POSTPARTUM ATYPICAL HEMOLYTIC UREMIC SYNDROME IN A YOUNG ADULT TREATED WITH ECULIZUMAB

Antreas Kourouklaris[1], Kyriakos Ioannou[1], Ioannis Athanasiou[1], Alexia Panagidou[1], Kyproula Demetriou[1], Michalis Zavros[1]

[1]Department of Nephrology, Nicosia General Hospital, Cyprus

INTRODUCTION

Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening disease caused by uncontrolled chronic activation of the complement alternative pathway, resulting in systemic microvascular thrombosis, organ ischemia and organ damage. Prognosis is poor: up to 65% of patients require dialysis, have permanent kidney damage or die despite treatment with plasma exchange/plasma infusion (PE/PI).

CASE DESCRIPTION

We describe the case of a 23-year-old female who after a pre-eclampsia induced premature delivery showed signs of thrombotic microangiopathy (TMA). The patient was admitted with tonicoclonic seizures, anasarca edema and high blood pressure while laboratory investigation revealed acute renal failure (creatinine 4.9 mg/dL), thrombocytopenia (platelets 40 x 10^9 /L) with elevated lactate dehydrogenase (LDH 3254 IU/L) and presence of schistocytes on blood smear. She was initially diagnosed with thrombotic thrombocytic microangiopathy (TMA) and intensive PE was initiated twice daily. She also received dialysis for 1 month. Three months after initial admission, the patient was discharged with non-dialysis dependent renal failure (creatinine 2 mg/dl) and without signs of hemolysis. In the next three months, the patient was readmitted with signs and symptoms of TMA. Further investigations showed a negative Coombs test and detectable ADAMTS13 activity excluding TTP. No genetic abnormality in complement genes was detected. Stool samples could not detect E. coli O157:H7/O104:H4 or Shiga toxin, excluding Shiga toxin E. coli HUS (STEC -HUS). The patient was diagnosed with aHUS. A renal biopsy was performed that showed TMA; the patient later developed signs of cardiomyopathy (left ventricular ejection fraction 25%). Due to failure of PE and dialysis to reverse TMA, the patient was started on eculizumab (complement inhibitor), which improved clinical and laboratory parameters. During long-term eculizumab treatment renal and cardiac functions were restored and TMA manifestations reversed. No further clinical symptoms and signs of TMA have been observed. The patient currently remains under chronic eculizumab treatment, without the need for any other invasive treatment.

DISCUSSION

Eculizumab is a humanized monoclonal antibody that binds to complement component C5 inhibiting its cleavage to C5a and C5b, and hence inhibits deployment of the terminal complement system including the formation of membrane attack complex (MAC) .Thus it reverses complement mediated TMA in patients with aHUS. The optimal duration of treatment remains to be determined.

CONCLUSIONS

Chronic eculizumab treatment can rapidly block complement activation, successfully reverse systemic TMA and improve organ function in aHUS patients. According to our knowledge this is the first case of postpartum aHUS treated with eculizunab. The patient is in persistent remission of aHUS for 2,5 years.

