A 50 year-old woman with iron deficiency anemia, renal failure and colitis: case report and brief review of literature

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Abstract

The hemolytic uremic syndrome (HUS) is defined by the triad of hemolytic anemia, thrombocytopenia, and acute renal failure. The typical presentation of HUS occurs following a diarrheal prodrome. Diarrhea is infectious, usually due to Shiga toxin-producing Escherichia coli. In typical HUS, the history may include exposure to contaminated food. Symptoms develop 24 hours to 8 days following ingestion of the offending agent. Atypical HUS (aHUS) is being described in a growing body of literature and is more commonly associated with neurologic impairment. Central nervous system involvement may occur in almost half of patients and symptoms vary from mild (lethargy, irritability) to severe (seizures, paresis, coma). Atypical HUS may be caused by a variety of etiologies, each with a different trigger resulting in the final common pathway of inflammatory cascade causing renal endothelial and vascular injury and resultant thrombotic microangiopathy. This report describes the case of a 50-year-old female who developed HUS.

Keywords: *hemolytic uremic syndrome, hemolytic anemia, iron deficiency, colitis*

Introduction

Hemolytic-uremic syndrome (HUS) is a clinical syndrome characterized by progressive renal failure that is associated with microangiopathic (non-immune, Coombs-negative) hemolytic anemia and thrombocytopenia. Hemolytic-uremic syndrome is classified into two main categories, typical and atypical HUS depending on whether it is associated with Shiga-like toxin or not. Typical HUS with Shiga-like toxin present is the classic form of hemolytic-uremic syndrome. This is largely a disease of children younger than 2-3 years and often results in diarrhea. Acute renal failure occurs in most of patients, but they have a favorable prognosis, and as many as two thirds of patients recover renal function.

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In atypical HUS, infection by Shiga toxin (Stx)-producing bacteria (STPB) is not the cause, and disease may occur year-round without a gastrointestinal prodrome. Overall, patients with non–Shiga toxin-associated HUS (non–Stx-HUS) have a poor outcome, and as many as half may progress to end-stage renal disease or irreversible brain damage. Some patients (approximately 20% of children and a similar percentage in adults) have a progressive onset with subclinical anemia and fluctuating thrombocytopenia during weeks or months and preserved renal function at diagnosis [1].

Case presentation

A previously healthy 50-year-old woman was admitted to the hospital in a superficial comatose state. She was found unconscious in a public place and brought by the ambulance to the Emergency Department. Clinical examination revealed pale skin with multiple ecchymosis on her upper and lower limbs, upper torso and abdomen thought to be

the result of domestic violence, but later denied by the family members who claimed that the injuries were caused by repeated accidental trauma brought on by alcohol consumption. She was admitted to the Gastroenterology Unit for further testing. On examination, the temperature was 38.5°C, the blood pressure 140/90 mm Hg, the pulse 84 beats per minute, and the respiratory rate 18 breaths per minute. The patient was awake, partially responsive to pain and verbal stimuli with slow responses, confused, with visual and auditory hallucinations. On neurologic examination, she followed simple commands inconsistently, with psychomotor slowing, a decreased ability to name objects, and an inability to read or to repeat words spoken to her. Her face was symmetric. Muscle strength was 3 out of 5 (where "5" indicates normal strength). The head CT ruled out any neurosurgical emergency such as a subarachnoid hemorrhage. Pale sclera was reported. The neck was supple and without jugular venous distention. Her personal and family history were unremarkable, except for mild intermittent mucosal bloody diarrhea accompanied by abdominal discomfort and marked fatigue 10 days prior to admission which the patient treated personally with antibiotics and anti-motility drugs. The abdomen was slightly distended, depressible and diffusely painful with a painless hepatomegaly two fingers below the costal margin. Splenomegaly was not noted. On admission, anemia, thrombocytopenia, and renal failure were detected. The initial laboratory data are available in Table 1.

