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

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**Introduction**
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, remobilization, 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 multi-step approach. We discuss the extensive workup of DITP in the context of this unusual case presentation.

**Patient Presentation**
This is a 66-year-old male with PMH of severe COPD, atrial fibrillation, and lung CA s/p two year period with COPD exacerbation and suspected pneumonia. He was admitted on separate occasions to our ICU 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 vancomycin (vanco) and piperacillin-tazobactam (pip-tazo) as an initial course, and in each circumstance he developed thrombocytopenia in a strikingly homogeneous temporal sequence. In every incident, platelets recovered only after the cessation of pip-tazo. On the third 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 notes followed in which he did not receive these antibiotics were not associated with thrombocytopenia.

<table>
<thead>
<tr>
<th>Admission</th>
<th>Days to recovery to baseline platelet count</th>
<th>Days to readmit following vanco and pip-tazo initial administration</th>
<th>Days to readmit following vanco and pip-tazo readmit administration</th>
<th>Days to readmit following vanco and pip-tazo initial administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/28/10</td>
<td>25</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>4/17/11</td>
<td>190</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>12/11/11</td>
<td>109</td>
<td>47 (72%)</td>
<td>75 (78%)</td>
<td>103 (83%)</td>
</tr>
<tr>
<td>3/6/12</td>
<td>616</td>
<td>47 (72%)</td>
<td>75 (78%)</td>
<td>103 (83%)</td>
</tr>
</tbody>
</table>

**Potential Etiology**
- **Sepsis**
  - Failure to meet criteria for two admissions. May not be cause for one day on each of two admissions. Clinically unlikely to be the primary cause.
- **LMWH**
  - Consumption
- **HIT**
  - Absent or negative, BP negative, HIT IgG negative

**Criteria**
1. **Evidence of an ADR**
   - 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.

**Discussion**
After extensive investigation, the evidence points to DITP secondary to pip-tazo. DITP is exceedingly uncommon, accounting in very rare cases to reported case reports and in even rarer cases to those published in scientific literature. The lack of serological confirmation, 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 1) which constitute “definite” probability for drug induced etiology. Additional support is seen with the utilization of an adverse drug reaction (ADR) probability scale.

**References**