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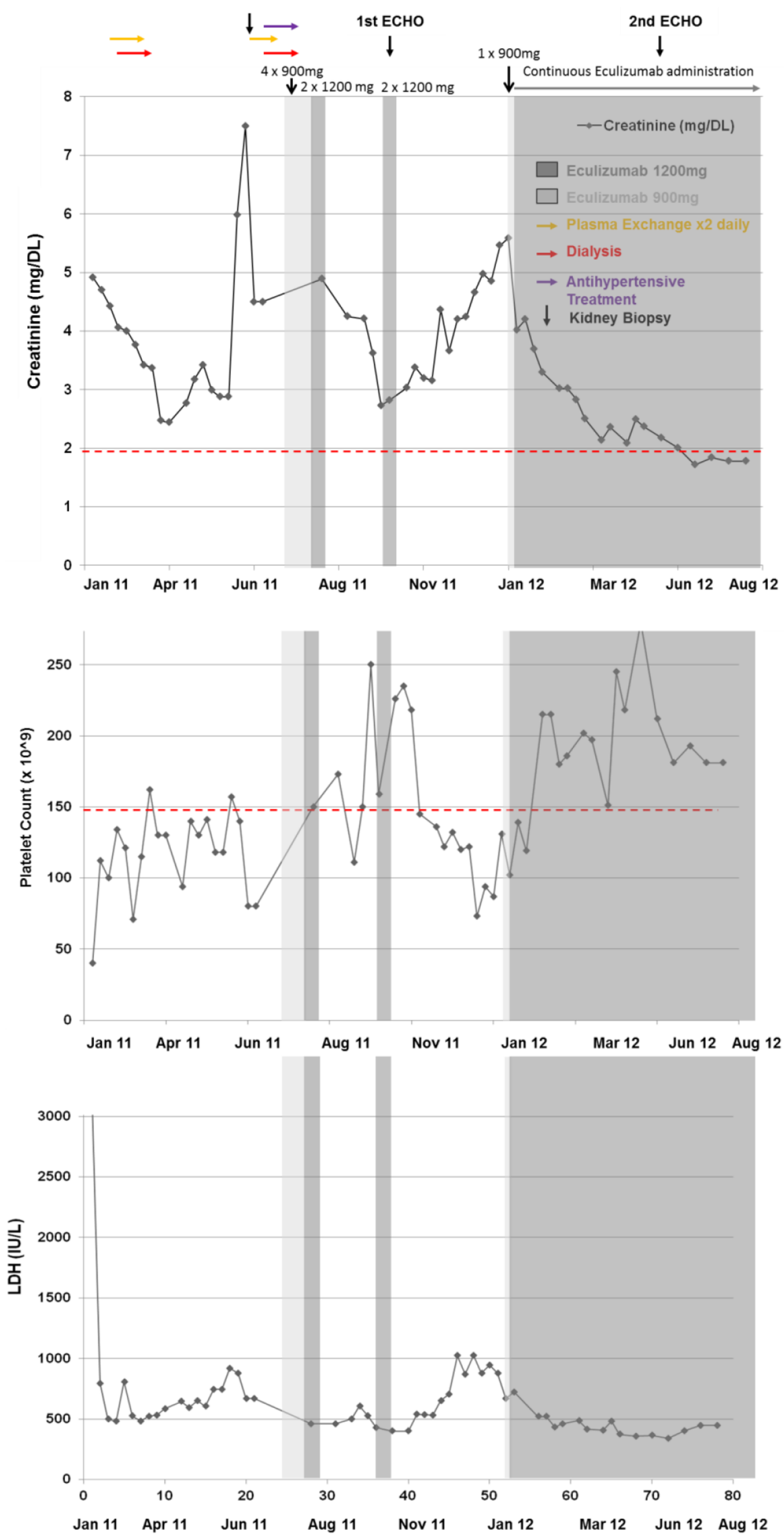

Figure 1. Response to eculizumab treatment in a young female adult who was diagnosed with aHUS following a preeclampsia induced premature delivery. At admission, laboratory results indicated thrombotic microangiopathy (TMA), acute kidney failure and thrombocytopenia; creatinine level; 4.9 mg/dL; LDH 3254 IU/L; platelets 40 x10^9/L, with the presence of schistocytes on peripheral blood smear. Plasmapheresis and dialysis managed to temporarily correct clinical indices, however following deterioration of clinical status the patient was started on eculizumab, 900 mg per week, in July 2011.Her clinical condition improved after the first infusion of eculizumab. One month after initiation of eculizumab patient presented with an episode of pneumonia and cardiac failure. She was admitted in the intensive care unit and treatment had to be stopped. Due to a new relapse of aHUS (thrombocytopenia; platelets 73 x 10^9/L, renal failure; creatinine 4.85 mg/dL; LDH 1024 IU/L), eculizumab was restarted in January 2012 at 900 mg followed by 1200 mg fortnightly. Clinical symptoms and laboratory findings of aHUS started to improve and patient achieved normal renal function 4 weeks after readministration of eculizumab. Patient remains on 1200 mg of eculizumab administered fortnightly, free of any symptoms of TMA and with stable renal function (creatinine level: 1,4 mg/dL) until today.