Table 1. Biochemical profile of the patient on admission

Parameter	Result	Reference interval
Hemoglobin(g/dl)	8.2	12.0-16.0
White-cell count (per mm³)	12.970	4000-10.000
Platelet count (per mm³)	61.000	150.000-400.000
Reticulocyte count (per µL)	0.02	0.003-0.009
Erythrocyte sedimentation rate (mm/h)	100	2-10
Iron levels (µg/dl)	19	50-170
Urea (mg/dl)	98	15-50
Creatinine (mg/dl)	6.63	0.50-0.90
Glucose (mg/dl)	191	74-106
Protein (mg/dl)	59.65	6.40-8.30
Total bilirubin levels (mg/dl)	0.7	0.1-1.20
Alanine aminotransferase (U/L)	48	5-31
Aspartate aminotransferase (U/L)	94	5-32
Gamma GT (U/L)	104	5-42
Total Cholesterol (mg/dl)	110	120-200
Lactic dehydrogenase (U/L)	1662	125-220
C-reactive protein (mg/dl)	2.9	0-0.5
Fibrinogen (mg/dl)	569	200-400
Uric acid (mg/dl)	7.9	2.5-6.0
Prothrombin time (%)	75	80-125%
INR	1.15	0.8-1.25
Sodium (mEq/L)	129	135-145
Potassium (mEq/L)	5.55	3.5-5.0

Serum protein electrophoresis and immunofixation revealed a diffuse increase of the IgA level. Urinary and blood cultures came back negative and her pulmonary X-ray showed no abnormality. Peripheral blood smear showed important anisocytosis and poikilocytosis with hypocrome microcytes predominance. Liver ultrasound showed a homogenous hepatomegaly, normal structure and dimensions of spleen and kidneys and no free fluid in the peritoneal cavity (Figure 1).

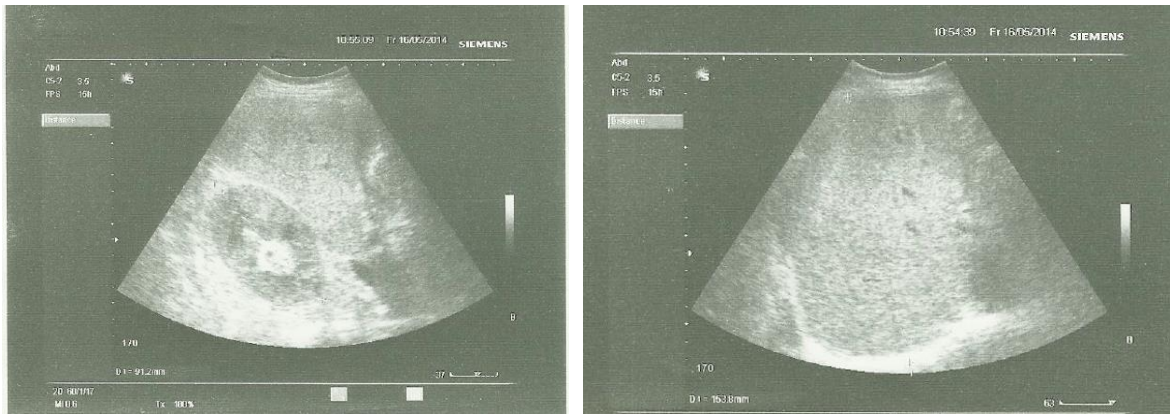

Fig. 1. 2D ultrasound images of liver and right kidney showing no structural abnormalities.

Head and pelvic X-ray showed a 3 cm geode at the parietal region (Figure 2). A hematological consult and bone marrow assessment were recommended.

The bone marrow aspiration and biopsy showed no signs of leukemia, multiple myeloma or myelodysplastic syndrome.

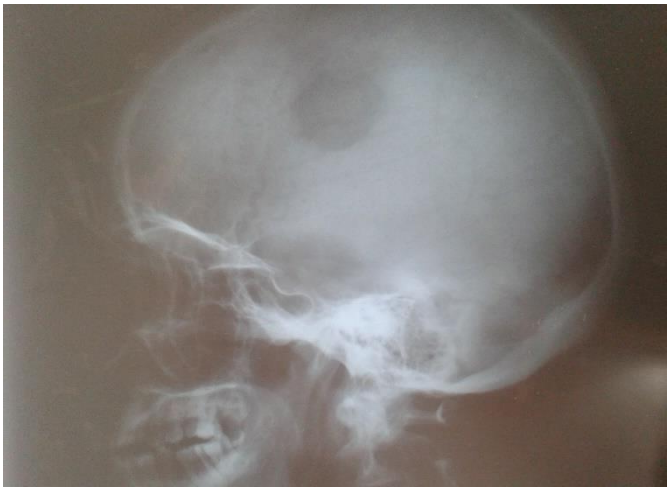

Fig. 2. Head X-Ray showing a 3 cm geode at parietal region.

The patient was tested for viral hepatitis and HIV infection which came back negative. Stool samples tested positive for occult hemorrhage and negative for *Clostridium difficile* toxins and negative cultures for Salmonella, Shigella and *Escherichia coli* strains.

