



Candida empyema at a tertiary care, medical-surgical and organ transplant center: Microbiology, risk factors, treatment and outcome

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INTRODUCTION

- Invasive candidiasis (IC) is the most common fungal disease among hospitalized patients
- Deep-seated candidiasis (DSC) includes entities like intra-abdominal candidiasis, empyema, endocarditis, osteomyelitis, septic arthritis, mediastinitis, and meningitis, which can occur with or without candidemia
- Data from a multicenter study suggested that approximately equal numbers of critical care patients with IC had candidemia, candidemia plus DSC, or DSC alone¹
 - Intra-abdominal candidiasis and candida empyema were the two most common DSC
- Review of 63 cases of *Candida* empyema from a two Taiwanese medical centers²:
 - Malignancy was the leading underlying disease
 - The crude mortality rate was 61.9%
- Another review from USA
 - Described *Candida* empyema only in patients with malignancy³
 - 6-week mortality was 31%
- Our medical center
 - Is an acute care, adult hospital with high referral from other hospitals, level 1 trauma center
 - Has 586 acute medical-surgical and 156 ICU beds
 - Operates a large organ transplant population

GOAL

- To assess the risk factors, potential sources of infection, microbiology, treatment and outcome of *Candida* empyema in our center

METHODS

- Retrospective review of cases from the University of Pittsburgh Medical Center – January, 2006 to December, 2015 (10 years)
- Inclusion criteria:
 - Isolation of *Candida* spp from pleural fluid obtained by
 - thoracocentesis
 - intraoperatively
- Exclusion criterion:
 - Candida* isolated from drains in place > 24 hours
- SPSS software was used for data analysis
 - Categorical variables – Fisher exact test
 - Continuous variables – Wilcoxon rank-sum test
 - Independent risk factors for bad outcome - multivariate logistic regression model

REFERENCES

- Antifungal Therapy for Patients with Proven or Suspected Candida Peritonitis : Amarcand2, a prospective Cohort Study in French Intensive Care Units. Montravers P *et al.* Clin Microbiol Infect. 2016 Oct 13
- Report of a 63-case series of Candida empyema thoracis: 9-year experience of two medical centers in central Taiwan. Lin KH *et al.* J Microbiol Immunol Infect, 2014
- Fungal empyema thoracis in cancer patients. Nigo M *et al.* J Infect, 2016

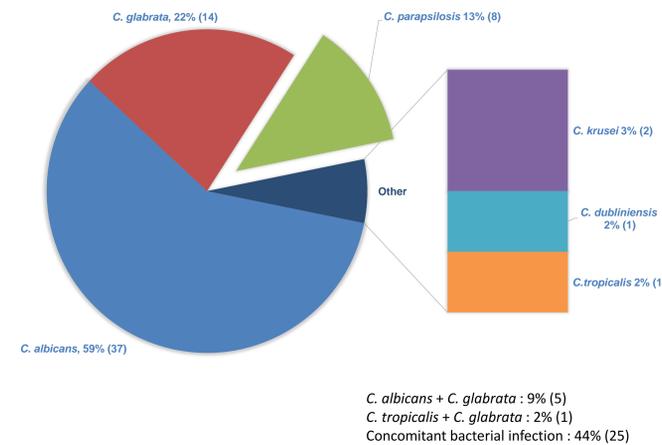
RESULTS

- Total 57 patients with empyema

Table 1: Demographics and underlying diseases

Clinical characteristics	Number of patients, n (%)
Age (years), mean ± SD	62 ± 15
Male, n (%)	37 (64.9)
Underlying diseases	
Malignancy	
Solid organ malignancy, n (%)	18 (31.5)
Hematologic malignancy, n (%)	0 (0)
Transplant	
Solid organ transplant, n (%)	11 (19.2)
Stem cell transplant, n (%)	0 (0)
Diabetes mellitus	9 (15.7)
Neutropenia	2 (3.5)
Cirrhosis	6 (10.5)
End stage renal diseases	2 (3.5)
Surgery within 90 days	40 (70.1)
Cardiothoracic, n (%)	28 (49.1)
Abdominal, n (%)	14 (24.5)
Others, n (%)	4 (7.0)

Microbiology



Outcomes

- Outcomes of treatment were assessed as follows
 - Treatment response – 49/57 (86%) patients
 - Resolution of empyema (clinical and microbiologic) with surgical drainage ± anti-fungal treatment
 - Treatment failure – 8/57 (14%)
 - Persistent infections, 2/57 (3.5%) – Patients with persistent signs and symptoms and culture positivity ≥ 7 days of source control and antifungal therapy
 - Recurrent infections, 6/57 (10.5%) – Recurrence of empyema after initial response
- Mortality
 - 14 -day mortality, 5/57 (8.8%)
 - 100-day mortality, 11/57 (19.3%)

