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ATYPICAL HEMOLYTIC UREMIC SYNDROME: REPORT OF A PEDIATRIC CASE

A TİPİK HEMOLİTİK ÜREMİK SENDROM: BİR OLGU SUNUMU

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Summary

Atypical hemolytic uremic syndrome (HUS) is a rare disease in childhood. The morbidity and mortality of this disease is found high. In this report, a 13 years old boy who had five times of HUS attacks was presented. The family history revealed that his uncle was on hemodialysis for chronic renal failure. The patient had acute renal failure, hemolytic anemia, thrombocytopenia, and dark urine when he was first hospitalized. HUS was diagnosed based upon his clinical and laboratory findings. During the follow-up, he developed three more attacks when he was five, six, nine and ten years old which all required admission to the hospital. The last attack occurred when he was ten years old and plasmapheresis required for five times. He had a quick response to it. We suggest that plasmapheresis is an effective treatment approach in cases with atypical HUS.

Key words: atypical hemolytic uremic syndrome, children, plasmapheresis

Özet

Atipik hemolitik Uremik sendrom (HÜS) çocukluk çağında nadir görülen morbiditesi ve mortalitesi yüksek bir klinik tablodur. Bu çalışmada 13 yaşında beş kez HÜS atakları ile izlediğimiz ve amcasına kronik böbrek yetmezliği nedeni ile hemodiyaliz uygulanan bir erkek olgu sunuldu. İlk defa iki yaşında akut böbrek yetmezliği, hemolitik anemi, trombositopeni, idrar renginde koyulaşma yakınmaları ile başvurdu. Bu bulgularla HÜS olarak değerlendirildi. HÜS atakları beş, altı, dokuz ve on yaşlarında yineledi. İzlemdeki olgu son atağında on yaşında olup, aynı yakınmalar ile başvurdu. Hipertansiyon, azotemi, trombositopeni, anemi ve oligüri saptanan olguya beş kez plazmaferez uygulandı. Hastada plazmaferez tedavisi ile daha kısa sürede klinik yanıt alındı. Atipik HÜS tedavisinde plazmaferezin etkin bir tedavi modeli olabileceğini düşünmekteyiz.

Anahtar kelimeler: atipik hemolitik sendrom, plazmaferez

INTRODUCTION

The hemolytic-uremic syndrome (HUS) typically presents in toddlers or older children after an episode of bloody diarrhea (D+) caused by Escherichia coli 0157:H7 (1,2). However, atypical presentations have been described, including familial and nön-diarrhea-associated (D-) cases (1). The pathogenesis of atypical hemolytic-uremic syndrome, which is rarely encountered in children, is poorly understood and its mortality and morbidity rates are high (1,3). In this report, we presented a case of HUS with recurrent attacks.

CASE REPORT

A two-year old boy with abdominal pain, weakness, pallor and darkening of urine was admitted to the clinic. On his physical examination, his skin and conjunctiva was pale; sclera subicteric and he had abdominal tenderness. Results of laboratory studies were as follows; hemoglobin (Hb): 5.6 g/dl, hematocrit (Hct): 16%, platelet (PLT): 80.000/mm3, reticulocyte: 4%, serum urea: 302 mg/dl, creatinine (Cr): 1.7 mg/dl, total bilirubin (TB): 1.9 mg/dl, indirect bilirubin (IB): 1.4 mg/dl. Serum complement 3 (C3) level was normal and

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direct coombs test was found negative. The peripheral blood smear showed fragmented erythrocytes and thrombocytopenia. HUS was diagnosed based upon these findings. The clinical and renal functions were recovered on the 10th day of admission by both fresh frozen plasma (FFP) infusions and supportive care. His family history revealed that his uncle was on hemodialysis due to chronic renal failure (CRF) with unknown etiology. The parents had consanguineous marriage. The second attack occurred 3 years later than the first attack. He was then admitted to the clinic with the same previous symptoms. The laboratory data were as follows; Hb: 6 g/dl, Hct: 18%, PLT: 90.000/mm^3, reticulocyte; 3%, serum urea: 294 mg/dl, Cr: 1.8 mg/d!, TB: 1.8 mg/dl and IB: 1.3 mg/dl. The peripheral blood smear showed anisocytosis, and burr cells. When he was 6 years old, the third attack occurred while he was in remission.

