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Gastroenteritis in an adult female revealing hemolytic uremic syndrome: case report

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**Abstract**

Nowadays acute gastroenteritis infection caused by *Escherichia coli (E coli)* O157:H7 is frequently associated with hemolytic uremic syndrome (HUS), which usually developed after prodromal diarrhea that is often bloody. The abdominal pain accompanied by failure kidney is a suspicious symptom to develop this disorder. Their pathological characteristic is vascular damage which manifested as arteriolar and capillary thrombosis with abnormalities in the endothelium and vessel walls. The major etiological agent of HUS is enterohemorragic *E. coli* strain belonging to serotype O157:H7. The lack of papers about HUS associated to gastroenteritis lead us to report this case for explain the symptoms that are uncommon. Furthermore, this report provides some strategies to suspect and make an early diagnosis, besides treatment approach to improving outcomes and prognosis for patients with this disorder.

**Key words**: Gastroenteritis; Gastrointestinal hemorrhage; Hemolytic-uremic syndrome; *Escherichia coli* O157; Shiga-toxigenic *Escherichia coli*

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**Core tip:** Bloody diarrhea and Hemolytic uremic syndrome are frequent caused by *E. coli* serotype O157:H7. The most causes of gastroenteritis are diagnosed as non-infectious illness and this could be the reason that clinicians did not usually associated with the hemolytic uremic syndrome development. This case report not only represents the importance of the diagnosis and the treatment approach, but also is one of the few studies where it is emphasized the gastrointestinal role and the critical symptoms that the clinical has to recognize it.

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# INTRODUCTION

Thrombotic thrombocyticpurpura (TTP) and hemolytic-uremic syndrome (HUS) are acute fulminant disorders characterized by thrombocytopenia and microangiopathic hemolytic anemia. Gastroenteritis is recognized as a precursor of the HUS, which is often accompanied by pain abdominal, vomiting and bloody stools. Other specific symptoms to establish the diagnosis are kidney failure and cognitive impairment[1].

# CASE REPORT

A 61-year-old woman with a history of hypertension, osteoarthritis and irritable bowel syndrome presented to the emergency department (ED) after 5 d of bloody diarrhea without mucus, after eating high-fat food. Her vital signs upon arrival in ED were within normal limits. Physical examination revealed diffuse abdominal tenderness on deep palpation without signs of peritonitis, spasms in the upper extremities, and muscle weakness.

The results of laboratory testing were: hemoglobin, 12.3 g/dL; platelet count, 250 × 103/μL; serum creatinine, 0.76 mg/dL; serum sodium, 133 mmol/L; serum potassium, 3.04 mmol/L; serum calcium, 6.2 mmol/L; and serum magnesium, 0.54 mmol/L. She was diagnosed with hydroelectric disequilibrium as a consequence of diarrheic syndrome and admitted for immediate treatment of hypocalcemia with fluids and electrolytes via central venous access; in addition intravenous antibiotic therapy with ertapenem was begun because culture showed the presence of extended-spectrum beta-lactamase (ESBL)-producing *E. coli*.Despite aggressive antibiotic therapy, she continued to clinically deteriorate with petechiae and ecchymoses appearing on her lower legs and her biochemical profile did not improve (Table 1).At that point, the results of blood tests were: hemoglobin, 9.8 g/dL; platelet count, 11 × 103; serum creatinine, 3.5 mg/dL; and lactate dehydrogenase, 3182 units/mL. She was diagnosed with microangiopathic hemolytic anemia. Her uremia required immediate hemodialysis after the insertion of a Mahurkar catheter. Overall, she required seven hemodialysis sessions and seven plasmaphereses during the 13 days after admission. Hematological tests showed a slight increase in her erythrocyte count, so she did not need erythrocyte transfusion until the sixth day of her hospital stay. Altogether, she required three transfusions of packed cells.

Finally, the patient showed slow improvement in her renal function, recovering diuresis after 3 wk. She was discharged with a platelet count of 213 × 103/μL.

# DISCUSSION

TTP and HUS have been considered rare diseases with high mortality. They continue to be rare in adults, although we have seen them more frequently than in the past. The prevalence of TTP is around 30%-40%, whereas HUS rate is approximately 4%-10%; their mortality ranges around 90% and 15%, respectively[2].The most important reason that our patient had a positive outcome was that we never excluded HUS as a possible diagnosis. The unusual features that led us to the diagnosis were the bloody diarrhea, abdominal and diffuse pain evolving over 5 days after eating high-fat food, and the abnormal blood test results, specifically the presence of hemolytic anemia and acute kidney failure[3].

