CLINICAL VIGNETTE

Drug-Induced Thrombotic Microangiopathy and Use of Eculizumab

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Case Report

A 31-year-old female was referred to nephrology for acute kidney injury. She was diagnosed with colorectal cancer at age 29, after presenting to her primary physician with a month history of nausea, vomiting and increasing bowel movements. The diagnostic work up showed large bowel obstruction which was adenocarcinoma on biopsy. She underwent surgical resection of the tumor with seven positive lymph nodes and involvement of the Visceral peritoneum.

She was started on chemotherapy with Fosaprepitant, Palonosetron and Oxaliplatin. Patient presented to her oncologist one day after receiving the second course of her chemotherapy with fever, generalized weakness, cola-colored urine, leg and back cramps and dizziness. Patient's physical examination showed stable vital signs with normal cardiovascular, gastrointestinal, pulmonary and neurological examination.

Laboratory test on the day of chemotherapy showed a Hgb of 11.0 mg/dl; Platelet of 237,000; and Creatinine of 0.7 mg/dl. Her repeat laboratory tests one day after receiving chemotherapy showed: Hgb of 8.6 mg/dl Platelet count of 106 X 10E/uL and creatinine of 3.3 mg/dl. Patient was admitted to the hospital and renal was consulted for acute kidney injury, acute anemia and thrombocytopenia.

A clinical diagnosis of acute kidney injury secondary to atypical hemolytic uremic syndrome (aHUS) related to medication, Oxaliplatin was considered. Other laboratory tests on admission showed: ADAMTS 13 activity of 72 (reference>67%); LD 1,864 U/L; Platelet 106 X10E3/uL (repeat Platelet count on the fourth hospital day decreased to 21 X 10E3/uL); creatinine 3.3 mg/dl (repeat creatinine on the fourth hospital day worsened to 8.35 mg/dl); Hemoglobin 8.6 g/dl (down to 8.0 g/dl on day 4 of hospitalization); Haptoglobin 28 mg/dl; urine test 2+ blood with 29 RBC in microscopic examination of urine. Patient's blood peripheral smear showed slight schistocytes. Ultrasound of kidneys was within normal limit.

The patient's clinical presentation and her laboratory tests were consistent with thrombotic microangiopathy (TMA). The history of receiving the chemotherapeutic agent, oxaliplatin, a day prior to acute kidney injury and laboratory tests were consistent with TMA and the diagnosis of drug induced TMA.

Treatment with Eculizumab was started on the second day of hospitalization. Patient was also started on hemodialysis for oliguric/anuric acute kidney injury. She received three doses of Eculizumab over twenty days of her hospitalization. Patient's laboratory test prior to discharge from the hospital showed: platelet 262 X 10E/uL; Hgb 9.3 g/dl; LD 275 U/L; and Haptoglobin 167 mg/dl. Patient did not have improvement in her renal function and was discharged on outpatient hemodialysis three times a week.

Discussion

Thrombotic microangiopathies are group of diverse disorders with common clinical, laboratory and pathological findings. The clinical manifestations include microangiopathic hemolytic anemia, thrombocytopenia and organ injury.[1] The pathologic features are manifested by arteriolar and capillary thrombosis with characteristic abnormalities in the endothelium and vessel wall.[2]

The focus of this case report is the role of eculizumab, a monoclonal antibody that blocks complement activity, on drug-induced thrombotic microangiopathy, (DITMA).[3]

Many drugs including chemotherapeutic and immunosuppressive agents are recognized as the cause of TMA in patients who have received them for treatment of underlying malignancy, organ transplant and immunologic disorders requiring immunosuppression. DITMA can be caused by direct toxic effects of the medication or develop as an immunologic reactions to the medication. The former is dose-and time- dependent while the latter is non-dose-related and idiosyncratic.[4,5] DITMA associated with immunologic reactions develop very rapidly and the patient can develop oliguric/anuric acute kidney injury within hours after exposure, like our case.[6] The recovery from acute kidney injury may be incomplete due to severity of kidney injury in immune-mediated DITMA. The thrombocytopenia should improve in few days. The patients with toxic dose-related DITMA typically develop gradual loss of kidney function and hypertension.[7]

The mainstay of therapy for DITMA is discontinuation of the offending drug and supportive care. There have been an increase use of eculizumab in patients with DITMA[8,9] and shiga toxin-mediated hemolytic-uremic syndrome (ST-HUS) over the past few years.[10-12] The ineffectiveness and/or harmfulness of plasma exchange (recognized as category IV by American Society of Apheresis) in patients with DITMA associated with

some drugs,[13] makes early diagnosis and initiation of eculizumab therapy an important task in order to improve the outcomes in this group of patients.

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