases in the negative empyema group submitted to T-D (p=0.01) - Table 5.

No significant difference was observed between patients with and without microbiological isolation, with respect to the mortality.

DISCUSSION AND CONCLUSION

Consistent with published epidemiology, this study shows that empyema is predominantly a male disease, most often affecting middle-aged people and is usually right-sided[7], and the main associated comorbidities basically are the same as those described in the literature like smoking, alcoholism, COPD and diabetes mellitus[3].

Regarding microbiological isolation rate, there are reports that range from 25%[8]-37%[9] to 60%[10]. In this study, the bacterial identification was 59.3%. A lot of causes can explain this number, such as the lack of harvest quality, previous antibiotic treatment or low-sensitive diagnostic tests, despite approaching the highest rates described in literature.

Another finding in line with the literature was microbiologic etiology, with particular emphasis on the predominance of genera Streptococcus, Staphylococcus, Pseudomonas and Enterococcus as well as anaerobes (Fusobacterium and Prevotella)[5,11,12]. In another study, Maskell et al[13] revealed a higher percentage of strepotococcal empyema (approximately 50%), but with similar percentages in relation to the other genera. In our sample, only 16.6% were polymicrobial, in contrast with Lieberman et al[14], where they observed multiple pathogens in up to 50% patients.

The median length of hospital stay was 29 days, similar to Nielsen et al[15]. The authors observed a tendency to longer length of hospital stay in patients with positive cultural empyema (32 days vs 23 days, p=0.056), regardless of the type of treatment performed (VATS-d, T-D or standard treatment), as well as a longer median length of hospital stay after surgery and higher surgical complications rate in this group of patients (Table

5), with statistically significant differences (p=0.032 and p=0.03, respectively). These results are in agreement with Okiror et al[6], which demonstrates that patients with positive empyemas had a longer duration of pleural drainage, longer length of hospital stay and are more likely to develop postoperative complications than those with no active bacterial pleural infection. On the other hand, Jimenez et al[5] did not notice any difference between positive and negative cultural pleural fluid patients, suggesting, therefore, that routine culture of pleural fluid in mild empyema should not be performed. However, although the sample in Jimenez et al[5] study contained 259 patients, the microbiological identification rate was only 19.3%, which may explain the similarity of results between positive and negative empyemas.

We also noted better results in patients undergoing VATS-d comparing with T-D, in terms of complications rate and length of hospital stay. This may be due to patients in earlier stages being offered VATS-d with the main purpose of efficient drainage and avoid T-D. Curiously, the isolation rate in VATS-d group was lower than the T-D group (41.9% vs 77.7%), which suggest a less advanced infectious process. These conclusions come in accordance with the study conducted by Okiror et al[6], where authors claim that, with VATS, there is a shorter duration of pleural drainage and hospital stay and less postoperative complications and pain with a mortality and morbidity benefit, when compared with T-D.

Finally, in this study, the authors observed a 6.2% overall mortality rate (n=5), in which 2 patients underwent thoracotomy, 1 underwent VATS-d and 2 were submitted to standard treatment. The three post-operative deaths occurred in patients with several comorbidities. The overall mortality presented was much lower than what was published by Nielsen et al15, but similar to Davies et al[4], Jimenez et al[5] (4.6% mortality), and Okiror et al[6] (5.6% overall mortality, without any case of post-operative deaths) which can be explained by and early and aggressive medical management of patients with pleural infection.

The limitations of this study relate to the retrospective design with its usual selection bias as well as its information bias. Some clinical records, mainly the older ones, had less clinical details that may be important to describe.

We therefore conclude that, in this group of patients, positive pleural fluid cultures seem to be associated with longer lengths of hospital stay and greater number of postoperative complications, which may lead to speculation that they were more advanced infectious processes at the time of diagnosis, when compared with negative ones. We also conclude that patients who present in earlier stages, with possibility of VATS debridement have better outcomes. This reflects the importance of early reference to specialized respiratory centers.

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