

# *Trichosporon montevidense* isolated from the descending colon of a patient with active severe Crohn disease: a case report

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*To the Editor:* A 13-year-old girl with Crohn disease (CD) from Shandong Province transferred to our inflammatory bowel disease (IBD) center during April 2013. Three months previously, the patient presented with hematochezia and fever, but antibiotic treatment was unsuccessful. After admission, a colonoscopy indicated manifestations of segmental lesions, cobble stoning, and stricture [Figure 1A]. Cytomegalovirus, Epstein-Barr virus, *Clostridium difficile*, and amoebae were excluded as possible causes. There were also no indications of Behcet disease, systemic vasculitis, or other autoimmune diseases. Our initial diagnosis was active severe CD (Vienna typing, A1L3B2). This study was approved by the Ethical Committee of First Hospital of Peking University (No. 2019153). An appropriate signed patient consent form was obtained.

Because intestinal tuberculosis could not be easily excluded, we initially administered a glucocorticoid to induce remission with antituberculosis therapy. However, there was no response, so we switched to infliximab. After three doses of infliximab (weeks 0, 2, and 6), we performed another colonoscopy [Figure 1B] and found that infliximab failed to improve the lesion. A biopsy was sent for culture to exclude specific infections, but the culture was positive for fungus [Figure 1C and 1D]. The fungus was subsequently identified as *Trichosporon montevidense* based on sequence analysis of internal transcriber spacers and intergenic spacer regions (Supplementary Material for the method, <http://links.lww.com/CM9/A219>). However, we considered *T. montevidense* colonization to be unrelated to the symptoms because this genus is common in the microbiota of normal intestines.<sup>[1]</sup>

After 3 months of infliximab therapy, abdominal pain and general well-being showed no improvement. Then, the patient suddenly underwent emergency surgery for intestinal bleeding, which included total colectomy and ileostomy.

After the operation, the patient developed high fever (39°C). Considering the long duration of glucocorticoid and infliximab treatments, we treated the patient with an antibiotic combination (meropenem, teicoplanin, and caspofungin acetate), but her temperature remained elevated after 72 h. There were no pathogens in a blood culture or a peritoneal lavage culture, and the (1, 3)- $\beta$ -D glucan test and galactomannan test were negative. Continuation of the high fever would place the patient in extreme danger.

The vast majority of yeast isolated from our intensive care units were from the genus *Candida*. Rare pathogenic fungi, such as *Cryptococcus* and *Trichosporon*, have also emerged (unpublished data). However, our center did not find *Candida* species that were caspofungin resistant (unpublished data). Therefore, we speculated that *Trichosporon* sp. may be the cause of her symptoms for several reasons. *T. montevidense* was previously cultured from her colon mucosa, *Trichosporon* sp. is considered the second most common cause of basidiomycetous yeast infections in humans, and gut translocation is considered the major source of infection.<sup>[1]</sup> Moreover, *Trichosporon* sp. is naturally resistant to caspofungin acetate.<sup>[1]</sup> Thus, we initiated treatment with voriconazole, to which *Trichosporon* sp. is susceptible. Encouragingly, the patient's temperature began to decrease after 24 h, and it returned to near normal after 3 days. Three months later, the patient recovered enough to be discharged home. Additionally, we found yeast in colon tissue by immunofluorescence [Figure 1E; Supplementary Material for method, <http://links.lww.com/CM9/A219>], so it is likely that the pathogen causing the fever was *Trichosporon* sp.

The role of *T. montevidense* in colitis is still unclear, although there is a close association between gut mycobiota and inflammatory bowel disease.<sup>[2]</sup> For example, *Candida albicans* and *Malassezia* spp. can aggravate colitis, whereas *Saccharomyces boulardii* can alleviate

