Catching CAPA: The Healthcare Impact of COVID-19-Associated Pulmonary Aspergillosis in an Academic Medical Center

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INTRODUCTION

- COVID-19 associated pulmonary aspergillosis (CAPA) is a known complication of COVID-19 and carries a high mortality rate.
- While there are proposed diagnostic criteria from the European Confederation of Medical Mycology (ECMM) and International Society for Human and Animal Mycology (ISHAM), CAPA remains likely underdiagnosed.[1]
- Our objectives were to evaluate markers of disease severity, bacterial coinfections, and outcome measures in order to assess the clinical impact of CAPA in patients admitted with COVID-19 disease.

METHODS

- Retrospective chart review on adult patients admitted to a single-center, tertiary hospital from March 1, 2020 to May 1, 2022 with a positive COVID-19 PCR and probable or proven CAPA based on ECMM/ISHAM consensus criteria. Probable CAPA criteria includes:
  - Clinical factors: ICU with ARDS, refractory fever, chest pain, pleural rub, hemoptysis
  - CT evidence: pulmonary infiltrate, cavitating lesion
  - Mycological evidence: BAL microscopy/cx and/or serum galactomannan (GM) >0.5, and/or BAL GM >1.0 or any combination of the above.
- Admission data, ICU status, CAPA diagnostic methods, days to CAPA diagnosis, respiratory and blood cultures, and 90-day all-cause mortality were analyzed.

RESULTS

- Roughly 2000 patients were admitted to our institution during the 2 year time frame. Of those, 14 patients of met criteria for probable CAPA.
- 71.4% (10/14) were immediately admitted to the ICU. By day 14, 92.9% (13/14) were intubated.
- The average time from admission to CAPA diagnosis was 31.3 days. 12 patients were initially diagnosed by BAL galactomannan, while 2 patients were diagnosed by mold growth on respiratory culture.

RESULTS

Table 1: Individual Case Descriptions (n=14)

Age/Sex	Comorbid Conditions	COVID-19 Treatments Received	CAPA Mycological Diagnostic Method	Time from Admission to CAPA diagnosis	Other Hospital Acquired Infections	90 day All Cause Mortality
68 M	HTN, obesity	Tocilizumab, dexamethasone	BAL galactomannan	24 days	MSSA bacteremia and pneumonia *Enterobacter aerogenes* pneumonia	Alive
58 M	None	Remdesivir, dexamethasone	Respiratory culture	27 days	*Serratia marcescens* bacteremia, *Serratia marcescens*/*Enterococcus faecalis* empyema, *Staphylococcus lugdunensis*/*Acinetobacter baumanii* pneumonia	Alive
33 F	HTN, pregnancy	Dexamethasone	BAL galactomannan + respiratory culture	41 days	MSSA pneumonia	Unknown
45 M	None	Remdesivir, dexamethasone, monoclonal antibody	BAL galactomannan	14 days	*Serratia marcescens* bacteremia and pneumonia, MSSA pneumonia	Alive
78 M	HTN, arrhythmias, Class 3 obesity	Remdesivir, dexamethasone	Respiratory culture	5 days	None	Expired
62 M	HTN, RA, asthma	Dexamethasone, monoclonal antibody	BAL galactomannan + respiratory culture	11 days	*Klebsiella oxytoca*/*Enterococcus faecalis* bacteremia, *Klebsiella oxytoca*/*Escherichia coli* pneumonia	Alive
56 M	DM2, obesity	None	BAL galactomannan	6 days	Candidemia, MRSA pneumonia	Expired
39 F	Obesity	Dexamethasone	BAL galactomannan + respiratory culture	44 days	MSSA bacteremia, ESBL-producing *Escherichia coli* pneumonia	Unknown
36 M	Asthma, HIV	Remdesivir, dexamethasone	BAL galactomannan + respiratory culture	139 days	*Pseudomonas mendocina*/MSSA pneumonia	Alive
58 M	None	Remdesivir, dexamethasone	BAL galactomannan + respiratory culture	20 days	None	Expired
49 F	HTN, obesity	Dexamethasone	BAL galactomannan	43 days	*Serratia marcescens* pneumonia	Expired
64 M	None	Dexamethasone	BAL galactomannan	6 days	*Enterobacter cloacae*/*Pseudomonas aeruginosa* pneumonia	Expired
51 M	HTN, current smoker	Dexamethasone	Serum galactomannan and BAL galactomannan	9 days	*Enterobacter cloacae* bacteremia and pneumonia, MSSA/*Klebsiella pneumoniae* pneumonia	Alive
66 M	HTN, arrhythmias, RA, COPD	Remdesivir, dexamethasone	BAL galactomannan	19 days	*Chryseobacterium indologenes*/*Klebsiella pneumoniae*/*Escherichia coli* pneumonia	Expired