On hospital day 3 her urine volume decreased and generalized edema developed. A urinary catheter was inserted to monitor volume repletion and urine output, diuretic therapy using intravenous furosemide and fluid restriction was initiated. On day 4, persistent systemic inflammation and marked leukocytosis with altered physical condition required the use of antibiotics for 7 days and corticosteroid therapy.

The presence of elevated uric acid, potassium, lactate and leukocytosis were indicative of hemolysis, but low iron levels with positive stool samples suggested chronic blood loss.

Therefore, upper and lower endoscopy was performed. Upper endoscopy showed no esophageal varices and mild gastritis with absent *Helicobacter pylori* infection. Lower endoscopy showed a congested inflamed colonic mucosa with a polypoid patchy aspect, multiple erosions and aphthous ulcerations which were biopsied (Figure 3).

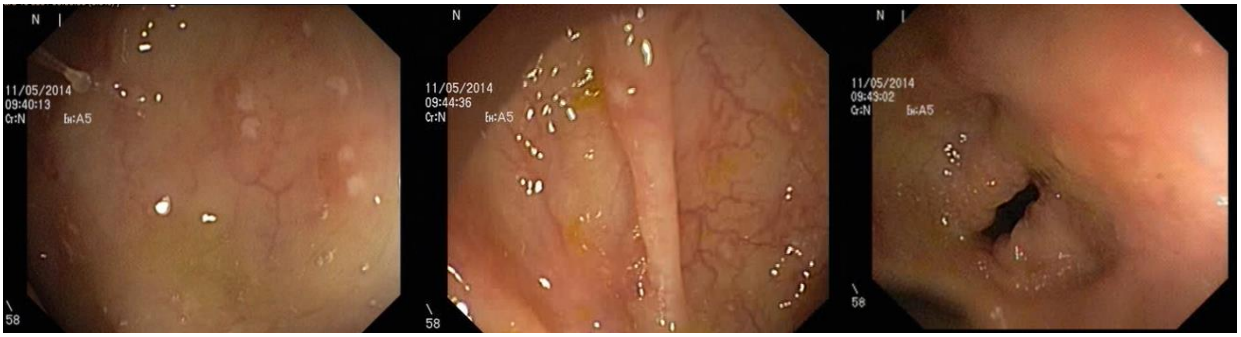

Fig. 3. Conventional endoscopic images of multiple nodular and aphthous lesions.

The pathology report showed a nonspecific aspect of chronic inflammatory colitis with no elements suggesting Crohn's disease or ulcerative colitis.

Biological markers showing disease onset and progression are presented in Figures 4 and 5.

After 16 days of treatment, the patient's condition was stabilized yielding normal diuresis as well as an improvement in renal function and the patient was released home.

Administration of intravenous fluids, supportive therapy, antibiotics, proton pump inhibitors, fresh frozen plasma, corticosteroids and diuretics amended the patient's clinical and biological parameters. No dialysis and no kidney biopsy were performed due to patient refusal.

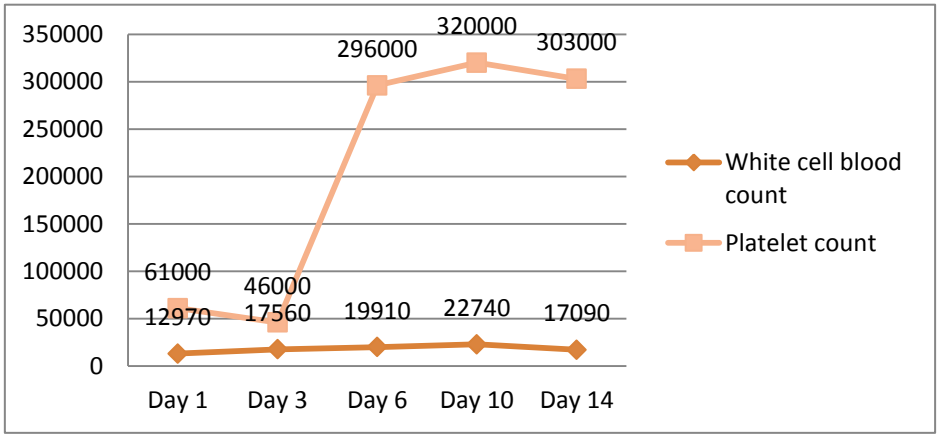

Fig. 4. Extreme leukocytosis during the second week of disease indicating systemic inflammation

