Antibiotic-Induced Thrombocytopenia in the ICU: Case Report of a Diagnostic Challenge

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Thrombocytopenia is the commonest coagulation problem in ICU patients and is an independent predictor of death among critically ill patients. Thrombocytopenia is generally defined as a platelet count below 100,000/μl. The causation is frequently multifactorial and driven by six distinct mechanisms: increased consumption, hemodilution, decreased production, sequestration, pseudo-thrombocytopenia, and increased destruction. The differential diagnosis of acute thrombocytopenia in an ICU patient is extensive. After eliminating the more common etiologies, drug-induced thrombocytopenia (DITP) should be considered as an often overlooked yet easily reversible cause of thrombocytopenia. Due to a lack of distinguishing clinical features and numerous other possible etiologies, diagnosis is often complex, requiring a multistep approach. We discuss the extensive workup of DITP in the context of this unusual case presentation.

Patient Presentation

This is a 68-year-old male with PMH of severe COPD, atrial fibrillation, and lung CA s/p exacerbation, BP stable, and lung CA s/p exacerbation, BP stable. He was admitted on four separate occasions to our institution over a two-year period with COPD exacerbation and suspected pneumonia. On each admission his presentation, workup, and treatment were similar. Repeatedly he was empirically treated with vanco (vancomycin) and tazobactam (pip-tazo) as an initial course, and in each circumstance he developed thrombocytopenia in a strikingly homogenous temporal sequence. In every instance, platelets recovered only after the cessation of pip-tazo. On the first admission, platelets continued to fall after vanco was stopped and pip-tazo was continued. On the final admission his platelets rose after cessation of pip-tazo while vanco was continued, strongly indicating that pip-tazo was the offending agent. Common and rare causes of thrombocytopenia were absent and anemia and neutropenia did not develop. Admission, during which he did not receive these antibiotics were not associated with thrombocytopenia.

Admission

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<tr>
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<tbody>
<tr>
<td>Admission Notes</td>
<td>C5AD2B, cultures negative, BP stable</td>
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<td>C5AD2B, cultures negative, BP stable</td>
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<tr>
<td>Initial Platelet Count</td>
<td>165</td>
<td>293</td>
<td>168</td>
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<tr>
<td>Platelet/leuk (3 drops from INR)</td>
<td>45 (72%)</td>
<td>118 (52%)</td>
<td>47 (75%)</td>
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<td>Days to read-following vanco and pip-tazo initial administration</td>
<td>0</td>
<td>7</td>
<td>5</td>
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<tr>
<td>Days to read-following vanco and pip-tazo initial administration</td>
<td>1</td>
<td>4</td>
<td>1</td>
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Thrombocytopenia resolved and remained normalized while heparin products were administered, while vanco testing was negative on several tests; thus eliminating heparin as the causative factor. Platelet count remained normal after discontinuation of suspected drug despite the resumption or continuation of other drugs. Thrombocytopenia improved after discontinuation of pip-tazo while vanco continued. On the 12/11/11 admission, platelet counts declined after vanco was stopped and only recovered when pip-tazo was discontinued.

Criteria for evaluating a causal relationship between a drug and thrombocytopenia:

1. Suspected drug administration preceded thrombocytopenia. Complete and sustained resolution of thrombocytopenia after suspected drug discontinued.
2. Platelet count remained normal after discontinuation of suspected drug despite the resumption or continuation of other drugs.
3. Criteria 1 and 2.
4. Re-exposure to the suspected drug was followed by thrombocytopenia.

Criteria 1. Vanc, pip-tazo, and heparin products all preceded thrombocytopenia.

Criteria 2. An extensive list of home medications was screened. Multiple home medications were continued throughout the admissions shown in figure 1 during the normalization of platelet count, thus exonerating them as the cause. Thrombocytopenia resolved and remained normalized while heparin products were administered, while vanco testing was negative on several tests; thus eliminating heparin as the causative factor.

Criteria 3. Any alternate etiology of thrombocytopenia would need to fit the time course of the acute drop in platelet counts shown in figure 1. Thus, many chronic and idiopathic causes of thrombocytopenia were eliminated from consideration. A potential drug etiology remained that was excluded by logic and investigation.

Potential Etiology:

- Sepsis
- Disseminated Intravascular Coagulation
- Thrombotic Thrombocytopenia Purpura
- Heparin-induced thrombocytopenia
- Dilution by fluid resuscitation
- Dilution by transfusions
- Sepsis on admission, no transfusions
- Multiple HIT tests negative on different admissions, eliminated HIT type

Differential diagnosis of acute thrombocytopenia in an ICU patient is extensive. After eliminating the more common causes, the more frequent etiology was drug-induced thrombocytopenia. Any potential etiologies remained that were excluded by logic and investigation.

Discussion

This case report of thrombocytopenia in a critically ill patient is an important addition to the current literature on DITP. The patient demonstrated a stepwise approach to the evaluation and management of DITP, which includes a thorough history and physical examination, laboratory testing, and if necessary, drug elimination and re-introduction. The patient’s presentation and course were consistent with the criteria for DITP, which include a suspected drug history, normalization of platelet counts after discontinuation of the suspected drug, and resolution of symptoms after re-administration of the drug.

References


Abbreviations

BP: Blood Pressure
COPD: Chronic Obstructive Pulmonary Disease
DITP: Drug-induced Thrombocytopenia
HIT: Heparin-induced Thrombocytopenia