CASE REPORT

RAPID RECOVERY AFTER EARLY INITIATION OF PLASMAPHERESIS IN ATYPICAL HUS: A CASE REPORT

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ABSTRACT

We report a case of a thirteen year old female diagnosed as aHUS, complicated by malignant hypertension and central nervous system involvement. The patient was treated with plasmapheresis(plasma exchange) and corticosteroids along with supportive care. The patient showed remission immediately and recovered after four weeks of hospital stay and three months later is well on antihypertensives.

Keywords: Plasmapheresis, HUS, Microangiopathic haemolytic anemia, Eculizumab

Abbreviations:

aHUS: Atypical Hemolytic Uremic Syndrome CRP: C- Reactive Protein; USG: Ultrasonography FFP: Fresh Frozen Plasma; LDH: Lactate Dehydrogenase ESRD: End Stage Renal Disease; RBC: Red Blood Corpuscle HPF: High Power Field; CAPD: Continuous Ambulatory Peritoneal Dialysis HD: Hemodialysis; ANA: Antinuclear Antibody; ASO- Anti-Streptolysin Titer

INTRODUCTION

World wide prevalence of aHUS ranges from 2.7-5.5 per million population with an incidence of 0.40 per million. Only 5-10% patients of HUS present with atypical form of HUS. It is a rare, life-threatening and progressive disease with a high mortality and morbidity[1]. A major cause of aHUS is the complement alternative pathway dysregulation[2], leading to arteriolar and inter-lobular arterial involvement causing end-organ damage[3].The complement system may be activated by the mutations in the complement regulatory proteins (factor H, factor I, or membrane cofactor protein) or by acquiring neutralizing autoantibody inhibitors of the components of complement system (anti-factor H antibodies)[1]. The patients may present with signs and symptoms of acute kidney injury, hypertension, encephalopathy, pancreatitis, lung complications, seizure, coma and others.[1,4,5]

We report a case of a thirteen year old female child with aHUS, complicated with hypertension, encephalopathy and seizure, and her therapeutic management.

CASE REPORT

A thirteen year old female child presented with a three day history of abdominal pain, low grade fever and vomiting. There was no history of loose motions/diarrhea or bloody stools. Past or family history is not contributory. Her laboratory evaluation showed Hb 9.8 gm%, Platelets 54000/c.mm. USG abdomen was normal. On the third day of admission, she developed headache, gross hematuria and oliguria (Urine output 0.7ml/kg/hr). This time the laboratory evaluation showed microangiopathic haemolytic anemia (Hb 6.8 gm%, Serum bilirubin 1.4 mg/dl, Serum LDH 2967 U/L, schistocytes 12-15% and Coomb's test negative), thrombocytopenia (platelet count 43000/c.mm) and acute renal insufficiency (Blood urea 137mg/dL, serum creatinine 3mg/dL). Her urine analysis revealed protein 4+, RBC >8-10/HPF and was positive for hemoglobinuria. Her serum C_3 level was found to be low 0.65g/L (Normal 0.9-1.8), ANA was negative, ASO titre was <200 and CRP was non-reactive. Malarial parasite and Dengue titers were negative. USG abdomen revealed stage I Medullary Renal disease. Hence she was diagnosed as D negative HUS (aHUS).

We started with plasmapheresis (plasma exchange) with FFP on sixth day of admission. We started first cycle with 20ml/kg of FFP and then increased to 35ml/kg for next four cycles. These were done on a daily basis. Patient showed signs of improvement after the third cycle. The plasmapheresis was stopped as the platelet count (1.64 x 10^3 / cmm) and serum

LDH (505 U/L) improved[2]. Complete hematological and renal recovery was found after five days of plasmapheresis. Our patient had hematological recovery on day eleven of admission. On day fifteen, she developed malignant hypertension and seizure, and she was put on a several antihypertensives (propranolol, nifedipine, prazosin, hydralazine, nitroglycerine) and anti convulsants (phenytoin sodium, phenobarbitone).

We had also put our patient on pulse methyl prednisolone therapy (three days) followed by oral prednisolone from day ten onwards. Oral prednisolone was continued for a month and stopped with gradual tapering.

