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POST-DIARRHEA HEMOLYTIC UREMIC SYNDROME MIMICKING SEVERE ACUTE COLITIS IN ADULTS: ABOUT A RARE CASE AND REVIEW OF THE LITERATURE

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ABSTRACT

Hemolytic uremic syndrome (HUS) is a thrombotic micro angiopathy (TMA) with renal tropism but extrarenal damage is possible. Typical or post-diarrheal HUS is well described in the pediatric population, but its incidence in adults is rare. The classic triad in HUS is hemolytic anemia, acute renal failure and thrombocytopenia. Resuscitation measures with adequate rehydration and dialysis if necessary remain the pillars of treatment. We report the case of a 17-year-old patient who presented with bloody post-diarrhea HUS and discuss the data in the literature.

KEYWORDS: HUS, TMA.

INTRODUCTION

Hemolytic uremic syndrome (HUS) is a micro vascular angiopathy defined by a classic triad associating mechanical hemolytic anemia with the presence of schizocytes, thrombocytopenia and acute renal failure. There are two categories of HUS: typical and atypical. Typical HUS or post-diarrhea usually affects infants and young children. The germ most implicated in HUS post diarrhea is Escherichia coli producing Shiga-toxins.[1-2] We present the case of a 17-year-old patient who presented with bloody post-diarrhea HUS. Our case highlights the diagnostic and therapeutic difficulties in front of a table of post-diarrhea HUS in adults.

CASE REPORT

A 17-year-old patient, with no particular history, admitted to our department for bloody diarrhea evolving for 1 week before admission at the rate of 5 to 6 bowel movements per day, associated with diffuse abdominal pain of moderate intensity with rectal syndrome hints, tenesmus and false needs, without other symptoms. She reported febrile sensations with asthenia.

The physical examination at admission had objectified a conscious patient with a frank anemic syndrome. Her blood pressure was 130/80 mmHg and her heart rate was 110 bpm. She was oliguric at 300 cc / 24h and feverish at 38.5 ° without signs of dehydration or undernutrition. The abdominal examination found a slight tenderness in the right iliac fossa without defense or contracture. The fingertip with digital rectal examination was stained with blood. There were no palpable lymphadenopathy or hepatomegaly or splenomegaly. The neurological examination showed a static cerebellar syndrome with dysarthria.

Emergency laboratory examinations objectified; normochromic normocytic regenerative anemia at 8.5 g / dl (MCV at 82.9 fl, MCHT at 28.5 pg, reticulocytes at 294600 / mm3), thrombocytopenia at 103.000 / mm3, predominantly neutrophilic hyperleukocytosis (white blood cells at 45360 / mm3, neutrophils at 40560 / mm3 and lymphocytes at 3080 / mm3). The renal function was impaired with creatinine at 53 mg / l, urea at 1.81 g / l and glomerular filtration rate (GFR) calculated at 13 ml / min / 1.73 m2. The CRP was at 237 mg / l, the natremia at 127 mmol / l and the serum potassium at 4.7 mmol / l.

The abdominal X-ray did not show any toxic megacolon. The abdominal CT scan without injection of contrast agent had shown a rectal, sigmoid and colonic circumferential thickening without signs of perforation.

A left colonoscopy objectified an erythematous recto-colic mucosa fragile bleeding in contact with superficial ulcers evolving in one piece without any interval of healthy mucosa and without signs of endoscopic gravity (Figure 1).

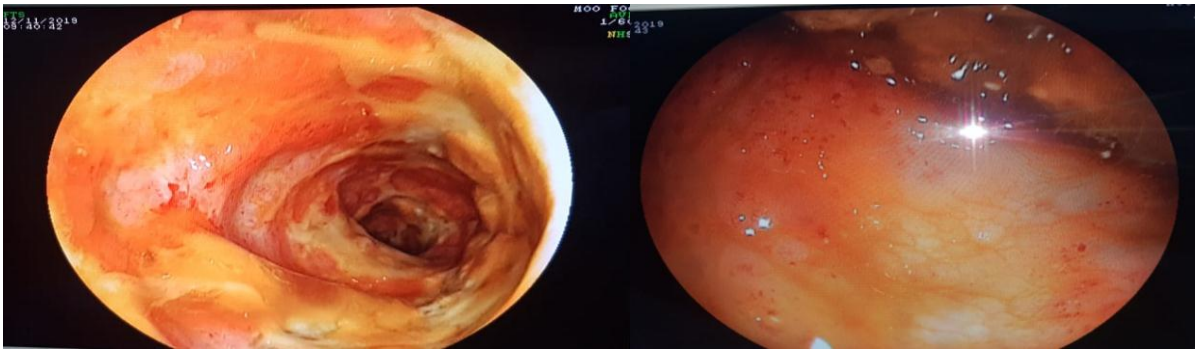

Figure 1: Erythematous recto-colonic mucosa fragile with superficial ulcerations.

