Therapeutic Plasma Exchange in a Case of Cerebral Hemolytic Uremic Syndrome

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ABSTRACT
A 19-year-old male presented with classical features of cerebral hemolytic uremic syndrome (HUS), namely hemolytic anemia, uremia, liver dysfunction, and altered sensorium. He was managed with therapeutic plasma exchange (PE) along with other supportive measures. Patient made complete recovery. The aim of reporting this case is to highlight the use of PE in the treatment of cerebral HUS, where it may be life-saving if started early.

Keywords: Hemolytic uremic syndrome, Plasmapheresis, Therapeutic plasma exchange.


Source of support: Nil
Conflict of interest: None

INTRODUCTION
Hemolytic uremic syndrome (HUS) is a condition characterized by thrombotic microangiopathy, thrombocytopenia, microangiopathic hemolytic anemia, renal dysfunction, neurologic deficits, and sometimes dysfunction of other organs.1,2 The worldwide incidence of HUS is reported to be 1 to 2 cases per 100,000 people per year. Hemolytic uremic syndrome is typically caused by Shiga-like toxin-producing bacteria, particularly Escherichia coli O157:H7, or nonenteropathic infections (such as with Salmonella pneumoniae).1

Atypical HUS (aHUS) is a rare disease characterized by hemolytic anemia, thrombocytopenia, and acute renal failure secondary to thrombotic microangiopathy. It is distinguished from typical or Shigatoxin-producing E. coli (STEC) HUS by the absence of STEC infection. In recent years, aHUS has been found to be associated with complement alternative pathway dysregulation. Stx-HUS is treated with supportive measures like management of anemia and bleeding, and correcting fluid and electrolyte disturbances, etc. Additionally, plasma exchange (PE) may be done especially in patients with severe central nervous system (CNS) involvement. Plasma exchange is also recommended as a first-line treatment in cases of aHUS in the very early stage of disease.3 Here, we report a case of cerebral HUS in a 19-year-old male who presented with a rapidly deteriorating course, but showed an excellent response when managed on PE along with other medical measures.

CASE REPORT
A 19-year-old male presented with complaints of high-grade fever with chills and headache, loose stools 4 to 5 times a day, which were watery and black-colored along with vomiting and hematemesis since 2 days. On examination, patient was icteric and mild hepatosplenomegaly and ascites were present. On second day after admission, the patient developed altered sensorium. Investigations revealed severe anemia (hemoglobin: 4.6 gm/dL) and thrombocytopenia (22,000/cumm) with very high lactate dehydrogenase (LDH) (1282 U/L) levels. Peripheral blood smear revealed pancytopenia with a hemolytic picture [abundance of schistocytes and fair number of elliptocytes, tear drop cells, helmet cells, spherocytes, and polychromatic cells with occasional nucleated RBCs (2 per 100 white blood cells)], suggestive of a microangiopathy. Bone marrow examination showed normoblastic erythroid hyperplasia, suggestive of hemolytic anemia with a possibility of microangiopathy. Fibrin degradation products were positive, and renal functions were deranged (creatinine: 2.58 mg/dL). Malaria rapid test, Leptospira, hepatitis A virus, hepatitis C virus, dengue virus, and scrub typhus serology were negative.

Patient was put on ventilator and given steroids along with therapeutic PE on three consecutive days. Replacement was done with fresh frozen plasma, saline, and albumin. The LDH levels started decreasing with the first PE and came to half the original levels (735 U/L) at the end of the first procedure. Patient regained consciousness in 3 days and was discharged on the 10th day with marked improvement in values of hemoglobin (11.5 gm/dL) and platelet count (339,000/cumm).
DISCUSSION

Hemolytic uremic syndrome is a serious clinical complication of enterohemorrhagic *E. coli* infection that contributes to acute kidney injury, often requiring dialysis and can progress to acute renal failure and death.1

Atypical HUS (aHUS) occurs at any age, from the neonatal period to the adult age. The disease has a relapsing course and more than half of the patients either die or progress to end-stage renal failure. Recurrence after renal transplantation is frequent.2 Diagnostically, HUS is defined by the triad of nonimmune hemolytic anemia (hemoglobin <10 gm/dL) with fragmented erythrocytes (schizocytes), thrombocytopenia (platelets <150,000/mm³), and renal impairment. High LDH and undetectable haptoglobin levels confirm intravascular hemolysis. The presence of schizocytes, undetectable haptoglobin, and high LDH levels confirm the microangiopathic intravascular origin of hemolysis.2 In 60% of aHUS patients, mutations in genes encoding complement-regulating proteins are reported.3

In another study, authors have suggested that serum levels of fibrinogen degradation product-E (FDP-E) may correlate with disease severity in patients with HUS and that serum levels of FDP-E may be a useful marker of HUS in clinical practice.4 Another study suggests that anemia, thrombocytopenia, elevated LDH, and FDP are the most frequent manifestations of HUS.7

A frequent complication is CNS involvement (10% of patients), manifested by irritability, drowsiness, seizures, diplopia, cortical blindness, hemiparesis or hemiplegia, stupor, coma. These patients need intensive care and dialysis and specialized care has contributed to the decrease of mortality, especially in young children in centers where dialysis and PE are daily practice.2

Cerebral HUS can manifest in several ways, including irritability, altered level of consciousness, and seizures, with signs occurring after onset of HUS. A previous report suggests that 3 to 41% of patients develop cerebral HUS.1 Treatment involves the institution of general supportive measures, antiplatelet and thrombolytic agents and thrombin inhibitors, selective use of antimicrobials, probiotics, toxin neutralizers (synthetic and natural binders, antibodies). Monitoring of hemoglobin, hematocrit, and platelet count is essential. Monitoring hemolysis with LDH and haptoglobin is also helpful.8

Experts recommend PE to be started as early as possible, within 24 hours of presentation should be performed daily until platelet count, LDH, and hemoglobin levels are normalized and renal function starts showing sustained improvement over several days.2 It decreases mortality rate from 50 to 25%.3 Plasma exchange is also reported to be effective in aHUS. Plasma exchange and immunoadsorption have been used in patients with severe disease and cerebral manifestations. Authors have reported potential future therapies like cell-permeable peptides for Shigatoxin-binding and complement inhibitors, such as eculizumab to amelioriate disease.1 Platelet count increments have presented the use of eculizumab and plasmapheresis as part of a renal transplant protocol for the treatment of aHUS in a patient with a known genetic defect deemed at high risk for recurrent disease.9

The 19-year-old patient in this case report developed a severe cerebral HUS with a rapidly deteriorating course but showed an excellent response when managed on PE along with other medical measures. The case is being reported to highlight the utility of this procedure, especially in cases of cerebral HUS where it can prove to be life-saving if started at the right time.

REFERENCES