IDCases 21 (2020) e00797

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case report

Clostridioides difficile co-infection with Enterohemorrhagic *Escherichia coli* (EHEC)—a potentially fatal combination

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ARTICLE INFO

Article history:
Received 15 April 2020
Received in revised form 3 May 2020
Accepted 3 May 2020

Keywords:
Clostridioides difficile
Co-infection
Shiga toxin
EHEC
Colitis

ABSTRACT

There has been a significant increase in hospital and community acquired *Clostridioides difficile* infection in the past decade. In addition to CDI, the rate of infection with enterohemorrhagic *Escherichia coli* (EHEC) has also increased by 28% in United States in the last five years. Concomitant CDI and EHEC infections are rare and if not identified early such co-infections can be fatal. We present the case of patient with hematochezia who was found to be positive for *Clostridioides difficile* and EHEC. She had a complicated hospital course that required timely identification of complications and management.

Introduction

About half a million people in United States are affected by *Clostridioides difficile* infection (CDI) annually, of which 41% infections are community-acquired [1]. The incidence and severity of CDI has been increasing at an alarming rate in the last few decades with up to 40% patients with community acquired CDI needing hospitalization [2]. *Escherichia coli* O157:H7 or enterohemorrhagic *Escherichia coli* (EHEC) is a Shiga-toxin producing strain of the bacteria [3]. EHEC transmission is generally through consumption of contaminated food and water [3]. Despite ongoing efforts to increase awareness about food hygiene, the incidence of EHEC has increased by 28% in United States between the year 2014 and 2017 [3].

We present the clinical course of a patient with concomitant *Clostridioides difficile (C. difficile)* and EHEC infection who developed fulminant colitis and had a steady recovery with time and close monitoring.

Case report

An 88 year-old woman with past medical history of hypertension presented to the emergency department with one day of 15–20 episodes of bloody diarrhea preceded by a week of non-bloody watery diarrhea. She denied any associated nausea, vomiting, fever or chills, recent infection, antimicrobial use or recent travel. She had never had a similar episode in the past. Patient stated that she generally eats home-cooked food and she denied eating any raw or undercooked food recently, which was confirmed by obtaining a detailed list of recently consumed food products. She denied any poultry or sick animal exposure. Additionally, she had never had a prior colonoscopy as she had refused it. She also denied any family history of gastrointestinal illnesses or malignancies.

On admission, vital signs and physical exam were unremarkable except for upper abdominal tenderness on palpation. She had normal bowel sounds, there was no rebound or guarding, no hepatosplenomegaly was noted and rectal exam did not reveal any blood. Laboratory tests showed white blood cell count of 9200/uL, hemoglobin 15.8 g/dL, platelet count 249000/uL, creatinine was 1 mg/dL. CT abdomen showed severe colitis of the ascending and transverse colon. Her stool tested positive for *C. difficile* using nucleic acid amplification test (NAAT) testing and specific toxin A and toxin B enzyme immunoassay (EIA). She tested positive for Shiga toxin by EIA. On culture and biochemical analysis *Eschericia coli* serotype O157:H7 was isolated. Shiga toxin 2 DNA was detected by PCR. She was started on oral vancomycin 125 mg four times a day for *C. difficile* infection. She developed leukocytosis of 12400/uL which later trended up to 24,500 u L; and the platelet count remained stable.

Although the frequency of hematochezia gradually decreased in the following days, by fourth day of admission her creatinine increased to 1.6 mg/dL and she began reporting diffuse abdominal

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https://doi.org/10.1016/j.idcr.2020.e00797

pain, abdominal distention and had some involuntary guarding on physical exam. Repeat CT abdomen showed worsening colitis involving the entire ascending, transverse and descending colon. Surgery was consulted at this point and closely followed her for signs of clinical deterioration which may warrant undergoing total abdominal colectomy. She was monitored closely for the rest of the week and rectal vancomycin 500 mg four times a day was started. Her symptoms briefly improved with resolution of hematochezia and decreased stool frequency (4–5 episodes of diarrhea per day), however, by the second week abdominal distention and diffuse tenderness restarted along with multiple diarrheal episodes (8–10 episodes per day). Intravenous metronidazole 500 mg three times a day was added to her treatment regimen and the possibility and benefits of early colectomy or fecal microbiota transplantation (FMT) were discussed with the patient. In the following days she reported few episodes of bowel movement that had mucus mixed with small amount of blood. By the end of second week, her abdominal distension had decreased, stool consistency and color was normalizing and she was tolerating diet. Her creatinine improved to her baseline of 0.9 mg/dL and platelet count remained stable throughout hospitalization (383000/uL at the time of discharge). Given how long the patient was ill and how slowly she responded, she was discharged with an extended course of oral vancomycin 500 mg four times a day for two weeks, then 500 mg once a day for one week followed by then 500 mg every other day for one week. On follow up at two weeks and at one and six months, patient remained without symptoms.

