

IMMUNE THROMBOCYTOPENIC PURPURA

Definition

Isolated thrombocytopenia with otherwise normal blood counts in a patient with no clinically apparent alternate cause thrombocytopenia (e.g. HIV infection, systemic lupus erythematosus, lymphoproliferative disorders, alloimmune thrombocytopenia, and congenital or hereditary thrombocytopenia).

Pathogenesis

- increased platelet destruction, likely due to autoantibodies to platelet membrane antigens
- in children, ITP is an acute, self-limiting disorder that resolves spontaneously

Clinical Manifestation

- onset is usually acute
- cutaneous bleeding
 - especially over the legs
- mucosal bleeding
 - palatal petechiae, epistaxis, haematuria, menorrhagia
 - gastrointestinal bleeding, intracranial haemorrhage
- absence of hepatosplenomegaly or lymphadenopathy
- thrombocytopenia, with normal haemoglobin and white cell count
- peripheral blood picture is normal apart from reduced, larger platelets
- prolonged bleeding time

Table 5. Other causes of thrombocytopenia

Neonatal alloimmune/ isoimmune thrombocytopenia if < 6 months old
Sepsis and infections including HIV infection
Drug-induced thrombocytopenia
Haematological malignancy <ul style="list-style-type: none">e.g. acute leukaemias
Congenital marrow failure syndromes <ul style="list-style-type: none">e.g. Fanconi anaemia, thrombocytopenia with absent radius
Autoimmune disorders <ul style="list-style-type: none">e.g. Systemic lupus erythematosus, Evan syndrome
Primary immunodeficiency syndromes <ul style="list-style-type: none">e.g. Wiskott-Aldrich syndrome

Diagnosis

- diagnosis is based on history, physical examination, blood counts, and examination of the peripheral blood smear, which should exclude other causes of thrombocytopenia

Threshold for performing a *bone marrow aspiration* is low and is indicated if:

- atypical features:
 - organomegaly, significant lymphadenopathy, abnormal blood counts
 - suspicious peripheral blood picture.
- before starting steroid therapy
 - (to avoid partially inducing an undiagnosed acute leukaemia)
- failure to respond to Immunoglobulin therapy
- persistent thrombocytopenia > 6 months
- thrombocytopenia recurs after initial response to treatment

Other tests may be indicated when there is atypical presentation

- Antinuclear factor
- Coomb's test
- ultrasound of abdomen
- HIV testing

Treatment

Not all children with diagnosis of acute ITP need hospitalization.

Hospitalization is indicated if:

- severe life-threatening bleeding (e.g. ICH) regardless of platelet count
- platelet count $< 20,000/\text{mm}^3$ with evidence of bleeding
- platelet count $< 20,000/\text{mm}^3$ without bleeding but inaccessible to health care
- parents request for admission

Most children remit spontaneously: 70% achieve a platelet count $> 50,000/\text{mm}^3$ by the end of the 3rd week.

Careful observation and monitoring of platelet count, without specific treatment, is appropriate for patients with:

- platelet count $> 20,000/\text{mm}^3$ without bleeding
- platelet count $> 30,000/\text{mm}^3$ with only cutaneous purpura

Treatment is indicated if there is:

- life threatening bleeding episode (e.g. ICH) regardless of platelet count
- platelet count $< 20,000/\text{mm}^3$ with mucosal bleeding
- platelet count $< 10,000$ with any bleeding

Choice of treatment include:

- oral prednisolone 4 mg/kg/day for 7 days, then taper and discontinue at 21 days
- IV Methylprednisolone 30 mg/kg/day for 3 days
- IV Immunoglobulin (IVIg) 0.8 g/kg/dose for 1 day or 250 mg/kg for 2 days.
- IV Anti-Rh(D) immunoglobulin (50 – 75 $\mu\text{g}/\text{kg}$) in Rhesus positive patients

Notes regarding treatment:

- *all are effective in raising platelet count much quicker compared to no treatment, with IVIG being the most effective. However there is no evidence that these treatments reduce bleeding complications or mortality or influence progression to chronic ITP.*
- *side effects of IVIG are common (15 – 75%): fever, flushing, headache, nausea, aseptic meningitis and transmission of Hepatitis C (older preparations).*
- *steroids should not be continued if there is no response or if there is a rapid relapse after withdrawal. The long-term side-effects in a growing child outweigh the benefits of either frequent high-dose pulses or titration of platelet count against a regular lower steroid dose.*
- *treatment should not be directed at increasing the platelet count above a preset level but rather on the clinical status of the patient.*

Intracranial Haemorrhage

- the most feared complication of ITP with 50% mortality rate
- cumulative risk of ICH in newly diagnosed ITP child within 1st year is $< 1\%$
- risk of ICH highest with platelet count $< 20,000/\text{mm}^3$, history of head trauma,
- aspirin use and presence of cerebral arteriovenous malformation.
- 50% of all ICH occurs after 1 month of presentation, 30% after 6 months
- early treatment with steroid or IVIG may not prevent late onset ICH

Emergency treatment of ITP with ICH (alone or in combination):

- IVIG 1 g/kg/dose/day for 2 days
- IV anti-Rh(D) 50 – 75 microgram/kg
- high dose IV Methylprednisolone 30 mg/kg/day for 3 days

- platelet transfusion
- neurosurgical intervention, if indicated.
- splenectomy if other modalities fail and if craniotomy required.

CHRONIC ITP

- persistent thrombocytopenia after 6 months of onset (occurs in 20%)
- wide spectrum of manifestations: mild asymptomatic low platelet counts to
- intermittent relapsing symptomatic thrombocytopenia to the rare stubborn and persistent symptomatic and haemorrhagic disease

Management

- every opportunity should be given for disease to remit spontaneously as the
- majority will do so if given enough time
- revisit diagnosis to exclude other causes of thrombocytopenia (Immunodeficiency, lymphoproliferative or collagen disorders or HIV infection).
- asymptomatic children can be left without therapy and kept under observation.
- symptomatic children may need short course of treatment to tide them over the relapse which include:
 - intermittent pulses of IVIG
 - intermittent anti-Rh(D) antibody treatment for those with Rhesus D positive
 - intermittent pulses of steroids
- care must be taken with any pulse steroid strategy to avoid treatment-related steroid side-effects. Aware of immunosuppression e.g. risk of severe varicella no justification for long-term continuous steroids

Splenectomy

- is indicated when:
 - persistence of disease after 12 months with
 - bleeding symptoms and
 - platelet count $< 10,000/\text{mm}^3$ (ages 3 – 12 years) or $< 10,000/\text{mm}^3$ to $30,000/\text{mm}^3$ (ages 8 – 12 years)
 - no response or only transient success with intermittent IVIG, anti-D or pulsed steroids
 - no contra-indications to surgery
- operative mortality $< 1\%$
- over 70% rate of complete remission post-splenectomy
- pre-splenectomy immunization against pneumococci, *haemophilus influenzae* type b and meningococci infection mandatory 2 weeks before surgery
- post-splenectomy penicillin prophylaxis

For post-splenectomy failure or relapse, consider:

- danazol, vincristine, azathioprine, cyclophosphamide, alpha-interferon, staphylococcal protein A immunoabsorption, cyclosporine, colchicine or dapsone.