Case of Complement-Mediated Atypical Hemolytic Uremic Syndrome

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Introduction

Hemolytic uremic syndrome (HUS) is defined by triad of thrombocytopenia, microangiopathic hemolytic anemia, and acute renal failure. Most commonly HUS is caused by Shiga toxin-producing bacteria Escherichia coli O157:H7. Other forms of HUS that are not caused by these bacteria are considered atypical HUS (aHUS). Common causes of aHUS include complement-mediated, chemotherapy, HIV, and antiphospholipid syndrome. Atypical HUS has a worse prognosis than typical HUS. Treatment with plasma exchange and eculizumab must be initiated promptly.

Case

A 58-year-old male with a past medical history of chronic lymphocytic leukemia (CLL) on ibrutinib, hypertension, hypothyroidism, and recent Covid-19 infection who presented with altered mental status after witnessed seizure-like activity at home. Initial laboratory studies showed low hemoglobin, platelet count and haptoglobin with elevated white blood cell count, lactate dehydrogenase, creatinine, uric acid, phosphorous, lipase, and lactate. Peripheral blood smear demonstrated 10+ schistocytes per HPF. Patient was intubated due to encephalopathy, emergent dialysis was initiated for acute renal failure with severe metabolic acidosis and was also given rasburicase for possible tumor lysis syndrome. Due to microangiopathic hemolytic anemia, patient was transferred to the intensive care unit for plasmapheresis and was started on methylprednisolone 1 mg/kg. Flow cytometry showed CD5+ B-Cell Lymphoma, lambda light chain restricted, compatible with CLL without evidence of Richter transformation. ADAMTS13 was 40% ruling out TTP. Despite plasmapheresis, patient continued to have greater than 10 schistocytes per HPF on peripheral blood smear.

Plasmapheresis and methylprednisolone were discontinued after four days, and patient was given eculizumab 900 mg for treatment of atypical HUS. Repeat peripheral blood smear showed 2-3 schistocytes per HPF. Complement gene testing showed low complement C3 of 44 mg/dL (normal 90-180 mg/dL) with otherwise normal complement C4, rheumatoid factor, antinuclear antibodies, myeloperoxidase antibodies, antineutrophil cytoplasmic antibodies. Low C3 supported complement-medicated hemolytic uremic syndrome. Patient was extubated after one week on mechanical ventilation, but unfortunately developed respiratory failure secondary to vocal cord paralysis, refused re-intubation, and was transitioned to comfort measures.

Discussion

Complement system is comprised of multiple different proteins and serves to protect the body from invading pathogens. The imbalance between complement activation and regulation on host cells drives aHUS. Low C3, as seen in this case, is detrimental because there is deficiency in white blood cell chemotaxis, decreased bacterial killing and decreased clearance of immune complexes. Low haptoglobin and elevated lactate dehydrogenase were consistent with hemolysis seen in aHUS. Historically, plasma exchange has been the gold standard treatment of aHUS. More recently, eculizumab, which works by preventing the final component complex in the complement pathway, has been shown to be beneficial in patients with aHUS and is replacing plasma exchange as the gold standard treatment. Eculizumab should be started immediately after TTP and Shiga toxin-producing bacteria are ruled out.

REFERENCES

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