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Intestinal Dysbiosis Disguised as a Rectal Fistula Treated With Autologous Fecal Microbiota Transplantation

Scibelli N, Singh P, Raynor K

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Background

- Fecal Microbiota Transplant (FMT): the process of infusing donor stool into the recipient's gastrointestinal tract via a colonoscopy or an upper gastrointestinal (GI) approach
- The most common indication for FMT is recurrent Clostridium difficile infection
- FMT has been applied in various extra-intestinal conditions, including metabolic diseases, neuropsychiatric disorders, autoimmune diseases, allergic disorders, Parkinson's disease, multiple sclerosis, myoclonus dystonia, chronic fatigue syndrome, idiopathic thrombocytopenic purpura, and tumors
- Autologous FMT is a newer application that uses one's own feces to help restore the microbiome of the gut

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Case

- A 69-year-old Caucasian male presented to his outpatient gastroenterology office with complaints of copious rectal discharge and for discussion of treatment options.
- History of present illness:
  - Trauma leading to a T7 spinal cord injury resulting in a thoracic arteriovenous malformation requiring surgical intervention eventually leading to paraplegia.
  - After 25 years, the patient developed a left ischial ulcer and a sacral decubitus ulcer with concomitant methicillin-sensitive Staphylococcus aureus (MSSA) bacteremia, status post multiple debridements and prolonged courses of broad-spectrum antibiotics.
  - Patient underwent sigmoid end-colostomy placement due to chronic constipation.
  - After another three years without complications, he presented with a new ischial wound and fevers, with wound cultures positive for MSSA, Streptococcus agalactiae, and Morganella morganii. He was treated surgery and prolonged course of antibiotics.
  - In the following months, he began to have new onset of copious, purulent rectal discharge, leading to poor healing and further debridement procedures for his wounds.

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Case continued

- According to patient, he had always suffered from minor mucus drainage from the anus but in the months leading to his presentation, the drainage increased in both volume and odor, with up to estimated 1 L daily of purulent rectal discharge.
- He was referred to a colorectal surgeon due to above-mentioned complaints.
- Physical Exam:
  - Paraplegia, flexion contracture of bilateral knees
  - Well-pouched colostomy in the left lower quadrant of the abdomen. No parastomal hernia was noted. Normal-appearing anus with some minor residual hemorrhoidal skin tags and obvious atrophy of both buttocks.
  - Digital rectal exam (DRE) demonstrated very low rectal tone without sensation and a large amount of thin, yellow purulent drainage from the rectum. A right ischial ulcer was present, measuring 5 cm in diameter, tracking medially and superiorly with easily palpated underlying bone.

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Work-up

- Anoscopy: large amount of purulence from the rectal wall in the right posterior location leading to concern for a rectal abscess with fistula
  - Magnetic resonance imaging (MRI) of the pelvis without contrast: soft tissue ulceration in the right ischial region extending from the skin to the ischial tuberosity and no evidence of focal fluid collection to suggest drainable abscess or other fluid collection (Figures 1,2).
- Anorectal examination under anesthesia and a flexible sigmoidoscopy (FS):
  - Large amount of purulent drainage to the top of the rectal stump. No connection to the sigmoid colon was found.
  - The rectal mucosa appeared atrophied and with some diversion proctitis, but no evidence of granulation tissue or pseudomembranes, and no clear source for the purulence was discovered.
  - The healed abscess cavity of the right ischial decubitus ulcer was aspirated and did not show evidence of purulent fluid.
- X-ray barium enema
  - No clear fistulous connections/fistula

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Figure 1

- Sagittal view of pelvic MRI. Red arrow indicates the rectal stump without any visible abscess or fistula.

