Hemolytic Uremic Syndrome – Case report

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\textbf{ABSTRACT}

Introduction: Typical hemolytic uremic syndrome (HUS) is a leading cause of community acquired acute kidney injury in infants and young children. It is defined as a triad of microangiopathic hemolytic anemia, thrombocytopenia and renal insufficiency associated with Shiga toxin-producing \textit{Escherichia coli}. In this case of HUS that we are going to present, hemolytic anemia and trombocitopenia were the major features, while renal involvement was less important.

Case report: We report the case of a one-year-old Caucasian girl, without significant medical history, who was found to have stool culture with positive enteropathogenic \textit{Escherichia coli} after an episode of diarrhea. The particularity of this case is that, even if the patient had prodromal diarrhea, thrombocytopenia and anemia in evolution, and the clinical features were consistent with typical HUS diagnosis, other diagnoses were considered due to the lack of apparent renal dysfunction.

Conclusion: Our patient presented some, but not all, abnormalities seen in typical HUS, making it difficult to establish the final diagnosis. Providers must keep in mind to raise the suspicion of typical HUS diagnosis even when some symptoms are missing, in order to establish a correct diagnosis and initiate supportive care.

Keywords: minimal renal involvement, \textit{Escherichia coli} O26, HUS differential diagnosis.

\textbf{INTRODUCTION}

Typical hemolytic uremic syndrome (HUS) is a leading cause of community acquired acute kidney injury in infants and young children. It is defined as a triad of microangiopathic hemolytic anemia, thrombocytopenia and renal insufficiency associated with Shiga toxin-producing \textit{Escherichia coli} (1).

Between February and November 2016, there was an outbreak of typical hemolytic uremic syndrome in Romania, with 32 reported cases that were admitted to the Nephrology Department of “Maria Sklodowska Curie” Emergency Children’s Hospital, Bucharest, Romania. The main clinical manifestations were represented by diarrhea (all cases), skin pallor reflecting the anemia (all cases), oligoanuria/anuria (18 cases), edemas (18 cases), vomiting (10 cases), petechiae (five cases) (2).

We report one case of HUS in which hemolytic anemia and trombocitopenia were the major features, while renal involvement was less important.

\textbf{CASE DESCRIPTION}

In February 2016, a one-year-old Caucasian girl was admitted to the Nephrology Department of “Maria Sklodowska Curie” Emergency Children’s Hospital, Bucharest, Romania, for diarrhea. The
onset of the disease was five days prior to the admission with anorexia and diarrhea.

On the second day of illness, a stool culture was performed, which was positive for enteropathogenic Escherichia coli. On the fourth day of illness, the patient presented two dark colored stools for which she was admitted to "Prof. Dr. Matei Bals" National Institute for Infectious Diseases of Bucharest, Romania. Laboratory work-up showed anemia (Hb=6.1 g/dL), thrombocytopenia (platelet count 40 000/µL), slightly increased serum urea 65 mg/dL, and normal serum creatinine of 0.4 mg/dL. Based on clinical and biological data and the context of an epidemic outburst of typical HUS in children in Romania (13 confirmed cases at that time), the suspicion of hemolytic uremic syndrome aroused and the patient was transferred to the Nephrology Department of “Maria Sklodowska Curie” Emergency Children’s Hospital for further investigations and treatment.

Her medical history revealed no significant information, except for an episode of gastroenterocolitis three weeks prior to the current presentation, for which the patient had received symptomatic treatment prescribed by her general practitioner, with symptoms relief.

On the day of presentation, physical examination revealed an alert but irritable and ill-appearing child with a normal body temperature, heart rate of 130 beats/min, blood pressure of 90/60 mm Hg, and oxygen saturation by pulse oximetry of 95%. The child’s weight at admission into hospital was 8700 g. The skin was pale, slightly decreased skin turgor, pale buccal mucosa, soft fontanelle, and capillary refill time of three seconds. Urine output was normal (390 mL/12 h – 3.73 mL/kg/hour). Heart and lung examination were normal, except for tachycardia; the abdomen was swollen, no hepatosplenomegaly. There were no signs of meningeal irritation; no peripheral edema either.

Laboratory tests showed: hemoglobin (Hb) 5.3 g/dL, platelet count 55 x 10³/µL, white blood cell (WBC) count 28 x 10³ /µL with left shift, reticulocytosis, blood urea 60 mg/dL, lactate dehydrogenase (LDH) 1630 U/L, aspartate aminotransferase (AST) 63 U/L, alanine aminotransferase (ALT) 16 U/L, C-reactive protein (CRP) 5.58 mg/L, peripheral blood smear showed poikilocytosis, elliptocytes, infrequent teardrop erythrocytes, frequent schizocytes, microspherocytes, consistent with microangiopathic hemolytic anemia. Urinalysis revealed leukocyturia, hematuria and proteinuria, and urine culture was positive with Escherichia coli (>100 000 CFU/mL).

