

Ideopathic thrombocytopenic purpura

Immune thrombocytopenia (ITP) is a type of thrombocytopenia involving the formation of autoantibodies against platelets. ITP may be a primary disease or occur secondary to a known trigger (e.g., SLE, HIV, hepatitis C, medications). It is commonly seen in children as a self-limiting illness following a viral infection, and in adults as a chronic illness. Most patients are asymptomatic, however, patients may occasionally present with minor mucocutaneous bleeding (e.g., petechiae, purpura, epistaxis) or, rarely, with severe bleeding (e.g., gastrointestinal or intracranial hemorrhage). Treatment recommendations vary depending on the presence and severity of symptoms. First-line medical therapy consists of corticosteroids, IVIG, or anti-D immunoglobulin, and is indicated for patients with non-life-threatening symptoms affecting their quality-of-life, and for adults with little-to-no symptoms and platelet counts below $30,000/\text{mm}^3$. Children with little-to-no symptoms can typically be managed with observation alone regardless of platelet count. Second-line treatments (i.e., thrombopoietin receptor agonists, rituximab, splenectomy) may be required for refractory, persistent or chronic cases. Patients with life-threatening hemorrhage, neurological symptoms, or those requiring urgent surgical interventions should receive immediate combination medical therapy (i.e., corticosteroids plus IVIG) along with platelet transfusions and hemostatic control interventions when necessary.

Definition

Immune thrombocytopenia has previously been referred to as idiopathic thrombocytopenic purpura, however, this term is outdated. 💬

- **Primary immune thrombocytopenia:** an autoimmune disorder characterized by isolated thrombocytopenia ($< 100,000/\text{mm}^3$) with no known precipitating cause [2]
- **Secondary immune thrombocytopenia:** an autoimmune hematologic disorder causing isolated thrombocytopenia that is secondary to an identifiable trigger (see "Etiology").
- **Newly diagnosed ITP:** all cases within the first 3 months of diagnosis 💬 [2]
- **Persistent ITP:** ITP lasting 3–12 months
- **Chronic ITP:** ITP lasting > 12 months

Epidemiology

- Prevalence: up to ~ 10 per 100,000 💬 [3][4]
- ♀ $>$ ♂ [3]
- Children
 - Highest prevalence in children < 5 years of age [3]
 - Typically self-limiting after a viral infection; 80% of cases resolve within 12 months [5]
- Adults
 - Highest prevalence in individuals > 55 years of age [3]
 - 80% of patients develop chronic ITP. [5]
 - An incidental finding on a routine CBC in 25% of cases [6]

Pathophysiology

Antiplatelet antibodies (mostly IgG directed against, e.g., GpIIb/IIIa, GpIb/IX) bind to surface proteins on platelets → sequestration by spleen and liver → ↓ platelet count → bone marrow megakaryocytes and platelet production increase in response (in most cases) 💬 [9]

Etiology

- Primary ITP: idiopathic (most common) [7]
- Secondary ITP associated with:
 - Autoimmune disorders: **SLE**, antiphospholipid syndrome
 - Malignancy: lymphoma, leukemia (particularly CLL)
 - Infection: **HIV, HCV**
 - Drugs: e.g., quinine, beta-lactam antibiotics, carbamazepine, heparin, vaccines, linezolid, sulfonamides, vancomycin, TMP-SMX, antiepileptics [8]

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Definition: Purpura characterized by:

- 1- Shortened platelets survival (^{51}Cr labeled platelets life span = few minutes to 1-4 hrs)
- 2- Due to antiplatelet antibodies .
- 3- Thrombocytopenia ($< 100.000 /\text{mm}^3$).
- 4- Increased megakaryocytes in bone marrow.
- 5- Absence of other identifiable thrombocytopenic disorders (diagnosis of exclusion).

1. IDIOPATHIC THROMBOCYTOPENIC PURPURA

- ✓ most common cause of acute onset of thrombocytopenia in an otherwise well child

ETIOLOGY

- ✓ 1-4 wk after exposure to a common viral infection, an autoantibody directed against the platelet surface develops → distracted in spleen (50-65%)
- ✓ Most common infectious viruses described in association with ITP= Epstein-Barr virus
- ✓ Autoimmune thrombocytopenia may be an initial manifestation of SLE, HIV infection, or rarely, lymphoma.
- ✓ Approximately 20% of patients who present with acute ITP have persistent thrombocytopenia for **>6 mo** and are said to have chronic ITP (**THINK OF:** SLE, HIV, type 2B and platelet-type von Willebrand disease, X-linked thrombocytopenia, WAS)

CLINICAL MANIFESTATIONS

- ✓ classic presentation of ITP is that of a previously healthy 1-4 yr old child who has sudden onset of generalized petechiae and purpura.
- ✓ Often there is bleeding from the gums and mucous membranes
- ✓ Splenomegaly, lymphadenopathy or pallor are rare.

