

Case Report

J Ped. Nephrology;2(1):39-42
<http://journals.sbmu.ac.ir/jpn>

Typical Hemolytic Uremic Syndrome with Diffused Brain Ischemia as a Complication: A Case Report of a Child in Iran

How to Cite This Article: Javadilarijani F, Sayarifard A, Javadilarijani F, Ataei N, Pajouhi A. Typical Hemolytic Uremic Syndrome with Diffused Brain Ischemia as a Complication: A Case Report of a Child in Iran. J Ped. Nephrology 2014;2(1):39-42.

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Received: Nov-2013

Revised: Dec-2013

Accepted: Dec-2013

Hemolytic uremic syndrome includes hemolytic anemia, acute kidney injury, and thrombocytopenia. In this article, a child with hemolytic uremic syndrome (HUS) and acute nervous system involvement is reported.

The patient was a 22-month-old boy who presented with hemorrhagic diarrhea and anuria. He was admitted by the impression of HUS and received supportive care such as acute peritoneal dialysis and packed cell infusion. During recovery period and after the beginning of the fifth session of dialysis, the child suddenly experienced loss of consciousness and focal convulsion in some extremities which led to hemiparesis of the left side of the body, and speech and swallowing impairment. The patient underwent a diagnostic and therapeutic process and was followed for one year. Any organ damage such as nervous system involvement and an appropriate period of follow up should be considered in a typical HUS syndrome, especially in pediatric patients.

Keywords: Hemolytic-Uremic Syndrome; Brain Ischemia; Infarction; Child; Iran.

Running Title: Typical HUS with Brain Ischemia

Introduction

The hemolytic uremic syndrome (HUS) presents as a microangiopathic triad which includes hemolytic anemia, acute kidney injury, and thrombocytopenia. HUS is categorized into two major groups: typical and atypical. The typical form is usually associated with the Shiga toxin of E-coli [1]. This form is also known as HUS with diarrhea, because it usually presents after a prodromal diarrhea and causes 90% of the disease in pediatric patients. About 50% of the patients with typical HUS require dialysis and 25% develop nervous system involvement as coma, convulsion, brain edema, hemiparesis, and focal neurological symptoms. In atypical HUS, the prodromal phase and gastrointestinal symptoms

are not seen. The outcome is poor and relapse or progression of the disease is probable [2]. Some severe acute neurological signs were reported in HUS cases in France [3] and some pediatric patients suffering HUS were reported to have neurologic involvement in London [4]. In this manuscript, we present a child with HUS and acute nervous system involvement.

Case Report

The patient was a 22-month-old boy who was admitted in Children's Medical Center, Tehran, Iran, with hemorrhagic diarrhea, paleness, agitation, and anuria. Diarrhea began 10 days before admission and was accompanied by abdominal pain, but no fever was detected. He was first taken to another hospital and was treated

with IV ceftriaxone and metronidazole. Oliguria and fatigue were added to other symptoms after three to four days and then he was transferred to our center. His mother gave a history of drinking rain water which was collected in a pit in a park. In past medical history, there was no history of sickness during the newborn period or any history of admission or surgery. The parents were first degree relatives and the mother had no history of abortion. Only one of the child's aunts had a positive history of foot thrombophlebitis during the post partum period. The physical examination which was performed immediately after admission included BP (100/70 mmHg), PR (130/minute), RR (40/minute), and T (36.5°C). The child was pale and agitated, the conjunctiva was pale, and no organomegaly or lymphadenopathy was detected. The neurological examination and other evaluations were normal, but mild rales were auscultated on the basis of both lungs. Laboratory findings showed decreased hemoglobin (6.2 g/dL) and platelet count (37000/mm³) and elevated BUN (71mg/dL) and creatinine (3.3 mg/dL) levels. The first stool exam in the first hospital showed many WBC, many RBC, and amebiasis but the stool exam in our hospital showed no ameba suggesting WBC was mistaken as amebiasis. A peripheral blood smear showed anisocytosis, mild spherocytes, Burr cells, and helmet cells. Direct and indirect Coombs' tests were negative. Coagulation profiles (including prothrombin, activated partial thromboplastin time, fibrinogen, and antithrombin III levels) were normal. According to history, physical examination, and laboratory findings (anemia, thrombocytopenia and acute renal failure), he received supportive care including acute peritoneal dialysis and infusion of packed cell with an impression of HUS. Ceftriaxone and metronidazole were discontinued and other diagnostic and therapeutic processes began for the child. Four to five days after dialysis and packed cell infusion, urine flow was established and levels of urea, creatinine, platelets and LDH reached their normal ranges gradually. As the patient recovered and after the beginning of dialysis in the fifth session, the child suddenly experienced fever and received cefepime by the impression of *Pseudomonas peritonitis*. Lack of consciousness and focal convulsion in some extremities happened just after the fever started. Emergent brain CT was done which was normal. Within hours after convulsion, hemiparesis of the left side including the face and the upper and lower limbs, and speech and swallowing

