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

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

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**Discussion**

"...when you have eliminated the impossible, whatever remains, however improbable, must be the truth." Sherlock Holmes

After extensive investigation, the evidence points to DTP secondary to pip-tazo. DTP related to pip-tazo is exceedingly uncommon, appearing in only 3 case reports and in 13 patients specifically tested for antibodies at Blood Center of WI (BCW) over 10 years. Furthermore, in the absence of a positive drug-induced anti-platelet antibody test it is even more rare. Despite the lack of seroconversion-confidence, a diagnosis of pip-tazo induced DITP can be made based on published clinical criteria. Our patient’s episodes of thrombocytopenia met all four of the criteria outlined by Rousan et al. (figure 2) which constitutes "definitive" probability for drug induced thrombocytopenia. Further support is seen with the utilization of an adverse drug reaction (ADR) probability scale. This case scored 11 out of a possible 13 points, where a score of n is equated with a “definitive” probability that his thrombocytopenia is due to an ADR.

A blood sample failed to show pip-tazo or vanco related anti-platelet antibodies when tested by immunofluorescent flow cytometry at BCW. However, there are several limitations to this test. These assays have high specificity but moderate sensitivity since a metabolite of the drug formed in vivo may be responsible for DITP and not the primary drug itself. Piperacillin is known to form metabolites which are normally not tested.

No change in coagulation values on any admission, suspicion clinically low sepsis was either very mild or not present. No change in coagulation values on any admission, suspicion clinically low sepsis was either very mild or not present.

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**References**


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**Table 1. Pattern of Thrombocytopenia across four admissions for similar clinical presentation and therapy.**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Admission Notes</td>
<td>CBOC exacerbation, PTTPa, cultures negative, BP stable</td>
<td>CBOC exacerbation, PTTPa, cultures negative, BP stable</td>
<td>CBOC exacerbation, PTTPa, cultures negative, BP stable</td>
<td>CBOC exacerbation, PTTPa, cultures negative, BP stable</td>
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</tbody>
</table>

**Figure 1. Thrombocytopenia & Antibiotics on Multiple Admissions**

- **Figure 2. Method of Investigation**

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**Table 2. Method of Investigation**

<table>
<thead>
<tr>
<th>Admission</th>
<th>Initial Platelet Count</th>
<th>Days to nadir following vanco administration</th>
<th>Days to recovery to baseline platelet count</th>
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</thead>
<tbody>
<tr>
<td>12/11/11</td>
<td>150</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>3/6/12</td>
<td>230</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>3/28/10</td>
<td>190</td>
<td>5</td>
<td>15</td>
</tr>
</tbody>
</table>

**Table 3. Patient Presentation**

- This is a 66 year old male with PMH of severe COPD, chronic cough, and lung CA slip upper lobe. 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. He was empirically treated with vancomycin (vanco) and piperacillin-tazobactam (pip-tazo) as an initial course, and in each circumstance he developed thrombocytopenia in a strikingly homogenous temporal sequence. In every incident, platelets recovered only after the cessation of pip-tazo. On the third admission platelets continued 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.

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**Figure 3. 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. Alternatives etiologies of thrombocytopenia were excluded.
4. Re-exposure to the suspected drug was followed by thrombocytopenia.

**Criteria**

- Vanco, pip-tazo, and heparin products all preceded thrombocytopenia.
- Thrombocytopenia resolved after the discontinuation of vanco and pip-tazo in 3 admissions; however, on the 3/6/12 admission the thrombocytopenia improved after discontinuation of pip-tazo while vanco continued. On the 12/11/11 admission platelets declined after vanco was stopped and only recovered when pip-tazo was discontinued.
- An extensive list of home medications was screened. Multiple home medications were continued throughout the admissions shown in figure 1 during the normalization of plateleted count, thus reexamining them as the cause. Thrombocytopenia resolved and remained normalized while heparin products were administered, while heparin testing was negative on several tests; thus eliminating heparin as the causative factor.

**Potential Etiology**

- Anti-platelet antibodies are known to have weak drug dependent interactions with normal platelets; however, there was no correlation shown between antibody strength measured by flow cytometry and the severity of thrombocytopenia.