We obtained the CFH antibody titre(anti-factor H autoantibodies) from AIIMS, New Delhi. It was found to be 2252 AU/ml. (Normal = <150 AU/ml). Genetic testing was not done due to its cost factor. This was only of diagnostic importance as the patient had already recovered. The lowest hemoglobin recorded was 3.6 gm%, lowest platelet count was 36000/c.mm, peak reticulocyte count was 6.4%, peak urea level was 150 mg/dL, and peak creatinine level reached was 3.6 mg/dL. Our patient had complete remission and was discharged on two antihypertensives after a total of four weeks of hospital stay.

After three months, on follow-up, the patient is stable and her laboratory reports are – Hb 13.3 gm%, Platelet count 2.15 x 10^3/cmm, Serum LDH 569 U/L, Serum creatinine 0.7mg/dL and blood urea is 27mg/dL. Her blood pressure is also well controlled on two drugs – Tab. Prazosin (2.5 mg) and Tab. Envas (2.5mg) OD.

DISCUSSION

Atypical HUS is rare and does not have a good prognosis. 33-40% patients die or develop ESRD with first attack of HUS. The treatment options for aHUS are good control of volume status, anemia, hypertension, electrolyte disturbances, peritoneal or hemodialysis, use of Eculizumab, plasma therapy (plasma infusion and/or plasma exchange) and kidney transplant. Eculizumab, a monoclonal humanized anti-C5 antibody, is indicated in first time diagnosed aHUS or already diagnosed and on other modality of treatment. For patients with aHUS who have kidney failure, eculizumab offers them the potential for a kidney transplant and an opportunity to restore their health and have a life free from the restrictions of dialysis and the need for frequent plasma therapy. For patients with active disease, eculizumab offers them the possibility of avoiding end stage renal failure, dialysis and kidney transplantation, as well as other organ damage. Results from the prospective studies showed that, compared with baseline, treatment with eculizumab improved systemic thrombotic microangiopathy activity and led to clinically significant improvements in kidney function and gains in quality of life by 26 weeks[8].

Plasmapheresis (Therapeutic plasma exchange) was initiated as Eculizumab is unavailable in India. The cost of therapy also is very high. We started the plasmapheresis, using the special plasma filter technique[6], with a lower volume to see for patient compliance and then we increased the dose of FFP[7]. Eventhough, the effectiveness of plasmapheresis is not demonstrated in inducing total disease remission, it is still the treatment of choice. It could prevent relapses and preserve the renal function if initiated early and rigorously[6]. It decreases the mortality from 50% to 25%[4]. In a case report by Georgaki-Angelaki H, et al[5]. their patient was initially started with peritoneal dialysis and plasma exchange was performed after six weeks. Post plasmapheresis (seven cycles) the patient started recovering (evidenced by the platelets and LDH levels). Due to complications, plasmapheresis had to be stopped, and the patient was later discharged on CAPD. Plasmapheresis helped in the gradual improvement of their patient. They however could not associate the patients renal function recovery with plasmapheresis. Their patient was found to be negative for anti-factor H autoantibodies. Inspite of this plasmapheresis was found to be beneficial, suggesting its effective role. In another case by Arnaud Lionet, et al[3]. they initiated plasmapheresis with FFP and intermittent hemodialysis and after four days patient showed signs of recovery. Plasmapheresis was stopped but patient became HD dependent. They restarted plasmapheresis. Anti CHF antibody titer was high.(positive) Corticosteroids and rituximab were started, and plasmapheresis gradually stopped, but patient was HD dependent till renal functions returned to normal.

We believe that early initiation of plasmapheresis and the addition of corticosteroids have helped in the favorable outcome in our patient. Hematological remission was complete after plasmapheresis, suggesting that removal of antibodies by plasmapheresis and suppression of formation of new antibodies by steroids may have played a contributory role[2,4,5]. There was no need to add rituximab / cyclophosphamide in our patient. The antihypertensives could be tapered off rapidly as the patients renal function was also normalized. We had not gone in for a renal biopsy to know the extent of renal parenchymal damage, but considering the rapid recovery of our patient, we assume it was minimal.

The final outcome of aHUS is unpredictable and is a matter of concern. It affects the patients quality of life and of the family as well. Our patients recovery suggests the same.

CONCLUSION

Early plasmapheresis contributes to the clinical and biochemical recovery in aHUS, along with cortico-steroids.

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