Clinical Characteristics and Outcomes in Patients Treated with Eculizumab for Suspected Atypical Haemolytic Uraemic Syndrome (aHUS) - A Single Tertiary Centre Experience

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Summary

- This study demonstrates the diverse clinical phenotype of patients with suspected aHUS
- As such, there is an argument for patients with aHUS to be referred to regional centres to facilitate comprehensive care for patients with a complex, rare disease.
- The majority of patients referred were initially suspected to have thrombotic thrombocytopenic purpura (TTP) and received plasma exchange (PEX) prior to Eculizumab.
- A proportion of patients presented critically unwell, with 7/11 patients requiring haemodialysis (HD)acutely.
- In most cases Eculizumab was delivered promptly where aHUS was felt to be the likely diagnosis, with 6/7 patients achieving HD independence.
- In more than half, Eculizumab was discontinued; however a proportion of patients required reintroduction due to disease relapse.

Introduction

aHUS is a rare, complement mediated thrombotic microangiopathy (TMA), commonly presenting with renal failure and hypertension [1, 2]. Prompt diagnosis and treatment with the anti C5 monoclonal antibody Eculizumab may improve patient outcomes [3].

Methods

This was a retrospective study reviewing clinical characteristics and outcomes of patients referred and treated with Eculizumab for suspected aHUS, in a centre providing a haematology-led specialist service for patients referred with TMAs. Data was collected from the centre's TMA patient database.

Results

Demographics

- 11 patients were treated with Eculizumab between 2013-2019
- Age at presentation: Median 34 years old (range 21-55 years old)
- Gender: Male 6, Female 5
- All patients were external referrals from a wide geographical distribution with a median distance from referring hospital of 40 miles (range 1-85miles).
- Suspected diagnosis at referral: TTP: 8/11, aHUS: 3/11

Characteristics at presentation

- Haemoglobin: median 81 g/L (range 50- 135 g/L)
- Platelets: median 56x10^9 /L (range 12-164x10^9 /L).
- Renal impairment 11/11
  - Creatinine: median 561 umol/L (range 135-1621 umol/L)
  - 7/11 patients requiring HD acutely
  - 0/8 patients with a final diagnosis of aHUS remain on HD.
- Combined renal impairment and moderate thrombocytopenia (platelet count >30x109) as classically seen in aHUS [2]: 8/11.
- Hypertension 10/11
  - Median systolic and diastolic blood pressure 178 and 100 mmHg respectively (range 139-260 mmHg systolic, 77-170 mmHg diastolic).
- Extra-renal manifestations: 4/11 (3 neurological, 1 cardiorespiratory).
- Pregnancy related: 4/11 patients presented within 1 week post-partum.

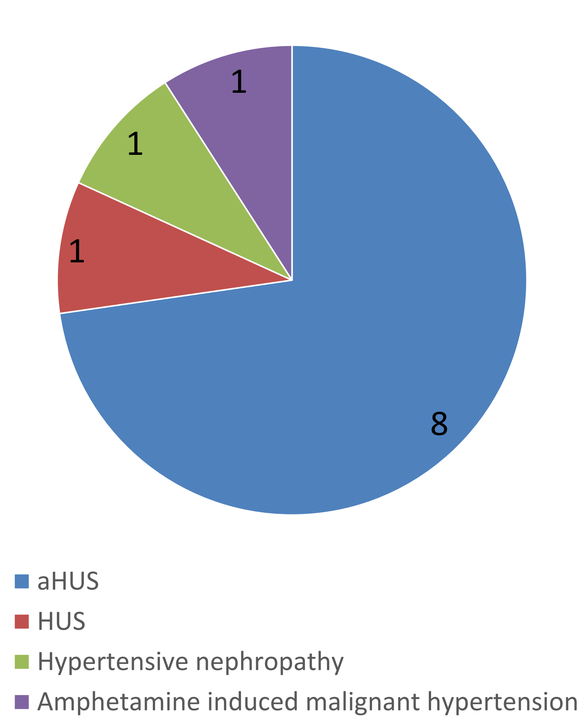

Figure 1: Final diagnoses of those treated with Eculizumab

Management

- Place of admission:
  - Intensive care unit: 9/11
  - Renal high dependency unit: 2/11
- Critical Care Support: 2/11 required intubation and ventilation (both of which had a final diagnosis of aHUS)
- PEX:
  - 10/11 patients received PEX prior to treatment with Eculizumab
  - Median duration of 3 days (interquartile range 5 days).
- Eculizumab:
  - Time to treatment: median 5 days (interquartile range 10 days)
  - Delays in eculizumab treatment (>7 days) were seen in 4 cases. This was where the differential diagnosis was malignant hypertension and blood pressure was being optimised.
  - Currently, 5/11 patients remain on Eculizumab (all delivered by a healthcare provider at home).

Outcomes

- Genetic Mutation analysis: 3/8 final aHUS diagnosis patients demonstrated a genetic complement mutation:
  - Complement factor H: 2/8
  - CD46: 1/8
- Renal biopsy: 8/11 patients underwent renal biopsy, 8/8 demonstrated TMA histology
- Discontinuation of Eculizumab: 6/11 patients
  - Reasons: 3/11 alternative diagnosis, 2/11 sustained renal recovery, 1/11 pre-conception.
  - 2/6 patients experienced a relapse of aHUS <6 months following discontinuation and successfully recommenced Eculizumab.

References

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