Gemcitabine Induced Hemolytic Uremic Syndrome Treated with Eculizumab
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Case Presentation:

57 year man with hypertension, type 2 diabetes, and metastatic urothelial cancer status post 4 cycles of gemcitabine/cisplatin, last received 7 days ago, presents from oncology clinic with nausea, vomiting, altered mental status, and a creatinine of 10.6mg/dL (baseline of 0.9mg/dL). Before his last round of chemotherapy he had been in his normal state of health with platelets at 575x10^9/L.

His admission physical exam was notable for confusion, but was otherwise normal. Labs were pertinent for an elevated LDH and low haptoglobin. With his altered mental status, acute kidney failure, and decreased platelets, we were concerned he may have atypical hemolytic uremic syndrome. On recommendations from hematology, we administered the monoclonal antibody Eculizumab atypical hemolytic uremic syndrome. On recommendations from hematology, we administered the monoclonal antibody Eculizumab atypical hemolytic uremic syndrome (aHUS) and thrombotic thrombocytopenic purpura (TTP).

Clinical Course:

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Atypical Hemolytic-Uremic Syndrome (aHUS)

- Category of thrombotic microangiopathies that includes Shiga-toxin induced hemolytic uremic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP)
- Defined by microangiopathic hemolytic anemia, thrombocytopenia or 25% reduction in baseline platelets, and end-organ damage, particularly the kidneys without the symptom of diarrhea with ADAMTS13 >5%
- Pathogenesis is theorized to be by intravascular complement activation leading down the alternative complement pathway and the generation of the membrane attack complex (MAC)
- Complement activation leads to endothelial injury leading to deficiency in nitric oxide which leads to the development of thrombotic microangiopathy

Causes of Atypical Hemolytic-Uremic Syndrome

- Hematopoietic stem cell transplant
- Solid organ transplant
- Neoplastic disorders
- Chemotherapeutic agents
- Hypertension
- Pregnancy
- HIV
- Autoimmune disorders
- Anti-VEGF drugs

Gemcitabine-induced aHUS

- Associated with cumulative doses exceeding 20,000mg/m² or number of doses exceeding 18 doses
- Can develop new-onset hypertension prior to developing aHUS
- In our patient:
  - Fewer than 18 doses and cumulative dosage of 11,000mg/m²
  - ADAMTS13 >5%

Management

- Plasma exchange reduces mortality from 50% to 25%, but many patients do not respond to therapy
- Eculizumab – Anti-C5 antibody. Stops creation of MAC, essentially stopping the complement cascade.

Epilogue:

After 2 treatments of eculizumab, the patient’s mental status recovered. With the patient’s mental status now at baseline, a goals of care discussion was performed on the last day of his hospitalization. It was decided that with the difficulties of his last round, chemotherapy would be put on hold and no further eculizumab was administered. The patient was discharged home with his family and to follow-up in the outpatient setting.

References

- Langhans, D. Syndromes of Thrombotic Microangiopathy. NAM. 2004