A Case of Thrombocytopenia

Ponlapat Rojnuckarin
A 85-yr-old man with left pleural effusion

Presented with dyspnea 3 m.
Dry cough, No fever
CXR: Pleural effusion Lt> Rt
Pleural Fluid: Cell 832/uL, M 86%
Protein 1.36/7.4 g/dL, LDH 94 U/L
Cytology: Negative for malignancy
AFB negative
Refer to KCMH
A 85-yr-old man with bleeding 2 weeks after pleural biopsy

KCMH: Try treat TB
Pleural biopsy as OPD case
3 days later: Dyspnea worsened
Hb dropped from 13.4 to 9.8 g/dL
Platelet count 229 x 10⁹/L
Pleural Tap: Hemothorax
ICD was inserted and removed

2 weeks after ICD bruises developed
Platelet 29 x 10⁹/L
<table>
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<th>15</th>
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2 weeks after ICD and 1 week after PRC
No fever, Skin Ecchymosis
Medication: IRZE and Imipenem
CBCL Hb 10.9 g/dL, MCV 83.1 FL, RDW 14.8%
W 7.03 x 10⁹/L, N 75%, L12.5%, M 8.4%, Eo 4%
Platelet 29 x 10⁹/L
Thrombocytopenia in hospitalized patients

- Thrombocytopenia in critically-ill patients: Sepsis, DIC, Dilutional, Catheter
- Drug-induced thrombocytopenia
- Heparin-induced thrombocytopenia
- Thrombotic Microangiopathy
- Post-transfusion purpura
- Underlying diseases: Immune thrombocytopenia or Marrow disease

DIC profile: PTT, PT, TT, Fibrinogen
Complete drug history including heparin lock
Blood smear, Reticulocyte, LDH, Cr
Drug-induced Thrombocytopenia (DIT)

Clinical presentations

• Unexplained acute thrombocytopenia

• After \textbf{5-14 days} of drug exposure, but within 24-48 hours of exposure to a sensitized drug

• Bleeding usually improves within 48 hours, and a PLT count is restored to normal within 1 week

• Occasionally, thrombocytopenia persists for 1-2 weeks
# Drug-induced thrombocytopenia

<table>
<thead>
<tr>
<th>Drug category</th>
<th>Individual drugs</th>
<th>Number of identified cases</th>
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</table>
| Antibiotics            | Sulfamethoxazole, vancomycin ceftriaxone, levofloxacin, piperacillin, rifampin, trimethoprim | >15  
                           |                                                                                  | 4-15                       |
| Cinchona alkaloid      | Quinine, quinidine                                                              | > 15                       |
| GP IIb/IIIa inhibitors | Abciximab, eptifibatide, tirofiban                                               | >15                       |
| Diuretic               | Furosemide                                                                      | 4-15                       |
| Cardiac                | Amiodarone                                                                      | 4-15                       |
| Anticonvulsants        | Carbamazepine, Phenytoin                                                        | >15  
                           |                                                                                  | 4-15                       |
| NSAIDs                 | Naproxen                                                                        | 4-15                       |

J Thromb Haemost 2009; 7: 911
DIT: treatment

- Discontinue all suspected drugs
- A role of IVIG and corticosteroid is uncertain
- Platelet transfusions often fail to elevate the PLT count during acute phase of thrombocytopenia
- Sensitivity to drugs that cause immune thrombocytopenia is usually permanent; patients should therefore be warned to avoid re-exposure.
Heparin-induced thrombocytopenia (HIT)

Heparin and Low molecular weight heparin can bind PF4.

Platelet activation
Thrombosis
Thrombocytopenia
Heparin-induced thrombocytopenia (HIT)

- Standard or low molecular weight heparin
- 5-10 days after heparin
  (Shorter if previously exposed)
- Median nadir 55 x10^9/L
  (90% between 15–150 x 10^9/L)
- No bleeding
- THROMBOSIS (May be fatal)

Warkentin, Chest 2005, BJH 2004
HIT management

• Stop heparin immediately
• Send HIT antibody screening test
• No warfarin, Reverse warfarin
• No platelet transfusion
• Pentasaccharide or DOACs?
• Negative HIT screening → HIT unlikely
• Positive HIT screening → Confirmatory test

Warkentin, Chest 2005, BJH 2004
Drug history review

• INH + Rifampicin + Ethambutol 27 days
• PZA 7 days
• Meropenem 4 days

• No heparin and no history of heparin lock

Stop all medications
Other work-up

• Blood smear: Thrombocytopenia, No MAHA, No abnormal cells
• LDH 258 U/L (125-220) Reticulocyte 1.2% Cr Normal
• Anti-HIV and Anti-HCV negative
• ANA 1: 2560 (Fine speckle), Anti-ds-DNA > 800 U/ml (< 100), RF 29.8 (< 15)
• Immunofixation: polyclonal gammopathy
• Bone marrow: Normal
Platelet counts of the patient

- Hemothorax
- LPRC 2 U
- SDP 1U
- LPPC 1 U
- SDP 1U
Onset/Severity of thrombocytopenia

Dx Male SLE
With Pleural effusion
Autoimmune Thrombocytopenia is possible,
But clinical course is NOT compatible.

