Does Candida Species Overgrowth Protect Against Clostridium difficile Infection?

To the Editor—We read with interest the article by Nerandzic et al [1] reporting the prevalence and acquisition of Candida species in stool of patients treated for Clostridium difficile infection (CDI). Although not specifically addressed in the article, the isolation of Candida spp from the stool of only 16% of pretreated patients is intriguing, given the high prevalence of Candida spp in the stool of normal healthy adults [2] and prior antibiotic exposure serving as a risk factor for both CDI and Candida spp overgrowth [3].

We recently performed a retrospective study of all hospitalized patients tested for CDI with concurrent (within 96 hours) stool cultures and seen in consultation by an adult infectious disease physician (F. A. M.) at Mercy, a 900-bed community hospital in St Louis, Missouri, from 1 September 2009 to 30 June 2012. Only the initial paired data during the study period were studied; patients on oral vancomycin at the time of either CDI testing or stool culture were excluded. CDI testing was performed by enzyme immunoassay (EIA; Premier Toxins A/B, Meridian Bioscience) from 1 September 2009 to 30 September 2010, and by polymerase chain reaction (PCR; Cepheid GeneXpert) from 1 October 2010 to 3 June 2012. Tryptic soy with 5% sheep blood and phenylethyl alcohol agar plates were used for isolation of targeted nonenteric pathogens including Candida spp. Growth covering ≥50% of an agar plate was considered “overgrowth.” Yeast was identified as either Candida spp presumptive albicans or Candida non-albicans (BactiCard, Remel). Exemption for patient informed consent was granted by the hospital institutional review board. Fisher exact test was used for statistical analysis with $P < .05$ considered significant.

Of 417 unique patients, 15 were excluded because of testing while on oral vancomycin. Of the remaining 402 patients, 360 (89.6%) were white; 215 (53.5%) were female. The age range was 19–94 years (mean, 62.5 years). CDI testing was performed by EIA and PCR in 150 (37.3%) and 252 (62.7%) cases, respectively. A total of 61 (15.2%) cases tested positive: EIA, 17 of 150 (11.1%) versus PCR, 44 of 252 (17.5%) cases ($P = .11$). Candida spp overgrowth was reported in 113 of 398 cases (28.3%); growth in 4 samples was not quantitated. Presumptive C. albicans grew in 87 (21.8%) and non-albicans Candida spp in 26 (6.5%) cases. Overgrowth of Candida spp was significantly less likely in CDI test-positive cases: 10 of 60 (16.7%) versus 103 of 338 (30.5%) cases (odds ratio, 2.2 [95% confidence interval, 1.1–4.5], $P = .03$).

To the best of our knowledge, this is the first report of a negative association between Candida spp overgrowth and CDI. A potential explanation for this finding includes prior antifungal therapy, a variable not examined in our study. Another explanation may be that C. difficile inhibits the growth of Candida spp; however, this is unlikely given decrease in yeast concentration in stool following CDI treatment reported by Nerandzic et al [1]. Alternatively,
*Candida* spp may protect against CDI by producing inhibitory substances as demonstrated against certain bacteria [4, 5]. Of interest, a recent study reported antifungal therapy as an independent risk factor for CDI [6].

**Note**

*Potential conflicts of interest.* Both authors: No reported conflicts.
Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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