Effective Management of Carfilzomib-Induced Thrombotic Microangiopathy in Multiple Myeloma Using Eculizumab

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Introduction: Carfilzomib, a proteasome inhibitor, is used to treat refractory multiple myeloma (MM). Although rare, there have been reports of carfilzomib-induced thrombotic microangiopathy (TMA), a serious condition characterized by thrombocytopenia, hemolytic anemia, and acute kidney injury. Early detection and appropriate management of TMA are crucial due to its high risk of mortality and morbidity. Currently, there are no established guidelines for managing carfilzomib-induced TMA. Here, we present a case of a 71-year-old woman with refractory MM who developed TMA following carfilzomib treatment and was successfully treated with eculizumab. Case presentation: The patient, with a history of relapsed IgG-kappa MM, presented with fatigue and shortness of breath. She had received her first dose of carfilzomib three weeks prior. Initial tests revealed acute kidney injury, anemia, and severe thrombocytopenia. Coagulation studies were unremarkable. Haptoglobin was undetectable, while D-dimer and lactate dehydrogenase were elevated. Peripheral blood smear showed schistocytes, supporting a diagnosis of microangiopathic hemolytic anemia. Imaging studies revealed right pneumonic infiltrate and bilateral pleural effusions but no intra-abdominal pathology. Plasmapheresis was initiated, and ADAMTS-13 activity, coming back at 91%, ruled out thrombotic thrombocytopenic purpura (TTP). Hemolytic uremic syndrome (HUS) and atypical HUS (aHUS) were also excluded through negative stool shiga-toxin and normal complement levels, respectively. Eculizumab was then administered, dramatically improving platelet count and hemolytic parameters within 24 hours. The patient was discharged and continues on weekly eculizumab treatment. Conclusion: Diagnosing drug-induced TMA is challenging as it requires ruling out conditions like DIC, TTP, HUS, and aHUS. Plasmapheresis, while commonly used,

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often has limited impact due to TMA's heterogeneous nature. Identifying the underlying cause and appropriate management are essential. This case highlights the potential of eculizumab in treating carfilzomib-induced TMA and may inform future treatment protocols and understanding of the disease.

Keywords: Carfilzomib, Drug-Induced Thrombotic Microangiopathy, Thrombotic Microangiopathy, Eculizumab

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