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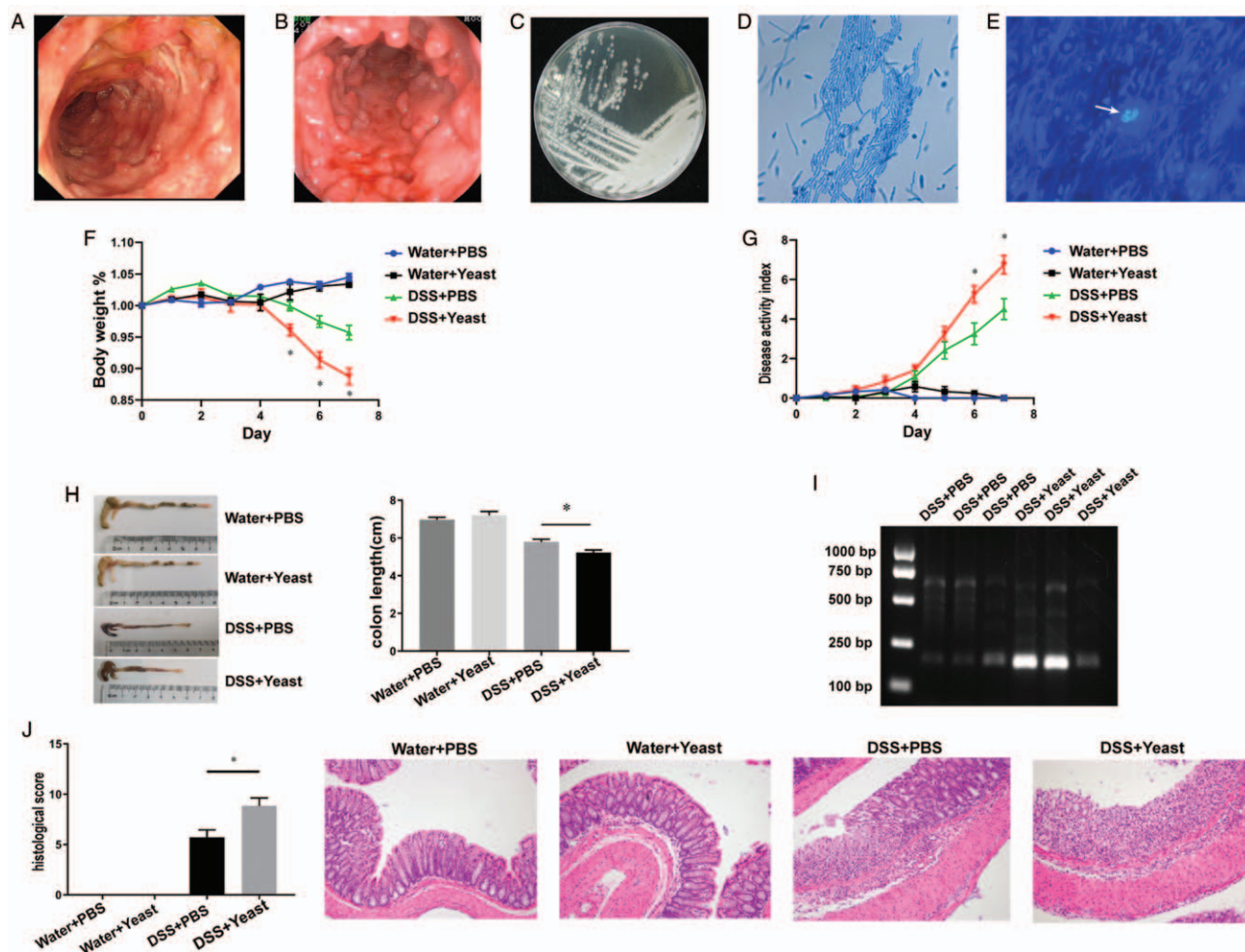
DOI:  
10.1097/CM9.0000000000000793

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Chinese Medical Journal 2020;133(10)

