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Brief Report

BRIEF REPORT

Escherichia coli O157: H7 sepsis following fecal microbiota transplant in an IgA-deficient inflammatory bowel disease patient

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Introduction

Clostridioides difficile infection (CDI) is a common gastrointestinal illness worldwide, with increased prevalence and worse outcomes in patients with inflammatory bowel disease (IBD) [1]. Fecal microbiota transplant (FMT) is an effective treatment for recurrent CDIs (RCDIs) with minimal serious adverse events (SAEs) reported [2]. While immunosuppressive medications increase susceptibility to infections, studies have shown that FMT does not increase SAE risk in immunocompromised patients (including IBD patients on immunosuppressive therapy) [3].

The US Food and Drug Administration (FDA) regulations for donor and stool screening are updated as new information emerges [4]. However, the screening process for recipients remains unguided by medical societies and unregulated by the FDA [5].

Case report

A 19-year-old male with growth hormone deficiency and asthma presented to his gastroenterologist with large-volume watery diarrhea. Four months prior, the patient was diagnosed with ulcerative colitis (UC) via colonoscopy, which revealed Mayo Score 3 pancolitis, and he was being treated with prednisone and infliximab. Stool testing was negative for *Escherichia coli* but revealed CDI (his third episode in 4 months—the previous two were treated with oral vancomycin). Thus, a decision was made to undergo FMT. Six days later, commercially sourced stool was placed in the cecum via colonoscopy; endoscopy again revealed severe pancolitis. Given the level of inflammation shown on colonoscopy, it was concluded that the patient was responding poorly to infliximab and he was switched from infliximab to tofacitinib and vedolizumab 8 days status post FMT.

Ten days after transplantation, the patient presented to the emergency department with explosive bloody diarrhea (20 episodes per day) and associated leukocytosis, tachycardia, high-grade fevers, chills, tenesmus, and abdominal cramping. Stool was negative for *C. difficile* but positive for enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli*, and Shiga toxin-producing *E. coli* (STEC) O157: H7. The patient received supportive care for 8 days, with moderate improvement. On day 9 of hospitalization, intravenous ciprofloxacin and metronidazole, and oral vancomycin were initiated. The patient underwent colonoscopy on day 10 that revealed Mayo Score 3 pancolitis, with pathology showing severe active chronic colitis in the rectum, and

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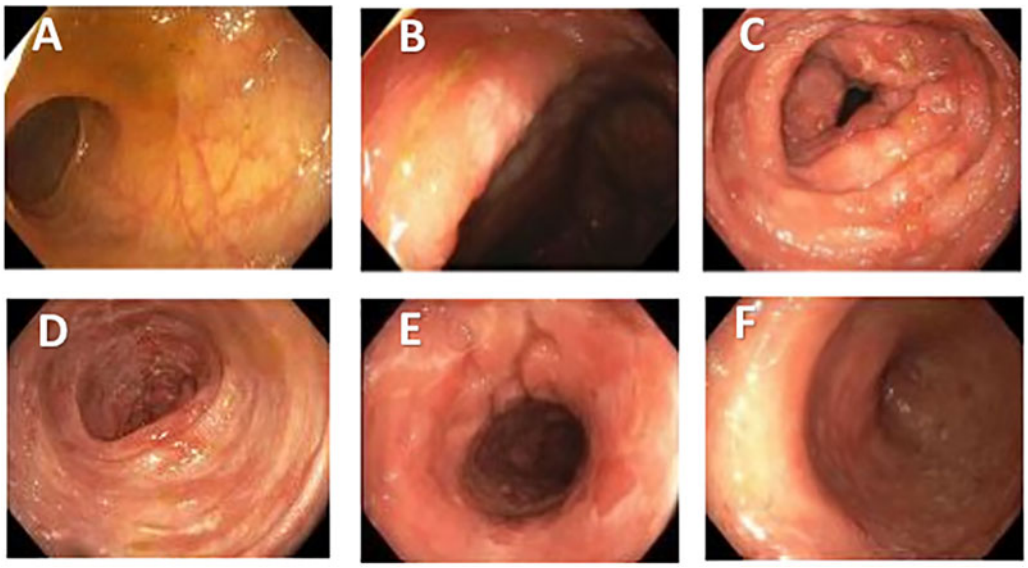

