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Adult intestinal toxaemia botulism in ulcerative colitis patient

ABSTRACT

Botulism is caused by neurotoxins produced by diverse members of the genus *Clostridium* and is rare in humans. Among the major forms is the adult intestinal toxaemia botulism caused by the insitu production of the neurotoxin from the toxigenic *Clostridium* spp. colonizing the intestines. Crohn's disease an inflammatory bowel disease, (IBD) is considered a predisposing factor for colonization of the intestines by *C. botulinum*. Here, we report the first case of botulism in a patient with ulcerative colitis (UC) who visited the gastrointestinal clinic complaining of intermittent diarrhea, abdominal distension, and acute pain. In addition, she experienced symptoms of cranial nerve palsies) diplopia and blurred vision (that lasted for a short time. *C. botulinum* was isolated from the stool of the patient, which led to the confirmed diagnosis of adult intestinal toxaemia botulism. Long antibiotic therapy and UC (another form of IBD) had likely promoted colonization by *C. botulinum*, leading to the symptoms of botulism that were overlooked by those of UC.

KEYWORDS: botulinum neurotoxins, *Clostridium*, inflammatory bowel disease, gastrointestinal disease

INTRODUCTION

Botulism is a rare but severe disease caused by a group of neurotoxins produced mainly by Clostridium botulinum in addition to many other members of the genus Clostridium (e.g., C. butyricum, C. baratii, etc.). The botulinum neurotoxins (BoNT) are serologically classified into seven distinct serotypes (A - G) (Zhang et al., 2017), and they are classified depending on their physiological properties and 16S rRNA gene sequences into four different groups (I – IV) (Austin et al., 2003). Groups I and II are associated with human disease, which have various forms: foodborne, infant, adult intestinal colonization, and wound botulism; group III is associated with animal disease, while group IV is not related to any disease to date. Botulism symptoms can vary from typical GIT symptoms (nausea, abdominal pain, vomiting, diarrhea) to neuro-muscular toxicity symptoms: symmetric descending acute flaccid paralysis progressing to respiratory compromise (Carrillo-Marquez et al., 2016). Due to the rarity of the disease, only a few cases of adult botulism due to colonization of the intestines are reported to occur. Antimicrobial therapy for extended periods promotes colonization by disrupting the intestinal microflora/microbiome.



Other risk factors for intestinal colonization are conditions related to the intestines, such as surgery, anomalies, inflammatory bowel diseases (IBD), and foodborne botulism (Harris et al., 2020). In the literature, only a few cases of botulism in Crohn's disease (CD) patients are reported (Griffin et al., 1997; Sheppard et al., 2012). Botulism is diagnosed by detecting the neurotoxin in the serum of a suspected patient or the food sample, isolating the neurotoxigenic *Clostridium*, or detecting its DNA.

Here we report a case of adult intestinal toxaemia botulism in an ulcerative colitis patient by isolating *C*. *botulinum* from the stool of the patient.

CASE REPORT PATIENT INFORMATION

A 43-year-old- female visited the GIT clinic at Ibn Sina Specialized Hospital complaining of standing stabbing abdominal pain, abdominal distension for 10 days, loss of weight for the last month, intermittent diarrhea (5 - 6 times a day), stool tinged with blood, and dry mouth with cracks in the lips. In addition, she suffered from diplopia and blurred vision, but she did not mention them on the first visit to the GIT clinic. The patient was non-alcoholic and non-smoker. She was in antibiotic treatment for 10 days with ciprofloxacin and metronidazole.

CLINICAL FINDINGS

Upon physical examination, pallor and abdominal distension were evident.

TIMELINE

In 2005, the patient suffered from very severe abdominal pain in the epigastrium and right and left lumbar regions associated with abdominal distension, vomiting, and diarrhea. Later, the symptoms were rectal bleeding and mucus discharges. Subsequently, the condition was diagnosed as ulcerative colitis. The patient was also diagnosed with diabetes in the last 2 years.

DIAGNOSTIC ASSESSMENT

The patient underwent an endoscopy and colonoscopy after the physical examination. Endoscopy and colonoscopy reports described extensive oesophageal candidiasis and LA grade B oesophagitis; no gastritis or duodenitis; normal mucosa and vascular pattern; neither piles nor anal mass were noticed. Duodenal and colonic biopsies were sent for histopathology to exclude dysplastic changes. The histopathology report of duodenal mucosa biopsies described typical villous architecture; the lamina propria showed mild chronic inflammatory cell infiltrate; no evidence of villous atrophy, increased intraepithelial lymphocytes, or crypt hyperplasia. Colonic mucosa biopsies revealed unremarkable crypt architecture, the lamina propria showed mild chronic inflammatory cell infiltrate; no cryptitis, crypt abscesses, dysplasia, or malignancy. Anaerobic stool culture yielded the growth of gram-positive rods. PCR with 16S rDNA primers followed by sequencing identified the organism as *Clostridium botulinum*.



