Clinics in Mother and Child Health
ISSN: 2090-7214

Badruddin and Rattani, Clinics Mother Child Health
2016, 13:1
DOI: 10.4172/2090-7214.1000229

Case Report Open Access

Atypical Hemolytic Uremic Syndrome in Tertiary Hospital, Pakistan

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Received date: December 10, 2015; **Accepted date:** January 28, 2016; **Published date:** February 17, 2016

Abstract

Atypical hemolytic uremic syndrome (HUS) is a rare disorder in children, therefore it may lead to misdiagnosis, delay in treatment, or acute kidney injury. Patients with atypical HUS present signs and symptoms of hemolytic anemia, thrombocytopenia, and higher lactate dehydrogenase and uric acid levels. The main risk factor highlighted is consanguinity, gene mutations, and viral infections. Eculizmab, a humanized anti-C5 monoclonal antibody, has been shown to be an effective treatment modality for such patients. This article will discuss atypical hemolytic uremic syndrome, present case report of a patient suffering with atypical HUS with bad prognosis and poor recovery.

Keywords: Atypical hemolytic uremic syndrome; Genes; Renal disorders

Introduction

Atypical Hus is one of the leading causes of acute kidney injury in children [1]. Atypical HUS can occur at any age, primary affecting children age less than two years. Final outcome of atypical HUS can be poor, around 25% of the patients die during the acute phase and 50% patients requiring long term dialysis [2]. Most cases of atypical HUS are idiopathic, but some are inherited, such as autosomal recessive or autosomal dominant traits. Such hereditary conditions consist of autosomal recessive atypical HUS with C3 deficiency, which is caused by mutations in factor H gene and congenital vitamin B12 deficiency [3]. These mutations have been accounted for 50 to 60% of the cases. The parents, who were first cousins, had half normal complement factor H protein (CFH) levels, indicating an inherited defect. In some cases, complete or partial CFH deficiencies have been reported in patients with atypical HUS [4]. Atypical HUS comprises the triad of microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury [5]. In this case report, author presented a child with atypical HUS that had very unusual presentation and unexpectedly poor outcome.

Materials and Methods

Case report

A one year four months old male child was presented in the emergency department (ED) of a tertiary hospital in Pakistan with complaints of fever, drowsy and shortness of breath. History revealed that one of his siblings had suffered from viral fever a few days ago and had recovered. Based on the history and the physical assessment, this child was diagnosed as having viral fever, treatment was prescribed, and the child was discharged from the emergency. After two days, that child again came to the ED with complaints of fever, cough, epistaxis, and decreased urine output, as observed by the mother during diaper changed. The child was presented with a heart rate of 140/min, respiratory rate 26/min and the blood pressures was 140/90 mmHg. Laboratory investigations revealed low hemoglobin (5.7 gm/dl), high white blood cell counts (18.4 × 10E9/L), low platelet counts (39 × 10E9/L), high lactate dehydrogenase (5444I.u/L), high uric acid (9.4 mg/dl), and high creatinine levels (1.3 mg/dl). The ultrasound of kidneys showed bilateral parenchymal disease.

Differential diagnosis made at that time was dengue fever, malaria, hemolytic uremic syndrome (HUS), and thrombotic thrombocytopenic purpura (TTP). Dengue and malaria were excluded as the patient's MP and Coomb's test were negative. One the basis of renal impairment, thrombocytopenia, and hemolytic anemia, the child was diagnosed as having atypical hemolytic uremic syndrome and TTP was excluded. Patient got intubated and peritoneal dialysis was immediately initiated as the patient condition got deteriorated. The condition was not improving despite getting dialyzed and plasmapheresis daily. The family was informed regarding medication that was found effective in the treatment of atypical HUS. They were also informed that aypical HUS is caused by the inappropriate complement activation and a humanized anti-C5 monoclonal antibody-eculizumab has been shown to be an effective therapeutic modality for the treatment of patients with aHUS. Sadly, eculizumab is the most expensive drug regimen, with treatment costs averaging 600, 000 USD per year. Due to unaffordability, this medication is not available in Pakistan and the parents were unable to bear the expenses to bring this medication from abroad. A few counselling sessions were conducted with the family and they were still hoping and praying that through some miracle their child would survive. This case study raised a number of questions:

What is atypical hemolytic uremic syndrome?

What treatment modalities are available to care for a child with atypical HUS?

Methods

A systematic and comprehensive search was done in September, 2015, to access research studies on the patients with atypical hemolytic uremic syndrome. Various words and phrases were used to guide the search that included: atypical hemolytic uremic syndrome, causes and treatment of aHUS, thrombocytopenia and acute kidney injury. Data bases such as CINAHL, Mosby Nursing Consult, PubMed, Sage, and Science Direct were used to guide the search. The search ranged from

2001 up to 2014. Total nine articles were included in a review after reading the abstracts.