Karpac *et al*[4] reported that the most common symptom associated with typical HUS is diarrhea; however, the majority of gastrointestinal diseases can cause this. In addition, the bloody diarrhea is often caused by *Campylobacter, E. coli* O157:H7, and other Shiga toxin-producing *E. coli*, *Salmonella, Shigella, and Yersinia*; however, *E. coli* O157:H7 is the most important pathogen, which usually causes abdominal tenderness, more than 5 watery stools in the last 24 h, and especially bloody diarrhea that frequently persists during first 8 h[5].Incidentally, Kuehne *et al*[6] demonstrated that the true STEC gastroenteritis incidence in a computed estimate was 32.3-fold higher than the incidence based on notified HUS cases.

In addition, Pedersen *et al*[7] showed that the incidence rate per 100000 persons of STEC infections was highest in children < 5 years of age (32.17) and in adults ≥ 65 years of age (11.64) compared to 15-64 years old population (7.89).

Regarding to the first symptoms of our patient, the appearance of ecchymoses and petechiae, besides the sudden decrease in platelets and the increase in serum creatinine confirmed our diagnosis of microangiopathy.

As indicated in the guidelines for management of microangiopathies, our first-line therapy was plasma exchange[2] combined with hemodialysis and aggressive antibiotic therapy because ESBL-producing *E. coli* was detected in blood cultures. However, at that time we could not differentiate between HUS and TTP. Later, the normal levels of ADAMTS 13 protease led us to the definitive diagnosis of HUS[8].

Differentiation of HUS and TTP remains complex. Acute renal failure is usually more severe in HUS[9],while TTP more frequently results in damage to the central nervous system. Moake[5,8] reported that systemic aggregation of platelets, especially in the central nervous system, usually indicates TTP because platelet aggregation in HUS is predominantly confined to the renal circulation.**8**In relation to ADMTS 13, a protein responsible for cleaving Von Willebrand factor, our patient had normal levels and this was another characteristic that assisted our diagnosis.

The key features of HUS treatment are firstly, fluid therapy with isotonic solutions to avoid the occurrence of oliguria, anuria, and the requirement for dialysis[10].In our patient, diuresis was less than 0.5 mL/kg/h for more than 12 h, meaning that hemodialysis was necessary[11].Secondly, the guidelines recommend blood transfusion when hemoglobin drops to 6 mg/dL, therefore, our patient required three transfusions of packed cells. Thirdly, patient needed antihypertensive therapy because patients with HUS develop arterial hypertension caused by an overexpansion of the intravascular volume and/or ischemia-induced activation of the renin–angiotensin system[12].Finally, management with low-molecular-weight heparin was necessary to prevent a thrombotic event.

In summary, our patient presented typical clinical features of HUS. This is an uncommon disease in adults, which has a relatively good prognosis with low mortality. The gastroenterologist may encounter the HUS as it presents with primarily intestinal symptoms or may assist in the management of the abdominal complications. Anticipation of the broad clinical scope of the HUS is essential for the optimal management of this serious entity.

After contaminated food is ingested, the *Shiga* toxin (Figure 1) is released into the blood circulation, which leads to damage of the intestinal mucosa and the renal endothelium. Damaged renal endothelial cells promote a prothrombic state with an increase in platelet adhesion and formation of microthrombi[13].Clinicians should consider *E. coli* O157:H7 when evaluating patients with diarrhea, especially those with a history of bloody diarrhea, and should be aware that patients with *E. coli* O157:H7 infection can get a wrong diagnosis with a non-infectious disease. Afterwards, that is the reason why it is necessary to perform culture stools for *E coli* 0157:H7 since may lead to early recognition of outbreaks and to implement public health control measures. Definitely, surveillance on the organism is needed to define more clearly the clinical illness, populations at risk of infection and risks and benefits of treatment methods.

**Article Highlights**

***Case characteristics***

A 61-year-old woman, with hypertension, osteoarthritis and irritable bowel syndrome, presented to emergency department after 5 d of bloody diarrhea without mucus.

***Clinical diagnosis***

The diagnosis of hemolytic uremic syndrome (HUS) was based on the presence of diarrheal prodrome, thrombocytopenia and the development of acute renal failure.

***Differential diagnosis***

Thrombotic thrombocytic purpura and other causes of thrombocytopenia.

***Laboratory diagnosis***

Moderate hydroelectrolytic disequilibrium, thrombocytopenia and microangiopathic hemolytic anemia.

***Pathological diagnosis***

The culture showed the presence of *E. coli* producing extended-spectrum β-lactamases.

***Treatment***

Fluid and electrolyte replacement, plasma exchange, hemodialysis and intravenous antibiotic therapy with ertapenem.

***Related reports***

HUS associated to gastroenteritis is a rare event in adults due to very few cases had been detected. However, this disorder has high mortality but good prognosis when it is diagnosed in early stages. The treatment should be based on syndromic approach according to guidelines.

