STEC colitis mimicking acute severe colitis with life-threatening consequences: a case report

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Abstract

Acute colitis is a common feature of infection with Shiga-toxin producing Escherichia coli (STEC) and can mimic acute severe ulcerative colitis. Early recognition is important as there is a risk of developing Shiga toxin-induced haemolytic uremic syndrome (STEC-HUS), defined by the triad of microangiopathic haemolytic anemia, thrombocytopenia and organ damage. In severe cases STEC-HUS can cause severe neurological complications and can be fatal.

Case: **We present a patient with a medical history of refractory ulcerative colitis, where making the diagnosis of STEC-HUS was challenging since the initial clinical presentation was difficult to differentiate from a flare of ulcerative colitis.**

Conclusion: **This case illustrates that STEC induced colitis can mimic acute severe ulcerative colitis. This finding is of utmost clinical importance because of the potential life-threatening complications of STEC-HUS. Therefore it should be excluded promptly in patients with acute severe ulcerative colitis by using multiplex-PCR assay on a faecal sample.** (Acta gastroenterol. belg., **2024,** 87, **37-39**).

Keywords: haemolytic uremic syndrome (HUS), thrombotic micro-angiopathy (TMA), ulcerative colitis (UC), inflammatory bowel disease (IBD), STEC-HUS.

Introduction

Shiga-toxin producing Escherichia coli (STEC) can cause colitis, which in up to 10% of cases can be complicated by the development of Shiga toxin-induced haemolytic uremic syndrome (STEC-HUS). STEC-HUS is part of the broad spectrum of thrombotic microangiopathy (TMA), defined by the triad of thrombocytopenia, Coombs-negative microangiopathic haemolytic anaemia and ischemic organ damage (1). At the early stage of STEC-related colitis, patients present with acute bloody diarrhoea, which can be difficult to differentiate from other infectious aetiologies as well as non-infectious causes (1,2); in particular ulcerative colitis.

Case

An 18 year-old Caucasian man with a 1-year history of refractory ulcerative colitis (primary non response to mesalazine, budesonide and azathioprin, secondary failure to adalimumab and primary non-response to vedolizumab) was hospitalized for an acute severe ulcerative colitis (ASUC) with symptoms of fever, bloody diarrhoea and abdominal pain for which he received treatment with antibiotics (ciprofloxacin and metronidazole intravenously (IV)) and methylprednisolone IV. An initial faecal culture was negative for enteric pathogens, negative for toxin-producing *Clostridioides difficile* and Shiga-toxin antigen. A sigmoidoscopy was performed and revealed an active ulcerative colitis with deep ulcerations and necrotic debris (Mayo 3 endoscopic score, figure 1). Biopsies and serological testing excluded cytomegalovirus (CMV) colitis. Computed tomography (CT) of the abdomen showed a severe pancolitis without evidence for perforation. Despite the treatment, the patient deteriorated with worsening of inflammatory parameters. He was started on high dose infliximab (10 mg/kg IV) and transferred to our hospital, a tertiary IBD referral center.

Shortly after admission the patient developed acute encephalopathy for which he was transferred to the Intensive Care Unit eventually necessitating protective intubation due to rapidly progressive obtundation with

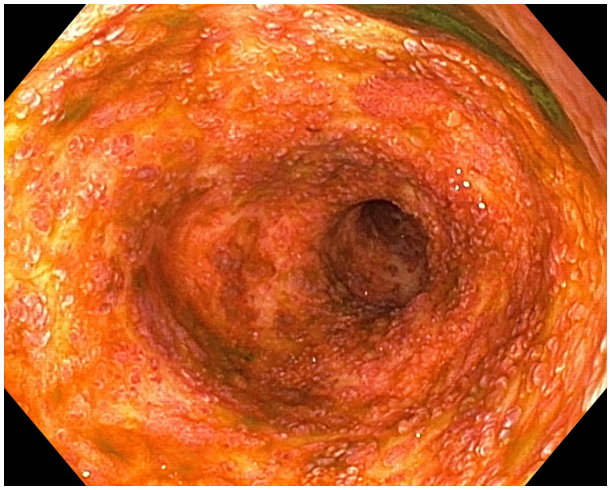

Figure 1. — Sigmoidoscopy upon admission revealed continuous inflammation with deep ulcers.
(Mayo score: 3 , Ulcerative Colitis Endscopic Index of Severity: 5).

