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Role of the Fecal Microbiote in the Treatment of Pseudomembranose Colitis at Purpose of a Clinical Case

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Abstract

Introduction: Pseudomembranous colitis is an inflammatory affectation of the mucose of the intestine, characterized by the formation of whitish plaques. It is associated with Clostridium difficult infection; it can be associated with other infections, with other non-infectious pathologies and without known cause.

Current disease and history: A 34-year-old male with a history of post-traumatic paraplegia who in January 2018 presented with an ulcerative lesion in the dorsal region, so they entered the local hospital where they indicated Meropenem, abdominal distension appeared, associated with generalized pain, absence of stools and vomiting.

Physical and paraclinical exam: In the cardiopulmonary examination without pulmonary or cardiac alterations, at abdominal level abdominal distension associated with tympanism, absence of intestinal noises, and the rest of the normal physical examination. The hematology shows an important leukocytosis. The rest of the exams were normal. He was taken to the operating room with an exploratory laparo to my which showed no alterations. He is taken to the special care area where his pseudo membranous colitis is suspected, he does not improve initially with antibiotic therapy, and he chooses to perform a colonoscopy study. The findings were consistent with this diagnosis, in the aforementioned case we chose to place stool enemas transplanted for a period of 2 days.

Discussion and conclusions of the case: Stool transplantation is an emerging little-known therapy; we consider it fundamental to conduct studies in our country because of its importance in the future in the management of pseudomembranous colitis in those cases where there is refractoriness to treatment.

Keywords

Enterocolitis Pseudomembranous; Anti-Bacterial Agents; Clostridium Infections; Fecal Microbiota Transplantation

Introduction

Pseudomembranous colitis (CSM) is an inflammatory affectation of the mucosa of the large intestine, characterized by the formation of characteristic and similar histological and endoscopic whitish plaques: the microscopic and macroscopic image are similar [1,2]. It is a descriptive term that, although characteristically associated with Clostridium Difficile (CD) infection, can be related to other infections, other non-infectious diseases and no known cause. From the opposite point of view, the CSM is but the most characteristic and classic picture, known for more than a century, within the clinical spectrum originated by CD, which includes from asymptomatic carriers to fulminating CSMs passing through very variable diarrheal symptoms clinical significance [3,4] (Table 1).

Below present a case of multidisciplinary management with interconsultartion of our service and thanks to a high clinical suspicious, an innovative therapy was achieved that resulted in the healing of the referred patient.

Case Presentation

This is a 34-year-old male patient, natural and from El Arenal, who reports onset of current disease approximately 4 months ago due to ulcer-like progressive skin lesion, located in the sacral region associated with unquantified thermal rises, so that he is

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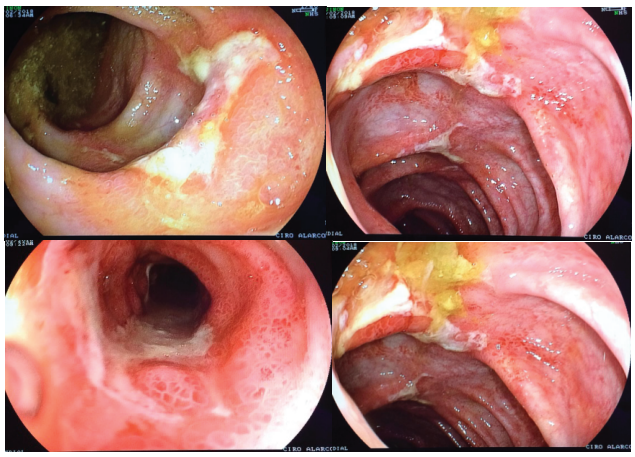

Images 1 to 4: The Colonoscopic study of the patient where extensive whitish lesions are evident in multiple areas during the examination of the patient compatible with Pseudomembranous colitis.

Mild	Moderate	Severe
Less than 6 stools per day Leukocytosis < 15000 / mm3	Profuse diarrhea (> 6 bowel movements a day) To develop in the course of diarrhea: Leukocytosis > 15,000 / mm^3 Abdominal pain (not acute abdomen) Low Albumin (albumin < 3 gr/dl)	Admission to a intensive care unit Fever > 38.5 ° c Low level of conscience Leukocytosis > 35,000 / mm3 or < 2,000 / mm^3 Any evidence of organ failure

Table 1: Severity classification of pseudomembranous colitis [5].

hospitalized for 13 days in a type III hospital, receiving treatment with Meropenem 1 g 3 times at day during his stay; After discharge, he presents progressive abdominal pain, diffuse, severe intensity colic type accompanied by vomiting (5 episodes / food content) and absence of bowel movements for 6 days, which is why he is brought to this center where his evaluation is decided after evaluation admission by the surgery service.