Table 2: Sources of infection

Sources of infection	No of patients (%)	
Contiguous spread – related to previous thoracic or abdominal surgeries	Thoracic surgery	29 (51)
	Abdominal surgery	8 (14)
	Thoracic + abdominal surgery	3 (5)
Contiguous spread – Thoracic, abdominal or head and neck event not related to surgery	Esophageal tear/ perforation	7 (12)
	Small intestinal perforation	2 (4)
	Previous thoracentesis	2 (4)
	Oral/neck abscess leading to mediastinitis	1 (2)
	Cryptic/ unknown source	5 (9)

Table 3: Treatment

	Total no. of patients		Total no. of patients (%)	Survival beyond 100 days (%)	Mortality at 100 days (%)
Surgical drainage	57	Chest tube/ pigtail drainage	48 (84)	39 (81)	9 (19)
		Open thoracotomy	10 (18)	8 (80)	2 (20)
		VATS	9 (16)	9 (100)	0 (0)
		Multiple operative interventions	6 (11)	4 (67)	2 (33)
		Antifungal treatment	47	Fluconazole	33 (70)
		Caspofungin	11 (23)	9 (82)	2 (18)
		Voriconazole	3 (7)	1 (33)	2 (67)
No antifungal	10			6 (60)	4 (40)

Note that all patients underwent ≥1 drainage of empyema

Table 4: Risk factors for treatment failure

	Treatment response (49), % (n)	Treatment failure (8), % (n)	Univariate analysis, p-value	Multivariate analysis, p-value
<i>C. parapsilosis</i>	8 (4)	50 (4)	0.010	0.014
Concomitant bacterial infection	47 (23)	25 (5)	0.444	
Transplant	14 (7)	50 (4)	0.037	0.243
Prior history of empyema (bacterial)	6 (3)	38 (3)	0.031	*
Community- acquired	45 (22)	63 (5)	0.457	
History of surgery within 1 year	76 (37)	63 (5)	0.422	
Antifungal treatment	84 (41)	75 (6)	0.619	
VATS	16 (8)	13 (1)	1.000	
Operative drainage	16 (8)	25 (2)	0.619	

* prior h/o empyema was correlated with *C. parapsilosis* (co-linearity), so it was not included in multivariate analysis

100 day survival: Kaplan-Meier curve

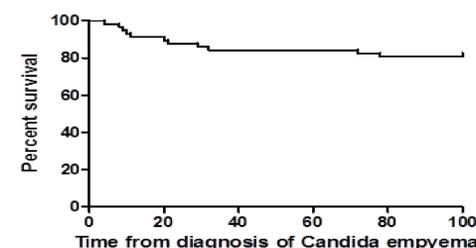


Table 5: Risk factors for mortality

	Number of patients	Factor present, % (n)	Factor absent, % (n)	P value
Presence of empyema on admission	26	22% (6)	16% (5)	0.74
Previous h/o empyema	6	33% (2)	18% (9)	0.32
Concomitant bacterial infection in pleural fluid	25	16% (4)	22% (7)	0.73
Concomitant blood culture positive	3	33% (1)	19% (10)	0.48
<i>C. parapsilosis</i>	8	25% (2)	18% (9)	0.64
Sepsis	14	50% (7)	9% (4)	0.002
Diabetes mellitus	9	33% (3)	17% (8)	0.35
Cirrhosis	6	33% (2)	18% (9)	0.32
SAPs II score ≥ 40	21/54	33% (7/10)	9% (3/10)	0.03
SOFA score ≥ 9	14/55	43% (6/10)	10 (4/10)	0.01
Admitted in ICU within 3 days of diagnosis	47	19% (9)	20% (2)	1.00
Previous antifungal prophylaxis and breakthrough empyema	5	20% (1)	19% (10)	1.00

DISCUSSION

- Candida* empyema is an uncommon clinical entity, but associated with poor outcome:
 - Treatment failure of 14%
 - 14- and 100-day mortality rate of 8.7% and 19%, respectively
- C. parapsilosis*, 3rd most common pathogen
 - Not recognized in previous studies
 - Associated with a prior history of bacterial empyema (p=0.03)
 - ? previous catheter drainage → contaminated with *C. parapsilosis* → biofilm → dislodge into pleural space
 - Independent risk factor for treatment failure, without any difference in mortality
- Better outcome was observed in our study compared to recently published studies^(2,3), probably secondary to
 - Fewer patients with malignancy
 - All patients achieved source control with drainage
- Significant risk factors for death: high SPS II and SOFA scores
 - 17.5% patient did not receive any antifungal treatment
 - Mortality was higher (40%) without antifungal vs 15 % with antifungal, (p=0.08)

CONCLUSIONS

- C. parapsilosis* is an emerging species for *Candida* empyema and associated with higher treatment failure
 - Its role in pathogenesis of empyema needs to be further studied
 - Propensity for persistence, biofilm, catheter-association?
- Mortality is associated with the severity of illness at the time of diagnosis
- Combined drainage/source control and antifungal is key to management
 - Candida* should be considered a pathogen, and all cases should be treated with an antifungal agent