Her basic metabolic panel revealed a sodium level of 136 mg/dL, potassium level of 3.92 mg/dL, and bicarbonate level of 20 mg/dL.

Stool culture demonstrated the presence of enteropathogenic Escherichia coli.

For further evaluation, abdomen ultrasound was done, which showed mesenteric lymphadenitis, and a non-obstructing calculus in the lower pole collecting system of the right kidney. A chest x-ray did not reveal any pathology.

Given the patient’s clinical manifestations (diarrhea, with two dark colored stools, pale skin and pale buccal mucosa) and the laboratory findings (microangiopathic hemolytic anemia, thrombocytopenia, increased serum urea, elevated lactate dehydrogenase), typical hemolytic uremic syndrome was the main suspicion. However, the fact that the patient had a positive urine output during hospitalization was an argument against this diagnosis. Therefore, other diagnoses were considered, including thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, glucose-6-phosphate dehydrogenase deficiency, autoimmune hemolytic anemia, and bacterial sepsis.

Further laboratory tests were conducted: direct Coombs test and indirect Coombs test, D-dimer level, hemoglobin electrophoresis, cytomegalovirus IgM antibodies, Epstein-Barr IgM antibodies, anti-HAV IgM antibodies, anti-HCV antibodies, anti-HIV 1+2 antibodies, anti-HBs antibodies, procalcitonin level, which were all within normal limits.

Multiplex PCR essay has been also performed and the results were obtained four days after the sample was taken (the fourth day of hospitalization), showing the presence of Escherichia coli O:26 and typical HUS caused by reaction to E. coli toxin was diagnosed.

During her hospitalization period, a temporary external jugular catheter was placed and the patient received transfusions of packed red blood cells (two administrations), intravenous fluid therapy, diuretic support was established.
with 16 mg/24 h Furosemide, antibiotherapy with 800 mg/24 h Ceftriaxone for three days and 520 mg/24 h Meropenem for seven days.

The patient had a favorable clinical evolution. Regarding the hematologic tests, the hemoglobin level had increased slowly, after packed red blood cells transfusion, with values of hemoglobin oscillating between 5.3 and 7.9 g/dL. Platelet decrease was less important and did not require platelet transfusion, with normal platelet level since the 7th day of admission. The diuresis was maintained during the entire hospital stay, so there were no indications for renal replacement therapy.

Laboratory studies at discharge included a hemoglobin of 7.6 g/dL, platelets of 480 x 10^3/uL, blood urea of 19 mg/dL, serum creatinine of 0.23 mg/dL and a LDH of 975 U/L.

On hospital day 11, she was discharged and received outpatient follow-up care. She was periodically reevaluated in the clinic, with favorable evolution and without apparent consequences.

**DISCUSSION**

This case highlights the challenges in diagnosing patients with typical hemolytic uremic syndrome.

Typical hemolytic uremic syndrome is most frequently triggered by Shiga-like toxin-producing *Escherichia coli* and it manifests with prodromal diarrhea.

The clinical manifestations of typical HUS include microangiopathic hemolytic anemia, thrombocytopenia and renal failure. Overall incidence of Shiga toxin-induced HUS is estimated at 2.1 per 100 000 cases, with a peak incidence in children under five (6.1 per 100 000) (3).

Shiga toxin-induced HUS is secondary to infection with the *E. coli* serotype O157:H7 in the majority of cases, being described in 70% of cases in North America and Western Europe. However, many other *E. coli* serotypes (O111:H8, O103:H2, O121, O145, O26, O113) have been reported (4).

Approximately two thirds of patients diagnosed with HUS require renal replacement therapy, with a majority of those patients experiencing renal recovery. About one third of the patients have milder renal involvement without the need for dialysis therapy (5).

Cases that developed a partial or incomplete form of HUS with thrombocytopenia, with or without anemia, have been reported, while serum creatinine concentration remained at normal values (6).

**CONCLUSION**

Our patient demonstrated a prodromal illness of diarrhea and development of thrombocytopenia and anemia. Given the epidemiological context, the clinical features were consistent with typical HUS diagnosis. However, because of the lack of apparent renal dysfunction, other diagnoses were considered.

Finally, *Escherichia coli* O26 was identified in the stool culture using polymerase chain reaction for virulence-associated genes of enterohemorrhagic *E. coli*.

Our patient presented some, but not all, abnormalities seen in typical HUS, making it difficult to establish the final diagnosis.

Providers must keep in mind to raise the suspicion of typical HUS diagnosis even when some symptoms are missing, in order to establish a correct diagnosis and initiate supportive care.

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**REFERENCES**


