

Intestinal Microbiota Transplantation and *Clostridiodes difficile*. A Relevant Case

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Received: June 19, 2023; **Published:** June 27, 2023

Abstract

After delving into numerous articles and having our own history of successful intestinal microbiota transplantation (IMT), we were fortunate that a new patient was referred, with pseudomembranous colitis; on this occasion, *Clostridiodes difficile* covered the entire colon.

The patient, 75 years old, and the history that her husband had died of sepsis caused by the same bacterium, and a series of comorbidities, which are explained in their corresponding place.

The first transplant was performed one week after the onset of diarrhea, due to failure with antibiotic therapy, using fecal microbiota of less than 8 hours of preparation, and given the severe findings, we point out the need for a new colon exploration, in not more than 72 hours. This was carried out a week later, where, surprisingly, we observed that the enormous amount of *C. difficile* had disappeared, leaving only minimal lesions in the rectum, for which reason we performed a second IMT, following the total cure of the pathological process.

Keywords: Intestinal Microbiota Transplantation (IMT); *Clostridiodes difficile* (CD); Intestinal Microbiota (IM); Probiotics, Prebiotics and Symbiotics (BIOT)

Introduction and Case Presentation

Female, 75 years old, who reports having suffered a fall due to arterial hypotension, bruising her right hemi-face, fortunately without fractures, only an echymotic process. Presence of type 2 diabetes mellitus, for 20 years. Arterial hypertension, for 18 years. She reports 3 - 4 semi-liquid diarrheal stools for a week, with a slight rise in temperature, as well as abdominal swelling and pain throughout the colic

framework. On physical examination, the patient presented a whitish tongue, due to moniliasis. Mild arterial hypotension. And abdominal swelling is corroborated, observing medium to intense pain throughout the colic framework. In the hypogastrium there is frank rebound, without muscular resistance. Bowel sounds are increased.

Chest x-ray within normal limits, for her age. CT scan with excess gas throughout the colon. No other alterations are observed. Laboratory studies with: Antigen for Covid -19 (SARS-CoV-2) Negative. Red formula: Erythrocytes 4.07, Hemoglobin 14.0 g/dL Hematocrit 39.1. Mean globular volume 96.1. Mean hemoglobin concentration 34.4. Red blood cell distribution index (RDW) 11.1. Platelets 241.0. Mean platelet volume 8.3. White formula: Total leukocytes 11.02. Total neutrophils 90.0%. Segmented neutrophils 90.0%. Band neutrophils 0.0%. Meta-myelocytes 0.0%. Myelocytes 0.0%. Pro-myelocytes 0.0%. Blasts 0.0%. Eosinophils 0.0%. Basophils 1.0%. Monocytes 5.0%. Lymphocytes 4.0% Erythro-sedimentation 0.0 mm/hr. Glycosylated hemoglobin (HB-A1c) 10.49%. Serum glucose 249 mg/dL. Serum urea 34.03 mg/dL. Ureic nitrogen 15.90 mg/dL. Serum creatinine urease 1.1 mg/dL. Creatinine imino-hydrolase Uric acid in serum 6.1 mg/dL. Uricase BUN/CREATININE ratio 14.45. Triglycerides 162 mg/dL. Aspartate amino transferase (TGO) 57 U/L. Alanine amino transferase (TGP) 56 U/L. Alkaline phosphatase 99 U/L 38.0. Lactic dehydrogenase (DHL) 302. U/L Pyruvate-lactate gamma glutamyl transpeptidase (GGT) 35 U/L. Serum calcium 9.0 mg/dL. Amylase in serum 61 U/L. Serum phosphorus 3.3 mg/dL. Serum magnesium 1.5 mg/dL. Atherogenic index 4.53. Serum sodium 128 mmol/L. Serum potassium 3.5 mmol/L. Chlorine in serum 100 mmol/L. Serum iron 23.0 ug/dL. Urine: Physical-chemical analysis: Specific density 1.015 pH 5.5. Negative glucose. Proteins 15 mg/dL. Blood 10/uL negative. Positive hemoglobin. Negative ketone bodies. Negative bilirubin. Normal urobilinogen. Negative nitrites. Leukocyte esterase negative. Microscopic analysis of sediment: Cellularity of origin leukocytes 0.8 - 10 erythrocytes/field. Hyaline casts 5-6/field. Moderate amorphous urates. Procalcitonin (PCT) 17.34 ng/mL. C Reactive protein 300 mg/L. *Clostridioides difficile* GHD. Toxin "A": Positive. Toxin "B": Positive. Prothrombin time (PT) 13.5 sec. % Concentration 66.5. INR 1.27. Control 100. Thromboplastin Time (APTT) 29.7 seconds. Witness 25.0. Ratio 1.19.

