

CASE REPORT

Stress involvement in pathophysiology of Diverticular Disease: case series and review of the literature

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ABSTRACT

Diverticular disease pathogenesis is still unknown in depth. Adaptation to a severe social stress possibly generates sustained dominance of the sympathetic over the parasympathetic activity, leading through a prolonged spasm of the sigmoid to the creation of diverticula and the related disease. Based on case series, we suggest an imbalance in autonomic nervous activity as a component of the multisystemic complex pathophysiology of diverticular disease.

Keywords: Diverticular disease, pathogenesis, stress, sympathetic nervous system

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INTRODUCTION

Diverticular disease is one of the most common conditions in the outpatient diagnosis and one of the most common findings identified in colonoscopy [1-3]. Epidemiological studies have confirmed the increase of hospital admissions for acute diverticulitis in recent years [4].

While the terms diverticulosis, diverticulitis, and diverticular disease are often used interchangeably, diverticulosis refers to the presence of diverticula in the colon, diverticulitis refers to the presence of peridiverticular inflammation and infection, and diverticular disease refers to the full spectrum of symptoms caused by the presence of diverticula including cramping, bloating,

pain, and fever. In an incidence rising with age people with colonic diverticula remain asymptomatic, making diverticulosis not a disease per se. Around 20% of those individuals will develop diverticular disease when they experience abdominal symptoms and 1-4% will evolve to acute diverticulitis. The pathogenesis of diverticular disease is thought to be multifactorial and include both environmental and genetic factors. It appears that the evidence for the role of dietary fiber deficiency in the development of diverticulosis is inconsistent, but that there likely exists some benefit to increased fiber intake in the reduction of diverticular disease complications [5-7]. Additional factors include vitamin D [9] levels, increased physical activity [5], non-steroid anti-inflammatory drugs use and the

pivotal context of mucosal inflammation which has several implications [8]. Firstly, inflamed microenvironment in the gut drives bacterial dysbiosis [10], favoring a vicious cycle between dysbiosis-driven inflammation and inflammation-driven dysbiosis. Secondly, mucosal inflammation and dysbiosis might lead to dysmotility [11], which is a critical step in diverticular disease pathophysiology. Hence, not well understood.

We herein report three cases of acute diverticulitis that illustrates the importance of identification of population at risk for the disease's development and the need for further investigation in accurate measurement of emotional stress factors.

CASE REPORTS

Case 1

A 63-year-old woman, with previous medical history of diabetes and high arterial blood pressure, was admitted in the Emergency Department of our clinic complaining about abdominal pain and vomiting. Regarding the social history of the patient, she reported her husband severely diseased 9 months ago. Physical examination revealed distention and tenderness of the abdomen, and no palpable mass. Laboratory investigations showed a slightly elevated white blood cell count (WBC 11.9 K/ μ L) and a C-reactive protein of 7 mg/l. All other laboratory data were within the normal range. Abdominal x-ray was performed and demonstrated multiple air-fluid levels and bowel dilatation. Under suspicion of acute

abdomen, a CT scan was performed and demonstrated mild diverticulitis of the descending colon, with wall thickening, a diverticulum, and mild stranding of the pericolic fat (Figure 1). She was transferred to the surgery unit. The patient was treated with bowel rest, intravenous fluids and broad-spectrum IV antibiotics, which resulted in reduction, and a few days later with complete resolution of the symptoms.



Figure 1. Case # 1. CT scan demonstrated mild diverticulitis of the descending colon, with wall thickening, a diverticulum, and mild stranding of the pericolic fat (arrow).

Case 2

A 49-year-old male patient was admitted in the Emergency Department of our clinic complaining about mild diffuse abdominal pain, with no specific location of tenderness. This pain commenced the previous day, along with fever up to 38.5°C. He did not mention any other symptoms, such

as nausea, appetite loss, or bowel dysfunction. His laboratory values included WBC 12.43 K/ μ L with 74.5% neutrophils and a C-reactive protein of 10 mg/l. His vital signs were between normal ranges. From his medical history he revealed two additional episodes of acute diverticulitis during the last year (nine months and one month before this admission), for which he followed conservative treatment. Regarding the social history of the patient, he had low socioeconomic status and a despondent divorce a year ago. At the time of admission, he was not on immunosuppressant or any other medication.



Figure 2. Case # 2. CT scan demonstrated sigmoid diverticulitis wall thickening (arrow), diverticulosis, and stranding at the root of the sigmoid mesentery.

A CT scan was performed and demonstrated sigmoid diverticulitis wall thickening, diverticulosis, and stranding at the root of the sigmoid mesentery (Figure 2). He was transferred to the surgical unit. The

patient was treated with bowel rest, intravenous fluids and broad-spectrum IV antibiotics, which resulted in reduction, and a week later in a complete withdrawal of the symptoms.

