HEPATOTOXICITY ASSOCIATED WITH ECULIZUMAB TREATMENT

Aysegul ORUC[1], Yavuz AYAR[1], Nimet AKTAS[2], Abdulmecit YILDIZ[1], Mahmut YAVUZ[1], Alparslan ERSOY[1], Kamil DILEK[1], Mustafa GULLULU[1]

1Uludag University Medical Faculty, Nephrology, Bursa, TURKEY, 2Cekirge State Hospital, Nephrology, Bursa, TURKEY.

OBJECTIVES

aHUS is a rare, life-threating disease characterized by systemic TMA which is associated with uncontrolled activation of C5 due to dysregulation in the alternative complement pathway [1] . Eculizumab is a recombinant humanized anti-C5 monoclonal antibody that blocks the cleavage and activity of complement factor 5, ultimately inhibiting complement-mediated cell lysis. It is first established for paroxysmal nocturnal hemoglobinuria (PNH) [2]. Historically, eculizumab promised successful results in aHUS with 2 case reports in 2009 [3, 4] and approved for aHUS treatment in 2011. Efficacy and safety of eculizumab in aHUS treatment have been reported in clinical trials [5, 6], but meningococcal infection is the most severe adverse event. The long-term safety of eculizumab is promising, but still remains uncertain. Hepatic side effects have been reported in a few pediatric cases after eculizumab treatment [7, 8], but not in adult patient. Herein, we presented an adult case of aHUS in whom hepatotoxicity was observed following eculizumab treatment.

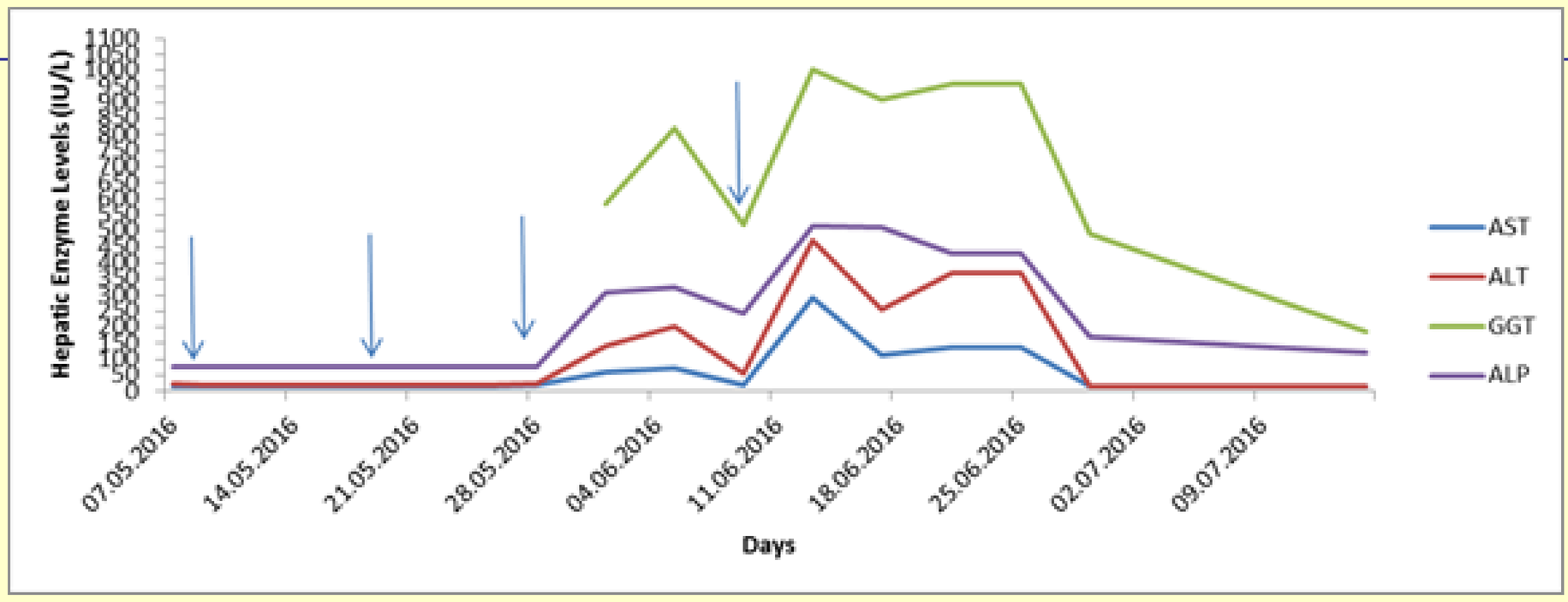

Fig Hepatic enzymes (AST, ALT, ALP and GGT) levels were presented during eculizumab treatment. Consecutive eculizumab doses were marked with arrows

CASE

A 39 year old male was referred to our center with acute renal failure, hypertension, blurred vision, and thrombocytopenia. After exclusion for possible causes of TMA, diagnosis of aHUS was considered and plasma exchange (PE) was initiated in the first 24 hours. Eculizumab was administered because of PE dependence and persistent renal failure after 19 PE sessions. Although TMA improved without recovery of renal functions under Eculizumab treatment, we had to withdraw Eculizumab treatment because of drug induced liver injury with elevated transaminases. After the 4th dose of Eculizumab marked elevation in enzyme levels (ALT 471 IU/L, x8 UNL (upper normal limit), ALP 516 IU/L, x4 UNL and GGT 1001 IU/L, x15 UNL) were observed and we had to stop Eculizumab because of fulminant hepatitis risk. Other causes for elevated transaminases were excluded and liver enzymes were normalized within 20 days with recovery after cessation. He continues to our outpatient clinic on anti-hypertensive treatment and free of TMA event with no abnormalities in liver enzyme levels

CONCLUSIONS

Drug induced liver injury should be kept in mind as an important adverse event related with Eculizumab which is not reported previously in adults. We suggest monitoring transaminase levels in patients receiving Eculizumab and further studies are required to evaluate hepatotoxicity risk. To our knowledge this is the first case report of severe hepatotoxicity associated with Eculizumab treatment

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