Treated one week with metronidazole 500 mg. Every six hours, as well as vancomycin 125 milligrams, every six hours.

An intestinal microbiota transplant is proposed to your attending physician, since the antibiotic scheme has not improved the condition, and they accept it, for which TMI is performed (Colonoscopy, figure 1), finding the entire colon lined with *C. difficile*. The endoscopist's report is: Starting from the rectum, the entire colon covered by whitish plaques of different diameters, with a cottony appearance, being more active from the rectum to the splenic angle, some of them presenting a halo with erythema. 200 ml are administered. preparation of fresh microbiota in ascending colon, 200 ml. in transverse colon, 200 ml. in descending colon and 200 ml. in straight. Observation and special studies are recommended to your treating Physician for the next 72 hours, given the intense process detected, which will surely require a new exploration through colonoscopy.

New studies are carried out and it is found: leukocytes at 20,780, procalcitonin 0.34, sedimentation rate at 31 and PCR 14. Persistent diarrheal stools, now mucous, with traces of blood, in number of 4, which decreased to two in 24 hours, the patient with hypothermia, and the need for a new examination was reiterated to the family. They decide a week later, finding only 4 small areas of probable *C. difficile* in the rectum. A polyp in the ascending colon (which is removed) and a new dose of microbiota is administered, similar to the first, fresh, throughout the colon.

Exit without problems. To date, the patient has not manifested gastrointestinal disturbances again.

Comments

More than 1,558 years would have to pass [1]. To resume what was started by Ge Hong, a Chinese doctor, when he successfully treated diarrhea with feces. We see, that the IMT. It has reappeared on the horizon of science; a Physician (Eisman B), carries out in Colorado,



Figure 1: Various whitish plaques of different diameters and cottony appearance are shown, which concur mainly in the right and splenic angle; some with halo (erythema).



Figure 2: Various whitish plaques of different diameters are shown, in the rectum with a cottony appearance, some with a halo (erythema).

United States of America, positive management of patients with Pseudomembranous enterocolitis [2]. Since then, not only retention enemas, but transplants have multiplied, becoming the United States of America, pioneers in this procedure [3]. Borody TJ and his group reiterate that TMI is not only useful in recurrent *Clostridioides difficile* infection [4]. But it can be carried out, with good results in: multiple sclerosis [5]; which leads other authors to use it in: metabolic diseases [6], inflammatory bowel disease [7], various diseases [8]. Gut microbiota dysbiosis, obesity, type 2 diabetes mellitus, neuropsychiatric disorders, irritable bowel syndrome, decompensated cirrhosis, cancers, and graft-versus-host disease [9].

Being the intestinal microbiota the great probiotic that improves both metabolic and immunological processes, based on the axis-intestine-brain, many researchers turn their eyes to it, since it modulates the processes and, therefore, patients improve [10]. Likewise, the minimal incidence of complications [11] and the rapidity of its performance, make it an accessible procedure [12].

Not all authors agree with the management of diseases other than *Clostridioides* [13]. And they refer that more time should be expected with IMT, as they fear the impact of other diseases [14].