Taking into account the age of the patient, the symptomatology, the positivity of the infectious assessment and the data from the colonoscopy; infectious colitis was initially suspected without being able to rule out the diagnosis of inflammatory colitis. The histological study of biopsies carried out showed acute non-specific ulcerative colitis with the presence of the bodies of blood-sucking amoebae.

Copro-parasitological examination of the stools revealed cystic forms of Entamoeba Histolytica and Entamoeba dispar but did not reveal the presence of Escherichia coli, Shigella dysenteriae or Salmonella. The intestinal PCR did not show any toxins. Cytobacteriological examination of the urine showed an Escherichia coli urinary tract infection susceptible to imipenem. The ultrasound study showed that the two kidneys were normal size, well differentiated. There were no stones or hydronephrosis. The brain MRI did not show any abnormalities.

The blood smear on peripheral blood showed the presence of schizocytes estimated at 9.26%. The LDH level was at 1910 IU / L and the combs test was negative. The dosage of the complement showed a normal level of C4 at 0.12 IU / l, while the level of C3 was low at 0.53 IU / l [normal: 0.9 –1.8 IU / l].

The rest of the biological balance showed aspartates aminotransferases (ASAT) 53 IU / L, alanine aminotransferase (ALAT) 30 IU / L, γ-glutamyl transpeptidase (γGT) 17 IU / L and alkaline phosphatase (PAL) 119 IU / L, total bilirubin 4.6 mg / dL, albumin 24.8 g / l.

The autoimmune workup was normal. The search for the human immunodeficiency virus (HIV) was negative in the same way as the other viral markers (hepatitis B and C, Ebstein-Barr virus, herpes simple virus and cytomegalovirus).

The diagnosis of typical HUS was made in the association of hemolytic anemia with the presence of schizocytes, thrombocytopenia and acute renal failure. A renal biopsy confirmed the diagnosis by showing signs of thrombotic micro-angiopathy with type of swelling of endothelial cells with enlargement of the endothelial space. The anti-ADAMTS-13 antibody assay was normal.

The patient's therapeutic approach consisted of transfusions of red blood cells with daily hemodialysis sessions. For urinary tract infection, antibiotic therapy adapted to the imipenem-based antibiogram was also prescribed.

From the third week of hospitalization, the bloody diarrhea and abdominal pain disappeared and the diuresis was restarted. Biologically; the platelet count normalized on the tenth day and kidney function around the twentieth day. Control of the albumin and LDH level was also normal (Table 1). A 1-month follow-up colonoscopy showed normal-looking colorectal mucosa (Figure 2).

Table 1: Evolution of the biological balance (note that for hemoglobin and renal function, the patient was transfused with hemodialysis sessions).

Hospital days	**1st day**	**5th day**	**10th day**	**15th day**	**20th day**	**25th day**
Hemoglobin (g / dl)	8.5	6	8.2	7.5	7.1	9.9
Platelets (/ mm3)	103.000	115.000	306.000	166.000	326.000	306.000
Creatinine (mg / l)	53	88.1	87	24.3	5.3	8.2
Urea (g / l)	1.81	2.7	1.63	0.49	0.15	0.44
DFG ml / min / 1.73m2	13	7.7	7.8	34.2	198.5	119.9
LDH (IU / l)	1910	-	3401	-	-	180
Albuminemia (g / l)	24.8	22.1	24.5	23.3	35.6	36.8
Blood smear	Normochromic normocytic regenerative anemia with schizocytes estimated at 9.26%.					

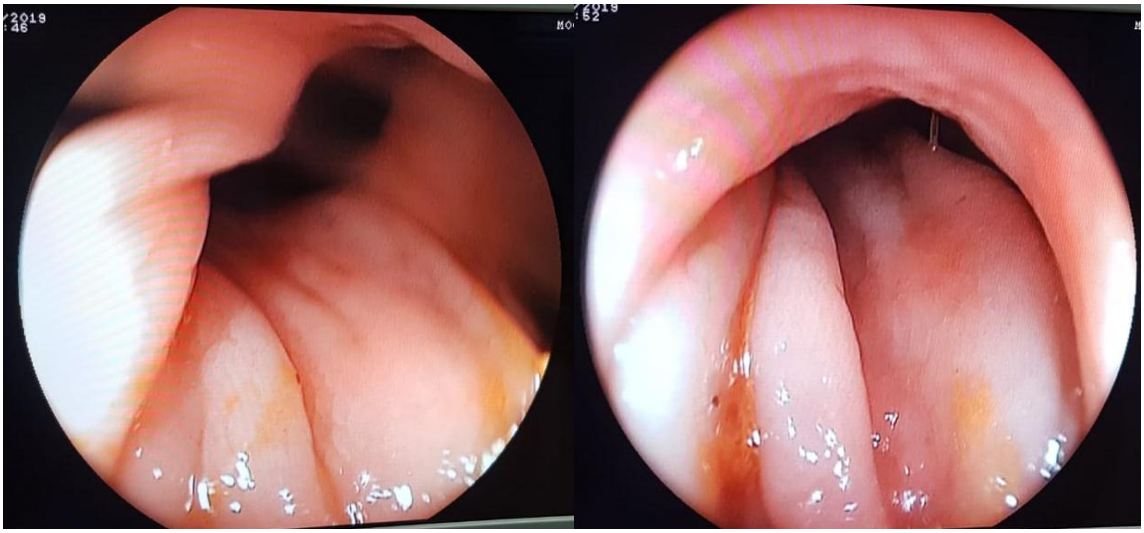

Figure 2: Colonoscopy after 1 month.