His laboratory findings were as follows; Hb: 6.t5 g/dl, Hct: 17%, PLT: 28.000/mm^3, reticulocyte: 5%, urea: 298 mg/dl, Cr: 3.2 mg/dl, TB: 1.5,mg/dl and IB: 1.1 mg/dl. The peripheral blood smear again demonstrated fragmented erythrocytes. Severe proteinuria was detected. The patient was given FFP and 1 unit packed red blood cell suspension and his clinical condition improved in 20 days. Renal biopsy was carried out later when his thrombocytopenia returned to the normal. The biopsy showed increased segmentation of mesangium, presence of erythrocytes in capillary lumen. By immune fluorescing staining, IgM and beta 1-C showed segmental staining at mesangium. These findings and widespread endothelial damage suggested HUS in the recovery phase. He had his 4th attack when he was 9 -years **old.** His complaints were abdominal pain, oliguria and pallor. The laboratory data were as follows; Hb: 7 g/dl, Hct: 21%, PLT: 31.000/mm3, reticulocyte: 4%, urea: 154 mg/dl, Cr: 1.4 mg/dl, TB: 1.8 mg/dl, IB: 1.3 mg/dl. The peripheral blood smear suggested hemolysis. FFP and supportive treatment were repeated. He was clinically improved in 12 days. He had last attack after a year with complaints of vomiting, abdominal pain, oliguria and urine darkening. Hypertension and oliguria were determined. The laboratory findings were as follows; Hb: 6 g/dl, Hct: 18%, PLT: 32.000/mm^3, urea: 302 mg/dl, Cr: 4.4 mg/dl, TB: 1.9 mg/dl, IB: 1.4 mg/dl. The patient's urine output returned to normal on 4th day. Serum complement (C-3.) and total complement (CH50) levels were detected as normal. He was treated with plasmapheresis (Immunadsorba TR 350, Asahi Medical Co., Ltd. Tokyo-Japan) and hemodialysis because of frequent attacks. He went into remission after 5 times of plasmapheresis and 3 times of hemodialysis. Our patient has been followed-up at remission for three years.

DISCUSSION

Atypical D-HUS cases usually have an insidious onset. However, its course could be progressive (2,3). Recurrences usually have been associated with nonspecific illness (1,4,5). Our patient was diagnosed as HUS when he was 2 years old. However, he had 5 attacks till the age of 10. All attacks had same symptoms such as abdominal pain, pallor and darkening of urine. The patient did not have any complaint between attacks. Fitzpatrick et al reported that 11 of 20 cases with atypical HUS had one or more recurrences (5). Neuhaus et al reported that 6 of 19 cases (32%) with atypical D-HUS had relapses (4). Atypical D-HUS is characterized by two subtypes as familial and sporadic. The prognosis of familial HUS is poor. It has been reported that pathogenesis of familial HUS has abnormality of serum complement (3,7). Kaplan et al (3) reported that individuals with familial HUS have abnormal C3 and CH50 levels (3). However, we did not determine abnormality of them in our case. Our patient was diagnosed as atypical HUS, because of both frequent recurrent attacks and lack of diarrhea during prodromal stage.

A wide variety of therapeutic approaches have been attempted and the literature contains numerous conflicting reports about the results of these different treatment ways. Prednisone, FFP infusions and plasma exchange transfusion are administered at different stages of the disease and satisfactory response is usually reached (2,4-6). Plasma exchange and drug therapy in patients with HUS were compared. It was shown that both of them had positive effects on remission, renal outcome and mortality rate (6). The study which was carried out in 22 patients with TTP/HUS while demonstrated that plasma exchange accomplished 86% complete remission, plasma infusion and drug therapy provided 57% complete remission (8). In a study carried out in children with HUS, it was demonstrated that there was no difference between plasma exchange and supportive treatment (6,8). Our case was followed-up for 11 years and during that time five attacks occurred. Because of frequent recurrences, plasmapheresis was performed at the last attack. The patient is still in remission for 3 years following the last attack. The effect of plasmapheresis for providing long term remission needs to be followed.

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