

Introduction

Haemolytic uraemic syndrome (HUS) is a rare disorder characterised by microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury. Gemcitabine, a nucleoside analogue used in the treatment of solid organ tumours has been causally associated with HUS with an incidence as high as 2.2% in treated patients. Gemcitabine-induced HUS (GiHUS) does not reliably respond to withdrawal of gemcitabine and despite corticosteroids and plasmapheresis, it often results in poor renal and mortality outcomes. Eculizumab is a monoclonal anti-C5 antibody recently NICE approved for the treatment of aberrant alternative complement pathway activation resulting from atypical HUS (aHUS) although its role in treating GiHUS is uncertain. Here, we report a complex case of GiHUS treated with Eculizumab.

Case Presentation

A 62-year-old caucasian female developed acute kidney injury and haemolysis following a course of gemcitabine therapy for recurrent pancreatic cancer. Her initial diagnosis in 2011 included local vascular invasion and mesenteric metastases but partial remission was achieved following surgical resection, radiotherapy and gemcitabine chemotherapy. Two years later, surveillance computed tomography (CT) scanning revealed progressive disease and gemcitabine therapy was re-commenced for a total of 12 cycles over 12 months (total cumulative dose 33,200mg).

During the final gemcitabine cycle, serum creatinine concentrations began to rise from 70µmol/L (0.79 mg/dL) to 109 µmol/L (1.23 mg/dL) and then 301 µmol/L (3.41 mg/dL) over the subsequent two weeks. In parallel, haemoglobin concentrations fell from 120g/L to 82 g/L; platelets from 326 to 89 x10⁹/L (normal range 150-450 x10⁹/L); and serum lactate dehydrogenase (LDH) rose to 1320 iU/L (normal range 105-333 iU/L). ADAMTS13 activity was 83% (normal range 50-160%). Peripheral blood smear revealed red cell fragments, thrombocytopenia and giant platelets confirming intra-vascular haemolysis and a diagnosis of likely GiHUS was made.

Daily plasma exchange (PEX; 3L of fresh frozen plasma (FFP)) was performed over 12 sessions with platelet counts recovering to normal range. However, three days following cessation of PEX, platelet counts dropped again and LDH began to rise. Kidney function and urine output deteriorated during this period, necessitating haemodialysis. Fluid overload and haemodynamic instability during dialysis rendered ultrafiltration difficult, culminating in an episode of acute respiratory distress necessitating respiratory support and continuous veno-venous haemofiltration for 48 hours on the intensive therapy unit. Echocardiography and left ventricular contrast studies revealed cardiac stunning consistent with a “Takotsubo” cardiomyopathy, making further PEX a high-risk treatment option.

The patient expressed a strong desire to continue with medical therapy in order to spend time at home. In light of persistent haemolysis and PEX being precluded due to haemodynamic instability, Eculizumab was administered at a dose of 900mg weekly for three doses. Haemoglobin, platelet count and LDH all stabilised within normal ranges. Although renal function did not recover to baseline function, she became dialysis independent allowing effective diuresis. The patient was thus clinically stable enough to spend some important time at home during her terminal disease. She died several weeks later through advanced cerebral metastatic disease.

Discussion and Conclusion

Two reports of using Eculizumab in the management of GiHUS have been published recently. The first single case study from Germany reported rapid normalization of platelet count and dialysis-independence achieved following a four-week course of Eculizumab (Starck, 2014). The second published report was a small case series from North America of four patients with GiHUS receiving Eculizumab with similarly positive outcomes (Ustwani, 2014). The case presented here supports emerging literature and offers the first UK report of Eculizumab to treat GiHUS, proposing it as a safe and effective alternative to previous conventional therapies.