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Case Report

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Hemolytic Uremic Syndrome secondary to *Entamoeba Histolytica* Intestinal Infection: A Case Report

Bassil Leghrouz* **and Juhina Hasassneh**

Abstract

Hemolytic uremic syndrome (HUS) is a rare disease that presents with a triad of microangiopathic heamolytic anemia, thrombocytopenia, and acute kidney injury, HUS is most often related to acquired causes such as intestinal infection mainly due to Shiga toxin-producing *Escherichia coli* (STEC), which is the most frequently observed cause.

Entamoeba histolytica is a protozoan parasite known to cause intestinal infection, and it is rarely reported to be complicated with HUS. We present here a case of a 3-year-old child with *E. histolytica* infection, which is complicated with HUS. The child initially complained of fever, abdominal pain, and bloody diarrhea, but the condition was complicated with rectal prolapse and HUS.

Stool samples revealed the presence of *Entamoeba histolytica* trophozoites, other common pathogens related to HUS were negative. The patient's kidney function deteriorated to the point of requiring hemodialysis for two days. Fortunately, her condition improved, and she was discharged home in good general condition after a few days.

This case shows an uncommon HUS secondary to intestinal infection by *Entamoeba histolytica*, which is infrequently described. It is important to recognize HUS as a potential complication of *E. histolytica* infection, and further research is needed to understand the mechanisms linking both conditions.

Keywords: *E. Histolytica*; Hemolytic Uremic Syndrome; HUS; Rectal prolapse

Background

Entamoeba histolytica is a protozoan known to cause intestinal amebiasis and other extraintestinal diseases. Although 90% of E. histolytica infections are asymptomatic, it has been estimated that almost 50 million people worldwide become ill yearly due to this infection, which results in around 100,000 deaths each year [1]. Very few reports describe the association between Entamoeba infection and hemolytic uremic syndrome (HUS) [2].

HUS is typically characterized by a triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury, induced by thrombi formation in the small vessels, leading to end-organ damage [3].

Children who develop HUS usually begin by manifesting infection-related symptoms such as crampy abdominal pain, bloody diarrhea, and fever followed by paleness and jaundice because of hemolysis, also high blood pressure can

Affiliation:

Department of Pediatrics, Al Ahli Hospital, Be'er Almahjar, Hebron, Palestine

***Corresponding author:**

Bassil Leghrouz, Department of Pediatrics, Al Ahli Hospital, Be'er Almahjar, Hebron, Palestine.

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be noticed because of volume overload and activation of the renin-angiotensin system by the ischemic kidneys [4]. Thrombocytopenia can cause petechiae, but major bleeding is rare. In addition, neurological involvement has been described in approximately 30% of HUS cases, manifesting with seizures, irritability, lethargy, encephalopathy, and coma [5]. In the acute phase of HUS, renal replacement therapy is needed in about 50%–70% of children due to oliguric acute kidney injury with signs of fluid overload [6].

HUS can be classified as infection-induced, complement-mediated, or medication-induced. The infection-induced HUS, which usually referred to classic diarrhea-associated HUS, is commonly due to Shiga toxin-producing E. coli (STEC) infection in most cases. Reports indicated that around 60% of HUS cases could be attributed to a preceding infection with STEC [7]. The other less common possible correlations include streptococcal pneumonia and exposure to certain viruses, such as influenza A or HIV, and rarely because of E. histolytica intestinal infection [7]. A link with amebic dysentery has also been described, but it is yet not clear whether this represents a cause-and-effect relationship [2].

As the association between amebic dysentery and HUS had been reported in a few cases, amebic infection should be considered if etiological studies for HUS are negative for most common causative organisms. Amoeba can be the leading cause of HUS if stool samples reveal numerous cysts and hematophagous trophozoites of E. histolytica [8].

In this article, we report a child who presented to our hospital with enteritis caused by E. histolytica, which was complicated by HUS with severe acute kidney injury (AKI) required two sessions of hemodialysis.

Case Report

A previously healthy 3-year-old girl was seen in the outpatient clinic with a 5-day history of fatigue, fever, and abdominal pain associated with frequent watery diarrhea that became bloody on the second day of her illness.