DISCUSSION

Hemolytic uremic syndrome (HUS) is a microangiopathy that affects the vascular endothelium. Its diagnosis is based on a triad that combines hemolytic anemia with fragmented red blood cells (schizocytes), thrombocytopenia and acute renal failure.[1] It represents the main cause of acute renal failure in children under three years of age.[3] There are two main entities of HUS: typical or pos-diarrheal HUS and atypical HUS without prodromal diarrhea. The latter is rare but more severe.

Typical HUS mainly affects infants and young children as a result of digestive symptoms. It is a rare disease in adults. The annual incidence of which has been estimated at approximately 0.1 cases per 100,000.[4] The largest adult HUS epidemic occurred in northern Germany in 2011, involving 845 confirmed cases of HUS unusually affecting a large number of predominantly female adults.[5-6]

In its typical form, HUS follows a generally brutal onset bloody diarrhea. It is associated with shigatoxin-secreting enterobacteria (STEC) such as Escherichia coli enterohemorrhagic (EHEC) 0157: H or E.coli entero-aggregative (EAEC) 0104: H.[7] Other infectious agents may be involved in the pathogenesis of HUS such as Shigella dysenteriae, Aeromonas, Streptococcus pneumonia and Parvo virus.[8–11]

The pathophysiology of HUS involves two phenomena: intravascular platelet aggregation and alteration of the properties of the endothelial cell.[12] The germ colonizes the intestine after being ingested in food or transmitted through direct contact with a person. It releases two verocytotoxins, shiga toxins (stx1 and stx2), which are responsible for damage to the intestinal wall.[13] After their release from the bacteria, sghigatoxins are transported by leukocytes and join the general circulation. Stx target organs express Gb3 receptors, particularly renal endothelial cells; brain, liver, heart, pancreas and hematopoietic cells. Once an organ is reached, the toxin binds to Gb3 and then internalizes it by endocytosis towards the endoplasmic reticulum. This results in an inhibition of protein synthesis in target cells such as glomerular endothelial cells ultimately causing cell death by apoptosis.[14-15] The detachment, apoptosis or necrosis of these cells leads to the exposure of the underlying basement membrane which will cause activation of platelets and activation of coagulation with the formation of micro-thromboses. The latter are responsible for the classic triad of HUS: consumption of platelets, mechanical destruction of erythrocytes and acute renal failure.[1,15]

The diagnosis of typical HUS is generally made on clinical presentation and laboratory abnormalities. Evidence of STEC infection includes stool culture and testing for toxins in stool samples.[13] Stool cultures may be unreliable because bacteria are present in the stool for a few days and even direct stool testing for shiga toxins may be unresponsive in low prevalence areas.[16-17] In a typical HUS, renal biopsy puncture is not indicated if there is no doubt about the diagnosis. If done, it shows endothelial swelling, detachment of endothelial cells and adhesion of platelets to the basement membrane with fibrin deposits.[1]

The management of typical HUS is symptomatic and is based on early and adequate rehydration with the use of dialysis if necessary.[18] The role of antibiotics is controversial in HUS due to STEC because they cause massive bacterial lysis in the digestive lumen with a new release of shiga toxins.[18-21]

The recent use of ecluzimab, which inhibits formation of the terminal complement complex, is based on the incrimination of the alternate complement pathway in the genesis of HUS lesions. Therefore potentially serious patients may benefit from short-term therapy with ecluzimab. Several studies have shown the efficacy of this treatment, especially in atypical HUS where the role of the complement pathway is well established.[21,22] In a

series of cases following an outbreak of STEC (E. coli O104: H4) in Germany, rapid clinical improvement after eculizumab has been reported.[23,24]

Plasma exchange therapy in typical HUS is controversial in adults in the absence of solid evidence of its effectiveness, but improvement has been noted in some severe neurological cases.[25,26] Intravenous immunoglobulins may also be beneficial.[27]

Admittedly, the prognosis for post-diarrheal HUS remains better compared to atypical HUS. In adults, the long-term prognosis remains unknown due to the lack of data. Pending further studies, periodic medical monitoring is warranted in any patient with HUS.

CONCLUSION

Post-diarrheal HUS is a rare disease in adults and poses diagnostic problems. Therapeutic management is symptomatic. Periodic medical follow-up is indicated in these patients due to the risk of renal failure after recovery.

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