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Hemolytic Uremic Syndrome in A Child: Clinical Case Report

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Abstract

Introduction: Hemolytic uremic syndrome (HUS) is one of the most common causes of acute kidney injury in children and is defined by the simultaneous occurrence of microangiopathic hemolytic anemia, thrombocytopenia when the small blood vessels in kidneys become damaged and inflamed.

Case presentation*:*A clinical case of post-diarrheal HUS in an 8-month-old child complicated by acute kidney injury. The analysis of the literary data from Medscape and Pubmed was carried out. During the examination, the diagnosis was specified. Postdiarrheal HUS. Acute renal failure, oligoanuria stage. Upon admission, the child's condition was severe, caused by impaired kidney function and, as a result, intoxication. The treatment was effective, and the patient's condition improved during the hospitalization period, although establishing the diagnosis required the cooperation of doctors of many specialties and many additional examinations.

Conclusions: This clinical case is a classic, "textbook" example of hemolytic-uremic syndrome in children, which is indicated by the presence of both a typical anamnesis (a clear connection with a previous infection) and a typical clinical picture ("triad"). There is a need to increase knowledge about this pathology among general practitioners and district pediatricians since managing patients with typical HUS in pediatrics requires a complex and multidisciplinary approach.

Keywords*:* hemolytic uremic syndrome, children, renal failure, acute kidney injury, AkI, Shiga toxin, Escherichia coli.

Introduction

Hemolytic uremic syndrome (HUS) is one of the most common causes of acute kidney injury in children. In Europe, the age category from 6 months up to 5 years is the most vulnerable **[1]**. The long-term consequences of this disease suffered in childhood are still being investigated. There is evidence that these children have a higher risk of developing CKD in adulthood, which correlates with the duration of the oligouric phase **[2]**. According to M.I. Burakovsky, the mortality rate in the USA and Western European countries is about 5-7%, and the same number of children have serious consequences (CKD, hemorrhages, hypertensive disorders) **[3]**. Therefore, such patients require long-term observation and are often lost from the medical workers' field of view, making the study of pathology even more difficult **[4,5]**.

The problem is in the difficulty of predicting the development of this syndrome: there are no reliable predictors for post-diarrheal HUS, and in the case of atypical, although a connection with heredity has been found, there is still a whole range of possible genetic markers, so their determination is not a routine test and is possible only in specialized laboratories **[6]**.

Establishing a diagnosis facilitates the choice of patient management tactics and improves the overall prognosis. Even though the forecast for HUS is generally favorable, there are still many unexplored problems, such as the probability of developing remote complications, the search for predictors, and the means of prevention.

Case Presentation

An 8-month-old child was admitted with complaints of decreased rate of diuresis, red color of urine, and discomfort during urination.

According to the patient's mother's information, the child fell ill on 06.07.2021 when mushy stools appeared after eating fresh greens. There was no increased body temperature. He was treated on an outpatient basis (enterosorbents, diet). On 06.17.2021, multiple liquid stools and refused to eat, which the mother associates with introducing milk mixture into the diet. He was hospitalized at his residence (Kramatorsk) and received treatment - antibiotic therapy and infusion therapy. On 06.19.2021, the pink color of the urine appeared, and the child began to strain when urinating. On 06.20.2021, he was transferred to the intensive care unit, and later, on 06.21.2021, he was again transferred to the intensive care unit in the hospital of Sloviansk. During the treatment, increased azotemia, anemia, thrombocytopenia, and a decrease in the rate of diuresis, proteinuria, and microhematuria were observed. HUS and AKI are suspected. The child was transferred to Kyiv Children's Regional Hospital. He was discharged after treatment on the 15 days. Currently,

he is under the observation of a hematologist in the oncology and hematology department of the Ternopil Regional Children's Clinical Hospital.

Anamnesis Vitae: The child is from 3rd pregnancy, 2nd childbirth. The pregnancy was uneventful; the labor was physiological. The child was born with a body weight of 3180 g, height of 56 cm, and 8.9 on the Apgar scale and vaccinated according to the calendar. There were no injuries or operations. Hereditary anamnesis is not burdensome. Allergological anamnesis is not overbearing.

Objective status upon admission: The general condition of the child is severe due to intoxication syndrome, oliguria, hyperazotemia, and anemia. The child is conscious, lethargic, and reacts to the examination by crying.

The skin is pale pink, warm, moist. The face is pasty; the limbs are swollen. T 36.8°C, BM – 10.4 kg. Respiratory rate - 38. min. During auscultation, it's puerile over the entire surface of the lungs without wheezing—SpO2 97-98%.