The patient was initially treated with metronidazole and an oral rehydration solution; however, her symptoms worsened, leading to her admission to the hospital, she was severely dehydrated, had severe abdominal tenderness on superficial palpation, along with rectal prolapse during the physical examination.

Her initial investigations showed leukocytosis with neutrophilic predominance, hyponatremia, otherwise kidney function test was within normal. Additionally, her stool examination was positive for Entamoeba histolytica cysts.

During hospitalization, she was started on intravenous metronidazole and rehydration therapy but without any improvement. On the next day, a follow up investigation revealed rising serum creatinine from 0.7 mg/dl to 2.3 mg/dl, while her hemoglobin dropped from 15 g/dl to 10 g/dl with drop in platelet count from 179 to 61/ µL, while her serum sodium reached 129 mEq/L.

The diagnosis of HUS was suspected, and she was transferred to our institution for further management. On evaluation, she found to have generalized edema, she was oliguric, for which intravenous fluid was discontinued. New laboratory studies were obtained (Table 1).

Abnormal test results of the patient included the following: dilutional hyponatremia; elevated serum creatinine (2.7 mg/dL); high blood urea nitrogen (BUN) (27 mg/dL); low hemoglobin (9 g/dL); low platelet count (52,000/µL); elevated lactate dehydrogenase (LDH) (3022 U/L); high reticulocyte count (1.3%); and metabolic acidosis with a pH of 7.3 and HCO3of 15 mEq/L.

The peripheral blood smear revealed a high percentage of schistocytes (8%). On three occasions, stool microscopic examination showed Entamoeba histolytica trophozoites. Urinalysis revealed the presence of hyaline and granular casts, but no proteinuria or hematuria.

Serological laboratory screening for rheumatological disorders revealed a low C3 level (36 mg/dL) and a low C4 level (6.2 mg/dL), with a negative antinuclear antibody (ANA) and (dsDNA)tests. Stool cultures were negative for Salmonella, Shigella, and Campylobacter. The culture for Escherichia coli O157 serotype in the stool was also negative.

During her hospital stay, the patient's kidney function deteriorated, accompanied by increased edema due to low urine output, metabolic acidosis, and hyponatremia. She was placed on fluid restriction and was given sodium bicarbonate infusion trying to correct the acidosis. At the peak of her illness, her serum creatinine reached (4.12 mg/dL), BUN was 54 mg/dL, and blood gas analysis revealed metabolic acidosis with an HCO_3 level of 10 mEq/L despite bicarbonate infusion. Additionally, her hemoglobin dropped to 4.8 g/dL, and her platelet count decreased to 16,000/µL.

During blood sampling, her blood appeared whitish, thick, and lipemic, for which a lipid profile was done and showed elevated cholesterol of 256 mg/dl, triglycerides of 743 mg/dl, LDL of 113 mg/dl, and HDL of 28 mg/dl.

She required two blood transfusions, and a central venous catheter was inserted to initiate hemodialysis. Bleeding from the catheter site required administration of fresh frozen plasma (FFP) twice along with platelet transfusions.

On the third day of admission, her symptoms worsened to the extent that she developed significant fluid overload and metabolic acidosis necessitated hemodialysis (HD). She underwent two HD sessions on the 3rd and 4th days of admission, and the patient improved following the dialysis.

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The patient's oral intake also improved, urine output gradually improved, and all the investigations and blood gases showed improvement on the daily follow-ups. She was discharged after 11 days of hospital stay, and she went home in good general health.

Follow-up after two weeks at the outpatient pediatric nephrology clinic revealed normal kidney function tests, hemoglobin, platelet count, and acid-base balance (Lab tests as shown in Table 1).

Discussion

After the initial positive result of our patient's stool analysis for Entamoeba histolytica, the analysis was repeated three times, with the continued presence of E. histolytica trophozoites. No other common enteric pathogens associated with HUS were found. Thus, we believe that our patient's HUS relates to her infectious diarrhea caused by Entamoeba histolytica. A similar case was reported in an 11-year-old healthy female but without rectal prolapse [2].

