GER-E-NEWS

URMC Division of Geriatrics & Aging March 2019

Thrombocytopenia in Older adults

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Background

- Thrombocytopenia (or low platelet count) is a common hematologic abnormality encountered in older adults
- Common causes of thrombocytopenia include (Table 1):
  - Immune-related [e.g. immune thrombocytopenia purpura (ITP)]
  - Drug-induced [e.g. heparin-induced thrombocytopenia (HIT)]
  - Bone marrow failure
  - Other: Infections (e.g. H. pylori, HIV, hepatitis), pseudothrombocytopenia (Figure 1), alcohol abuse, liver cirrhosis, blood transfusion, thrombotic thrombocytopenia purpura (TTP), and hemolytic-uremic syndrome (HUS), thyroid disease

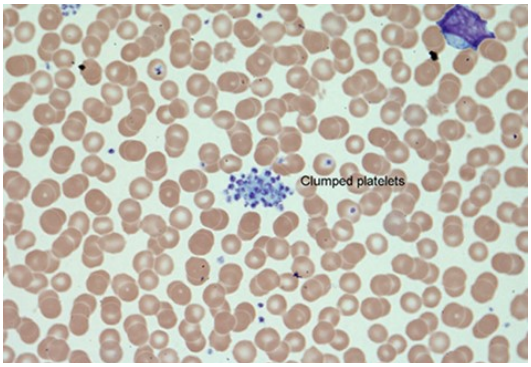

Figure 1: Peripheral smear showing clumped platelets (pseudothrombocytopenia — falsely low platelet count)

- Age-related changes in the organ and vasculature systems increase the risks of thrombocytopenia on hemostasis
- Factors that may enhance bleeding in older adults. These include:
  - Comorbidities
  - Medications
  - Loss of subcutaneous tissue
- Age-specific factors that may prevent bleeding in older adults include enhanced platelet aggregation and increased fibrinogen, factor V, and von Willebrand factor
- Thrombocytopenia is often multifactorial in older adults.

Table 1: Quick Facts on Thrombocytopenia

PATHOPHYSIOLOGY	
Immune Thrombocytopenia Purpura	**Drug-Induced**
• Increased platelet clearance in the reticulo-endothelial system of bone marrow, spleen, and/or liver • Inadequate platelet production due to megakaryocyte inhibition by IgG antibodies	• Impaired production (direct marrow toxicity or megakaryocyte-specific inhibition) • Increased platelet clearance (indirect immune clearance, antibody-specific immune clearance, miscellaneous immune -mediated) • Often suppress other cell lines

CAUSES	
Immune Thrombocytopenia Purpura	**Drug-Induced**
• Often idiopathic • Can be associated with underlying hematologic abnormalities (e.g. myelodysplastic syndrome, chronic lymphocytic leukemia)	See Table 2
INCIDENCE RATES	
Immune Thrombocytopenia Purpura	**Drug-Induced**
• 4.62 per 100,000 adults aged >60 years vs. 1.94 per 100,000 adults aged <60 years • Similar rates in women vs. men in the older population	• Unclear • Rates higher in hospitalized patients and those in the intensive care unit
DIAGNOSES	
Immune Thrombocytopenia Purpura	**Drug-Induced**
• Diagnosis of exclusion • Thrombocytopenia is often isolated (normal Hb, differential, and WBC)	• High index of suspicion (careful history) • See criteria (Table 3) • For heparin-induced thrombocytopenia, use the 4Ts criteria
WORK-UP	
Immune Thrombocytopenia Purpura	**Drug-Induced**
• Labs (to rule out other causes): CBC/diff, CMP, HIV, hepatitis panel, H.pylori, thyroid tests, peripheral smear (e.g. platelet clumping) • Bone marrow biopsy (optional; goal is to rule out primary hematologic malignancies)	• Labs (to rule out other causes): CBC/diff, CMP, HIV, hepatitis panel, H.pylori, thyroid tests, peripheral smear (e.g. platelet clumping) • Drug-dependent antibiotics (though not commonly tested and antibiotics cannot always be detected) • For heparin-induced thrombocytopenia, antibodies against heparin PF4 and/or serotonin assay
TREATMENT	
Immune Thrombocytopenia Purpura	**Drug-Induced**
• Treatment is usually initiated if platelet count is <20-30k/µL (risk vs. benefits of therapy) • Options: splenectomy, steroids, intravenous immunoglobulin (IVIG; beware of infusion reactions), and thrombopoietin receptor agonists (e.g. elthrombopag, romiplastim) • Platelet transfusion generally does not increase platelet count	• Drug discontinuation • Platelet transfusion if platelet count is <10k/µL or clinically significant bleeding • Steroids, IVIG, or plasma exchange (commonly used, benefit not proven) • For heparin-induced thrombocytopenia, initiate alternative anticoagulant (do not use low-molecular weight heparin)

Table 2: Mechanisms of and common medications associated with thrombocytopenia

Drug-induced Thrombocytopenia	Mechanism	Medications
Impaired production	Direct marrow toxicity	• Cytotoxic chemotherapy (e.g. paclitaxel) • Anticonvulsants (e.g. valproic acid)
	Megakaryocyte-specific inhibition	• Quinine • Bortezomib • Thiazide diuretics
Increased platelet clearance	Indirect immune clearance	Hapten-mediated (e.g. penicillin)
	Antibody-specific immune clearance	GP IIb/IIIa inhibitors (abciximab) Ranitidine, rifampin
	Miscellaneous immune-mediated	Heparin-induced thrombocytopenia

*Common drugs that cause thrombocytopenia (https://ouhsc.edu/platelets/ditp.html)

Table 3: Criteria used to evaluate causative relationships in drug-induced thrombocytopenia

Criterion	Description
1	Therapy with the candidate drug preceded thrombocytopenia.
2	Recovery from thrombocytopenia was complete and sustained after therapy with the drug was discontinued.
2	The candidate drug was the only drug used before the onset of thrombocytopenia or other drugs were continued or re-introduced after discontinuation of therapy with the candidate drug with a sustained normal platelet count.
3	Other causes for thrombocytopenia were excluded.
4	Re-exposure to the candidate drug resulted in recurrent thrombocytopenia.
Level of Evidence	
I	Definite: Criteria 1, 2, 3 and 4 are met.
II	Probable: Criteria 1, 2, and 3 are met.
III	Possible: Criterion 1 met.
IV	Unlikely: Criterion 1 not met.

The Bottom Line

When to refer to a hematology

- When platelet count is <50k/µL (or <100k/µL if you are uncomfortable)
- Worsening thrombocytopenia
- Suspected hematologic malignancies or bone marrow failure
- Bleeding complications
- Referral is generally indicated for ITP, TTP, HUS, and HIT

References

1. McMahon BJ, Kwaan HC. Thrombocytopenia in older adults. Seminars in thrombosis and hemostasis. 2014;40(6):682-687.
2. Aster RH, Curtis BR, McFarland JG, Bougie DW. Drug-induced immune thrombocytopenia: pathogenesis, diagnosis, and management. Journal of thrombosis and haemostasis : JTH. 2009;7(6):911-918.