**CLINICAL VIGNETTE**

# An Uncommon Cause of Drug-Induced Thrombocytopenia Suggested by Reviewing the MAR

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***Case Presentation***

A 69-year-old male with multiple medical problems including rheumatoid arthritis, interstitial lung disease, cervical spinal stenosis, OSA, and obesity hypoventilation syndrome was transferred from an outside hospital where he had developed respiratory failure and was treated for pneumonia. He did not require intubation. As his respiratory status had improved to near baseline, he was transferred to undergo previously scheduled cervical laminectomy.

He developed recurrent respiratory failure and sepsis soon after transfer and was intubated on hospital day 2. He had a long hospital course requiring tracheostomy on hospital day 15 but ultimately had cervical spinal surgery on hospital day 18. He had second episode of sepsis due to respiratory infection on hospital day 23 but recovered. As he was awaiting transfer to long-term acute care hospital for further rehabilitation, his platelets were noted to be decreasing. At admission, his platelet count was mildly low at 139,000/uL; over the course of hospitalization, they had increased and remained stable in mid-200,000s/uL until noted to be trending downward on hospital day 43 when platelets were 113,000/uL.

The patient reported no new symptoms and clinically appeared unchanged. Medications known to be associated with decreased platelets were stopped including pantoprazole and heparin. He had additionally recently completed a 2 week course of cefepime. In further review of medicine administration record (MAR), inhaled tobramycin was started on hospital day 35, the immediate day prior to the start of downward trend in platelet count (from 230,000/uL to nadir of 101,000/uL on hospital day 44). Thus, tobramycin was also stopped. Given intermediate concern for heparin-induced thrombocytopenia (HIT) based on 4T's score, fondaparinux was also started for DVT prophylaxis.[1] The platelet count was essentially unchanged the following day but then began to rise on hospital day 46. In regards to HIT, screening heparin associated platelet antibody (HAPA) returned as weakly positive with absorbance of 0.520, but confirmatory serotonin release assay (SRA) was negative. PPI and heparin were resumed without effect on platelets.

***Discussion***

Thrombocytopenia is defined as a platelet count less than 150,000/uL and is rarely noticed until the platelet count decreases to around 100,000/uL as it was in this case.[2] It is a very common diagnosis encountered in hospital-based medicine with frequent, if not daily, blood work obtained for many patients. The differential diagnosis of thrombocytopenia is long and varied, and it ranges from benign to life threatening, making recognition and determination of the underlying etiology very important.

Adverse drug effects are common, and drug-induced thrombocytopenia should always be considered in hospitalized patients with thrombocytopenia. In the case above, review of the MAR revealed several medications well-known to be associated with thrombocytopenia including pantoprazole, cefepime, and heparin. Heparin, in particular, requires special consideration as failure to stop it in setting of heparin-induced thrombocytopenia (HIT) can lead to severe morbidity and/or mortality from acute thrombosis. However, the patient had been receiving heparin since at least hospital day 1 (as well as receiving enoxaparin at outside facility just prior to transfer) and pantoprazole since hospital day 2, arguing against these as the underlying cause; additionally, cefepime had already been stopped. A close review of the MAR for new medications suggested inhaled tobramycin as a possible underlying etiology. Although unable to definitely prove this, after stopping the inhaled tobramycin, the patient's platelets increased.

In review of the literature, tobramycin is infrequently associated with thrombocytopenia. The drug insert for injected tobramycin lists thrombocytopenia under 'other adverse reactions possibly related to tobramycin.'[3] However, no such adverse reaction is listed on the drug insert for inhaled tobramycin.[4] Commonly used and easy to navigate clinical resources such as Micromedex and Lexicomp (which UpToDate uses for drug information) likewise list thrombocytopenia as a possible adverse effect of injection tobramycin, but not for inhaled tobramycin.[5,6] This case suggests some amount of the inhaled medication was absorbed leading to systemic affects.

***Conclusion***

Thrombocytopenia is often missed in clinical practice until the platelet count decreases significantly to around 100,000/uL. When diagnosing thrombocytopenia, a review of recent medication history and temporal relationship to platelet decrease should always be done as adverse medication effects are common, including drug-induced thrombocytopenia. Although uncommon even with injection tobramycin, given

the temporal relationship between initiation of inhaled tobramycin and platelet decrease, inhaled tobramycin appears to be the culprit medication in this case and highlights how reviewing the medical administration record can help lead to a diagnosis.

## REFERENCES


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