Pediatr Pract Res 2020; 8(2): 43-45
DOI: 10.21765/pprjournal.824099

CASE REPORT
OLGU SUNUMU

A Case of Atypical Hemolytic Uremic Syndrome with STEC Positivity and Myocardial Involvement

Myokardit ve STEC Pozitifliği ile Seyreden Atipik Hemolitik Üremik Sendrom Tanılı Olgu

Eylül Şahin[1], Fatma Devrim[2], Büşra Koç[2], Özlem Dur[2], Aslı Kantar Özşahin[2], Gülhan Atakul[1], Pınar Seven[1], Hasan Ağın[1], Nida Dinçel[2]

[1] Department of Pediatric Intensıve Care, Dr. Behçet Uz Children's Diseases and Surgery Health Practice and Research Center, University of Health Sciences, İzmir, Turkey
[2] Department of Pediatric Nephrology, Dr. Behçet Uz Children's Diseases and Surgery Health Practice and Research Center, University of Health Sciences, İzmir, Turkey

ABSTRACT

Hemolytic uremic syndrome (HUS) is a thrombotic microangiopathy characterized by intravascular hemolysis, thrombocytopenia and acute kidney injury. HUS is generally classified into two types. While typical HUS follows a gastrointestinal infection with shiga-toxin producing E. coli (STEC), atypical HUS (aHUS) is associated with autoantibodies or mutations that lead to irregular complement activation. However, according to some recent studies, it was observed that diarrhea and multisystem involvement were seen in both HUS types. STEC positivity was also detected in a little percent of aHUS cases. Histopathological findings compatible with myocarditis were found in postmortem examinations in some cases. Although our case was diagnosed with atypical HUS, typical HUS symptoms such as bloody diarrhea and Shiga toxin 2 positivity were reported and myocardial involvement was observed as a rare complication.

Keywords: HUS, atypical HUS, STEC, myocarditis

ÖZ

Hemolitik üremik sendrom (HÜS), intravasküler hemoliz, trombositopeni ve akut böbrek yetmezliği ile karakterize trombotik bir mikroanjiyopatidir. Hastalık genellikle shiga-toksin üreten E. coli (STEC) enfeksiyonu ile birliktelik gösteren tipik HÜS ve kontrolsüz kompleman aktivasyonu ile ortaya çıkan atipik HÜS (aHÜS) olarak sınıflandırılmaktadır. Ancak son zamanlarda yapılan bazı çalışmalara göre diyarenin her iki HÜS tipinde de görüldüğü, aHÜS olgularında da STEC pozitifliği ile karşılaşıldığı ve her iki HÜS tipinde de multisistemik tutulumun olduğu görülmüştür. Bazı postmortem incelemelerde miyokardit ile uyumlu histopatolojik bulgular saptanmıştır. Bu raporda kanlı ishal ile başvuran, Shiga toksin 2 pozitifliği göstermesine rağmen aHÜS olarak değerlendirilen ve nadiren görülen miyokard tutulumu gözlenen bir olgu sunulmuştur.

Anahtar Kelimeler: HÜS, atipik HÜS, STEC, miyokardit

INTRODUCTION

Hemolytic uremic syndrome (HUS) is one of the most common causes of acute kidney failure in children and infants. Infections, drugs, systemic diseases, genetic mutations have been accused in ethiology. The pathophysiology involves irregular complement activation due to genetic mutations or external factors which helps to determine the type of the disease (1). While typical HUS follows a gastrointestinal infection with shiga-toxin producing E. coli (STEC), atypical HUS (aHUS) is associated with autoantibodies or mutations that lead to irregular complement activation. Intravascular hemolysis, trombosis, trombocytopenia and renal failure presents and multisystemic involvement is reported in both types (1). Although typical cases are thought to

Corresponding Author: Büşra Koç
Address: Department of Pediatric Nephrology, Dr. Behçet Uz Children's Diseases and Surgery Health Practice and Research Center, University of Health Sciences, İzmir, Turkey
E-mail: bsrkoc@hotmail.com

