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BACKGROUND

- Critically ill patients with coronavirus disease 2019 (COVID-19) are at the theoretical risk of invasive pulmonary aspergillosis (IPA) due to known risk factors.

METHODS

- We performed a retrospective chart review of all COVID-19 patients with *Aspergillus* isolates in respiratory samples during March 21 and April 22, 2020, at Mount Sinai Beth Israel, an acute care hospital in New York City.
- We used the clinical algorithm for ICU patients to classify pulmonary aspergillosis as either putative IPA or colonization (*Asp/ICU* algorithm)

RESULTS

- A total of 7 patients with COVID-19 who had one or more positive respiratory cultures for *Aspergillus fumigatus* were identified, all of whom were mechanically ventilated in the ICU.
- 4 patients were classified as putative IPA. The median age was 79 years, and all patients were male. The patients had been mechanically ventilated for a mean of 6.8 days (range: 1-14 days) before *Aspergillus* isolation.
- Serum galactomannan level was positive for only one patient.
- The majority of our cases received much higher doses of glucocorticoids than the dosage with a proven mortality benefit.
- All 4 patients died. The 3 patients classified as colonization also died. Causes of deterioration included Candidemia, Enterobacter bacteremia and *Stenotrophomonas maltophilia* pneumonia.

TABLE. Clinical characteristics of critically ill COVID-19 patients with putative invasive pulmonary aspergillosis.

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	82	79	77	77
Gender	Male	Male	Male	Male
Comorbid conditions				
Hypertension	No	Yes	No	No
Diabetes	No	No	No	Yes
Coronary artery disease	No	Yes	No	No
Chronic obstructive pulmonary disease	Yes	No	No	No
History of cerebrovascular accident	No	Yes	No	No
History of cancer	Yes	Yes	No	No
Dementia	No	No	No	No
Timing of positive culture for <i>Aspergillus fumigatus</i> (hospital day)	Day 15 and 20	Day 7, 10, and 16	Day 10 and 14	Day 10
Clinical features at <i>Aspergillus</i> isolation				
Fever	No	No	Yes	No
Respiratory status at <i>Aspergillus</i> isolation	Mechanical Ventilation	Mechanical Ventilation	Mechanical Ventilation	Mechanical Ventilation
New radiographic abnormalities on chest CT or X-ray	Worsening infiltrates	Opacities with dense consolidations	Cavitary pneumonia	Diffuse interstitial and patchy hazy opacities
White blood cell count (10 ³ /uL)	32.9	21.1	20.1	20.2
Platelet count (10 ³ /uL)	376	146	420	123
Procalcitonin (ng/mL)	0.16	0.30	3.30	9.34
Lactic acid (mmol/L)	1.0	3.6	1.6	3.7
Total bilirubin (mg/dL)	2.4	1.1	1.4	2.9
Serum creatinine (mg/dL)	2.6	3.1	1.5	4.1
Serum galactomannan	NA	0.71	Negative	Negative
Vasopressor support	Yes	Yes	Yes	Yes
Inpatient medications				
Glucocorticoids				
Cumulative dose in prednisone equivalent (mg)	932	1000	870	87
Starting date (hospital day)	Day 8	Day 2	Day 2	Day 10
Duration (day)	10	10	12	3
Tocilizumab	No	Yes	No	No
Antibiotics	Cefepime + Vancomycin	Cefepime + Vancomycin	Meropenem + Vancomycin	Cefepime + Vancomycin
Antifungal therapy	Voriconazole	Voriconazole	Voriconazole	Caspofungin

DISCUSSION

- Reports of pulmonary aspergillosis complicating severe COVID-19 required mechanical ventilation are emerging. Most patients did not have underlying immunocompromising conditions.
- Early diagnosis of IPA is critical but challenging in mechanically ventilated patients with COVID-19, because 1) Bronchoscopy and transbronchial biopsy are rarely performed given the risk of complications and transmission of the virus, and 2) pneumonia due to SARS-CoV-2 obscures the radiological findings of IPA.
- The performance characteristics of *Asp/ICU* algorithm for COVID-19 have not been validated.
- The diagnostic value of serum galactomannan for CAPA seems less promising.
- Too high dose of steroids could have contributed to high mortality of CAPA in our case series.

CONCLUSIONS

- Vigilance for secondary fungal infections will be needed to reduce adverse outcomes.
- Clinicians should have a high index of suspicion for CAPA when a critically ill COVID-19 patient in the ICU develops further respiratory decompensation, fevers, or new or worsening radiographic abnormalities of the lungs, particularly if there is no response to empiric antibacterial therapy.

REFERENCES

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