Covid-19 Associated Pulmonary Aspergillosis (CAPA)

Suspect in critically ill COVID-19 patients with refractory respiratory failure for more than 5–14 days, despite receiving all support recommended for COVID-19 patients who are critically ill.

Diagnosis

Clinical and radiological features may be non- specific

Imaging

Lesions suggestive of Invasive Pulmonary Aspergillosis (IPA) can be hidden or mimicked by lung involvement in severe COVID-19 patients. eg: halo sign is a characteristic radiological feature of IPA, due to local infarction. But endotheliopathy in severe COVID-19 cause thrombosis and local infarction leading to halo sign.

However, **multiple pulmonary nodules with cavitation** described in CAPA patients are rarely seen with COVID-19 alone. Therefore, urgent investigations are indicated to exclude IPA.

Risk factors

- ? COVID-19 infection itself
- Chronic corticosteroid therapy
- Dexamethasone treatment
- Anti-IL-6-directed strategies

Clinical features

- Refractory fever for > 3 days without an obvious cause
- New fever after a period of defervescence of longer than 48 h during appropriate antibiotic therapy, without an obvious cause
- Worsening respiratory status (eg, tachypnea or increasing oxygen requirements)
- Pleural rub
- Chest pain
- Haemoptysis

Mycological evidence

Preferred specimens for fungal diagnostics are respiratory samples

Bronchoscopy

Allows direct inspection of the trachea and bronchi to identify patients with aspergillus trachea-bronchitis

But, due to aerosol generation and high risk of viral transmission, diagnostic bronchoscopy is not done usually in patients with COVID-19

Bronchoscopy is primarily indicated in patients with suspected secondary infection, especially if the patient has already tested negative for SARS-CoV-2

Specimens

- Bronchoalveolar lavage fluid (BAL) and lung biopsy samples
- BAL samples for fungal culture

Container

Sterile screw capped container

Transport

At room temperature ASAP accompanied with a duly filled request form

Lung biopsy samples

Sterile screw capped container with sterile saline for fungal studies accompanied with a duly filled request form

Sterile screw capped container with formal saline for histopathology accompanied with a duly filled request form

Tissue culture and tissue microscopy showing invasive growth of septate fungal hyphae represent the diagnostic gold standard in proving infection

Aspergillus galactomannan antigen (GM)

Main diagnostic test to diagnose secondary IPA in patients with severe viral infection. Detection of GM in BAL fluid is highly indicative of IPA, as the antigen is released during active fungal growth. However, it does not prove tissue invasion, and the likelihood of infection is increased if serum GM is detected, though its sensitivity is low in CAPA.

Specimen

- BAL
- 2cc serum

Container

- Sterile screw capped container (for BAL)
- Sterile plain tube (for serum)

Transport

Send to the laboratory at room temperature, as soon as possible, accompanied with a duly filled request form.

Proven CAPA

Histopathological or direct microscopic detection, or +/- aspergillus recovered by culture from material obtained by a sterile aspiration or biopsy from a pulmonary site

Probable CAPA

Clinical factors: Pulmonary infiltrate or cavitating infiltrate (not attributed to another cause)

Combined with mycological evidence ≥1;

positive BAL direct smear

positive BAL culture

serum GM index >0·5 or BAL GM index ≥1·0

Possible CAPA: Pulmonary infiltrate or cavitating infiltrate or nodules (not attributed to another cause) + mycological evidence (eg: fungal culture, or GM) obtained via non-bronchoscopic lavage

Treatment

First line treatment for possible, probable, and proven CAPA is IV or oral voriconazole

Voriconazole	Body weight	Day 1	Day 2 onwards
IV	-	6mg /kg 12 hourly	4mg/ kg 12 hourly
Oral	body weight > 40kg	400 mg 12 hourly	200 mg 12 hourly
	body weight < 40kg	200 mg 12 hourly	100 mg 12 hourly

- Duration – depends on the serum galactomannan titre. Need to treat until the titre is <0.5

Drawbacks to use of voriconazole in patients with severe COVID-19

- Narrow therapeutic window
- Drug–drug interactions due to metabolism via Cytochrome P450
- Prolongation of QT interval

Primary alternative for treatment of CAPA

- Amphotericin B deoxycholate - IV 1 mg / kg / day
- Liposomal amphotericin B - IV 3-5 mg / kg / day

Nephrotoxicity may further decline renal function, especially in patients who already have AKI by renal trophic COVID- 19 virus

*In pregnancy and lactation: Avoid voriconazole (FDA risk category D), alternative is any preparation of amphotericin B (FDA risk category B)

References

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