Rare case of hemolytic uremic syndrome associated with only one transient low platelet count

Kalpita Hatti · Maria Rojas · Peter Kouides

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Abstract Hemolytic uremic syndrome (HUS) is the most common cause of acute renal failure in children and the incidence of this syndrome is increasing worldwide. The classic triad of features for HUS consists of hemolytic anemia, thrombocytopenia, and acute renal failure. HUS presenting with normal platelet count is extremely rare. There is one case report of a 13-year-old boy presenting with atypical HUS with normal platelet counts. We report a second case of a young 18-year-old girl presenting with HUS and normal platelet counts.

Keywords Hemolytic uremic syndrome · Low platelet count · Acute renal failure

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K. Hatti (✉)
Rochester General Hospital Internal
Medicine Residency Program,
1425 Portland avenue,
Rochester, NY 14621, USA
e-mail: hatti.kalpita@gmail.com

M. Rojas
Rochester General Hospital,
1425 Portland avenue,
Rochester, NY 14621, USA

P. Kouides
Rochester General Hospital, Mary M. Gooley
Hemophilia Center, Hemophilia Thrombosis
Research Society, University of Rochester School
of Medicine and Roswell Park Memorial Cancer Institute,
1425 Portland avenue,
Rochester, NY 14621, USA

To the Editor

Typical (diarrhea-associated) hemolytic uremic syndrome (HUS) is the most common cause of acute renal failure in children and the incidence of this syndrome is increasing worldwide [1]. It leads to significant morbidity and mortality during the acute phase. Death or ESRD occurs in about 12% of patients with diarrhea-associated HUS and 25% of survivors demonstrate long-term renal sequelae [2]. The classic triad of features for HUS consists of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. HUS presenting with normal platelet count is extremely rare [3, 4]. A normal platelet count in the setting of anemia and renal failure typically leads the clinician to alternative diagnoses. We reviewed the literature for HUS with normal platelet counts. There is one case report of a 13-year-old boy presenting with atypical HUS with normal platelet count in 2009 [5]. We hereby report a case of Shiga toxin associated HUS with a single transient borderline low platelet count and concurrent infection with *Escherichia coli* strain O145.

Our patient is an 18-year-old female with no significant past medical history who presented with the chief complaint of bloody diarrhea and abdominal cramping. She was evaluated a week prior for similar complaints at which time a colonoscopy was done which revealed segmental patchy colitis that could be infectious or inflammatory. She was discharged home on oral antibiotics but was readmitted to our hospital for persistent abdominal pain and bloody diarrhea. At that time she was noted to be in acute renal failure. She was found to have a hematocrit of 14, which led to an urgent hematologic evaluation.

On physical examination, she was afebrile with BP 116/80, heart rate of 86, and saturating 100% on room air. Abdominal exam revealed mild diffuse tenderness with no evidence of organomegaly. Neurological exam was intact.

Laboratory data: as in Table 1.

Table 1 Laboratory data

Date	Time	Events	HCT (35–47)	Platelet count (150–450 k)	BUN (8–20)/creatinine (0.5–0.9)	LDH (90–200)
First admission	10.30	Admission at outside hospital	30	268	7/0.8	
6 days after prior admission	15.05	Re-admission at our hospital	16	124	47/5.1	736
Day #2 Re-admission	9.20	Plasma exchange initiated	14→22	208	43/3.7	741
Day #3 Re-admission	5.30	Clinical improvement	28	267	36/2.6	344
Day #4 Re-admission	3.00	Transfer out of ICU to medical floor	32	354	32/2.2	368
Day #19 Re-admission	9.00	Hematology outpatient follow-up	36	289	79/0.8	231

Urine analysis was within normal limits without evidence of proteinuria.

Peripheral smear revealed multiple schistocytes (4+) with some of the helmet cells [shown by yellow arrow in Fig. 1] and others fragmented.

Platelets were not reduced [shown by yellow arrow in Fig. 2].

Stool cultures were positive for *E. coli* O145 strain. Stool immunoassay revealed Shiga toxin.

She was admitted to the MICU and received plasma exchange for 2 days. She transiently dropped her platelet count to 124,000/mcl on one occasion. Her renal function normalized with no need for renal replacement therapy and she improved clinically over the next few days.

Discussion

The presence of TTP–HUS should be suspected when a patient presents with the characteristic set of clinical and laboratory findings without another clinically apparent etiology. It is uncommon for all components of the pentad (thrombocytopenia, microangiopathic hemolytic anemia,

neurologic and renal abnormalities, and fever) to be present in the same individual. When acute renal failure is dominant and neurologic abnormalities are minimal or absent, the disorder is considered to represent HUS. A severe deficiency of ADAMTS13 (a disintegrin-like and metalloprotease with thrombospondin type 1, member 13) as detected by current assays, less than 5% of normal activity, appears to be specific for TTP [6].

The etiology and pathogenesis of childhood and adult Shiga-toxin-associated HUS are the same, but renal and neurological involvement are usually more severe and sequelae more frequent in adults than in children [7]. The overall incidence of typical HUS is estimated to be 2.1 cases per 100,000 persons/year, with a peak incidence in children who are younger than 5 years [3].

The most common mode of infection in USA for HUS is ingestion of hamburger meat contaminated with *E. coli* O157:H7 [8, 9]. In our case a new strain of *E. coli* was isolated. Of note there was an outbreak of *E. coli* O145 in USA in May 2010 which was linked to romaine lettuce in which CDC reported 23 confirmed cases around Columbus, Buffalo, and Tennessee [10]. State and county public health epidemiologists along with New York State Health Department's (DOH) Wadsworth Center laboratory played pivotal

Fig. 1 Peripheral smear revealed multiple schistocytes **Fig. 2** Normal platelet count

roles in the identification of this lettuce as the source of the *E. coli* O145 outbreak and to date, four confirmed including our case and three probable cases of *E. coli* related to the outbreak have been identified in New York State [10]. The lettuce processing company issued a recall of lettuce produced at their facility as a result of the evidence obtained. In 2009, Fratamico et al. described PCR assays to identify enterohemorrhagic *E. coli* serogroup O145 and to detect low levels of the pathogen in food [11]. Certainly one needs more evidence to definitively associate it with HUS in the absence of thrombocytopenia.

Most importantly, the prognosis for TTP/HUS has changed over time from a fatal disorder associated with the classic pentad to a syndrome associated with 80% survival in the plasma exchange era. The treatment of HUS with normal platelet counts remains the same including aggressive supportive management and if needed dialysis [12]. Plasma exchange is considered in severe cases especially in factor H dysfunction or inability to differentiate HUS from TTP with ADAMTS13 deficiency. Single center experiences with adult patients with typical HUS receiving therapeutic plasma exchange in view of the higher mortality rate of nearly 90% have been published [13]. Recent analyses have shown that typical HUS is not a benign disease in the long-term and initiation of judicious management could be of utmost importance to improve prognosis [14]. Our case is a reminder for adult hematologists that normal platelet counts should not preclude the diagnosis of HUS nor consideration for timely therapeutic interventions in HUS if the anemia is of the microangiopathic hemolytic type and the renal failure is acute.

Conflict of interest The authors declare that they have no conflict of interest in the submission of this case report.

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