Introduction

A 23 year old man was admitted to hospital having collapsed on a flight back to the UK from Spain. He had begun to feel unwell the evening before with fever, diaphoresis, vomiting and severe myalgia. In the morning he struggled to get to the airport due to worsening leg pain and eventually collapsed in the airplane toilet during the flight. His past medical history was notable for paroxysmal nocturnal haemoglobinuria (PNH), for which he had been receiving infusions of eculizumab, a monoclonal antibody which binds complement C5 and prevents formation of the membrane attack complex (Figure 1), for the preceding two months.

He was attended by a fellow passenger, an off-duty paramedic, who noted a non-blanching rash on his limbs and made a diagnosis of meningococcal sepsis. On arrival, the plane was met by an ambulance crew who administered intramuscular benzylpenicillin and rushed the patient to hospital. In the emergency department he was hypotensive, tachycardic and tachypnoeic with a fever, had a rapidly progressing purpuric rash mainly affecting his lower limbs (Figures 2, 3 and 4), and a mild headache but no meningoencephalitis. Venous lactate was 8.3mmol/L, CRP 91mg/L, Neutrophils 7.35x10^9/L, with normal renal function and liver enzymes. He received intravenous ceftriaxone and fluids and was transferred to the Intensive Care Unit for inotropic support. Household contacts were given ciprofloxacin prophylaxis.

Clinical Images and Results

Figure 1. PNH erythrocytes lack complement inhibitors CD55 and CD59, resulting in complement-mediated intravascular (CD59) and extravascular (CD59) haemolysis. Eculizumab blocks C5, preventing formation of the membrane attack complex (MAC), which kills both CD59- intravascular erythrocytes and Neisseria spp. through the insertion of a pore into the cell membrane.

Figure 2. 200c spine, (W135 strain) was identified by PCR from an EDTA blood sample taken on admission; blood cultures and throat swab were negative.

Figure 3. Trends of ALT and ALP from admission to discharge.

Discussion

Anti-complement therapy is the most effective way to reduce haemolysis and thrombosis in PNH, which are a result of complement-mediated haemolysis due to the absence of cell surface complement regulatory proteins (CD55 and CD59). Invasive meningococcal disease is significantly more common in patients receiving eculizumab, and it is a standard practice to give meningococcal vaccines in addition to penicillin prophylaxis. Despite this, there have been reports of meningococcal disease despite such precautions.

6 cases of meningococcal sepsis have been seen in patients receiving eculizumab from the Leeds PNH Service, but purpuric rash is rare (seen only in this case). The rate of meningococcal infection on eculizumab is 0.25 infections/100 patient years on therapy.

Conclusions

This case highlights:
- the importance of heightened awareness of this disease in this small subset of patients, particularly as it may present atypically
- the importance of rapid identification of and prompt antimicrobial and supportive treatment for sepsis
- the important role of molecular diagnostics (PCR in this case) in determining the cause of infection

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References


3. Personal communication, Professor Peter Hillman, Consultant Haematologist, St James’s University Hospital, Leeds.

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