The tones of the heart are muffled and rhythmic. Heart rate – 117. min, blood pressure – 139.79 mmHg. Capillary filling - 2 s.

No neurological deficit was detected at the time of examination. Pupils D=S, photoreaction preserved.

The abdomen is soft, symmetrical, distended, and accessible to deep palpation. Auscultatively - the noise of peristalsis. There are traces of pink urine in the diaper. There are no stools at the time of inspection. The complete blood count revealed leukocytosis with a shift of the leukoformula to the left, which was observed only in the first days after admission, moderate anemia and thrombocytopenia, which persisted for about a week, increased ESR and reticulocytosis **(Table 1)**. In the biochemical analysis of blood, a significant increase in urea and creatinine is noticeable, which indicates impaired kidney function **(Table 2)**. The coagulogram showed hypofibrinogenemia and a slight rise in APTT, which were successfully corrected during treatment **(Table 3)**.

Among the changes in urinalysis - macrohematuria and massive proteinuria **(Table 4)**.

No changes were detected during instrumental examination and specific laboratory tests **(Table 5-6)**.

Table 1. Complete blood count in dynamics.

Paramether.date	26.06	29.06	01.07	03.07	07.07	11.07	13.07	19.07	21.07	27.07
WBC*10^9.L	10,1	7,3	7,3	3,9	7,7	7,9	6,3	11,8	9,4	10,24
Hb g/l	83	74	123	67	97	128	130	125	132	145
RBC *10^{12}.L	2,91	2,49	4,08	2,31	3,55	4,54	4,70	4,36	4,85	5,03
PLT 10^9.l	87	34	183	41	115	231	215	579	682	466
Bands %	12	9	12	5	7	30	7	3	5	2
Segmented neutrophils %	39	33	39	40	63	57	48	57	57	25
Lymph %	39	45	31	34	17	12	23	13	15	29
Monocytes %	10	9	16	14	9	1	7	7	9	8
Eosinophil %	0	4	2	6	3	0	7	20	13	
Basophil %										
Reticulocytes %	14,9	8,2	6,7		4,7		1,6			
ESR мм. hours	20	25	12	36	21	11	9	11	16	

Table 2. Biochemical profile in dynamics.

Parameter	26.06	28.06	01.07	03.07	05.07	08.07	10.07	12.07	14.07	27.07	Referent norm
ALT	25		14							6	Before 39
AST	80		45							18	before
Amylase.U.l	16										28-100
Total bilirubin mmol.l	18,4	19,7	19	17,7	19,5	6,0	15,0	7,7	9,2	5,0	17,0
Conjugated bilirubin	4,0	2,1	6,1	5,6	6,5	3,2	5,6	3,5	3,3	1,0	
Unconjugated bilirubin	14,4	17,6	12,9	11,1	13,0	2,8	9,4	4,2	5,9	4,0	
Na											5,1

K											128,5
Ca	1,98										
Cl											
P	2,0										
Fe	33,2										
Mg	2,24										
Glucose mmol.l	5,11	5,44	7,26	5,11	4,96	7,75	6,73	9,26	5,55	3,64	3,33-5,89
Urea	26	12,8	19,1	21,9	2,9	14,7	16,5	10,7	11,9	25,2	
Creatinine mmol.l	291	177	293	276	43	272	230	138	112	65	
Total protein g.l	49,3	48	55,9	52,1	65,4	62,4		52,8	60,8	72,8	60-80
Albumin	30,9		33,7	32,6	43,9						
Lactate	1,64		1,68		1,39						
CRP	0,60					61,29					Less 0.5

Table 3. Coagulogram in dynamics.

parameter	25.06	27.06	30.06	01.07	Referent norm
APTT sec	20,6	36,2	25,3	22,2	24-36
Thrombin time sec	22,3				8-14
Fibrinogen g.l	1,32	1,04	1,42	2,33	2-4
Prothrombin time sec	14,6	15,5	16,0	16,3	9-16
INR	1,1	1,03	1,08	1,1	0.85-1.23
PT Quick	94	94,4		86,3	60-130%
Antithrombin III	107,6				

Table 4. Urinalysis in dynamics.

