Challenges of COVID-19 and invasive fungal infections

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All identified organisms as a proportion of total number of organisms per pathogen

<table>
<thead>
<tr>
<th>Pathogen type: Bacteria</th>
<th>Co-infection (N = 1910) No. (%)</th>
<th>Superinfection (N = 480) No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>148 (7.7)</td>
<td>13 (2.7)</td>
</tr>
<tr>
<td><em>Haemophilus influenza</em></td>
<td>127 (6.6)</td>
<td>6 (1.3)</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>82 (4.3)</td>
<td>6 (1.3)</td>
</tr>
<tr>
<td><em>Acinetobacter spps</em></td>
<td>78 (4.1)</td>
<td>107 (22.3)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>73 (3.8)</td>
<td>33 (6.9)</td>
</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>10 (0.5)</td>
<td>18 (3.8)</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>189 (9.9)</td>
<td>28 (5.8)</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>156 (8.2)</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em></td>
<td>29 (1.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><em>Bordetella</em></td>
<td>3 (0.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em></td>
<td>32 (1.7)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td><em>Pseudomonas</em></td>
<td>67 (3.5)</td>
<td>52 (10.8)</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>14 (0.7)</td>
<td>22 (4.6)</td>
</tr>
</tbody>
</table>

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## All identified organisms as a proportion of total number of organisms per pathogen

<table>
<thead>
<tr>
<th>Pathogen type: <strong>Viruses</strong></th>
<th>Co-infection (N = 1910) No. (%)</th>
<th>Superinfection (N = 480) No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-SARS-CoV-2a coronavirus strains</td>
<td>38 (2.0)</td>
<td>9 (1.9)</td>
</tr>
<tr>
<td>Human influenza A</td>
<td>426 (22.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Human influenza B</td>
<td>73 (3.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>72 (3.8)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td>17 (0.9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td>20 (1.0)</td>
<td>9 (1.9)</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>68 (3.6)</td>
<td>11 (2.3)</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>35 (1.8)</td>
<td>2 (0.4)</td>
</tr>
</tbody>
</table>
All identified organisms as a proportion of total number of organisms per pathogen

<table>
<thead>
<tr>
<th>Pathogen type</th>
<th>Co-infection (N = 1910)</th>
<th>Superinfection (N = 480)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Fungi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucor</td>
<td>6 (0.3)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Candida spp.</td>
<td>19 (1.0)</td>
<td>90 (18.8)</td>
</tr>
<tr>
<td>Aspergillus</td>
<td>128 (6.7)</td>
<td>65 (13.5)</td>
</tr>
</tbody>
</table>

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Clinicians’ challenges in managing patients with invasive fungal diseases in seven Asian countries: An Asia Fungal Working Group (AFWG) Survey

- Physicians in Asia lack access to many advanced diagnostics in mycology.
- Among 292 respondents, 51.7% were infectious disease (ID) specialists.
- Only 37% of respondents had received formal training in medical mycology.
- They handled only around 2–4 proven cases of each fungal infection monthly, with invasive candidiasis the most common.
Clinicians’ challenges in managing patients with invasive fungal diseases in seven Asian countries: An Asia Fungal Working Group (AFWG) Survey

- Laboratory support, the majority had access to direct microscopy (96%) and his to pathology (87%).

- Galactomannan and azole levels were available to 60% and 25% of respondents.

- 74% of respondents used the empirical approach. Only 30% had an antifungal stewardship program in their hospital.
In this study, we found that ~28% of the mechanically ventilated patients had positive culture for mold species. Among whom almost 76% had positive GM on BAL. While BDG and GM using serum samples showed much lower sensitivity. Radiological imaging did not differ in those with CAPMI and those without. Our experience suggests that BAL culture and BAL GM represent the most useful diagnostic tools.
Autopsy-proven IMD occurred in 11 (2%) of 677 decedents:

- 8 CAPA, 2 unspecified IMD & one disseminated mucormycosis.
- Among 320 decedents who received mechanical ventilation, 6 (2%) had IMD.
The presence of either co-infection or superinfection was associated with poor outcomes, including increased mortality.
بیمار آقای ۶۲ ساله بعلت تب، لرز و تنگی نفس با %77 = Spo2 در تاریخ ۱۴۰۰/۱/۲۴ در بخش کووید بستری و ۵ روز بعد (۱۴۰۰/۱/۲۹) بعلت افت ساجریشن (۵۵/%) به بخش ICU منتقل می‌شود.

بیمار تحت درمان پروتکل های استاندارد کووید قرار می‌گیرد. در سابقه بیمار فشار خون + CAD دیابت و آنتی کوآگولان + نازوسین + پیرفنکس قرار می‌گیرد.