Studies have shown that the severity of E. histolytica infection can be effectively predicted by the virulence of a strain, environment, host genetic susceptibility, immune status, age, and gender [9].

The pathogenesis of *E. histolytica* is primarily dependent on the factors of the parasite rather than the host; therefore, there is extended research to explain the molecular differences between pathogenic and non-pathogenic *E. histolytica*. Pathogenic amoebas lyse, phagocytose, and destroy diverse cells and tissues in the host due to three major virulence factors: Gal/GalNAclectin, ameba pore, and proteases [10]. Moreover, it was reported recently that the interaction of the host's intestinal flora with E. histolytica may result in more aggressive behavior and the creation of more dangerous strains [9].

The presence of some gut bacteria can enhance the production of proinflammatory cytokines, thus leading to more damage in the intestinal lining, making the invasion of the parasite easier [9].

E.histolytica trophozoites lack the typical cellular structures commonly found in higher eukaryotes. They rely on lipids to express virulence, requiring cholesterol and phospholipids for the biosynthesis of internal and plasma membranes and other functions. However, the parasite is unable to produce its cholesterol and must acquire it from the environment, such as from cultured cells or the intestine and liver cells of live organisms. The trophozoites show enhanced virulence when cultured with a high cholesterol concentration [11]. Increased lipid levels have been associated with E. histolytica infection in the literature [12]. As evidenced by our patient's lipid profile, which revealed elevated triglyceride and cholesterol levels.

Conclusions

Though most E. histolytica infections are asymptomatic, some pathogenic strains can cause a range of complications, including liver abscess and fulminant amebic colitis. Additionally, other studies have demonstrated the fact that E.

Table 1: Patient Lab Findings Over 11 Days.

Day of Hospitalization	1	2	3	4	5	6	7	8	9	10	11
BUN	27	48	62	75	68	57	56	58	53	54	44
Creatinine	2.7	4.15	4.74	5.28	4.42	3.85	4.14	3.77	3.15	2.23	1.4
Serum NA	125	129	129	129	133	132	134	136	135	137	139
Serum K	3.3	3.7	3.8	3.7	3.1	3.3	2.7	2.9	3.6	3.6	4.9
HB	11.1	7.6	6.22	9.5	6.32	5.87	4.87	7.73	6.52	6.33	9.34
PLT	52	49	16	31	21	30	54	109	156	262	308
Blood gas PH	7.31	7.4	7.39	7.45	7.38	7.56	7.43	7.42	7.57	7.57	7.36
Blood gas HCO3	14	11.5	10	9.5	12	14	16.5	20.1	21.8	20	21
Blood gas PCO2	31	22.8	19.9	13	24	24.8	32.3	38.4	24.1	18	35.5
cholesterol	-	-	-	-	-	-	-	-	-	240	256
HDL	-	-	-	-	-	-	-	-	-	23	28
LDL	-	-	-	-	-	-	-	-	-	104	113
Triglycerides	-	-	-	-	-	-	-	-	-	743	692
Serum Albumin	2.7	2.3	2.3	2.5		2.8	3	-	-	3.4	3.6
C3	-	36	-	-	-	-	-	-	-	-	126
C4	-	6.2	-	-	-	-	-	-	-	-	27.9
D-Dimer	-	22060	17340	11398	3966	21936	6336	-	-	-	3765
LDH	3022	3112	4185	4709	3351	2533	-	-	-	1404	-

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histolytica could be a cause for the development of Hemolytic Uremic Syndrome (HUS) as an unusual complication. The potential for some pathogenic strains to cause severe complications underscores the need for further research and vigilance in the diagnosis and management of this condition. Understanding how E. histolytica might lead to HUS is very important for building effective strategies for its prevention and treatment. More studies and clinical observations are necessary to fully grasp the association between E. histolytica and HUS and to advance medical approaches for addressing this rare but serious complication.

Conflicts of interest:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be a potential conflict of interest.

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The study is exempt from ethical approval in our institution at Al-Ahli Hospital.

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