CLINICAL VIGNETTE

Anti-Thymocyte Globulin Induced Hemolytic Anemia

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Case Presentation

A 24-year-old female with end stage renal disease secondary to focal segmental glomerulosclerosis (FSGS) status underwent living unrelated renal transplant one year ago. Post-transplant course included history of recurrent Clostridium difficile infections, cytomegalovirus colitis, thrombocytopenia and recovered cardiomyopathy presented with acute kidney injury. The patient and her family members had gastroenteritis nine days prior to admission. She initially developed nonbloody, nonbilious emesis followed by significant watery diarrhea which improved. She later developed fatigue, loss of appetite, nausea and pain over her transplant site. She presented to an outside facility near her home and was found to have an acute kidney injury (AKI) with creatinine of 4.5 from a baseline creatinine of 1.0 and subsequently presented to the Emergency Department for further management.

Kidney transplant ultrasound did not show evidence of hydronephrosis. She underwent a renal transplant biopsy which was consistent with acute cell-mediated rejection. The renal transplant team recommended methyleprednissolone 300mg intravenously for 3 days though she continued to have worsening renal function. The renal transplant team recommended initiation of intravenous immunoglobulin (IVIG) with the patient. She declined given history of significant side effects in the past. She was agreed to start anti-thymocyte globulin (ATG) and received ATG 1.5mg/kg for three days. She developed worsening thrombocytopenia and anemia and received a half dose of ATG on the fourth day with worsening of her thrombocytopenia and anemia, further doses of ATG were held. Her anemia was consistent with hemolysis given haptoglobin less than 10, lactate dehydrogenase elevated to 535 and total bilirubin elevated to 1.4. Her peripheral blood smear had a low schistocyte burden with 1-2 schistocytes per high power field. Hematology/oncology was consulted and was suspicious for ATG-induced hemolysis. There was also consideration of tacrolimus-induced thrombotic microangiopathy (TMA) though this was less likely given no evidence of TMA on the renal biopsy. After holding ATG, the hemolysis labs and platelets improved.

Discussion

Antithymocyte globulin (ATG) is a polyclonal gamma-immunoglobulin derived from rabbits or horses which is effective against human thymocytes and works to deplete the T lymphocytes of the graft or the host.[1,2] ATG has been used for a variety of clinical conditions including prevention and treatment of acute rejection in solid organ transplant recipients, graft-versus-host-disease, autoimmune diseases and aplastic anemia.[2] ATG has been associated with several side effects. The most common adverse effects reported by the FDA include abdominal pain, hypertension, nausea, shortness of breath, urinary tract infection, headache, chills, hyperkalemia, thrombocytopenia and leukopenia.[3]

A few case reports also describe hemolytic anemia as an adverse effect of ATG. One 21-year-old woman received thymoglobulin as induction immunosuppressive therapy after kidney transplantation and subsequently developed severe hemolytic anemia and thrombocytopenia.[4] Her course was further complicated by perirenal hematoma requiring surgical intervention and transfer to the intensive care unit. Thymoglobulin was suspected to interact with a common Fc-receptor epitope which caused the hemolytic anemia and thrombocytopenia. A 62-year-old man with aplastic anemia received ATG for four days.[5] After the first infusion, his hemoglobin decreased with increase in serum lactate dehydrogenase. His course was further complicated by renal failure. The hemolytic anemia was thought to be secondary to lysis of complement-sensitive red blood cells.

Conclusion

ATG is associated with numerous adverse effects. Though thrombocytopenia and leukopenia have been reported, there are few reports of hemolytic anemia as an adverse effect of ATG. Though less common, hemolytic anemia should be considered and further evaluated in patients receiving ATG and with decreasing hemoglobin.

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