Case 3

A 42-year-old male patient was admitted in the Emergency Department of our clinic complaining about lower abdominal pain. The pain presented the previous day, along with fever up to 38°C and diarrhea. Prior to our examination, the patient was scheduled to have a blood test and an X-ray examination of the abdomen. His laboratory values included WBC 15.93 K/ μ L and a C-reactive protein of 4 mg/l. A CT scan was performed which revealed diverticulitis of the sigmoid colon associated with a pericolic abscess, without free fluid or air in the abdomen. (Figure 3).



Figure 3. Case # 3. CT scan demonstrated diverticulitis of the sigmoid colon associated with a pericolic abscess (arrow).

Regarding the social history, he is a Syrian immigrant suffering from both the war that led to his expatriation a few months ago and a dangerous and physically demanding sea travel. He was transferred to the surgery unit. The patient was treated with bowel rest, intravenous fluids and broad-spectrum IV antibiotics, which resulted in reduction, and a few days in complete withdrawal of the symptoms.

DISCUSSION

Diverticular disease is quite common, but still pathophysiology details are missing. Dysmotility seems to be a key feature of this process. The hypermotility appears to predominate in the descending and sigmoid colon, while motility is normal in the transverse colon [11] while etiology of this uncoordinated and excessive activity is unclear. In addition, the sigmoid is the narrowest part of the colon and the one with the strongest wall muscle as the 3 taenia coli merge at the sigmoid wall forming a complete external muscle layer. Segmentation movements at an empty sigmoid was initially suggested as a causative factor for the protrusion of the mucosa through the vessel openings penetrating the colonic wall layers [11,12].

Associations between increased colonic activity and emotional stress have been confirmed [13,14]. In our cases, which were selected in a cross-sectional design from all diverticulitis cases admitted in 3 large volume centres in Greece within one day, we have found three out of four cases having a

remarkable stressful personal/emotional history. The common ground in all is that the stress leads to increased colonic spasm like (p.e. in segmentation) like the one happening in increased sympathetic tone, and not the effective peristaltic movement enhanced parasympathetic activity. Stress that leads to imbalance towards the sympathetic may be the missing link in the pathogenesis of diverticulitis.

Heart rate variability (HRV) is established as a real time biomarker for ANS activity [15]. Previously, reduction of HRV indices has been reported in healthy participants (endotoxin model) and in patients with various infectious conditions from viral infections like dengue fever, HIV and chronic hepatitis to severe bacterial infections and sepsis [16-19]. In particular, HRV has been extensively studied in patients with sepsis and septic shock in the ICU. These studies also showed that the reductions of HRV indices (both in the time domain and frequency domain) were correlated with the severity of sepsis and mortality [16]. Although there is limited research done in the field substantial HRV depression in relation to acute uncomplicated diverticulitis has been found, and these reductions were associated with elevated biomarkers for clinical bacterial infection [20].

CONCLUSION

Diverticular disease pathogenesis is still unknown in depth. Based on the observation of diverticular disease cases, an imbalance in autonomic nervous activity is proposed

etiology. Physical adaptation to a severe social stress possibly generates sustained dominance of the sympathetic over the parasympathetic

activity, leading through a prolonged spasm of the sigmoid to the creation of diverticula and the related disease.

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ΠΑΡΟΥΣΙΑΣΗ ΠΕΡΙΣΤΑΤΙΚΟΥ

Η συμμετοχή του στρες στην παθοφυσιολογία της εκκολπωματικής νόσου: σειρά περιπτώσεων και ανασκόπηση της βιβλιογραφίας

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ΠΕΡΙΛΗΨΗ

Η παθογένεια της εκκολπωματικής νόσου είναι ακόμη άγνωστη σε βάθος. Η προσαρμογή σε ένα έντονο κοινωνικό στρες προκαλεί πιθανώς διαρκή ενεργοποίηση του συμπαθητικού νευρικού συστήματος και υπεροχή έναντι της παρασυμπαθητικής δραστηριότητας, οδηγώντας μέσω ενός παρατεταμένου σπασμού του σιγμοειδούς στη δημιουργία εκκολπωμάτων και της αντίστοιχης νοσολογικής οντότητας. Με βάση σειρές περιπτώσεων που αντιμετωπίσαμε, προτείνουμε μια ανισορροπία στην αυτόνομη νευρική δραστηριότητα ως σημαντικό συστατικό της πολυσυστηματικής σύνθετης παθοφυσιολογίας της εκκολπωματικής νόσου.

Λέξεις-ερευρηρίου: εκκολπωματική νόσος, παθογένεια, στρες, συμπαθητικό νευρικό σύστημα

Σ. Βούλγαρης, Χ. Μπαρτσώκας, Π. Βασιλείου. Η συμμετοχή του στρες στην παθοφυσιολογία της εκκολπωματικής νόσου: σειρά περιπτώσεων και ανασκόπηση της βιβλιογραφίας. *Επιστημονικά Χρονικά* 2022; 27(1): 179-184