Başvuru Tarihi/Received: 11.11.2020
Kabul Tarihi/Accepted: 26.11.2020

be starting with STEC infections and bloody diarrhea, and atypical cases being younger than 6 months, having family history or recurrent hemolytic attacks, classification according to clinical conditions is quite difficult. Because the treatment protocols are different, it is important to be careful when diagnosing the type of the disease. It was found that STEC positivity may present in cases that do not describe diarrhea. Although STEC positivity is common in the typical HUS, it was observed in 30% of aHUS cases in studies, either. Multisystemic involvement were also seen in both types (2,3). Histopathological findings compatible with myocarditis were found in postmortem examinations in some typical HUS cases (4,5). Although our case was diagnosed with aHUS, it started with typical HUS symptoms such as bloody diarrhea, Shiga toxin 2 positivity, and myocardial involvement was observed as a rare complication.

CASE REPORT

A six months old boy was admitted to emergency department for convulsions. Diarrehea, bloody stool and decrease in urine output was also added to the symptoms 3 days ago. His skin was pale and extremities were edematous in the physical examination. Biochemical analysis revealed elevated serum creatinine of 2.9 mg / dL, urea of 39 mg / dL, lactate dehydrogenase (LDH) of 2828 IU / L. Complete blood count revealed a hemoglobin of 6.9 gr / dL, leukopenia (3900 / mm3) and thrombocytopenia (44000 / mm3). Schistocytes (5%), helmet cells, fragmented erythrocytes were detected in blood smear in several areas.

When the case was evaluated with clinical findings and workup results showing acute kidney injury hemolytic anemia and thrombocytopenia, hemolytic uremic syndrome was considered as diagnosis. Kidney replacement therapy as started for the patient with an anuric course in Pediatric Intensive Care Unit. Eculizumab treatment was given to the patient at the 24th hour of hospitalization with a pre-diagnosis of atypical HUS, considering history of seizures and age of 8 months. Tachycardia and hypotension developed at the 48th hour of continuous veno-venous hemodiafiltration (CVVHDF) therapy. Pericardial effusion was revealed and ejection fraction was calculated as 50% in the echocardiography. Cardiac markers were high in Troponin: 7.5-17.5ng / ml, in CK-MB: 60.3ng / ml. Myocarditis was diagnosed with echocardiographic findings. On the 20th day of the total treatment, plasmapheresis treatment was performed for 3 days in the patient whose hemolysis findings continued. On the 3rd day of plasmapheresis treatment, hemolysis findings stopped and urine output started. ADAMTS 13 activity was normal and Shiga Toxin 2 was detected in tests before treatment. Genetic results revealed p.Glu566Ala (heterozygous) mutations in the CFB gene and p.His402Tyr (homozygous) mutations in the CFH gene. Based on the genetic work-up of CFB, he was diagnosed as a likely aHUS and has given eculizumab.

DISCUSSION

It has been shown in studies that mutations affecting the alternative complement pathway were detected in half of the patients with atypical HUS (6). Although the most common mutations are seen in the CFH gene 20-30%, more than one mutation may also occur. In our case, mutations in Complement factor B (CFB) and Complement factor H (CFH) genes were detected. There are studies in which the types of mutations are associated with the effectiveness of treatment. In the case report of Galvanuso et al, it was stated that long-term response to Eculizumab treatment of a case diagnosed with atypical HUS may be related to Complement factor I (CFI) and Thrombomodulin (THBD) gene mutations (6).

Although 2 of 3 patients diagnosed with HUS require renal replacement therapy, patients with mild renal involvement have been reported, especially in the group with typical HUS (7). In some patients diagnosed with atypical HUS, which is rarely seen in adults, the clinical picture did not show renal involvement at the beginning, became distinctive later and kidney biopsy was required to clarify the diagnosis (8). Considering the importance of kidney involvement in prognosis, physicians should be careful in the diagnosis stage. In a patient reported in Sri Lanka in 2020, hypertension, sepsis and appendicitis were observed at the onset of the disease, and it was reported that the atypical HUS table developed and treated with long-term plasma exchange treatments (9).