THERAPEUTIC INTERVENTION

The patient was under a regimen of IBD treatment with mesalazine) Pentasa tabs (and insulin for diabetes. The patient was advised to continue with this medication.

FOLLOW-UP AND OUTCOMES

The symptoms of cranial nerve palsies (diplopia and blurred vision) improved with time and subsided completely, but the abdominal pain persisted.

DISCUSSION

Botulism is diagnosed by detecting *C. botulinum* or any other neurotoxigenic clostridia or neurotoxin in the samples (Harris et al., 2020; Angulo et al., 1998). Here, we report a case of adult intestinal toxaemia botulism by isolating C. botulinum from the stool of a patient with UC. As a known UC patient, she visited the GIT clinic complaining only of symptoms related to UC and did not mention any other symptoms. However, when the stool culture results were obtained, the patient was contacted to enquire about any symptoms of neurotoxicity. The patient disclosed that she had experienced diplopia and blurred vision, which lasted for a short period. Unlike the aggressive type A botulism, chronic cases of visceral botulism are associated with a short-lived BoNT E (Rodloff and Kruge 2011). In a thorough literature review conducted by Harris, Annibali and Austin (Harris et al., 2020) on adult intestinal toxaemia botulism, only three cases were found that relate to IBD, specifically CD. They suggested that CD is predisposed to intestinal colonization by the neurotoxigenic Clostridium; IBD has been associated with dysbiosis, leading to a change in the intestinal microbiome (Barko et al., 2018), which may favour the conditions for colonization by these bacteria. Prolonged antibiotic therapy affects the equilibrium of the microbial communities in the intestines, which may favor colonization by non-usually hosted bacteria, such as C. botulinum. It is a common practice in Sudan that people take antibiotics without proper diagnosis and medical prescription. In addition, the patient in the present report came from a rural area where health-care facilities are limited and, therefore, people take medicines on advice from their relatives and older adults. The patient had visited Ibn Sina Hospital as a referral center for GIT after being under antibiotic therapy for 10 days. It was unclear whether this therapy predisposed the patient to colonization by C. botulinum. However, the contrary could be possible. Metronidazole is active against anaerobic bacteria and is a known regimen for reducing the risk of Clostridioides difficile infection. It may have shortened the colonization by C. botulinum and reduced its burden, so the neurotoxicity symptoms resolved sooner. The source of the infection was also unclear. The area from which she came (East Nile region) is known for animal botulism, according to reports by a field veterinary doctor (Omima Osman, Department of Animal Health and Epidemics Control, Khartoum State, personal communication). The patient had no contact with animals, but contamination of food or water directly by this soil-borne organism or by fecal material from animals harboring human toxigenic serotypes is possible.

Adult intestinal toxaemia botulism is rare, and few reports are available in the literature (Rodloff and Kruge 2011; Harris et al., 2020). It is more likely that many cases are mistaken or overlooked due to the mild symptoms, as in the present case. Therefore, we screened stool samples from patients over 6 months to look for other possible cases of intestinal colonization by *C. botulinum*. It was astonishing that a sample from



another diarrhoeic patient yielded growth of *C. botulinum*, as identified by initial culture and 16S rDNA PCR followed by sequencing. Unfortunately, the patient's record was incomplete, and his contact details were incorrect. Therefore, it was not possible to obtain any further information about him.

CONCLUSIONS

The symptoms of the overlaying disease (UC) in this case were more or less similar to those of early intestinal toxemia botulinum when excluding those of neurotoxicity (cranial nerve palsies). The case described here represents the first case of this disease in a patient with UC. It points out that many cases of adult botulism resulting from intestinal colonization by BoNT-producing *Clostridium* species are overlooked.

Abbreviations

- UC Ulcerative Colitis
- IBD Inflammatory Bowel Disease
- CD Crohn's Disease
- BoNT Botulinum Neurotoxin
- GIT Gastrointestinal Tract
- PCR Polymerase Chain Reaction

Declarations

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee, of Ibn Sina Specialized Hospital. The patient gave written and oral consent for the use of her anonymous data and samples. Informed consent was obtained from all subjects whose samples were involved in the study.

Consent to publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

All data supporting our findings are contained within the manuscript. Further details can be provided upon written request to the corresponding author

Competing interests

All authors have no reported conflicts of interest.



Institutional Review Board Statement

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Informed Consent Statement

The patient gave written and oral consent for the use of her anonymous data and samples. Informed consent was obtained from all subjects involved in the study.

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Conflicts of Interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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