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GCS of 5/15 (E3M1V1). Laboratory studies were most remarkable with a new onset severe thrombocytopenia (19 x 10**9/L, normal value: 150-450 x 10**9/L) no anemia (haemoglobin value 17.4 g/dL, normal value 14.0-18.0 g/dL), doubling of serum creatinine from baseline (1.89 mg/dL, normal value 0.67-1.17 mg/dL), elevated blood urea nitrogen (99 mg/dL, normal value ≤ 49 mg/dL), increased lactate dehydrogenase (LDH) (761 IU/L, normal value 130-250 IU/L), normal haptoglobin (0.61 g/L, normal value 0.30-2.00 g/L), elevated inflammatory markers (C-reactive protein 196 mg/dL, normal value ≤ 5.0 mg/dL). Urine analysis revealed microscopic dysmorphic haematuria and proteinuria (2+ on dipstick, normal value 0). CT scan of the brain showed cerebral oedema most pronounced in the basal ganglia. Urgent magnetic resonance imaging (MRI) of the brain revealed symmetrical brain lesions with cytotoxic and vasogenic oedema of the basal ganglia, thalami, hypothalamus, mesial temporal structures, cerebellar vermis and brainstem. An intracranial pressure (ICP) device was placed via neurosurgical intervention. The next days, we were confronted with a rapid decline in kidney function with worsening creatinine value (4.77 mg/dL, normal value 0.67-1.17 mg/dL). A postrenal cause was excluded with an abdominal ultrasound. The patient was started on renal replacement therapy. Further laboratory investigations to exclude thrombotic thrombocytopenic purpura (TTP) or HUS indicated a slight schistocytosis (15-20 schistocytes/ 1000 red blood cells). Since there was no overt haemolytic anaemia and the serum levels of haptoglobin were normal not all the typical features of HUS were fulfilled. However, based on the clinical characteristics, radiological and laboratory findings there was a high suspicion of TMA and plasmapheresis was started because of the differential diagnosis with TTP until the results of ADAMTS13 was known. This demonstrated a reduced (29.5%, normal value 40%-124%) von Willebrand Factor protease (ADAMTS13) activity. However, given the value was more than 10% TTP could be excluded and plasmapheresis treatment was stopped. Shortly afterwards, the results of a stool multiplex PCR assay surprisingly demonstrated the presence of STEC (stx2), supporting the diagnosis of STEC-HUS. Because of the high risk of abdominal sepsis in the context of refractory UC a subtotal colectomy with terminal ileostomy was performed. In the context of perioperative bleeding and high bleeding risk we abstained from performing a kidney biopsy.

Anatomopathological examination of the colectomy specimen showed a homogenous, chronic ulcerative colitis compatible with UC. The post-operative phase was complicated by an early post-operative haemorrhage requiring urgent surgical intervention with surgical haemostasis of an arterial pancreatic bleeding. Gradually, we obtained a clinical and neurological improvement with conservative treatment (IV fluid resuscitation, renal replacement therapy).

Discussion

This case report highlights the importance of excluding an infectious aetiology in patients presenting with ASUC and an atypical clinical course.

In our case a difficult-to-treat ASUC turned out to be an infectious colitis with life-threatening multivisceral complications. Earlier reports already suggested that infection with STEC can mimic ASUC, which is of clinical importance since 9% of patients with ulcerative colitis initially present with ASUC (2,3). STEC should therefore be included when making a differential diagnosis in IBD onset and flares. (Bloody) diarrhoea, abdominal pain, nausea, and vomiting are the most reported gastro-intestinal symptoms of STEC colitis (4). In these cases, renal involvement ranges from asymptomatic urine sediment abnormalities to severe renal failure requiring renal replacement therapy (1). In the context of widespread use of immunosuppressive therapy and antibiotics in IBD it is important to know that both of them can increase the risk of developing STEC-HUS (5,6). Although it is generally assumed that antibiotics do not benefit infected patients, some studies suggest that use of azithromycin is associated with lower frequency of long-term shedding (6,7).

The neurological picture of our patient evolved from an unexplained lethargy and disorientation into coma with diffuse cerebral oedema. Neurological involvement is indeed one of the most worrisome complications as it is responsible for the majority of deaths in STEC-HUS (8). Coma and seizures are the most common manifestations, but various focal defects, pyramidal or extrapyramidal syndromes have been described (8).

The pathophysiology of STEC infection can be attributed to its ability to produce a Shiga toxin (Stx), a ribosome-inactivating protein which exists as two immunologically types: Stx1 and Stx 2. Stx 2 is more often associated with haemorrhagic colitis and HUS compared to Stx 1 (1,2). Stx reaches target organs via the bloodstream and binds glycosphingolipid globotriaosylceramide (Gb3), present in lipid rafts on the surface of microvascular endothelial cells (1,9). Stx leads to apoptosis by causing ribotoxic stress, inhibition of protein translation and activation of multiple stress signalling and apoptotic pathways. Next to its cytotoxic effect, vascular dysfunction is a hallmark of its pathophysiology with a net effect that transforms endothelial cells into a more prothrombotic phenotype (1,2,9). As a consequence, STEC-HUS belongs to the spectrum of TMA and is characterised by a triad of features: thrombocytopenia, mechanical haemolytic Coombs-negative anaemia with schistocytosis and ischemic organ damage (9). "Typical" HUS is caused by a gastrointestinal infection with STEC (and occasionally other pathogens) whereas "atypical" HUS results from alternative complement pathway dysregulation (1,10). In our case, the presentation of HUS was somehow unusual since there was no overt anaemia present (although LDH was elevated, haemoglobin, bilirubin and haptoglobin

were normal; however the latter is an acute phase reactant and will be increased in the presence of inflammation). In addition, earlier stool cultures were negative for STEC and diagnosis was made by a multiplex PCR. This is probably due to a higher diagnostic accuracy and sensitivity of a multiplex PCR compared to the traditional cultured based methods (11). According to literature, diagnosis relies greatly on the detection and distinction of genes encoding Shiga toxins (Stx1 and/or Stx 2) by PCR. These are generally picked up by multiplex PCR tests and allow an earlier diagnosis compared to traditional methods and immune-assays, which have a lower sensitivity (1). As shown in our case, confirming STEC infection in stool can be challenging and should be performed quickly since it's generally detected for only a few days following diarrhoea occurrence (9).

Conclusion: STEC colitis is difficult to distinguish from ASUC and can lead to a severe, life-threatening condition that is called HUS. It is recommended to perform thorough investigations by early multiplex PCR tests on stool cultures to exclude an infectious aetiology in IBD patients presenting with acute severe colitis.

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