Discussion

Patients presented with atypical HUS have presented signs of hemolytic anemia, thrombocytopenia, higher lactate dehydrogenase and uric acid levels, and signs of renal impairment [4]. Atypical Hus usually presents abruptly with paleness, anorexia, vomiting, edema, hypertension and oliguria [1]. Before discussing further, it is important to understand hemolytic anemia and thrombocytopenia. The Joint Committee of JSN/JPS defined microangiopathic hemolytic anemia based on a hemoglobin level of <10 g/dl. The presence of microangiopathic hemolytic anemia should be confirmed based on increased serum lactate dehydrogenase levels, a marked decrease in serum haptoglobin and the presence of red blood cell fragments in a peripheral blood smear [5]. Thrombocytopenia is defined as platelet count of <150, 000/uL. For pediatric cases, the serum creatinine should be increased to a level that is 1.5 fold higher than serum creatinine reference values based on age and gender issued by Japanese Society of Pediatric Nephrology [5].

It has been reported that approximately 50% of the aHUS patients have gentic abnormalities in complement regulatory factors, including complement factor H. Uncontrolled hypertension is also associated with hemolytic anemia. The complement system plays vital part of immune systems of living organisms. It is activated through 3 pathways, the classical, alternative and lectin pathways. As a result of the activation of hosts' alternative and classical pathways, C5b-9, a membrane attack complex, is generated and destroys cell by forming transmembrane pores. The alternative pathway is involved in the beginning of aHUS. The regulators involved in the alternative pathway include complement factors H and I, which are humoral factors and membrane cofactors protein and thermbomodulin, which are membrane bound factors. If these factors are unusual, the consequent failure of regulation will hyper activate the complement proteins, leading to the prominent onset of aHUS [5].

The earlier sign presented in this patient was fever and lethargic before the presentation of kidney failure appeared. Later the patient got hypertension and central nervous system manifestations include drowsiness. Malignant hypertension is characterized by fibrinoid necrosis; clots in the lumen of arterioles cause luminal narrowing, leading to excess accumulation of erythrocytes that increases pressure on the kidneys and causes decrease in glomerular filtration rate (GFR) [6]. Atypical Hus has a wide spectrum of presentation, therefore, hemodynamic monitoring, good nutrition, and electrolyte status is important for good management. Management of atypical HUS is supportive. Strict monitoring of fluid balance is important in detecting early renal failure. Hypertension should be controlled and treated with antihypertensive agents. If renal failure develops, renal replacement therapy such as peritoneal dialysis, hemodialysis, and continuous renal replacement therapy should be started. Peritoneal dialysis helps create osmotic pressure in the peritoneal cavity and helps remove toxic substances from the body. Peritoneal dialysis has been suggested to potentially enhance the clearance of plasminogen activator inhibitor I, thereby facilitating renal recovery [7]. It is also suggested that treatment with plasmapheresis should be initiated within 24 hours from presentation, since its delay can increase the frequency of failure. Plasma exchange has been found to be relatively more effective than plasma infusion because it helps to remove potentially toxic substances from the circulatory system of the patients. Despite the poor prognosis of atypical HUS, plasma therapy has dropped the mortality rates from 50% to 25% [8]. It should be noted that complications of atypical HUS are severe and can involve neurological, renal, and gastrointestinal systems; the more severe complication is end stage renal disease. There is a 10% chance that patients with aHUS may end up with coma, hemiparesis or stroke [9].

In cases where renal transplant has been suggested but the prognosis of kidney function and the recurrence rate after kidney transplantation develops vary on the type of genetic abnormalities present. A discussed in case report, a HUS is a disease that may frequently cause renal failure and can be life threatening if it is misdiagnosed and not properly treated at early stages of disease onset [5].In cases where aHUS is connected with complement dysregulation, the eculizumab has brought revolution as a medical treatment modality. Eculizumab and Retuximab have been found effective to control kidney disease and central nervous system manifestation. Eculizumab inhibits the complement system by binding to the complement component C5, this medicine stops the generation of C5a and C5b-9 [1].

Conclusion

In conclusion, our case report shows that atypical HUS have atypical presentation such as hypertension and renal failure and can have poor prognosis. Atypical HUS is an unusual disorder; this can result in delay in diagnosis and treatment in developing countries. Such patients are presented at the tertiary health care facility when they become critically ill, thus result in delay of treatment. In the case presented above, based on the history, examination, and the fact that the child was unable to receive proper treatment due to unaffordability of medication expenses. Hence, none of the interventions helped him to recover and death was the outcome.

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