Figure 1: Level of Care Required on Admission

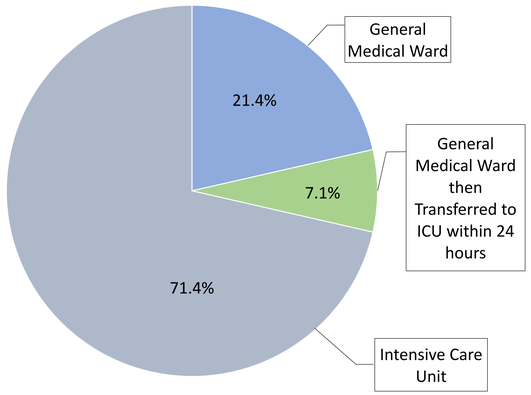
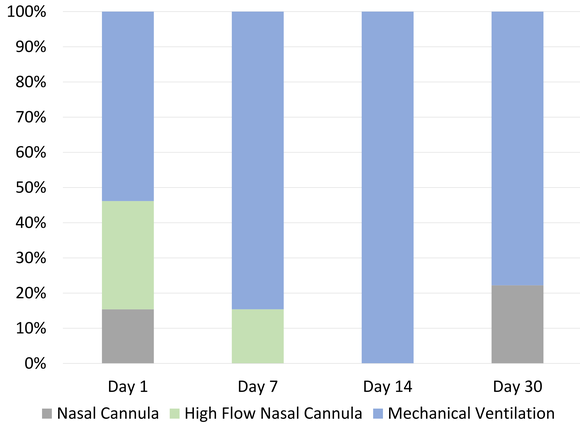


Table 2: Average Time (days)

Symptom Onset to Admission	9.9
Admission to CAPA Diagnosis	31.3
Days on the Ventilator	33.1
ICU Length of Stay	36.4
Total Hospital Length of Stay	43.6

Figure 2: Oxygen Requirements over Time



- 85.7% (12/14) also had bacterial growth on respiratory cultures. The most common pathogen was *Staphylococcus aureus* (6/14).
- 8 patients developed acute kidney injury, 5 of whom required new-onset hemodialysis. 3 developed acute liver injury and 3 had cardiac injury.
- All-cause mortality was 42.8% (6/14) at day 90. In patients with a CAPA diagnosis, the average length of ICU stay was 36.4 days and average total hospital length of stay was 43.6 days, compared to 6.3 and 12.5 days, respectively, for all patients admitted with COVID-19 disease.

DISCUSSION

- All patients were considered to have probable CAPA as no patients had available histologic evidence. Probable CAPA was rare at approximately 0.7% of all patients admitted with COVID-19 at our institution. However, patients with CAPA had higher mortality rates and longer hospitalizations.
- This population also had a very high rate of hospital acquired coinfections (85.7%) compared to bacterial (20.97%) and fungal (12.60%) coinfection rates in all patients hospitalized with COVID-19 disease.[2]
- Only one patient had a positive serum galactomannan, demonstrating the importance of obtaining a galactomannan from the respiratory tract for improved sensitivity.
- A majority of patients developed extra-pulmonary complications during hospitalization, potentially attributable to systemic effects of COVID-19, CAPA, or their treatment.
- The substantial burden of CAPA on hospital systems with already strained resources prompts further investigation for early diagnosis and management.

REFERENCES

1. Koehler P, Bassetti M, Chakrabarti A, et al. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. *Lancet Infect Dis.* 2021;21(6):e149-e162. doi:10.1016/S1473-3099(20)30847-1
2. Pakzad R, Malekifar P, Shateri Z, et al. Worldwide prevalence of microbial agents' coinfection among COVID-19 patients: A comprehensive updated systematic review and meta-analysis. J Clin Lab Anal. 2022 Jan;36(1):e24151. doi: 10.1002/jcla.24151. Epub 2021 Dec 1. PMID: 34851526; PMCID: PMC8761407.