

Ask a Pathologist

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Question:

My patient had a normal platelet count on admission but became acutely thrombocytopenic several days later. How do I distinguish heparin-induced thrombocytopenia (HIT) from drug-induced thrombocytopenia caused by other medications?

Answer:

Several different drugs may cause thrombocytopenia. Heparin-induced thrombocytopenia (HIT), most often associated with unfractionated heparin, occurs when the antigen-binding fragment (Fab) of pathogenic IgG binds to a complex of heparin and platelet factor 4 (PF4). The crystallizable region (Fc) of the antibody then binds to platelet FcγIIa receptors, resulting in platelet activation and a hypercoagulable state. The thrombocytopenia in HIT is usually mild to moderate in severity, with a mean platelet nadir of around $60 \times 10^9/L$. Due to the risk of thrombosis, platelet transfusion should be avoided.

Other drugs may also induce immunologic thrombocytopenia. Besides heparin, the two drugs most commonly implicated are quinine (in the outpatient setting) and vancomycin (in the inpatient setting). For both of these drugs, the Fab portion of the antibody binds to platelet surface glycoproteins, while the Fc portion binds to receptors on phagocytic cells. This results in accelerated platelet clearance by the reticuloendothelial system and a severe thrombocytopenia, usually with a platelet nadir of less than $20 \times 10^9/L$ or a drop in platelets beyond 50% of original platelet count. Drug-induced thrombocytopenia from these medications is associated with an increased risk of bleeding, and patients may be refractory to platelet transfusion as the transfused platelets are also quickly destroyed by antibodies.

In severely ill hospitalized patients, heparin and vancomycin may be simultaneously administered, making it difficult to determine if the thrombocytopenia is caused by underlying disease or by one of the medications. A sudden severe thrombocytopenia, particularly if the platelet count falls below $20 \times 10^9/L$, should raise suspicion that a non-heparin drug such as vancomycin may be responsible. Vancomycin-induced thrombocytopenia should be suspected in patients who have initiated treatment within the past 6-8 days. If drug-induced thrombocytopenia from vancomycin or another drug is suspected, the drug should be discontinued immediately. The platelet count will usually return to baseline within a few days of stopping the drug.

If you suspect drug-induced thrombocytopenia from a non-heparin medication, contact your pathologist, who can assist with ordering the appropriate reference lab testing to confirm the diagnosis.

References for evaluating a patient with possible drug-induced thrombocytopenia can be accessed using <http://www.ouhsc.edu/platelets/ditp.html>, which is maintained by the University of Oklahoma and provides a comprehensive survey of drugs that have been reported to cause drug-induced thrombocytopenia.

Suggested references:

- Hoffman R, Benz EJ, Silberstein LE, et al. *Hematology: Basic Principles and Practice*. 6th Edition (2013).
- Greinacher A. Heparin-Induced Thrombocytopenia. *N Engl J Med* 2015; 373:252-261.
- Von Drygalski A, Curtis BR, Bougie DW, et al. Vancomycin-Induced Immune Thrombocytopenia. *N Engl J Med* 2007; 356:904-910.