impairment gradually occurred. The brain CT was repeated after twelve hours which showed diffused ischemic infarction in the right hemisphere; enoxaparin was prescribed and changed to warfarin after three days to reach an INR of 2. EEG showed abnormal waves so phenytoin was administered for seizure control. Also, FFP was prescribed for the patient and levels of all coagulatory factors were measured which showed normal results. After ten days of supportive treatment, the platelet level raised, hemoglobin increased to 8- 9 g/dL, and creatinine reduced to the normal range. The work-up for ANA, ds DNA titer, C3, C4, CH50, lupus anticoagulant, factor V, protein C, protein S, homocystein, anti phospholipid IgG and IgM, and anti Cardiolipin IgG and IgM was normal. Volume overload signs including pleural effusion, ascites, and pulmonary edema were reported in chest x-ray and abdominal sonography. Laboratory findings were suggestive of typical HUS. All laboratory tests and paraclinic investigations were performed in Tehran Children's Medical Center. He received hospital care for about 26 days. When he was discharged, swallow was normal, but he was not able to speak. Also, the child still suffered from left hemiparesis and inability to move. Phenytoin and warfare were prescribed and he was referred to occupational therapy and physiotherapy centers. In addition, weekly evaluation of the renal function was recommended. Laboratory findings at the time of discharge were as follows:

Hb=9.8 g/dL; platelet= 129000/mm³; WBC= 42200/mm³; PT= 13.5"; INR=2; BUN= 10 mg/dL; Cr= 0.6 mg/dL; Na= 136 mEq/L; K= 4.2 mEq/L; LDH= 818 U/l

The brain MRI was as follows:

Three months after discharge: Chronic ischemic infarction in the right hemisphere in the territory of MCA is seen. Basal ganglia destruction due to the mentioned infarction is also seen with small right thalamus. Secondary ipsilateral ventriculomegaly from volume loss is remarkable. Six months after discharge: Encephalomalacia in the right temporoparietal lobe in favor of old infarction is seen. Brain MR venography shows superficial and deep venous structures including superior and inferior sagittal sinuses, lateral sinuses, straight sinus, internal cerebral vein and vein of Galen are normal. During one year of follow up, the patient continued to have left

hemiparesis of the face, speech impairment, inability to move the left wrist and fingers, and paresis of the left lower extremity. Renal function tests remained intact.

Discussion

The patient was a typical case of hemolytic uremic syndrome with bloody diarrhea as the prodromal symptom. During recovery, he experienced a sudden extensive impairment in central nervous system which resulted in poor prognosis while most typical HUS cases in pediatric patients have a good prognosis and less common cases of atypical HUS have higher morbidity and mortality [1]. CNS dysfunction is seen in 17-50% of the pediatric population which is the most dangerous complication of HUS. Brain CT scan in these patients may show infarction or hypo density which is more common in the basal ganglia [4]. Severe forms of atypical HUS associated with regulator mutation of the complements in two reports suggest that certain genetic backgrounds in children experiencing acute HUS with verotoxigenic *E. coli* may make them more sensitive to complications and they may experience more severe forms [5]. Erikssone [4] followed 22 children suffering from HUS from 1985 to 1999 in London. All of the children had neurological involvement at the acute phase of the disease. In that study, all patients had prodromal gastrointestinal signs similar to our case; moreover, some patients had several acute neurological involvements. In a retrospective study by Nathanson [3], 52 patients with HUS and neurological involvement were studied in France. There was no correlation between specific characteristics of localization in early MRI and the prognosis in MRI results of those patients. In the study by Nathanson [3], almost all patients with severe neurological involvement also suffered from kidney injury which led to dialysis similar to our patient. Furthermore, in both our and Nathanson's cases, high blood pressure was not necessary for the beginning of neurological symptoms. The other aspect of our case was hemorrhagic diarrhea that prevented us from prescribing any antibiotics to avoid HUS, but the positive result for ameba in his first stool exam made the first physician in the first hospital prescribe antibiotics which could contribute to the start of HUS. Several factors could play a role in the mechanism of CNS damage such as local microangiopathy, hypertension and hyponatremia

[3]. Parenchymal ischemia was described as the main result of CNS damage in typical HUS in a study, which was directly related to local microangiopathy in the brain [6]. In our case, thrombosis was described as the cause of brain ischemia. HUS neurological complications lead to death in 17% of the cases, cause severe sequels in 23% of the cases although 50% of the cases show complete neurological recovery [3]. Unfortunately, the neurological sequelae including left hemiparesis and aphasia did not resolve in our case. Treatment of these patients includes volume control, correcting electrolyte imbalances, blood pressure, anemia and supportive care for acute renal failure. Although plasmapheresis is recommended in atypical HUS, the role of plasma in treatment is under discussion [7]. Since plasmapheresis is not allowed in children less than 2 years of age according to the guidelines of the Blood Transfusion Center, we had to collect the patient's blood and send it to the Blood Transfusion Center; then, the plasma and packed cell of the sample were transfused to the patient. The risk of contamination and infection during the process of transfusion in this way was high, and we preferred to continue supportive care and wait for laboratory results to rule out atypical HUS. All laboratory findings were suggestive of typical HUS and after one year of follow-up, no relapse or recurrence was seen; therefore, we believe the best decision was made for this patient. The child discussed in this report had a benign progression of typical HUS at first, but thrombosis and severe CNS involvement happened during the recovery period. Hence, it is recommended to take care of other organ involvements such as the neurological system, especially in pediatric patients with typical HUS progress, and keep in mind to observe and follow patients for a while. Parent education in order to make them aware of the causes of this syndrome such as contaminated water, raw foods, and poor hygiene (for example hand washing especially during the period this syndrome is more common) should be kept in mind as prevention.

Acknowledgment

The authors wish to acknowledge all the people who helped us to prepare this case report.

Conflict of Interest

None declared

Financial Support

None declared

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