Received: 13-01-2020 Edited by: Li-Shao Guo



**Figure 1:** *Trichosporon montevidense* in the descending colon of a patient with Crohn disease (A–E) and *T. montevidense*-mediated aggravation of disease in a mouse model of colitis (F–J). (A) Endoscopic image of the descending colon after admission. (B) Endoscopic image of the descending colon after three doses of infliximab. (C) Phenotype of an isolate on Sabouraud dextrose agar. (D) Microscopic features of an isolate in an agar block smear (stained with lacto-phenol cotton blue, original magnification  $\times 400$ ). (E) Immunofluorescence staining of fungi in colon samples (original magnification  $\times 400$ ) and yeast cells (white arrow). (F) Changes in body weight in male C57BL/6J mice (10 weeks old) that were randomly divided into 4 groups (12 mice per group): Water + phosphate buffer saline (PBS): free access to water and 0.2 mL of PBS by gavage once per day; Water + Yeast: free access to water and 0.2 mL of PBS with  $10^8$  *T. montevidense* cells by gavage once per day; Dextran sodium sulfate (DSS)+PBS: free access to 2.5% (wt/vol) DSS and 0.2 mL of PBS by gavage once per day; DSS + Yeast: free access to 2.5% (wt/vol) DSS and 0.2 mL of PBS with  $10^8$  *T. montevidense* cells by gavage once per day. (G) Changes in the disease activity index of mice in the 4 groups (12 mice per group). (H) Colon lengths of mice in the 4 groups (Water + PBS,  $n = 5$ ; Water + Yeast,  $n = 5$ ; DSS + PBS,  $n = 12$ ; DSS+Yeast,  $n = 12$ ). (I) Agarose (1.5%) gel electrophoresis of amplified *Trichosporon* DNA from DSS group mouse colon tissue. (J) Hematoxylin and eosin-stained sections of colons (original magnification  $\times 200$ ) and mean histopathological scores in the 4 groups (Water + PBS,  $n = 5$ ; Water + Yeast,  $n = 5$ ; DSS + PBS,  $n = 7$ ; DSS + Yeast,  $n = 7$ ). Data in F, G, H, and J are expressed as the means  $\pm$  standard error of means and differences were analyzed using Student's *t* test. \* $P < 0.05$ .

colitis.<sup>[1,3]</sup> The presence of antibodies against *Saccharomyces cerevisiae* is a marker for susceptibility to IBD.<sup>[2]</sup> Caspase recruitment domain 9 (Card9) is a key regulator of immunity to fungi, and certain Card9 polymorphisms are associated with IBD.<sup>[2]</sup>

A previous study reported the presence of *Trichosporon* spp. in the intestinal mucosa of patients with CD.<sup>[4]</sup> Iliev *et al*<sup>[5]</sup> found increased amounts of *Trichosporon* spp. during colitis in mice, suggesting that these fungi may be adapted to the inflammatory environment. Thus, we examined the effect of our clinical isolate of *T. montevidense* (BMU 07526) in a mouse model of colitis, in which disease was induced by dextran sodium sulfate (DSS).<sup>[5]</sup> These experiments were approved by the Peking University First Hospital Laboratory Animal Welfare and Ethics Committee (No. 201913). The experimental mice received a gavage

with  $10^8$  *T. montevidense* cells each day. The results indicated that *T. montevidense* had no effect on the control (non-colitis) group but exacerbated colitis in the DSS group. Moreover, relative to control mice, mice treated with yeast had greater weight loss, shorter colon lengths, higher disease activity scores, and higher histopathology scores [Figure 1 F–H, J; Supplementary Material for method, <http://links.lww.com/CM9/A219>]. Moreover, we detected by polymerase chain reaction the *Trichosporon* spp. from the colon mucosa of mice that received the yeast gavage [Figure I; Supplementary Material for method, <http://links.lww.com/CM9/A219>].

These results indicated that *Trichosporon* spp. are capable of gut colonization, can cause invasive infections, and can exacerbate the symptoms of colitis. We suggest that clinicians consider intestinal colonization by fungi,

especially *Trichosporon* spp., in patients with CD who present with fever, hematochezia, and colon biopsy cultures that are positive for fungi.

### Conflicts of interest

None.

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**How to cite this article:** He SD, Li RY, Chi Y, Wan Z, Wang HH. *Trichosporon montevidense* isolated from the descending colon of a patient with active severe Crohn's disease: a case report. Chin Med J 2020;133:1245–1247. doi: 10.1097/CM9.0000000000000793