CASE REPORT

Rapid recovery of membrane cofactor protein (MCP; CD46) associated atypical haemolytic uraemic syndrome with plasma exchange

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SUMMARY

Atypical haemolytic uraemic syndrome (aHUS), unlike typical HUS is due to complement dysregulation. At least one abnormality of the complement system can be identified in 70% of patients. aHUS is associated with a poor prognosis with 25% mortality and 50% progress to end-stage renal disease. Genetic abnormalities in the complement system, proteins including *CFH*, *CFI*, *CFB*, *C3*, *CFHR1/3* and *MCP* (*CD46*) lead to uncontrolled complement activation in aHUS. We presented the second reported case of aHUS associated with a heterozygous c.191G > T mutation in exon 2 of *MCP* who responded rapidly to plasma exchange.

BACKGROUND

Typical haemolytic uraemic syndrome (HUS) is usually linked with *Escherichia coli* 0157 infection. Secondary causes of HUS have been described in the literature including: infections (*Streptococcus pneumoniae*, HIV and H1N1 influenza A), malignancy, chemotherapy and systemic disease.^{1–3} Ten per cent of the cases are described as atypical, where genetic mutations in members of the complement pathway lead to uncontrolled complement activation.⁴ Thirty per cent of cases of aHUS are idiopathic.¹ The overall prognosis of aHUS is poor with 25% mortality³ and 50% progress to end-stage renal disease.⁴

We reported the second known case of aHUS associated with a heterozygous c.191G>T mutation in exon 2 of the membrane cofactor protein (*MCP*; *CD46*), who responded rapidly to high-dose corticosteroids and plasma exchange.

CASE PRESENTATION

A 16-year-old man with no previous medical history of note presented with jaundice, systemic malaise, oliguria and a petechial rash. There was no history of diarrhoea, or relevant drug or family.

INVESTIGATIONS

Laboratory investigations demonstrated acute kidney injury (urea 38 mmol/L, serum creatine 460 mmol/L), severe thrombocytopenia (platelets $7 \times 10^9/L$), hyperbilirubinaemia (bilirubin 60 $\mu\text{mol/L}$) and anaemia (Hb 10.6 g/L). Lactate dehydrogenase (LDH) was elevated at 2975 U/L and blood film demonstrated microspherocytes and fragments (figure 1), consistent with a diagnosis of microangiopathic intravascular haemolysis. Microscopic

Figure 1 Peripheral blood film demonstrating red cell fragments, microspherocytes and true thrombocytopenia.

haematuria progressed to overt macroscopic haematuria.

DIFFERENTIAL DIAGNOSIS

Stool cultures were not possible due to constipation. ADAMTS13 activity was within the normal range at 87%, excluding a diagnosis of thrombotic thrombocytopenic purpura.

There was no evidence of a pneumococcal trigger from the clinical history, radiography, viral throat swab or repeated blood cultures. The HIV test was also negative.

Serum C3 and C4 were repeatedly within normal range. Plasma levels of complement factor H (*CFH*) and factor I (*CFI*) were also normal. Complement genotyping demonstrated no abnormalities of *CFH*, *CFI*, *CFB*, C3 and *CFH*-related proteins. Mutation screening of the membrane cofactor protein (*MCP*, *CD46*) demonstrated a heterozygous missense mutation in exon 2 (c.191G>T, p.Cys64Phe).

TREATMENT

Following confirmation of the diagnosis of aHUS, the patient was started on high-dose corticosteroids with gastroprotection. Central venous access was difficult in view of his thrombocytopenia and absolute contraindication for platelet transfusion.⁵ He initially received haemodialysis and 4 units of fresh frozen plasma (Octaplas). Plasma exchange was started on day 2 and volume restitution was with Octaplas. Transfusion of red cells were also required on haemodialysis to maintain target

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Figure 2 Plasma exchanged on day 2.

haemoglobin (Hb) >10 g/L. A plasma exchange was performed daily for 8 days with complete recovery of the platelet count, LDH and Hb, and renal function normalised. Comparative images of the plasma exchanged on day 2 and 8 are demonstrated in figures 2 and 3.

OUTCOME AND FOLLOW-UP

At the 2 months follow-up, renal function, repeated complement levels and a urine dipstick were normal on a reducing regime of oral steroids.

DISCUSSION

Excellent reviews of aHUS have recently been published in the literature.^{1 2} A number of mutations in the complement pathway have been described in aHUS and prognosis varies according to genotype, with *CFH* mutations associated with the worse outcome.¹ *MCP/CD46* mutations accounts for 10–15% of cases of aHUS.² These patients typically have frequent episodes of recurrence of aHUS followed by complete recovery of

renal function.⁶ It is associated with <20% risk of progression to end-stage renal disease.² To our knowledge, there is only one other reported case of aHUS caused by a heterozygous c.191G>T mutation in exon 2 of *MCP* and is associated with decreased expression of *MCP*.⁷ There is limited evidence to date that plasma exchange is beneficial in patients with *MCP* mutations.¹ Our patient responded rapidly to plasma exchange with complete recovery of platelet count, LDH and Hb, and normalisation of renal function by day 8 of treatment.

Learning points

- ▶ Haemolytic uraemic syndrome (HUS) is characterised by a triad of non-immune haemolytic anaemia, thrombocytopenia and renal impairment.² Ten per cent of cases are atypical, as they are neither caused by Shiga-toxin producing *Escherichia coli* nor Streptococci.³
- ▶ Platelet transfusions are contra-indicated in aHUS as they can potentiate thrombotic microangiopathy.⁵ Plasma exchange is the mainstay of treatment of aHUS.
- ▶ In 70% of cases of aHUS, at least one abnormality of the complement system can be identified.¹
- ▶ Through complement genotyping response to plasma exchange and progression to end-stage, renal disease can be predicted.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Figure 3 Changes in appearance of the plasma exchanged on day 8.

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