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Evolving therapeutic strategies for fungal infections

INTRA-ABDOMINAL CANDIDIASIS IS ASSOCIATED WITH HIGH MORTALITY, REPEATED SURGERY AND ECHINOCANDIN RESISTANCE, AND OFTEN NOT INITIALLY TREATED WITH ANTIFUNGAL AGENTS

C.J. Clancy[1], R.K. Shields[1], **M.H. Nguyen**[1]

[1]Medicine, University of Pittsburgh, Pittsburgh PA, USA

Objectives. Intra-abdominal candidiasis (IAC) is accepted as the second most common form of invasive candidiasis, but it is less well-studied than candidemia. Our objectives were to describe the epidemiology, clinical manifestations, and outcomes of IAC at our center.

Methods. We performed an observational study of patients with ≥1 sterile abdominal culture (+) for Candida in 2010-11. IAC included peritonitis and intra-abdominal abscesses, and was classified as primary (spontaneous or dialysis-associated), secondary (seeded during GI perforation or surgery) or tertiary (persistence/recurrence).

Results. 199 patients had invasive candidiasis. Candidemia, IAC, IAC+candidemia and other deep-seated candidiasis accounted for 28%, 53%, 7% and 13% of invasive candidiasis, respectively. IAC was primary and secondary in 15% and 85% of patients. Secondary IAC resulted from surgery (45%), perforation (30%), transmural colitis including *C. diff* and Crohns (16%), and other causes (9%). 51% of patients with post-surgical IAC had a colon procedure, 24% small bowel procedure, 15% liver procedure and 10% esophagus procedure. 63% of perforations involved small bowel, 25% G-tube displacement and 11% colon. 11% of IAC were breakthrough infections during echinocandin therapy. 50% of patients with IAC had abscesses, 42% peritonitis and 8% peritonitis+abscesses. 58% of IAC was due to *C. albicans*, 23% *C. glabrata*, 8% *C. parapsilosis*, 4% *C. tropicalis*; 65% of patients were co-infected with bacteria. All patients had (+) intra-abdominal cultures for Candida, but only 12% had (+) blood cultures. *FKS* mutant strains were responsible for 5% of IAC, and represented 18% and 1.4% of *C. glabrata* and *C. albicans*, respectively. *FKS* mutants were recovered in 38% of breakthrough IAC, *vs.* 0.9% of non-breakthrough ($p<0.0001$). The mortality rate among patients with IAC was 23%; mortality was worst for patients with perforation (50% vs 11%; $p=0.046$). 27% of survivors developed tertiary IAC that required prolonged antifungal therapy and/or repeated surgeries. Overall, 38% of patients with IAC did not initially receive an antifungal agent; 50% of these patients developed persistent IAC, and 20% died.

Conclusions. IAC was the most common cause of invasive candidiasis at our center, and was associated with high mortality, need for repeated surgeries, and emergence of echinocandin resistance (particularly with breakthrough *C. glabrata* infections). Clinicians could not reliably identify patients who were cured with surgical drainage alone, indicating that all patients require antifungal therapy in addition to surgery. Blood cultures have poor sensitivity, and IAC is under-recognized because of a dependence on intra-abdominal cultures for diagnosis.