Paremeter	date			
	26.06	28.06	14.07	16.07
Color	yellow	red	yellow	Light yellow
Clarity				
Specific gravity	1010		1008	1004
pH	6,5	8,0	7,5	8,0
Protein g.l	+++ (3,0)	+++ (3,0)	+++ (3,0)	+++ (3,0)
Glucose	-	+.-	-	-
Ketones	-	-	-	-
Blood	+++ (250 RBC.ul)	+++ (250 RBC.ul)	+++ (250 RBC.ul)	+.- (10 RBC.ul)
RBCs.hpf	60-62 15-17	Fresh 18-20 Little changed 22-24	Fresh 3-4 Little changed 5-6	fresh 0-1 Little changed 4-5
WBCs.hpf	2-3	1-2	2-3	2-3
Squamous epithelial cells.hpf	0-1	0-1	0-1	0-1
Casts	-	-	-	-
Mucus	A little	-	A lot	A little
Crystals	-	-	-	-
Bacteria	-	-	-	-

Table 5. Other lab tests.

Date	Paremeter	Value	Unit of measurement

	PTH		Pg.ml
26.06	PCT	1,90	Ng.ml
	Anti-HIV		
	HBsAg, A-Hbc (IgM+IgG) A- HCV (IgM+IgG)	Not found	
	Blood group and Rh		
	DNA – EBV DNA – CMV, HHV-6		
30.06	Coombs test	Negative	

Microbiological cultures

1. Nose 26.06 and 08.07 – growth of microflora was not detected.
2. Pharynx 26.06 – hemolytic streptococcus; 08.07 – Escherichia coli – III.
3. Blood 08.07 – Staphylococcus epidermidis.
4. Blood (vein) 08.07 - Acinetobacter baumannii, fungi not detected.
5. Blood (catheter) 08.07 - Acinetobacter baumannii, Staphylococcus epidermidis.
6. Blood, subclavian catheter 01.07 - Staphylococcus epidermidis; 09.07 – Staphylococcus epidermidis, no fungi detected.
7. Stomach contents 25.06 – C. Lusitarae.
8. Feces 26.06 – fungi of the genus Candida; 10.07 – pathogenic escherichia, salmonella, and shigella were not detected.
9. Urine 26.06 – C. Lusitarae; 08.07 – BI not detected
10. PD-liquid 08.07 – Acinetobacter baumannii, no fungi detected; 07.19 – microflora growth was not detected. Fungi were not detected.

Table 6. Instrumental examinations.

Examination	Date	Conclusion
Abdominal ultrasound	29.06	Liver: enlarged - right lobe 69 mm, parenchyma homogeneous Gallbladder is anechoic, content is homogeneous Pancreas: head - 6 mm, body - 3.5 mm, tail - 5.5 mm, uniform, parenchyma of medium echogenicity. Spleen: not enlarged, parenchyma is homogeneous Right kidney: typical position, 69x30 mm, increased echogenicity, cortico-medullary differentiation smoothed. Blood flow 1 st. Left kidney: typical position, 71x31 mm, increased echogenicity, cortico-medullary differentiation smoothed. Blood flow 1 st. Free fluid: interloop minimal effusion. It is dry in the pleural cavities
Echocardiogram	29.06	Heart cavities, valves are not changed. There are no pathological currents. Myocardial contractility is good. EF - 73%, oval window - 8 mm, there is no effusion in the pericardium.
Neurosonography	29.06	The middle structures are not displaced. CSF spaces are slightly expanded. BA up to 4.5 mm. The ventricles of the brain are not expanded. Brain parenchyma without focal changes.
Chest X-ray	26.06	The lungs are expanded, pneumatized, without focal, infiltrative changes. The costo-phrenic angles are equal. The contour of the diaphragm is clear and even. The roots are not extended, they are structural. The shadow of the mediastinum is not displaced, not expanded.
Genetics of the Center for Disease Control and Prevention	30.06	A: this condition must be differentiated first of all from lysosomal storage disease, as well as from other congenital disorders of the metabolism of amino acids and acylcarnitines. Dynamic observation in the health care center.

An ophthalmologist, neurologist, hematologist, and surgeon consulted the patient.

The prescribed treatment.

1. Antibacterial. Antimycotic therapy: Zivox, Ceftriaxone, Ceftum.
2. Efferent methods of detoxification: peritoneal dialysis, plasmapheresis, prolonged hemodiafiltration.
3. Infusion therapy and electrolyte solutions: NaCl 0.9%, NaCl 10%, glucose 5%.
4. Hypotensive therapy: Berlinpril, Amlodipine.
5. Blood components: erythrocyte mass, Albumin 20 %, platelet concentrate.
6. Symptomatic therapy.

Clinical diagnosis: Acute intestinal infection. Postdiarrhealhemolytic uremic syndrome. KDIGO-3, oligoanuria stage.

Anemia of moderate severity. Mild thrombocytopenia. Dysmetabolic encephalopathy.

Discussion and Review of The Literature.