Clinical picture

I- **Bleeding** → usually spontaneous but may follow minor trauma

- Purpura.
- External bleeding e.g. epistaxis, oral bleeding, ...
- Rarely; internal bleeding e.g. intra cranial hemorrhage.

II- **No significant organomegaly:** Tip of spleen is palpable in $< 10\%$.

III- **No pallor** except with significant bleeding or with Evans syndrome

Outcome

- ☆ Spontaneous recovery occur in 70- 80% of acute ITP over 6 months.
- ☆ 10-20% go onto **chronic ITP** :
 - Defined as persistent thrombocytopenia for more than 6 months.
 - Incidence is higher in:
 - Older females children & adolescents.
 - May be a manifestation of a systemic illness as SLE or chronic HIV.

LABORATORY FINDINGS

- ✓ Severe thrombocytopenia (platelet count $<20 \times 10^9/L$) is common
- ✓ platelet size is normal or increased
- ✓ hemoglobin value, white blood cell (WBC) count, and differential count should be normal.
- ✓ Hemoglobin may be decreased if there have been profuse nosebleeds or menorrhagia.
- ✓ Bone marrow examination is normal with characteristically normal or increased numbers of megakaryocytes (do if atypical presentation- after 2 weeks of steroids).

Investigations

- ITP is still clinical diagnosis: thrombocytopenia in well appearing child with normal CBC(Platelets antibodies tests are still unreliable to confirm or exclude diagnosis)
- i- Bleeding time: - Prolonged.
- ii- CBC :
 - Platelet count $\rightarrow$ always $< 100.000 / mm^3$.
 - Normal WBCs. & RBCs.
- iii- BM. ex.:
 - Megakaryocytes hyperplasia
 - Normal myeloid & erythroid cells (exclude aplasia & leukemia).

Treatment

1. Observation:

- For asymptomatic case without bleeding with platelet count $>20.000/mm^3$.
- Avoid trauma, aspirin, contact sports.

2. Steroids:

- | | |
|--------------------|--|
| <u>Value</u> | - $\downarrow$ Platelet antibodies production.
- $\downarrow$ Phagocytosis of antibody coated platelets |
| <u>Indications</u> | - Bleeding orifices
- Count $< 20.000/mm^3$
- Extensive eruption.
- Persistent > 2 weeks |
| <u>Dose</u> | - 2 mg/kg/day for 3 weeks course with gradual tapering . |

3. Intravenous Immunoglobulin:

- | | |
|--------------------|---|
| <u>Value</u> | - Block phagocytes Fc receptors $\rightarrow$ protect platelets from destruction |
| <u>Indications</u> | - Alternative to steroids (can be used together)
- Used in acute and chronic ITP |
| <u>Dose</u> | - 0.8 – 1 gm/kg for 1-2 days |

4. Intravenous Anti D (Win Rho):

- | | |
|--------------------|---|
| <u>Value</u> | - Coat RBCs $\rightarrow$ block phagocytes Fc receptors $\rightarrow$ platelet escape destruction with transient mild hemolysis |
| <u>Indications</u> | - Chronic ITP
(Patient must be Rh positive , unsplenctomized with Hb % > 9 gm/dl) |
| <u>Dose</u> | - 50 μ gm/kg per dose |

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5. Splenectomy:

Indications

- Acute ITP with life threatening bleeding unresponsive to platelet transfusion, steroids and intravenous immunoglobulin
- Chronic ITP in older patient ; uncontrolled medically

6. Other therapies for resistant cases:

- 1. Rituximab:** - Nature: Anti CD20 monoclonal antibody
- Role : Eleminate autoreactive B cells
- Dose : 375 mg/kg/m² IV weekly for 4 weeks

2. Cytotoxic drugs

3. Plasmapheresis

Treatment of life threatening bleeding episode:

- 1- Adequate resuscitation(ABC; including blood transfusion if needed)
- 2- Platelet transfusion (especially if platelets count $< 20.000/mm^3$).
- 3- I.V. methylprednisolone.
- 4- I.V. immunoglobulin.
- 5- Emergency splenectomy.