Personal history

Post-traumatic paraplegia since 2014 that conditions forced recumbency, so it presents a sacral ulcer and repeated urinary infections. Denies family history.

Denies epidemiological background.

Denies allergic history.

Functional and Physical Exam

Functional examination

Patient refers to abdominal pain with significant distention.

Physical examination of admission: TA: 90/50 mm Hg FC: 107 bpm FR: 22rpm, looks in regular clinical conditions, feverish, dehydrated, mild mucocutaneous pallor. Normocephalus without alteration. Skin: sacral region: 5x5cm diameter ulcer, dirty bottom, with moderate non-fetid serohematic secretion and poorly defined edges, mobile neck, no palpable nodes, depressed venous pulse, symmetric thorax, normoexpansible, audible vesicular murmur without aggregates , normophontic, rhythmic heart sounds, with both respected silences, distended abdomen, absent bowel sounds, tympanic, poorly depressible, painful to superficial and deep palpation diffusely, symmetric extremities without edema, neurological: oriented surveillance, fluid and coherent language, no agnosias or apraxies, no cranial nerve deficit, Motor: MSD 5/5 MSI 5/5 MID and MII 0/5, anesthesia at T-11 level, patellar reflex and bilateral aquilea, hypotrophy in both lower limbs without signs of irritation meningeal

Exams and evolution

Enter the general surgery service under IDX.

1. Septic shock from abdominal point.

1.1 Obstructive surgical acute abdomen

1.1.1 Intestinal obstruction secondary to flanges.

On 01/24/2018: they perform exploratory laparotomy discarding the presence of visceroparietal adhesion that could condition the presence of obstruction, for which they request assessment by Internal Medicine.

Multiple studies such as complete hematology are carried out, the platelet count and the red series are normal.

The Leukocyte response was found in 29,000 cells at the expense of 87% segmented.

The normal renal function as well as the rest of the chemistry, amylase and lipase times only high but did not reach 2 times the maximum peak. The stool test only showed an increase in intestinal flora and the presence of fecal leukocytes.

The uronalisis within normal. The simple Abdomen RX showed significant hydric and air levels and the thoracic right parahilar air bronchogram. It is based on the history of hospitalization where the patient received Meropenem the presence of a clinical picture compatible with pseudomembranous colitis. After 5 days of admission, exams are ordered according to the case once the patient has Bristol 6 stools without mucus or blood, a stool test with the presence of fecal leukocytes and absence of parasites, Beta Toxin in stool is ordered for Clostridium Dificcile being negative . A colonoscopy is proposed to the Gastroenterology department.

This patient receives multiple antibiotic schemes that included the combination of Metronidazole IV and oral Vancomycin, however, despite complying fully, no improvement was obtained, so the Gastroenterology Service proposed to perform a healthy donor microbiota transplant. This therapy is not as innovative as in April 2013, the US Food and Drug Administration (FDA) drafted its first guide to the use of fecal transplants, considering donated fecal material as a medicine.

It is described in the literature the use of this both rectally and orally being a field not explored on a large scale in Medicine, in the mentioned case it was decided to place enemas or fecal transplanted every day on 2 occasions. On the second day, a very important improvement was observed with the absence of diarrheal evacuations and the signs of systemic inflammatory response. It should be noted that it is not frequent to observe this association with the use of Carbapenemic, however this was the only group of antibiotics used in this patient before the development of it. In the remaining time, oral Vancomycin and Metronidazole IV were maintained for 21 days [5]. The Biopsy report obtained 30 days later reported findings compatible with an inflammatory process of the nonspecific mucosa.