This clinical case illustrates the typical course of HUS - the presence of the classic triad – microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury **[1,7]**. This child is at increased risk of developing this disease (children under 5 years old) **[3]**.

Usually, Escherichia coli, which is capable of Shiga toxin production, is the etiological factor in the development of the HUS8. The most common serotype is O157:H7, but there are cases caused by other serotypes, including O111:H8, O103:H2, O121, O145, O26, and O113, as well as other pathogens, such as bacteria of the Shigella spp. and Streptococcus pneumoniae **[9,10,11]**.

Even though Escherichia coli was not isolated from this child during stool culture, this is not an exclusion criterion. From the anamnesis, it is known that an extended period (12 days) passed between the appearance of symptoms of intestinal infection and kidney damage, which proportionally reduces the probability of identifying an ecotropic factor, according to the study of Mody R.K. et al., published in 2012 **[12]**. The previous administration of antibiotics is also essential.

When the diagnosis of HUS is established, it is essential to determine its clinical form - typical (associated with diarrhea) or atypical (not associated with infection, genetically induced), since the pathogenesis of both types is slightly different. This will help determine the treatment strategy. For a HUS, there is an orthotropic treatment - factor C5 inhibitor Eculizumab, but due to its high cost, it is not very accessible to patients **[13]**.

In the case of the HUS, which is present in this patient, the basis of treatment is supportive therapy. The most critical points are the well-timed start of correction of blood system changes and early liquid resuscitation. However, the approach to infusion therapy must be individual and consider both the degree of renal dysfunction and the total blood volume loss since patients with HUS can be both hypovolemic (due to dehydration) and hypervolemic (due to fluid retention caused by renal dysfunction). In several independent studies (Poland, 2018; Germany, Hamburg, 2016), it has been proven that the early start of infusion contributes to a better prognosis of HUS, but in fluid-overloaded patients, it can cause heart failure, so all infusion solutions and blood products should be administered slowly andunder constant monitoring of vital signs **[14,15]**. When correcting anemia, it is essential to balance the hemoglobin index and the volume of allocated blood components since the consequences of volemic overload for the myocardium are more dangerous than anemia itself. It was also crucial for this patient to start renal replacement therapy as soon as possible—the method of choice - peritoneal dialysis, which is the "gold standard" for children **[18]**.

As for changes in the hemostasis system, both hyper- and hypocoagulation are possible for HUS. Hypercoagulation is more typical for the beginning of the disease, and hypercoagulation – is for the terminal phase due to the consumption of coagulation factors. However, options for the treatment of this syndrome are different. Currently, no advantages of therapy with heparin, streptokinase, or other anticoagulants over adequate supportive therapy have been found **[16]**. There is a hypocoagulation syndrome in this clinical case, but it was successfully corrected during the treatment with blood components. The duration of thrombocytopenia in this patient was 11 days, which is consistent with other researchers' data regarding the average time of this syndrome in children (13.7 days) **[17]**.

Despite the typical clinical picture of HUS in a patient, diagnosis is still problematic at the primary and secondary level of medical care due to the low frequency of cases in the world (from 0.2 to 3.4 cases per 100,000 children) **[3]**.

Therefore, we have found the necessity for a complex and multidisciplinary approach to managing patients with typical HUS in pediatrics and increasing knowledge about this pathology among general practitioners and district pediatricians.

Conclusions

1. This clinical case is a classic, "textbook" example of hemolytic-uremic syndrome in children, which is indicated by the presence of both a typical anamnesis (a clear connection with a previous infection) and a typical clinical picture ("triad").

2 .There is a need to increase knowledge about this pathology among general practitioners and district pediatricians since managing patients with typical HUS in pediatrics requires a complex and multidisciplinary approach.

Author Contributions

S.O. and M.V. were responsible for the diagnostic procedures, clinical diagnosis, and treatment decisions. S.O.

And O.Y. wrote the manuscript. A.I., I. A was responsible for the data acquisition. S.O., I.A., and O.Y.

They were responsible for collecting and assembling the articles/published data and their inclusion and interpretation.

In this review. All authors contributed to the critical manuscript revision for valuable intellectual content. All authors have read and agreed to the published version of the manuscript.

Compliance with Ethics Requirements

"The authors declare no conflict of interest regarding this article. "

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), and the national law. Informed consent was obtained. from the patient included in the study. "No funding for this study. "

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List of abbreviations

HUS- Hemolytic uremic syndrome

AKI-Acute kidney insufficiency

CKD - chronic kidney disease

KDIGO-3- kidney disease: Improving Global Outcomes

APTT- Activated partial Thromboplastin time

INR-international normalized ratio

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