

Toxic Together: Partners in Pancytopenia

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Introduction

Pancytopenia occurs when there are decreases in the three major blood cell lines including white cells, red cells, and platelets. Bone marrow failure, destruction, and sequestration are the three major categories of causative etiologies. More specifically these etiologies can include nutritional deficiencies, infections, medications, leukemias and lymphomas, myelodysplastic syndromes, fibrosis, autoimmune diseases, toxins, and chemotherapy or radiation. The objective for this clinical vignette is to explore the work up for pancytopenia in an acutely ill patient and the importance of medication reconciliation including medications taken in the recent past and recognition of drug-drug interactions.

Case Presentation

- An 81-year-old female with a medical history of psoriatic arthritis
- Methotrexate (MTX) was started 3 months prior to presentation
- Presented from an outside facility due to hypotension and weakness over 3 days. A CBC showed she had pancytopenia (Table 1).
- Notable, two weeks prior to presentation, she presented to her PCP with complaints of urgency and dysuria and was started on trimethoprim/sulfamethoxazole (TMP-SMX) for 10 days for a urinary tract infection.
- Blood cultures, hepatitis panel, HIV, flow cytometry for leukemia/lymphoma, SPEP, immunofixation, parvovirus B19 antibodies, EBV and CMV antibodies, aspergillus galactomannan antigen, and ANA were all negative.
- Copper, B12, and folate levels were within range and she had no known toxin exposures.
- Neutropenic prophylaxis was initiated with ciprofloxacin, acyclovir, and fluconazole and folic acid was started
- Hematology was consulted and recommended granulocyte colony stimulating factor due having one of four blood cultures being positive which was later determined to be a contaminant
- Neutropenia prophylaxis medications were stopped, and her symptoms improved. Notably, one week after discharge, her WBC was 7.68 k/mcL.

Table 1. Laboratory Values

	Labs 8 months prior to presentation	Initial Lab Work	Two days after colony stimulating factor
WBC	5.5 k/mcL	0.84 k/mcL	19.23 k/mcL
Absolute neutrophil count	3.0 k/mcL	0.13 k/mcL	11.34 k/mcL
Hgb	12.3 g/dL	8.6 g/dL	7.9 g/dL
Platelets	218 k/mcL	34 k/mcL	198 k/mcL

Discussion

- This case highlights the importance of medication reconciliation before prescribing medications
 - Pancytopenia is a known complication of giving methotrexate and trimethoprim/sulfamethoxazole simultaneously

How Does Toxicity Occur?

- Both agents inhibit dihydrofolate reductase therefore reducing folate metabolism leading to myelosuppression
- Both have the potential to cause nephrotoxicity which can lead to elevated levels of the drug(s) in the body
- Due to competitive binding, TMP-SMX can cause increased free levels of methotrexate

- Providers should order the appropriate monitoring labs when prescribing medications (Table 2). This patient did not have any follow up blood work after starting the methotrexate, so we were unsure how long she was pancytopenic but her symptoms of fatigue and malaise started just after taking the course of TMP/SMX.

Table 2. Suggested Monitoring Labs for Methotrexate

Duration since starting treatment	Monitoring Lab Work
First 3 months of therapy	Every 4 weeks – CBC, LFTs, creatinine, albumin
Months 4-6 of therapy	Every 8 weeks - CBC, LFTs, creatinine, albumin
After 6 months of therapy	Every 12 weeks - CBC, LFTs, creatinine, albumin

Conclusion

This case represents a case of pancytopenia due to medications adverse effects and drug-drug interactions. There are known possible adverse effects of MTX and TMP-SMX when given simultaneously since SMX can increase the dose of MTX in the bloodstream, increasing the likelihood of toxicity. This case emphasizes the importance of completing a thorough medication reconciliation before starting a new medication for a patient as well as the importance of monitoring labs when starting a medication with possible side effects like MTX. It is important to keep a broad differential to detect the etiology. It is also important to consider mitigating factors when starting a high-risk medication such as MTX. Folic acid supplementation could be considered to reduce the risk of adverse events.

References

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