Concurrent Trimethoprim-Sulfamethoxazole Induced Immune Hemolytic Anemia and Thrombocytopenia Following Allogeneic Stem Cell Transplantation

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Introduction

Drug induced immune hemolytic anemia (DIHIA) and drug induced immune thrombocytopenia (DIT) are rare but dangerous complications of pharmacotherapy which may be under-recognized in hematopoietic stem cell transplant (HSCT) patients due to overlap of other medication effects and post-transplant complications.

Patient Presentation

A 61 year old female with NK cell deficiency and GATA-2 associated myelodysplastic syndrome was referred to our institution for HSCT (day +58) presented with 3 days of severe back pain, muscle cramps, and dark urine. Her medications were notable for Acyclovir, Tacrolimus, and Trimethoprim-Sulfamethoxazole (TMP-SMX). On assessment she was found to be febrile (38.3°C) with scleral icterus, bilateral upper and lower extremity edema, an erythematous maculopapular rash and oliguria. She was admitted for further evaluation and management.

Presenting Labs

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<td>110-220</td>
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<td>AST</td>
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<td>135-450</td>
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Clinical Course

Patient received 2 units of rPRBCs and underwent dialysis before receiving a renal biopsy. Given the near absence of schistocytes, this made TTP-HUS less likely. A peripheral blood smear at 10x magnification demonstrating marked hyperchromia, borderline macrocytic anemia, and thrombocytopenia. Red arrow denotes erythocyte clumping, yellow arrows denote toxic granulations.

Figure 1. Left Top: Kidney biopsy demonstrating acute tubular injury with sloughing of tubular epithelium, most suggestive of toxic type etiology. Left Bottom: Scattered pigmented casts most likely representing free Hgb casts. Right: Peripheral blood smear at 10x magnification showing severe microcytic anemia and thrombocytopenia. Red arrow denotes erythocyte clumping, yellow arrows denote toxic granulations.

Figure 2. TMP-SMX had been prescribed on a weekend dose schedule with doses received on post transplant days +36, +43, +45, and +47 (black arrows) prior to admission. Tacrolimus on a twice daily dose schedule had been taken since day -2 of transplant. Both TMP-SMX and Tacrolimus were held on admission.

*Note Day 0 = Day of Transplant.

Figure 3. CD19+ NK cells were markedly increased on flow cytometry.

Discussion/Conclusion

DIHIA and DIT are rare and potentially fatal complications of pharmacotherapy. To date, the literature reports 7 and 50 cases of each, respectively, with no reported cases of concurrent hemolytic anemia and thrombocytopenia due to TMP-SMX use.1,2 TMP-SMX is one of the most commonly used agents in the world and is often the first line treatment for PJP prophylaxis in immunosuppressed patients following HSCT. It is generally well tolerated both in its recommended thrice weekly regimen and in its alternate regimen of weekend administration only.3,4

This case illustrates the fact that concomitant occurrence of both DIHIA and DIT is rare and can present a diagnostic challenge in the setting of polypharmacy, utilization of intermittent medication (weekend only) dosing and a complicated clinical scenario with many potential drug sequelae. More specifically, it highlights the difficulty in assessing the cause of hemolysis and thrombocytopenia in HSCT patients, where overlap of signs and symptoms with other potential comorbidities makes clinical suspicion for this rare entity quite low. Hopefully, presentation of this case will encourage providers to consider this potential diagnosis when the appropriate clinical scenario is encountered.

Patient Follow-Up

During the patient’s hospital course, TMP-SMX and Tacrolimus continued to be held pending appropriate renal recovery. Her clinical and laboratory status improved with continued hemodialysis and a brief course of steroids. She was discharged home after 15 days in stable condition. A trend of the patient’s hemoglobin, platelets, and creatinine is depicted in Figure 2

Drug-dependent antibody testing with TMP-SMX and Tacrolimus resulted 3-days prior to when the patient was scheduled to restart her medications. Mixing the patient’s serum with TMP-SMX revealed drug antibody immune complexes to RBCs. Further testing with platelets also revealed TMP-SMX-inducted platelet antibodies. This was consistent with drug induced immune hemolytic anemia and drug-induced immune thrombocytopenia.

REFERENCES