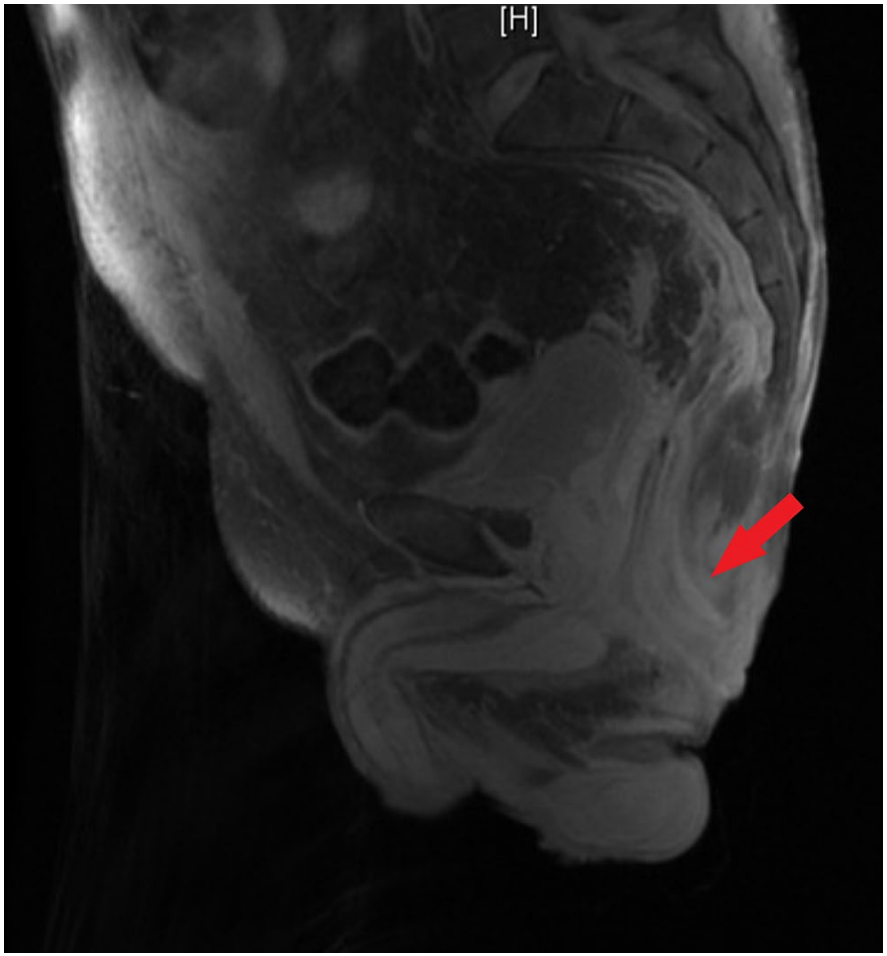

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Figure 2

- Coronal view of pelvic MRI. Red arrow indicates the rectal stump without any visible abscess or fistula.

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FMT treatment

- At this point, it was suspected that intestinal dysbiosis may be contributing to the patient's current symptoms and a decision was made to treat him with autologous FMT.
- Treatment:
  - Daily enemas with a mixture of approximately 50 cc of feces from his ostomy with 50 cc of distilled water and retained for 20 minutes or as long as possible.
- The patient noted immediate improvement within two days when the rectal discharge had stopped completely.
- Eventually symptoms began to return and the patient and his colorectal surgeon ultimately decided to move forward with a rectal mucosectomy, removing the mucosa of the rectum. The patient had slow wound healing following this procedure but decreased rectal discharge.

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Discussion

- Intestinal dysbiosis: alterations of the gut microbiota that can occur secondary to diet, toxins, drugs, and pathogens which result in local and systemic inflammation, further disturbing the barrier function of the gut.
  - Enteric pathogens
  - Antibiotics
    - Directly: microbial diversity can be depleted due to the broad-spectrum activity of antibiotics with both pathogenic bacteria and commensal bacteria are indiscriminately killed.
    - Indirectly: the homeostatic state of the gut can be disturbed and bacteria that once lived through symbiosis and codependency may no longer have the necessary nutrients they require to survive. Commensal bacteria and sensitive strains of pathogenic bacteria are eliminated, while antibiotic-resistant strains of bacteria will have a growth advantage in this unstable microbiome [7].
- In our patient, after multiple rounds of empiric antibiotics, deleterious effects to the microbiome developed. This disruption led to the emergence of pathogenic bacteria that were resistant to the empiric antibiotics being given.

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- Prolonged inactivity of the gut.
  - Studies performed on patients who underwent loop ileostomy showed that the de-functioned intestine had significant atrophy compared to functional tissue.
- Our patient had very clear intestinal atrophy in the distal, or efferent, bowel limb as visualized during FS and no fistula. This validated that there were no nutrients provided to the distal arm of the gut, thereby leading to starvation and large decrease in both bacterial load and bacterial diversity.

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Current Utility of Autologous FMT

- In a controlled study, autologous FMT was used in patients undergoing allogeneic hematopoietic stem cell transplant (allo-HSCT) treatment to treat dysbiosis.
  - Following treatment with allo-HSCT, gut microbiota diversity was severely depleted due to routine antibiotic use from immunosuppression. Autologous FMT was performed and compared to patients who did not receive the intervention.
  - Rapid improvement in bacterial microbiome was seen in the patients who received autologous FMT
- In IBD, studies have taken a patient's own stool during a time when the patient is in remission and then re-introduced to the patient when they are having a flare.
  - Autologous FMT has cure rates as high as 90% in some patient cohorts. In addition, the transmission of communicable and noncommunicable diseases is avoided with the use of autologous FMT [4].

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Conclusion

- In our patient, we theorize that an overgrowth of pathogenic bacteria after broad-spectrum antibiotic use occurred in the distal or efferent bowel limb.
- This inactive portion of bowel was especially susceptible to dysbiosis as it was deprived of enteral nutrition.
- By performing enemas composed of his own feces, symptoms improved temporarily and the patient experienced improved quality of life.
- Although for this patient the solution was not permanent, it was low risk compared to surgical intervention.
- We propose that further randomized studies should be done to investigate the utility of autologous FMT in patients suffering from intestinal dysbiosis after end colostomy in the distal limb of the intestine, especially if initiated early.

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