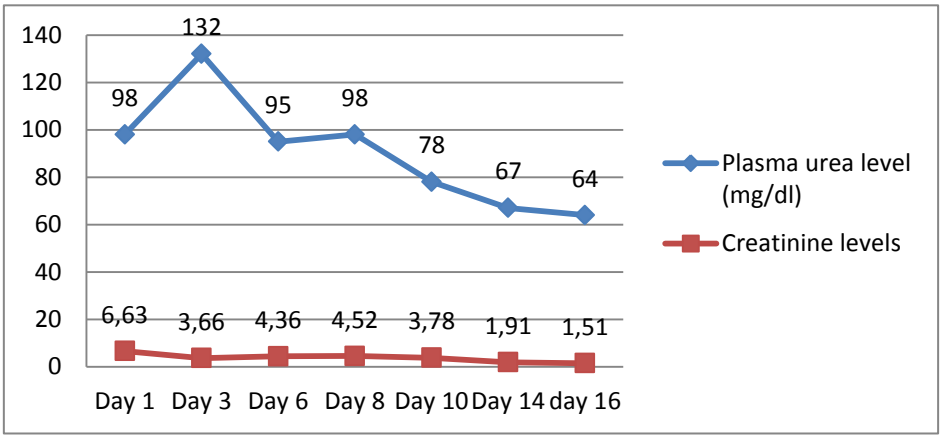

Fig. 5. Recovery of renal function. Plasma creatinine and urea levels gradually improve towards the end of the hospitalization.

Discussion

Most cases of HUS (90%) occur following infection with Shiga toxin-producing Escherichia coli typically serotype O157 [2]. However, in approximately 5–10% of the cases, no evidence of Escherichia coli or other infection is found [3]. Typical HUS occurs due to bacterial verotoxin production in the colon. Patients may present bloody diarrhea, abdominal pain, pale skin, irritability, fatigue, fever, unexplained bruises or bleeding, decreased urination, hematuria, confusion or seizures. Only 5% of all HUS and 38-43% non-diarrheal HUS are reported in association with invasive Streptococcus pneumoniae infection [4].

The first breakthrough was the emergence of a new clinical picture of aHUS. aHUS is no longer considered as an exclusively pediatric disease but also, if not predominantly, an renal disease affecting adults [5]. aHUS represents 5 -10% of HUS in children, but the majority of a HUS is diagnosed among adults. More than 1000 aHUS patients investigated for complement abnormalities have been reported [6, 7].

The occurrence of colitis is not uncommon and can be mistaken for acute appendicitis, ulcerative colitis because the site of intense inflammation may be in the right or left lower part of the abdomen. If this leads to an appendectomy, the appendix is almost always found to be normal. If a colonoscopy is conducted, severe inflammation, ulceration and pseudo-membranes are found. Ten percent of cases are associated with rectal prolapse with colitis [8].

Unfortunately, there are no treatment guidelines. Several studies conducted on the management of HUS concluded that the mainstay of treatment for typical HUS is supportive care: volume resuscitation, fluid and electrolyte monitoring, transfusion of blood products and in non-responsive cases dialysis. Also, there is no consensus on antibiotic use, but several meta-analyses show that no harmful outcome and apparently no benefit were detected after antibiotic usage. Corticosteroid use is also controversial.

Recent studies indicate that the amount of parenteral hydration given to a patient before the development of hemolytic uremic syndrome, especially the amount of sodium, is crucial in preventing anuria and, ultimately, dialysis [9].

In our patient, the diagnosis was made retrospectively. Given the sudden onset of bloody diarrhea before hospital admission, the particular neurologic presentation and laboratory findings of anemia, low platelet count, renal failure the diagnosis was delayed. The particularity of the case was the presence of iron deficiency anemia and positive stool for occult bleeding due to colonic ulcerative lesions making the diagnosis even more difficult.

Conclusions

Hemolytic uremic syndrome is a complex disorder, affecting both children and adults. Diagnosis of typical HUS is usually clinical, based on history and laboratory findings. Typical hemolytic uremic syndrome is a self-limiting disease with spontaneous recovery, although close monitoring and treatment of symptoms are essential. Because hemolytic uremic syndrome has a wide spectrum of clinical presentations, supportive therapy is crucial for a good outcome. Genetic, drug-induced, or idiopathic hemolytic uremic syndrome is heterogeneous, is not preceded by diarrhea, and has a poor prognosis, with incomplete recovery in most cases.

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