TREATMENT

- ✓ No therapy other than education and counseling of the family and patient for patients with minimal, mild, and moderate symptoms (**80% spontaneous resolution**)
- ✓ TREATMENT WITH:
 1. IV-IG (1g/kg/d) - 1-2 days
 2. iv ANTI-D for RH+(50-75ug/kg/dose)
 3. Prednisone (2-4mg/kg/day) for 2 WEEK
- ALL INCREASE PLT COUNTS WITHIN 2 DAYS BUT IN PRESENCE OF CONTINUOUS DISTRUCTION.
- ✓ platelet transfusion in ITP is usually contraindicated unless life-threatening bleeding is present
- ✓ The role of splenectomy in ITP should be reserved for 1 of 2 circumstances.
 1. The older child (≥ 4 yr) with severe ITP that has lasted >1 yr (chronic ITP)
 2. symptoms are not easily controlled with therapy
- ✓ Splenectomy is successful in inducing complete remission in 64-88% of children with chronic ITP

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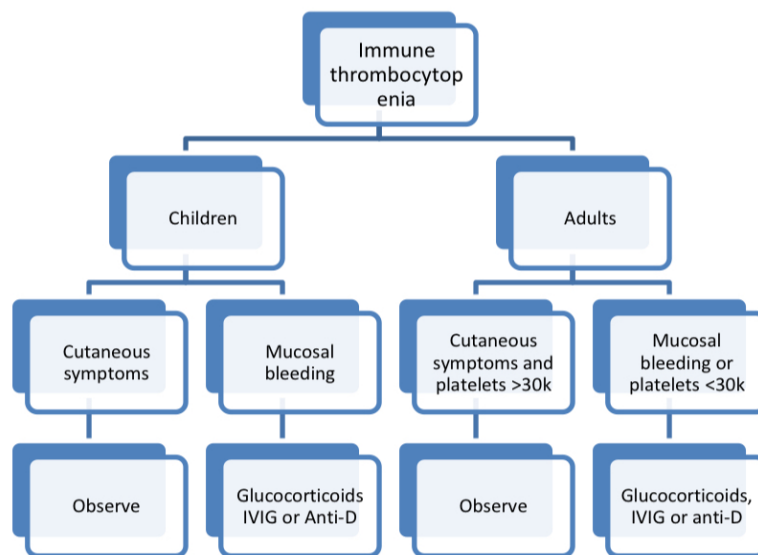
To Sum up:

IMMUNE THROMBOCYTOPENIA

1. Preceded by viral infection
2. Presents with
 - a. Petechiae
 - b. Purpura
 - c. Mucosal bleeding
 - i. Epistaxis
 - ii. Hematuria
 - iii. GIT bleeding
3. Most cases resolve within 3 months
 - a. Adolescents with mild initial presentation and NO PRECEDING viral trigger are more likely to develop chronic ITP
4. Labs
 - a. Isolated thrombocytopenia
 - i. Normal to large platelets present on peripheral smear due to increased platelet turnover
5. Evaluation
 - a. Chronic ITP
 - i. Bone marrow examination
 - ii. Blood tests for:
 1. Infection (eg, HIV, Hep C, CMV)
 2. Autoimmune disorder (eg, SLE, thyroid disease)
 - b. If these evaluations are negative, manage chronic ITP along the same course as acute ITP

Immune thrombocytopenia	
Etiology	• Platelet autoantibodies • Preceding viral infection
Clinical findings	• Petechiae, ecchymosis • Mucosal bleeding (eg, epistaxis, hematuria)
Laboratory findings	• Isolated thrombocytopenia $<100,000/\text{mm}^3$ • Few platelets (size normal to large) on peripheral smear
Treatment	• Children ◦ Observe if cutaneous symptoms only ◦ Glucocorticoids, IVIG, or anti-D if bleeding • Adults ◦ Observation if cutaneous symptoms AND platelets $\geq 30,000/\text{mm}^3$ ◦ Glucocorticoids, IVIG, or anti-D if bleeding or platelets $<30,000/\text{mm}^3$

6. Management:



Note: give anti-D if Rh-positive and Coombs-negative

7. Second-line treatments (splenectomy, rituximab and thrombopoietin receptor agonists) are reserved for
 - a. Catastrophic bleeding
 - b. Chronic ITP refractory to intravenous immunoglobulin and glucocorticoids
8. Platelet transfusion is considered in very severe cases of ITP (e.g, intracranial bleeding) but it is typically avoided as it can lead to further platelet destruction
 - a. Transfusion is the treatment for congenital platelet abnormalities which present with very large platelets on smear

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