Cardiac complications are rare in patients with HUS and may occur during or after the course of the disease (5). The frequency of cardiomyopathy characterized by atypical HUS-related systolic dysfunction can be up to 10%. The pathophysiology of cardiac involvement is explained by microvascular coagulation and necrosis developing in the heart muscles, or infectious myocarditis developed by infectious verotoxins. In the case reported by Campbell et al. in 2020, a cardiac biopsy was performed on a patient who was diagnosed with atypical HUS and heart failure. Thrombotic microangiopathy characterized by obliterations in intramyocardial arterioles and fragmanted erythrocytes rolled up in subintimal region were observed in pathology. It was reported that cardiac functions improved in the controls after months of eculizumab treatment (10).

Myocarditis was detected in our patient in the early period of aHUS, which was complicated by renal failure and convulsions. Accordingly, even if it is rarely seen,

cardiac complications should be taken into consideration and echocardiographic examinations should be routine in HUS patients.

CONCLUSIONS

In atypical HUS cases, shiga toxin can be a triggering factor. Therefore, it should be remembered that cases with STEC positivity may be aHUS. In addition to the typical organ and system involvement of HUS, it can also go with different systemic findings and myocarditis, a rare condition.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Yürük Yıldırım ZN, Yılmaz A. (2014) Atipik Hemolitik Üremik Sendrom, Çocuk Dergisi 14(3):108-115
2. Davin JC, Majoie C, Groothoff J, Gracchi V, Bouts A, Goodship TH, Loirat C. (2011) Prevention of large-vessel stenoses in atypical hemolytic uremic syndrome associated with complement dysregulation. Pediatr Nephrol. 26:155–157.
3. Neuhaus TJ, Calonder S, Leumann EP. Heterogeneity of atypical hemolytic uremic syndromes. (1997) Arch Dis Child; 76(6): 518-21.
4. Hosler GA, Cusumano AM, Hutchins GM. (2003) Thrombotic Thrombocytopenic Purpura and Hemolytic Uremic Syndrome Are Distinct Pathologic Entities. A Review of 56 Autopsy Cases, Arch Pathol Lab Med; Jul;127(7):834-9.
5. Eckart P, Guillot M, Jokic M, Maragnes P, Boudailliez B, Palcoux JB, Desvignes V. (1999) Cardiac Involvement During Classic Hemolytic Uremic Syndrome, Arch Pediatr, Apr;6(4):430-3.
6. Calvaruso L, Naticchia A, Ferraro PM,Vischini G, Costanzi S. (2019) Deterioration in Clinical Status Is Not Enough to Suspend Eculizumab: A Genetic Complement-Mediated Atypical Hemolytic Uremic Syndrome Case Report. Case Rep Nephrol. doi:10.1155/2019/9264824.
7. Costin M, Cinteza E, Balgradean M. (2019) Hemolytic Uremic Syndrome – Case report. Maedica (Buchar). Sep;14(3):298-300.
8. Mohammed SK, Mubarik A, Nadeem B, Khan K, Muddassir S. (2019) Atypical Hemolytic Uremic Syndrome:A Case Report.Cureus. May 10;11(5):e4634.
9. Basnayake BMDB, Wazil AWM, Nanayakkara N, Samarakoon SMDK, Senavirathne EMSK, Thangarajah BUEWDR, Karunasena N, Mahanama RMBSS. (2020) Atypical hemolytic uremic syndrome: a case report. J Med Case Rep. Jan 13;14(1):11.
10. Campbell CM, Cassol C, Cataland SR, Kahwash R. (2020) Atypical hemolytic uremic syndrome: a case report of a rare cause of reversible cardiomyopathy. Eur Heart J Case Rep. Mar 12;4(2):1-6.