Correspondence

Clostridium difficile Infection and Candida Colonization of the Gut: Is There a Correlation?

To the Editor—We read with interest the article of Manian and Bryant about the possible protective role of gut colonization by Candida species against Clostridium difficile infection (CDI) [1]. Although Candida has been involved as part of the normal intestinal microbiota [2], no recent data seem to confirm the authors’ results. Conversely, an opposite role for non-albicans Candida (NAC) colonization was suggested by Nerlandzic et al in a trial on 548 patients with CDI [3]. Recent observations conducted in our 1300-bed teaching hospital Policlinico “Umberto I” in Rome showed that patients treated for severe CDI developed at least 1 episode of candidemia, thus hypothesizing a link between CDI and candidemia [4].

We designed a prospective case-control study in diarrheic patients with suspected CDI from November 2013 until June 2014 to investigate whether Candida colonization of the gut and CDI may be linked. Stool specimens (n = 140; Bristol stool chart 5–7 [5]) from consecutive patients were evaluated for glutamate dehydrogenase and CD toxin A/B by immunochromatography tests (C-Diff Quick Check Complete, Techlab); positive samples were screened for the C. difficile Pa-Loc gene and for 027 ribotype by reverse transcription polymerase chain reaction (RT-PCR) (GeneXpert, Cepheid, Sweden). Candida was revealed by plating 10 µL of all samples on Sabouraud-chloramphenicol agar (Liofilchem, Italy), incubated for 24–48 hours at 37°C. Candida colonization was defined as the growth of ≥10⁵ colony-forming units per milliliter of stool sample. The yeasts were typed through their biochemical profiles (Api ID 32 C, bioMérieux). Mantel-Haenszel test and Stata 11 software were used for statistical analysis; an α error <.05 was accepted.

The 140 patients averaged 65 ± 22.98 years of age, and 52% were male. One hundred patients had negative results and 40 positive results for CDI, as revealed by both the immunochromatography reactivity and by the RT-PCR for the Pa-Loc gene presence, which showed that 10 patients were infected by the 027 ribotype. CDI was significantly associated with Candida colonization (83% CDI positive vs 67% CDI negative; \( \chi^2 = 3.91; P < .05 \)). Candida albicans was the species more often implicated (\( \chi^2 = 4.82; P = .02; \) Table 1). All except 1 of the ten 027 ribotype-infected patients were colonized by the yeast, 7 of which were C. albicans (\( \chi^2 = 0.37; P = .5 \)). Our data provided evidence that Candida colonization and CDI are linked, thus suggesting a role for the yeast during CDI. The prevalence of yeasts observed in our study was higher than that reported by others [1, 3], probably due to differences in the cultural and typing methods, or to different study populations. Indeed, Manian and Bryant evoked a protective role for Candida in competing with C. difficile, as they observed a lower prevalence of Candida colonization in only 16.7% of the CDI-positive patients. Unfortunately, the authors did not perform any quantitative assessment of Candida growth, referring only to the overgrowth of the yeast covering >50% of an agar plate [1]. Similarly, the higher prevalence of NAC observed in Nerlandzic et al’s study (68% NAC vs 32% of C. albicans) can be affected by the storage conditions used in their study [3]. Further studies are in progress to find out a correlation between CDI and candidemia and to reveal the pathogenic mechanisms underlying this association.

Table 1. Yeast Prevalence in Clostridium difficile Infection—Positive and Negative Patients

<table>
<thead>
<tr>
<th>Yeast Colonization</th>
<th>CDI Positive (%)</th>
<th>CDI Negative (%)</th>
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<tbody>
<tr>
<td>Candida albicans</td>
<td>61% (24)</td>
<td>34% (34)</td>
</tr>
<tr>
<td>Non-albicans Candida</td>
<td>22% (8)</td>
<td>32% (32)</td>
</tr>
<tr>
<td>None</td>
<td>17% (7)</td>
<td>34% (34)</td>
</tr>
</tbody>
</table>

Data are presented as % (No. of patients).

Abbreviation: CDI, clostridium difficile infection.

Notes

Financial support. This work was partly supported by a grant of Sapienza University of Rome “Ateneo 2010.”

Potential conflicts of interest. All authors: No potential conflicts.

All 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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Clinical Infectious Diseases® 2014;59(11):1648–9
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DOI: 10.1093/cid/ciu637