***Term explanation***

ADAMTS13 - a disintegrin-like metalloproteinase with thrombospondin motif type 1 member 13 - cleaves Von Willebrand factor anchored on the endothelial surface, in circulation, and at the sites of vascular injury.

***Experiences and lessons***

The gastroenterologist may encounter the HUS as it presents with primarily intestinal symptoms or may assist in the management of the abdominal complications. Anticipation of the broad clinical scope of the HUS is essential for the optimal management of this serious entity.

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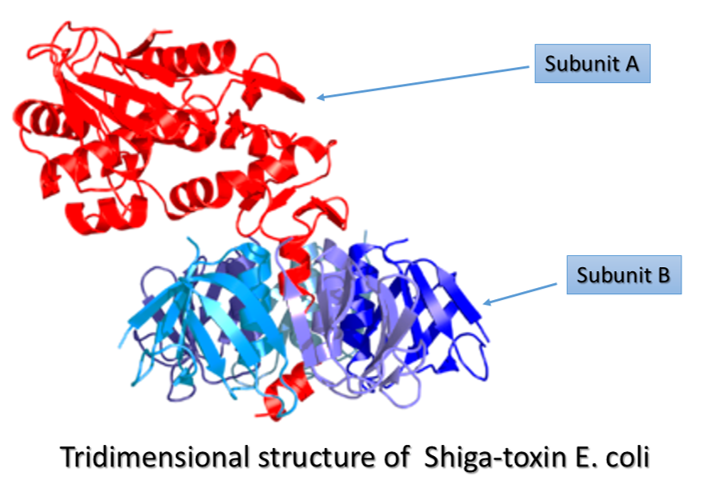
Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**Table 1 Biochemistry Test evolution of patient with gastroenteritis linked to hemolytic uremic syndrome**

|  |  |  |  |
| --- | --- | --- | --- |
| **Test** | **Initial evaluation** | **Middle evaluation** | **Final evaluation** |
| Hemoglobin | 12.3 g/dL (13-17 g/dL) | 6.8 g/dL | 9.7g/dL |
| Platelets | 250 × 103/µL (150-450 × 103/µL) | 37 × 103/µL | 213 × 103/µL |
| Leukocytes | 7.9 × 103/µL (4.5-11 × 103/µL) | 6.6 × 103/µL | 5.3 × 103/µL |
| Neutrophils | 84.3 % (40%-75%) | 75% | 88% |
| Lymphocytes | 10.7% (12%-46%) | 14% | 8.0% |
| Blood urea nitrogen | 4.9 mg/dL (8.0-20 mg/dL) | 70.4 mg/dL | 59.5 mg/dL |
| Urea | 10.5 mg/dL (17.1-42.8 mg/dL) | 150.7 mg/dL | 127.3 mg/dL |
| Creatinine | 0.76 mg/dL (0.44-1.03 md/dL) | 6.24 mg/dL | 1.97 mg/dL |
| Sodium | 133 mmol/L (136-144 mmol/L) | 129 mmol/L | 139 mmol/L |
| Potassium | 3.04 mmol/L (3.60-5.10 mmol/L) | 2.95 mmol/L | 4.27 mmol/L |
| Calcium | 6.7 mg/dL (8.9-10.3 mmol/dL) | 6.9 mg/dL | 8.5mg/dL |
| Magnesium | 0.52 mg/dL (1.80-2.50 mg/dL) | 2.03 mg/dL | 1.41 mg/dL |
| Partial thromboplastin time | 31.9 s (24.8-31.8 s) | 29.4 s | 25.3 s |
| Fibrinogen | 249 mg/dL (177-410 mg/dL) | 223 mg/dL | 221 mg/dL |
| D-dimer | 4620 ng/mL (0-199 ng/mL) | 2520 ng/mL | 321 ng/ mL |
| Alanine aminotransferase | 48 U/L (14-54 U/L) | 37 U/L | 20 U/L |
| Aspartate aminotransferase | 251 U/L (15-41 U/L) | 121 U/L | 35 U/L |
| Dehydrogenase lactic | 3182 U/L (98-192 U/L) | 1781 U/L | 314 U/L |
| Albumin | 4.0 g/dL (3.5-4.8 g/dL) | 2.5 g/dL | 3.5 g/dL |



**Figure 1 Tridimensional structure of Shiga toxin**. Shiga toxins are a family of related toxins with two major groups, Stx1 and Stx2, expressed by genes considered to be part of the genome of lambdoidprophages. The most common sources for Shiga toxin are the bacteria *S. dysenteriae* and the shigatoxigenic serotypes of *Escherichia coli*, which includes serotypes O157:H7, O104:H4, and other enterohemorrhagic *E coli.*