Discussion

We have seen a dynamic change in the epidemiology and associated risk factors of CDI in the last decade [4]. Recent or prolonged hospitalization, recent antimicrobial use and advanced age are some of the well-known risk factors of CDI. However, in the last decade there has been an exponential rise in the rates of non-antimicrobial associated CDI, increased incidence of CDI in pediatric population and in adults with no underlying co-morbidities [2,4,5]. Of the traditional risk factors for CDI, our patient did have an advanced age. Concomitant *Clostridioides difficile (C. difficile)* and EHEC infections are rare and if not identified early such co-infections can be fatal. Literature on such co-infection is sparse. To our knowledge and after extensive literature review, there have been eight cases of *C. difficile*-associated atypical hemolytic uremic syndrome (HUS) reported. One of the characteristic defining feature of atypical HUS is a negative STEC (Shiga toxin-producing E. coli) [6]. Ours is the first case of CDI-EHEC co-infection in an adult where *C. difficile* and Shiga-like toxins were both positive. Our patient tested positive for *C. difficile* with NAAT and EIA. EHEC was identified on culture and biochemical analysis and Shiga toxin 2 DNA was detected by PCR. To our knowledge, there is no known cross reactivity between *C. difficile* NAAT toxin assay and EIA for Shiga toxin.

Both CDI and EHEC carry the risk of fatal complications. The clinical features of a symptomatic CDI infection range from mild symptomatic diarrhea to acute fulminant colitis [7]. Up to 3% patients with CDI can develop fulminant colitis which has a mortality rate of 34.7% [4]. Therefore, in addition to close monitoring, early involvement of general surgery is also critical in these patients. The incidence of HUS is approximately 5–15% in EHEC infections [8]. Our patient was carefully monitoring for HUS. Her platelet count and hemoglobin remained stable during the course of her hospitalization. Her creatinine did increase to 1.6 mg/dL by fourth day of hospitalization and then gradually improved with improved oral intake.

Due to lack of guidelines and the limited literature on *C. difficile* co-infection with EHEC, management and outcome of such infections remains unclear [9]. While the Infectious Diseases Society of America guidelines recommend initiation of empiric antimicrobials if CDI is suspected, antimicrobial use in E. coli O157:H7 infection could possibly increase the risk of HUS [4,10]. Kennedy et al. reported the case of a 75 year-old man, with no prior risk factors for CDI, who was found to have pseudomembranous colitis-like lesions on flexible sigmoidoscopy [10]. Interestingly this patient tested negative for *C. difficile* toxin, however, stool test was positive for *E. coli* O157:H7. He was initially empirically treated for CDI with metronidazole and vancomycin which were discontinued after he was found to be positive for *E. coli* O157:H7. The patient had a complicated clinical course with development of HUS and an episode of seizure. He was then empirically treated for sepsis with broad-spectrum antimicrobials and eventually recovered. On the other hand, delay in diagnosis can also prove fatal. Guillard et al. reported the case of a 71 year old man with a diagnosis of CDI who developed HUS due to atypical EHEC [11]. Despite being on antimicrobial therapy, hemodialysis and plasmapheresis, the patient suffered from progressively declining renal and neurological functions. He eventually died due to cardiovascular collapse [11].

In conclusion, we present the case of a patient with CDI who was found to have co-infection with Shiga-toxin producing EHEC. Such co-infections, although rare, require a high index of suspicion and close monitoring due to the risk of fatality associated with them [11]. Our patient had a relatively early diagnosis and received appropriate treatment. Despite this her clinical course worsened with the development of pancolitis. However, she made a gradual recovery with close monitoring.

Authors contributions

Farah Deshmukh: Drafting of the article; critical revision of the article for important intellectual content; final approval of the article.

Upasana Agrawal: Critical revision of the article for important intellectual content; final approval of the article.

Nancy Merrell: Patient treatment and management, critical revision of the article for important intellectual content, final approval of the article.

All authors confirm that this work is original and has not been published previously.

Funding

None.

Informed consent

Written informed consent was obtained from the patient for publication of this case report.

Declaration of Competing Interest

None.

Acknowledgement

None.

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