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Fecal Microbiota Transplantation as First-Line Treatment for Immune-Mediated Colitis

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Introduction

Immune-mediated colitis (IMC) is a potential adverse drug effect following treatment with immune checkpoint inhibitors (ICIs) and poses a significant obstacle to effective cancer management, mitigating the potential success of immunotherapy. Current guidelines for IMC management recommend the initiation of corticosteroids at 1-2mg/kg for diarrhea/colitis of Common Terminology Criteria for Adverse Events (CTCAE) grade of 2 or higher and biologics for refractory cases. Our previous case series of 15 patients demonstrated that fecal microbiota transplantation (FMT) was effective for treating refractory disease, successfully treating 75% of patients. Immunosuppressant use is associated with significant morbidities. FMT as a first-line treatment for IMC has not been studied previously and has the benefit of minimizing the complications of immunosuppression. In this case report, we present three IMC cases who received front-line FMT as part of a research protocol.

Clinical characteristics

The patients in this case report were enrolled on MD Anderson clinical trial 2018-0663 (NCT04038619) investigating the efficacy of first-line fecal transplant for IMC. All the patients underwent FMT prior to receiving any treatment with steroids or biologic agents. All three patients were diagnosed with metastatic renal cell cancer and received different immune checkpoint inhibitor regimens, either as monotherapy or dual therapy. Work-up for all included ruling out infection (GI multiplex panel, C. diff testing etc) and measuring fecal calprotectin and lactoferrin values. All patient presented with abnormal lactoferrin and calprotectin values that subsequently improved following the procedure. Clinical symptoms severity was measured by CTCAE, and endoscopy colitis severity was graded by Mayo endoscopy score.

Case 1

Patient A is a woman in her 50s who developed grade 3 diarrhea within one week of initiating nivolumab (received 5 cycles of pembrolizumab prior). She presented with grade 3 diarrhea. Colonoscopy at presentation was consistent with Mayo 3 colitis, with a calprotectin above 1000mcg/gm. Her symptoms improved one day following FMT with a sustained clinical response lasting 13 months. Calprotectin values returned to baseline within 2 months accompanied by dramatic mucosal healing. Repeat colonoscopy at one and two months showed Mayo 1 colitis, despite restarting nivolumab for three cycles within the following 3 months. Her most recent cancer staging showed a favorable cancer response. Endoscopy images are displayed on the right.

Case 2

Patient B is a man in his 70s who presented with grade 3 diarrhea and grade 2 colitis after two cycles of nivolumab/ipilimumab combination therapy. His initial colonoscopy showed Mayo grade 2 colitis and a calprotectin of 244mcg/gm. He received FMT with initial improvement of his diarrhea and colitis symptoms, but he was admitted within a week for recurrent symptoms. Subsequently, he was started on intravenous methylprednisolone and vedolizumab for refractory IMC which achieved clinical remission and remained in remission for 10 months with histological resolution. His cancer was stable at last staging. Endoscopy images are displayed on the right.

Case 3

Patient C is a man in his 70s with end stage renal disease on hemodialysis and heart failure who presented with grade 3 diarrhea and grade 2 colitis four months after initiation of ICIs (4 cycles of nivolumab/ipilimumab combination therapy and 1 cycle of nivolumab monotherapy). He had a three-week history of grade 3 diarrhea and grade 2 colitis and colonoscopy showed Mayo 3 colitis with a calprotectin of 718mcg/gm. He achieved partial symptom response following FMT with more formed stool and less episodes of incontinence within one month post-FMT. He was planned to undergo a second FMT but developed worsening hypotension and deterioration of heart condition for which he passed away 6 weeks later. Findings from his first endoscopy can be found on the right.

Discussion

This is the first study investigating the efficacy and safety of first-line FMT in treating IMC. It has demonstrated a favorable safety profile and a promising therapeutic effect. All patients showed signs of symptom improvement following FMT with only one experiencing a recurrence of symptoms. Additional investigation in larger patient cohorts is warranted to further assess the utility of FMT as a first-line treatment for IMC and its impact on cancer outcomes.

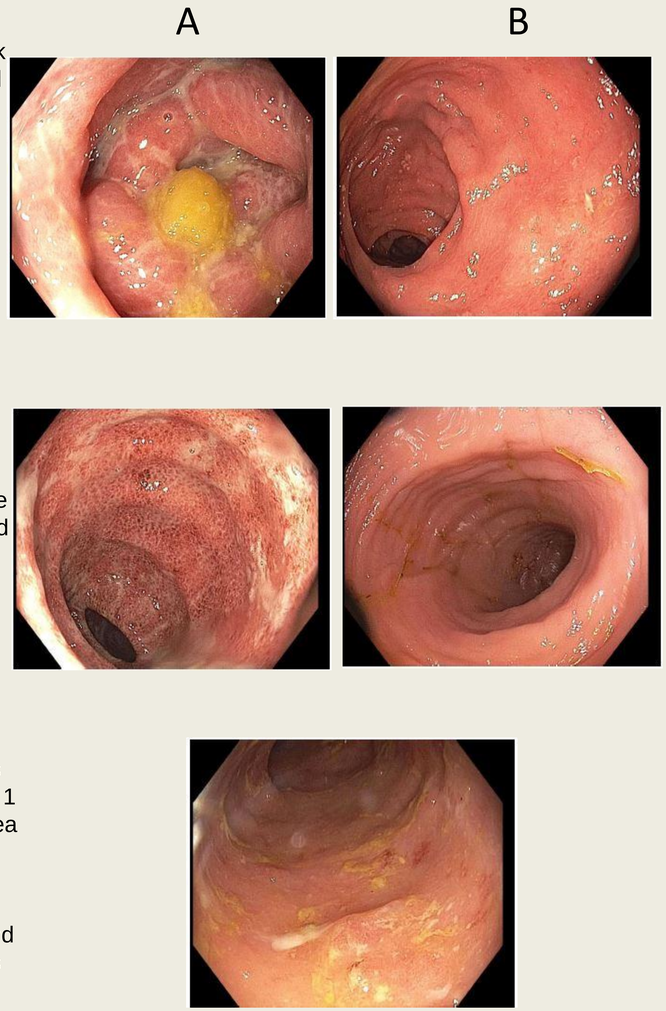

Figure 1. Gross colonoscopy findings A) at time of FMT and B) at follow-up. The first row = patient A. The second row = patient B. The final row = patient C, who passed away before a follow-up scope could be done.