Intra-abdominal candidiasis is associated with high mortality, repeated surgery and echinocandin resistance, and often not initially treated with antifungal agents

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**Background**
- Candidemia is generally accepted as the most common type of invasive candidiasis (IC), and it accounts for the overwhelming majority of cases included in clinical trials and other studies. Other types of IC are less well-characterized.
- A review at our center in 2010-2011 demonstrated that deep-seated candidiasis (DSC) accounted for 65% of IC, compared to only 35% for candidemia. Moreover, intra-abdominal candidiasis (IAC) accounted for 83% and 60% of abdominal candidiasis (IAC) represented 83% and 60% of DSC and IC, respectively.
- Our data and the limited published experience suggest that IAC is more common than recognized, and is associated with significant morbidity and mortality.

**Objectives**
- To describe the epidemiology, risk factors, treatment and outcome of patients with IAC

**Methods**
- Observational study of patients at our center with ≥1 sterile site culture positive for Candida spp. over 15 months (2010-11).

**Definitions**
- *Intra-abdominal candidiasis* (IAC) is defined by steriley-collected abdominal fluid cultures that are positive for Candida spp., in the setting of signs and symptoms consistent with an active infection. IAC generally results from gastrointestinal perforation or surgical leak.
- *Intra-abdominal infection* (IAI) refers to intra-abdominal abscesses (IAA) and peritonitis, which can be due to bacteria or Candida
- *Peritonitis* is defined as infected fluid in the peritoneal cavity with evidence of an inflammatory response
- *IAA* is defined as a localized pocket of infection that is walled-off by the host inflammatory response
- IAC was classified as:
  - Primary (spontaneous or dialysis-associated)
  - Secondary (seeded from GI tract during perforation or surgery)
  - Tertiary (persistence/recurrence after seemingly adequate treatment).

**Results**

**Background**

- IAC was more common than candidemia, accounting for 52% of 199 cases of IC

**Classification of IAC:**
- **Primary IAC** (15%): spontaneous ascites or peritoneal dialysis infections
  - Small bowel, 63%
  - Gastric feeding tube displacement, 25%
  - Colon, 11%
- **Secondary IAC** (85%)
  - post-abdominal surgery: 45%
  - gut perforation: 30%
  - transmural colitis, 16%
  - others (pancreatitis, cholangitis, etc.), 9%

**Types of abdominal surgery among patients with post-surgical IAC:**
- colon, 51%
- small bowel, 24%
- liver, 15%
- esophagus, 10%

**Characteristics of patients infected with FKS mutants**

<table>
<thead>
<tr>
<th>Isolate</th>
<th>Source</th>
<th>Days of Prior IC</th>
<th>FKS Mutation</th>
<th>Candida spp.</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca 674</td>
<td>DM, Obese</td>
<td>8</td>
<td>FKS1 – R674I</td>
<td>C. glabrata</td>
<td>Failure</td>
</tr>
<tr>
<td>Ca 1910</td>
<td>Multisystem TAP</td>
<td>68</td>
<td>FKS1 – S645P</td>
<td>C. tropicalis</td>
<td>Failure</td>
</tr>
<tr>
<td>Cg 102</td>
<td>Short gut syndrome</td>
<td>46</td>
<td>FKS2 – D632H</td>
<td>C. glabrata</td>
<td>Failure</td>
</tr>
<tr>
<td>Cg 35</td>
<td>Multisystem TAP</td>
<td>102</td>
<td>FKS2 – D632H</td>
<td>C. albicans</td>
<td>Failure</td>
</tr>
<tr>
<td>Cg 129</td>
<td>Coda’s Disease</td>
<td>9</td>
<td>FKS2 – D632H</td>
<td>C. glabrata</td>
<td>Failure</td>
</tr>
<tr>
<td>Cg 187</td>
<td>Coda’s disease</td>
<td>117</td>
<td>FKS2 – D632H</td>
<td>C. glabrata</td>
<td>Failure</td>
</tr>
<tr>
<td>Cg 309</td>
<td>Liver abscess</td>
<td>64</td>
<td>FKS1 – D632H</td>
<td>C. albicans</td>
<td>Failure</td>
</tr>
<tr>
<td>Cg 999</td>
<td>Multisystem TAP</td>
<td>122</td>
<td>FKS2 – D632H</td>
<td>C. glabrata</td>
<td>Failure</td>
</tr>
<tr>
<td>Cg 705</td>
<td>Esophaged CA, GI Perfor</td>
<td>7</td>
<td>FKS2 – D632H</td>
<td>C. glabrata</td>
<td>Failure</td>
</tr>
</tbody>
</table>

59% (30/51) of isolates were collected from patients with intra-abdominal candidiasis (n=51)

- All abscesses were drained prior to inclusion

**Outcomes**

- Mortality rate: 23%
  - IAC from GI perforation: 50%
  - IAC from other causes: 11%
  - p-value = 0.046

- Among the survivors, 27% developed tertiary IAC, requiring multiple surgeries and prolonged antifungal agents

- 38% were treated with surgical interventions without antifungal:
  - 20% died
  - 50% developed persistent Candida infection requiring antifungal subsequently

**Risk factors for FKS mutations among UPMC Candida isolates**

**Conclusions**

- IAC was the most common cause of IC at our center, and was associated with high mortality (especially following perforation), need for repeated surgeries, and emergence of echinocandin resistance
- All patients require antifungal therapy in addition to surgery, as clinicians cannot reliably identify patients who can be cured with surgical drainage alone
- Blood cultures have poor sensitivity, and IAC is under-recognized because of a dependence on IA cultures for diagnosis