

## CASE REPORT

## How atypical can Atypical Hemolytic Uremic Syndrome be?

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### Key Clinical Message

A 24-year-old man with diarrhea found to have acute renal failure with microangiopathic hemolytic anemia (MAHA). A diagnosis of hemolytic uremic syndrome (HUS) was made. He was initiated on plasma exchange and hemodialysis. On day 6, he was started on eculizumab. His renal functions progressively improved. His main complication during eculizumab therapy was hypertension-related posterior reversible encephalopathy syndrome.

### Keywords

Atypical hemolytic uremic syndrome, eculizumab, malignant hypertension, posterior reversible encephalopathy syndrome.

## Introduction

Atypical Hemolytic Uremic Syndrome (aHUS) is a life-threatening and progressive disease due to uncontrolled complement activation. We describe a case of aHUS on Eculizumab and coexisting malignant hypertension.

## Case

This is the case of a 24-year-old gentleman who had presented to the Emergency Department with 5 day history of nausea and vomiting and mild diarrhea. The diarrhea was loose watery with no associated blood or mucous. He had no significant past medical history. On examination, he looked comfortable and was not in distress. He was afebrile with pulse rate of 95/min and blood pressure of 156/96 mm Hg with normal saturation at room air of 98%. On physical examination, he looked mildly dehydrated; the rest of the examination was unremarkable. His investigation on day 0, 1, and 2 are listed in the Table 1.

He had a peripheral smear done which revealed fragmented RBC. The differential diagnosis included Hemolytic Uremic Syndrome, which was more likely given the classical picture of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. The second possibility could be Thrombotic Thrombocytopenic

Purpura; however, the patient had no neurological symptoms. Disseminated Intravascular Coagulation was unlikely given normal coagulation profile and absence of sepsis. On day 2, we received further investigations (Table 2). He then proceeded to have a renal biopsy, which is shown in Figure 1.

## Follow-up

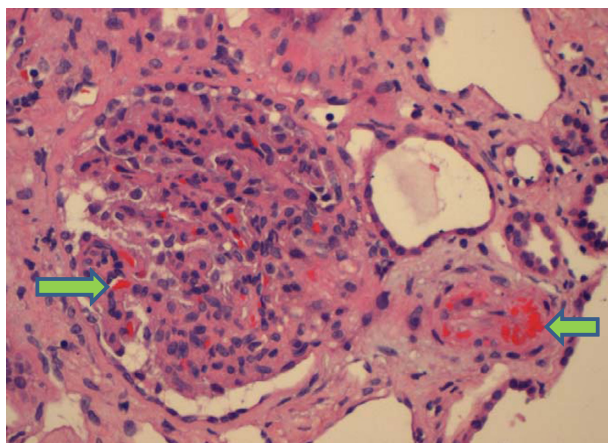
He was commenced on daily plasma exchange (PE) with fresh frozen plasma. On days 3 and 4, his PE was continued and concurrently initiated on hemodialysis due to worsening renal function. He, however, continued to have ongoing thrombotic microangiopathy and on day 6 of his

**Table 1.** Lab investigations.

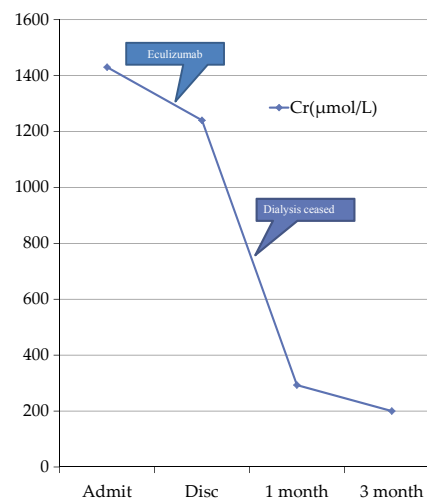
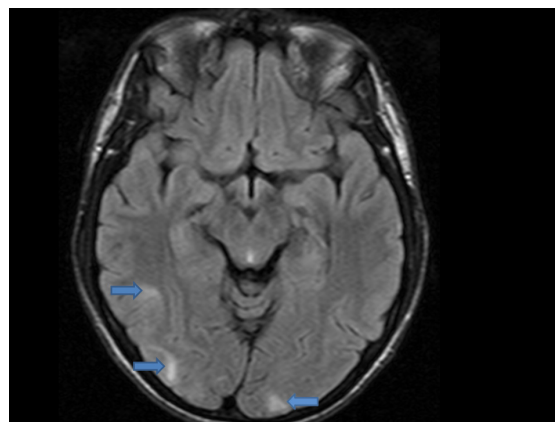
Investigations	Day 0	Day 1	Day 2	Day 58
Hb (g/L)	106	94	49	119
WBC	8.2	3.1	8	4.6
Platelets	102	89	83	231
Na (mmol/L)	127	126	132	140
K (mmol/L)	3.2	4.4	3.6	4.0
Urea (mmol/L)	36.2	40.1	37.4	15.2
Cr ( $\mu$ mol/L)	1430	1550	1370	244
LDH (U/L)		1130		200
Stool culture	Negative			