Figure 1. Endoscopic images of the patient on day 10 of hospitalization that revealed Mayo Score 3 pancolitis. No inflammation in the terminal ileum (A). Moderate active chronic colitis in the cecum (B). Severe active chronic colitis in the ascending (C), descending (D), sigmoid colon (E), and rectum (F).

descending and ascending colon, and moderate active chronic colitis in the cecum (Figure 1). After 17 days, he was discharged on oral vancomycin, tacrolimus, and a prednisone taper. Blood cultures were negative throughout hospitalization. Two years status post FMT, although he has experienced severe UC flares, he has had no recurrence of CDI.

Unbeknownst to his gastroenterologist before transplantation, the patient also had primary IgA deficiency (diagnosed while growing up in the Czech Republic). Immunoglobulin testing in 2014 and repeated in 2015 showed <1 mg/dL IgA with normal IgM, IgE, IgG, and IgG subclasses. His sister had similar laboratory results and was also diagnosed with IgA deficiency. The patient had not experienced any severe infections throughout his lifetime, although, according to his mother, he had several mild colds every winter that did not require regular antibiotics.

Following hospitalization, laboratory testing was performed to further characterize his level of immunodeficiency. Flow cytometry and CH50 were within normal limits. CD4/8 testing revealed 41% CD8 cells (reference range, 11%–30%) and 33% CD4 cells (reference range, 35%–60%), leading to a 4/8 ratio of 0.82 (reference range, 1.25–4.50). The patient received all age-appropriate vaccinations and was found to have protective IgG titers to diphtheria and tetanus, but non-protective IgG titers to *Haemophilus influenzae* type b and varicella. He was found to have protective titers to 3 of 14 *Streptococcus pneumoniae* serotypes. He was then given the Pneumovax-23 vaccine and was retested 6 weeks later, which showed that he still only had protective titers to 3 of 14 serotypes.

Discussion

Per literature review, this appears to be the first reported instance of an individual with primary IgA deficiency undergoing FMT and also the first reported instance of FMT-introduced *E. coli* O157: H7 infection.

This incident was reported to the stool bank that sourced the donor stool and the FDA. Several months later, the FDA released a safety alert stating that four different patients who had received stool from the same donor developed STEC infections following FMT for RCDI [6]. The company noted that the donor's stool had initially tested negative for STEC via enzyme immunoassay. They retested safety aliquots from those patients, which were again negative via enzyme immunoassay, but positive via nucleic acid amplification testing (NAAT) [7]. Subsequently, the FDA instituted new regulations that all past and future donor stool must be tested for EPEC and STEC via NAAT [8]. While our patient is almost certainly one of the four STEC infections referenced by the stool bank and FDA, due to lack of bacterial isolates from our patient's stool, it could not be confirmed that the STEC in the donor stool was genetically identical to the STEC in our patient's stool.

According to the stool bank, this particular donor was previously used for FMT in other patients with no SAEs reported. We do not know whether there were any differences between the STEC-infected recipients and those without SAEs. Although it is impossible to know whether our patient would have experienced a similarly detrimental outcome if he was an immunocompetent patient with UC, his complete lack of IgA was likely an important contributor, if not the primary catalyst for his disastrous response to FMT.

This case highlights the importance of reporting suspected SAEs to the FDA and, in this case, the stool bank. Due to this incident and subsequent reports, the donor was permanently excluded from providing stool and FDA regulations were updated, which will hopefully help to prevent future FMT-derived infections.

Although the FDA now requires donor screening and stool testing for specific pathogens, they do not currently mandate screening for recipient co-morbidities or immunodeficiencies. Similarly, medical societies have not published guidelines addressing recipient screening. Given the understood importance of secretory IgA in mucosal immunity against gastrointestinal infections [9] and the outcome presented in this study, we strongly recommend rigorous screening of recipient medical history for immunodeficiency. If immunocompetence is uncertain, a basic immunoglobulin panel could be considered prior to FMT.

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Conflict of Interest

None declared.

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