Discussion

In the microbiota of the intestine of an adult human being, it is estimated that there are approximately one billion of microorganisms per milliliter of fecal content, which houses 500 to 1,000 different bacterial species [6]. The microbiota prevents colonization of the intestine by pathogenic bacteria such as Escherichia coli, Salmonella, Clostridium (C) and Shigella [7]; In addition, it is involved in a wide variety of functions in the host, including modulation of the immune system and metabolism [8,9]. The fecal transplant was documented for the first time in fourth-century China; It was known as yellow

soup. It has been used for more than 100 years in veterinary medicine and used regularly for decades in many countries as the first line of defense or treatment of choice for C. difficile. Fecal transplantation has been used sporadically in the United States since the 1950s, without much regulation [10]. The first use of the TMF fecal microbiota transplant in humans dates back to a case of 1958, in a series of four patients with pseudomembranous enterocolitis. Of the more than 700 cases reported to date, the transplantation of fecal mycrobiote has demonstrated a rapid response and one, so it could be explained that in the latest investigations this has been used to treat pseudomembranous colitis caused by C. difficile in refractory cases [11,12].

In the summer of 2013, the FDA announced that fecal matter would be considered as a new investigational drug (NID) and a biological one, and that only doctors with approval for the use of NID could continue with the development of TMF [13]; however, due to the success rate of transplants, the FDA reversed its position in the same year [14]. Mentioned the foregoing, it is very important to establish a series of controls for the execution of the TMF and on the selection of donors and the follow-up of cases for the identification of medium and long-term conditions. To this end, criteria have been created that define the inclusion and exclusion of donors for TMF [15]. The procedure for donor determination will consist of the following steps:

A. Identification: the identification of the possible candidate to donate will be in charge of the patient; It could be a relative or an unrelated person

B. Questionnaire: once the potential donor (s) has been identified, you will complete the questionnaire that will be delivered to you in the clinical laboratory area.

C. Interview: Subsequently, a brief medical interview will be conducted to determine the presence of medical or infectious conditions using the guide questionnaire, a physical examination and, finally, the detection by laboratory tests. In certain cases, it will be necessary to ask both questions and additional laboratory tests according to the donor's background (Table 2,3).

Conclusion

The value of TMF in the treatment of pseudomembranous colitis is clear, but its possible long-term consequences, both beneficial and harmful, are unknown [16]. A priori knowledge is not available regarding the impact of the transfer of these communities of complex microorganisms from one person to another [17]. Although many studies in mice indicate that the composition of the intestinal microbiota may affect the susceptibility of the host to diseases, critical data such as donor / recipient detection, fecal preparation, delivery modality and practices are lacking. patient consent [18]. There is information about the effectiveness of this therapy in the short term; however, this does not systematically carry long-term safety data [19]. The only information available is case reports published in the literature [20]. Therefore, we consider it essential to conduct studies in our country because of the future importance of this treatment in the management of pseudomembranous colitis in those cases where there is refractory treatment.

Criterials
1 Age between 18 and 65 years
2 No history or symptoms present suggestive of gastrointestinal disease
3 Without presence of major medical comorbidities
4 Minimum medication that does not affect the viability of feces, including antibiotics in a period of 3 months.

Table 2: Donor inclusion criteria for fecal microbiota transplantation [15].

zzzzzzzzz1 Riesgos de agentes infecciosos
• Known infections (HIV, HBV, HCV)
• High-risk sexual activity (multiple partners, prostitution)
• Use of illicit drugs
• Tattoos or piercings less than six months old
• History of travel to endemic areas with high prevalence of diarrheal diseases
2 Gastrointestinal Comorbidities
• History of inflammatory bowel disease
• History of irritable bowel syndrome, chronic constipation, chronic diarrhea
• History of gastrointestinal malignancy or presence of polyps, a history of colorectal cancer
3 Factors that may alter the composition of the microbiota
• Use of antibiotics or probiotics within three months
• Use of immunosuppressive medications (steroids, etc.)
• Systemic antineoplastic agents
• Members of the same household with active gastrointestinal infection
4 Other conditions
• Systemic autoimmunity (example: multiple sclerosis, connective tissue diseases)
• Atopic disease (example: moderate to severe asthma, eczema, eosinophilic disorders
• Metabolic syndrome, obesity with body mass index > 30 or moderate to severe malnutrition
• Chronic pain syndromes (example: chronic fatigue syndrome, fibromyalgia
• History of malignant diseases or oncological treatment

Table 3: Donor exclusion criteria for fecal microbiota transplantation [15].

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