Greinacher A, Warkentin TE. Hemostasis and Thrombosis 2013
Post-transfusion purpura (PTP)

- 1: 330,000 transfusion
- Alloantibody to platelet-specific antigen or Human Platelet Antigen (HPA)
- 21 HPA systems: HPA-1, HPA-2, etc
- Biallelic gene: HPA-1a is more common than HPA-1b in Western population
- Patients with uncommon alleles e.g. Homozygous HPA-1b (2.5%) may produce antibody against transfused HPA-1a platelets and also destroy their own platelets.
## Human Platelet Antigens (HPA)

<table>
<thead>
<tr>
<th></th>
<th>Synonyms</th>
<th>Glycoprotein</th>
<th>Sequences</th>
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<tbody>
<tr>
<td>HPA-1a</td>
<td>Pl\textsuperscript{A1}, Zw\textsuperscript{a}</td>
<td>GpI\text{ll}a</td>
<td>Leu33</td>
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<td>Pl\textsuperscript{A2}, Zw\textsuperscript{b}</td>
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<td>HPA-2a</td>
<td>Ko\textsuperscript{b}, Sib\textsuperscript{b}</td>
<td>GpI\text{lb}\text{α}</td>
<td>Thr145</td>
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<td>GpI\text{ll}b</td>
<td>Ser 843</td>
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Post-transfusion purpura

- Previous pregnancy or transfusion
- Onset 5-12 d post PRC/WB transfusion (platelet contamination)
- Anti-HPA also destroys patient platelets despite antigen-negative
- Abrupt onset: \( \text{Nadir} < 20 \times 10^9/\text{L} \) within 12-24 h with bleeding
- 30% major bleeding, 10% death
- Recovery in 7-28 d

Murphy MF and Pamphilon DH. Practical Transfusion Medicine 2009
Post-transfusion purpura

Diagnosis
- Detection of alloantibody to HPA
  - Anti-HPA-1a most common in Caucasians
  - Thais are different
- HPA genotyping of the patients

Treatment
- Intravenous immunoglobulin
- Future transfusion: HPA-compatible

Murphy MF and Pamphilon DH. Practical Transfusion Medicine 2009
Platelet antibody tests in this patient

• Autoimmune thrombocytopenia is possible, but PTP is more likely by the clinical course

• Platelet Antibody Screening
  Positive for Anti-HLA and Anti-HPA

<table>
<thead>
<tr>
<th></th>
<th>HPA-1</th>
<th>HPA-3</th>
<th>HPA-4</th>
<th>GPIIb/IIa</th>
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<td>1b</td>
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</table>
Platelet counts of the patient

- Hemothorax
- LPRC 2 U
- LPPC 1 U
- SDP 1U
- IVIG

Dx PTP
Steroid can be avoided.
Post transfusion purpura (PTP)

Definition
- **Definitive**: Alloantibodies against HPA with thrombocytopenia AND decrease in platelets to < 20% of baseline.
- **Probable**: Alloantibodies against HPA with thrombocytopenia. AND platelets to levels 20-80% of baseline.

Imputability
- **Definite**: Occurs 5-12 days post-transfusion AND Patient has no other conditions to explain thrombocytopenia.
- **Probable**: Occurs < 5 or > 12 days post-transfusion OR There are other potential causes but transfusion is the most likely.
- **Possible**: Alternate explanations for thrombocytopenia are more likely, but transfusion cannot be ruled out.
Severity of Transfusion Reactions

• **Grade 1 (Non-severe)**
  • Symptomatic treatment

• **Grade 2 (Severe)**
  • Admission, Prolonged admission, Long-term organ dysfunction

• **Grade 3 (Life-threatening)**
  • Requirement of life-saving treatment e.g. Assisted ventilation, ICU admission

• **Grade 4 (Death)**
Take home messages

• Thrombocytopenia in hospitalized patients: Review medications, Time course, Nadir, Blood smear, DIC profile, TMA

• Always think of Transfusion Reactions (Hemolysis, Sepsis, Respiratory distress, Anaphylaxis, Severe thrombocytopenia) and report to Blood Bank for investigations

• Diagnosis of PTP is helpful for patient management: Acute phase and Future transfusion