شرايط بيمار به نحوی است كه انتقال به بخش امکان پذير نيست. حدود يك ماه بعد بيمار بطور ناگهاني دچار تب، افت شديد ساجریشن و پلي پنه مي شود و در رادیوگرافی ريه انفلترياسيون دو طرفه ريه مشاهده مي شود.
Guidance on clinical management of CAPA

- Any of the following clinical findings:
  - refractory fever for more than 3 days or a new fever after a period of defervescence of longer than 48 h during appropriate antibiotic therapy, in the absence of any other obvious cause;
  - worsening respiratory status (eg, tachypnoea or increasing oxygen requirements);
  - Haemoptysis
  - pleural friction rub or chest pain

can trigger diagnostic investigations for CAPA in patients with refractory respiratory failure for more than 5–14 days despite receiving all support recommended for patients with COVID-19 who are critically ill.
Despite all of the limitations previously given, the following statement can be made for critically ill patients with COVID-19: **multiple pulmonary nodules or lung cavitation should prompt thorough investigation for IPA**, as they are rarely seen with COVID-19 alone and have been described in a small proportion of patients with CAPA to date.
اقدامات انجام شده جهت بیمار شامل موارد ذیل است:

ارزیابی سریع اولیه شامل:

A

1- کشت خون
2- کشت خلط
3- کشت ادرار
4- گالاكتومانان سرم

PCT - 5
CRP- CBC- 6
D-dimer- 7
اقدامات انجام شده جهت بیمار شامل موارد ذیل است (ادامه):

B: درمان امپریکال آنتی بیوتیکی:
- مروپن
- کلستین
- لینزولید
- وریکونازول؟؟

C: درمان امپریکال ضد قارچی؟

D: مشاوره ریه، بیهوشی، قلب؟
New clinical algorithm including fungal biomarkers to better diagnose probable invasive pulmonary aspergillosis in ICU

- Proven cases were defined by positive histological examination with visible hyphae or positive culture on sterile material.
- Possible cases were defined by the presence of host factors and radiological criteria.
- Probable cases were defined by host factors, radiological and microbiological criteria (culture, galactomannan (GM) antigen).

Aspergillus quantitative polymerase chain reaction (qPCR) has been included as microbiological criterion in the 2019 update.
Several studies analyzed the occurrence of pulmonary aspergillosis associated with COVID-19 reporting an incidence ranging from 1.7% to 34.4%.

Different risk factors were identified to be correlated with invasive Aspergillus infection. COVID-19 associated lymphopenia might be a crucial factor, as it is a well-known risk for opportunistic infections.

Moreover, mechanical ventilation and admission to ICU greatly increase the risk of fungal colonization potentially leading to invasive pulmonary aspergillosis.
Furthermore, corticosteroids currently represent the standard of care for patients hospitalized with COVID-19.

Other immunosuppressive agents (such as tocilizumab) are employed in specific groups of subjects, potentially increasing the risk of opportunistic infections.

Associated with an increase of IL-10, IL-6 levels.

The incidence of invasive aspergillosis was estimated to be 10-14% with an overall mortality of 48-55%.
Invasive fungal infections in patients with COVID-19: a review on pathogenesis, epidemiology, clinical features, treatment, and outcomes

INVASIVE CANDIDIASIS

- Invasive candidiasis usually presents as fever and worsening of clinical conditions in critically-ill and/or immune-suppressed patients.
- Signs and symptoms of candidiasis occurring at skin or mucosal surfaces could also be present.
- The majority of subjects do not show specific symptoms, and the diagnosis relies on the microbiological isolation of *Candida spp.* from a sterile site (typically blood cultures) or on the histopathological evidence of fungal infection in sterile tissue samples.
Invasive fungal infections in patients with COVID-19: a review on pathogenesis, epidemiology, clinical features, treatment, and outcomes

INVASIVE CANDIDIASIS

- The measurement of fungal cell wall component mannan, coupled to anti-mannan antibodies, and the detection of (1,3)-β-D-glucan in patients’ body fluids could be useful to rule in and rule out the disease.
Invasive fungal infections in patients with COVID-19: a review on pathogenesis, epidemiology, clinical features, treatment, and outcomes

INVASIVE CANDIDIASIS

Risk Factors:

- The presence of intravascular catheters
- Hospitalized patients with COVID-19, especially if severely ill, are almost invariably treated with antibiotics
- Earlier reports suggested a possible association between the use of tocilizumab, an anti-IL-6-receptor agent, and the development of candidiasis
- Small case series suggested an increased risk of candidemia in patients receiving corticosteroids.
- SARS-CoV-2 infection could be by itself associated with a heightened risk of candidiasis.
Thanks for your attention