Parsing Out Platelets
How I Approach Thrombocytopenia

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Disclosures

FINANCIAL DISCLOSURE

Grants/Research Support: None

Speaker bureau/Honoraria amounts: None

Consulting fees: None

Other: Roche Pharmaceuticals- Local Investigator
Objectives

1. Be aware of conditions commonly associated with thrombocytopenia in clinical medicine

2. Use an algorithm to guide investigation of a patient with thrombocytopenia

3. Be aware when urgent hematologic referral is indicated for a patient with thrombocytopenia
Dear Dr.

Please assess this 35 year old female with thrombocytopenia, incidentally noted on bloodwork. She is otherwise asymptomatic.

Results:

- WBC 6.0 x 10⁹/L, normal differential (4.5 -10)
- Hb 135 g/L, normal indices (120-160)
- Platelet 40 x 10⁹/L (130-400)
Definition

• Thrombocytopenia- platelet count that is less than normal

• Normal is 130 to 400 x 10e9/L

• Clinical definition is a platelet count of less than 100 x 10e9/L

• Treatment usually not indicated until platelet count is less than 30 x 10e9/L

• Very important that the blood film is examined to ensure it is true thrombocytopenia
Pseudothrombocytopenia

• Platelets are recorded as falsely low by the hematology analyzer

• Causes include:
  • EDTA-induced platelet aggregation
  • Platelet satellitism
  • Familial Macrothrombocytopenia
EDTA-Induced Platelet Aggregation

• Time-dependent

• *In vitro*

• Antibody crosslink
Platelet Satellitism

- Platelets adhere to WBC leaving the automated platelet count low
- Also the result of EDTA
Macrothrombocytopenia

- Most are familial
- Large platelets counted as red cells by the hematology analyzer
Causes of True Thrombocytopenia

- Decreased bone marrow production of platelets
- Sequestration of platelets
- Increased destruction of platelets
  - Immune
  - Non-immune
Decreased Bone Marrow Production

- Rare cause of isolated thrombocytopenia - alcohol

- Usually associated with leukopenia, anemia, and/or abnormal bone marrow pathology - pancytopenia algorithm

- Referral to hematology consideration of bone marrow examination
Increased Sequestration of Platelets

- Rare cause of isolated thrombocytopenia
- Usually associated with leukopenia (and normal hemoglobin)
- Causes are those of hypersplenism
  - Portal hypertension
  - Other causes of splenomegaly
- Need imaging of liver/spleen
Non-immune Destruction of Platelets

- Causes of microangiopathic hemolytic anemia
- TTP, HUS, DIC
- Urgent hematology consult
Immune Destruction of Platelets

- Primary
- Secondary
  - Autoimmune diseases
  - Lymphoproliferative Diseases
- Infections
  - HIV
  - Hepatitis B and C
  - EBV, CMV
Workup of Isolated Thrombocytopenia

- **History:** viral illness, autoimmune disease, LPD, bleeding

- **Medications:** amiodarone, beta lactams, carbamazipine, GpIIb/IIIa inhibitors, heparin, ibuprofin, mirtazepine, phenyoin, rifampin, quinidine, quinine, TMP/SMX, vancomycin - need to stop offending drugs

- **Physical Exam:** hepatosplenomegaly, lymphadenopathy, autoimmune disease, peteciae/bleeding
Workup of Isolated Thrombocytopenia

• If results do not make sense, repeat CBC first

• CBC, retic count, INR, direct antiglobulin test, ABO and Rh

• Review of peripheral blood smear

• Renal function, liver enzymes, (ANA/autoimmune panel)

• HIV, Hepatitis B and Hepatitis C serology (EBV, CMV)
Referral of Immune Thrombocytopenia

- Emergent referral if platelet count less than $30 \times 10^9/L$ and/or platelet count less than $50 \times 10^9/L$ with bleeding
- Urgent referral if platelet count between 30 and $50 \times 10^9/L$
- Routine referral if platelet count between 50 and $100 \times 10^9/L$
- Referral not required if platelet count greater than $100 \times 10^9/L$
Work-Up of THROMBOCYTOPENIA

Peripheral Blood Smear
Platelets $130 \times 10^9 / L$

Artificial thrombocytopenia
(Pseudothrombocytopenia)

Real thrombocytopenia

Pseudothrombocytopenia
(EDTA phenomenon)

Thrombocyte Satellitism

Familial Macrothrombocytopenia

Isolated thrombocytopenia

Direct Antiglobulin Test Negative

Direct Antiglobulin Test Positive

Evans Syndrome

Other Cells

Schistocytes

Leukopenia Normal Hb

Bone Marrow Infiltration

MAHA

Hypersplenism

Bone marrow examination

Immune thrombocytopenia

Drug induced

Congenital thrombocytopenia

Infections

Pregnancy (Gestational)

Alcohol

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Pathways are subject to clinical judgment and actual practice patterns may not always follow the proposed steps in this pathway.
Take Home Messages

• Peripheral blood film review rules out pseudothrombocytopenia and the presence of other abnormal cells

• Most cases of isolated thrombocytopenia are immune

• Need to think about medications as the cause but relatively few medications cause significant thrombocytopenia

• Urgent referral required if platelet count less than $30 \times 10^9/L$ and/or platelet count less than $50 \times 10^9/L$ with bleeding


Questions?

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2. Which of the following drugs is not likely to cause thrombocytopenia?
A. Quinine
B. Acetaminophen
C. Ibuprofen
D. Amiodarone
E. Heparin
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