Probiotics, prebiotics and symbiotics (BIOT)

CD, as an opportunistic gram-positive bacterium, with a high mortality rate, recurs very frequently, and in addition to IMT, probiotics can reduce its pathogenicity, by balancing the intestinal microbiota (IM), affecting dysbiosis [15]. Although the role of probiotics in *Clostridioides* infection is not clear, *Lactobacillus* and *Saccharomyces boulardii* have been reported to be effective [16].

As far as prebiotics are concerned. In 8102 patients, only eight BIOT had been used, and oligofructose with *Saccharomyces boulardii*, were effective [17]. Finally, the synbiotics used in recurrent diarrhea processes due to CD are positive, since the number of Lactobacilli tends to increase [18].

Paraprobiotics: Non-viable microbes, which could produce health benefits similar to those produced by live probiotics. They are inactive microbial cells or cell fractions [19]. In people with decreased immunity, paraprobiotics may be helpful.

Postbiotics: These bioactive compounds produced by probiotic bacteria, when they consume prebiotics, have been given importance lately. They are defined as: Preparation of inanimate microorganisms and/or their components that confers benefits to the health of the host [20]. And, since they benefit, it could be preventive in the management of *C. difficile*.

Conclusions

- Intestinal microbiota transplantation is definitely superior to any other procedure to treat recurrent *Clostridioides difficile* infection.
- Usually, one IMT is enough to treat the infection. Sometimes up to three are required.
- The use of BIOT in the post-transplant period decreases the risk of new infections.
- Do not stop thinking about post-transplant management based on paraprobiotics or postbiotics.

Conflicts of Interest

The authors declare that do NOT have affiliation or participation in organizations with financial interests.

Ethical Approval

This report does not contain any study with human or animal subjects carried out by the authors.

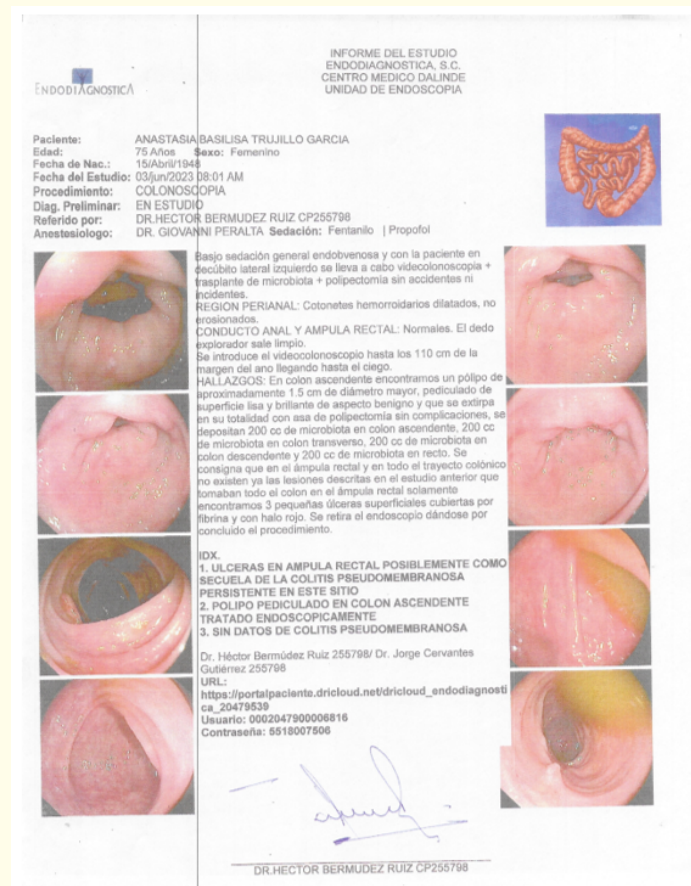


Figure 3: The condition caused by *Clostridioides difficile* has disappeared, leaving only ulcers in the rectal ampulla.

Informed Consent

The authors obtained informed written consent from the patients, in order to develop this article.

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Volume 10 Issue 6 June 2023

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