**Table 2.** Lab investigations on Day 2.

Haptoglobin	0.03 (low)
Coombs test	Negative
Vasculitic markers	Negative
C3, C4	Normal
ADAMTS 13	Normal 69 (40–130)
Stool culture	Negative

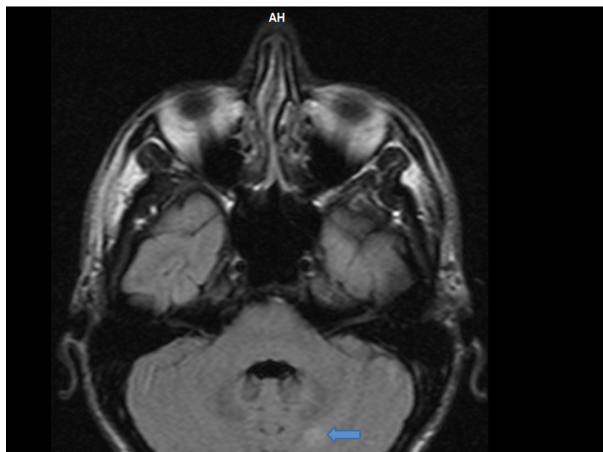
**Figure 1.** Showing red cells in the glomerulus and arteriole characteristic of thrombotic microangiopathy.

admission was initiated on Eculizumab. Eculizumab is a recombinant humanized monoclonal IgG<sub>2/4</sub> antibody that specifically binds to the complement protein C5, inhibiting its cleavage by the C5 convertase which prevents the generation of the terminal complement complex C5b-9. On day 6, as well his PE was ceased and he was discharged home. His dialysis was stopped after 3 weeks due to progressive improvement of his renal functions (Fig. 2). He was hypertensive which was initially managed on a single antihypertensive with systolic blood pressure at 140 and diastolic blood pressure being 80–90. Eculizumab was initially given at a dose of 900 mg every week for 4 weeks, followed by 1200 mg at week 5, and then 1200 mg every fortnight. During the treatment course, after 58 days since the initial presentation, he had an episode of accelerated hypertension with generalized tonic-clonic seizures with MRI confirming posterior reversible encephalopathy syndrome (PRES, Figure 3, 4). His hemolytic screen revealed no evidence of recurrence of aHUS (Table 1). His seizures were initially managed with antiepileptics and tight blood pressure control. He is currently off antiepileptics with no further seizures and well-controlled blood pressure (120/70) on three agents with ongoing fortnightly course of Eculizumab.

**Figure 2.** Progressive renal function improvement.**Figure 3.** MRI brain T2 hyperintensity signal involving subcortical white matter of the occipital lobes bilaterally greatest on the right.

## Discussion

Neurological involvement in the acute phase of aHUS occurs in 17–52% in a study among children, with generalized or partial seizure activity contributing in more than half of them [1–5]. The pathogenesis of CNS involvement in aHUS is multifactorial secondary to metabolic abnormalities, uraemia, hyponatraemia, or hypocalcaemia [6]. Also, toxin-mediated mechanisms resulting in focal vascular endothelial injury or multifocal thrombotic pathology may occur [7]. Hypertension has been cited as an additional factor [8]. Seizures usually are early in the course of the disease. This case report describes the uncommon finding of late onset seizures with hemolytic uremic syndrome with MRI findings consistent with PRES.



**Figure 4.** MRI brain T2 hyperintensity signal involving cerebellar hemisphere greatest on left.

The cause of PRES could be multifactorial. There was an issue of noncompliance with antihypertensive medication in this particular patient. Recurrence of Atypical HUS could be a possibility, however, unlikely with normal hemolytic parameters during the episode. Also, it was unlikely to be treatment-related as there has been no previous documented adverse event with Eculizumab and he continues to be seizure-free with ongoing therapy with Eculizumab. This case provides an example of aHUS coexisting with malignant hypertension and requires both complement-mediated thrombotic microangiopathy and hypertension to be controlled.

## Conflict of Interest

None declared.

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