
بسم الله الرحمن الرحيم

pediatric ITP

overview,epidemiology,diagnosis, physiopathology

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ITP

Definition

PLT<100,000/mm3

Autoimmune mechanism

ITP

Classification

-Duration(Acute,persistent,chronic)

-Etiology (primary,secondary)

-Clinical manifestation(No symptom,mild,severe)

-Response to treatment (Early response,initial Response , durable response ,corticostroid dependent,refractory,remission)

-Age:(pediatric,Adult)

ITP PREVALENCE

Immune thrombocytopenia (ITP) is one of the most common acquired bleeding disorders, occurring in ~5 to 10 per 100 000 children per year and 3.3 per 100 000 adults per year

Characteristic differences and similarities between pediatric and Adult ITP

- One of the most well-documented epidemiological distinctions between childhood and adult ITP is the predominance of females among adults affected with ITP. This female predominance (~2:1 ratio) is consistently documented throughout the literature.
- The increased percentage of female patients in the adult ITP population is generally thought to be related to the increased incidence of systemic autoimmune disease in adult females.

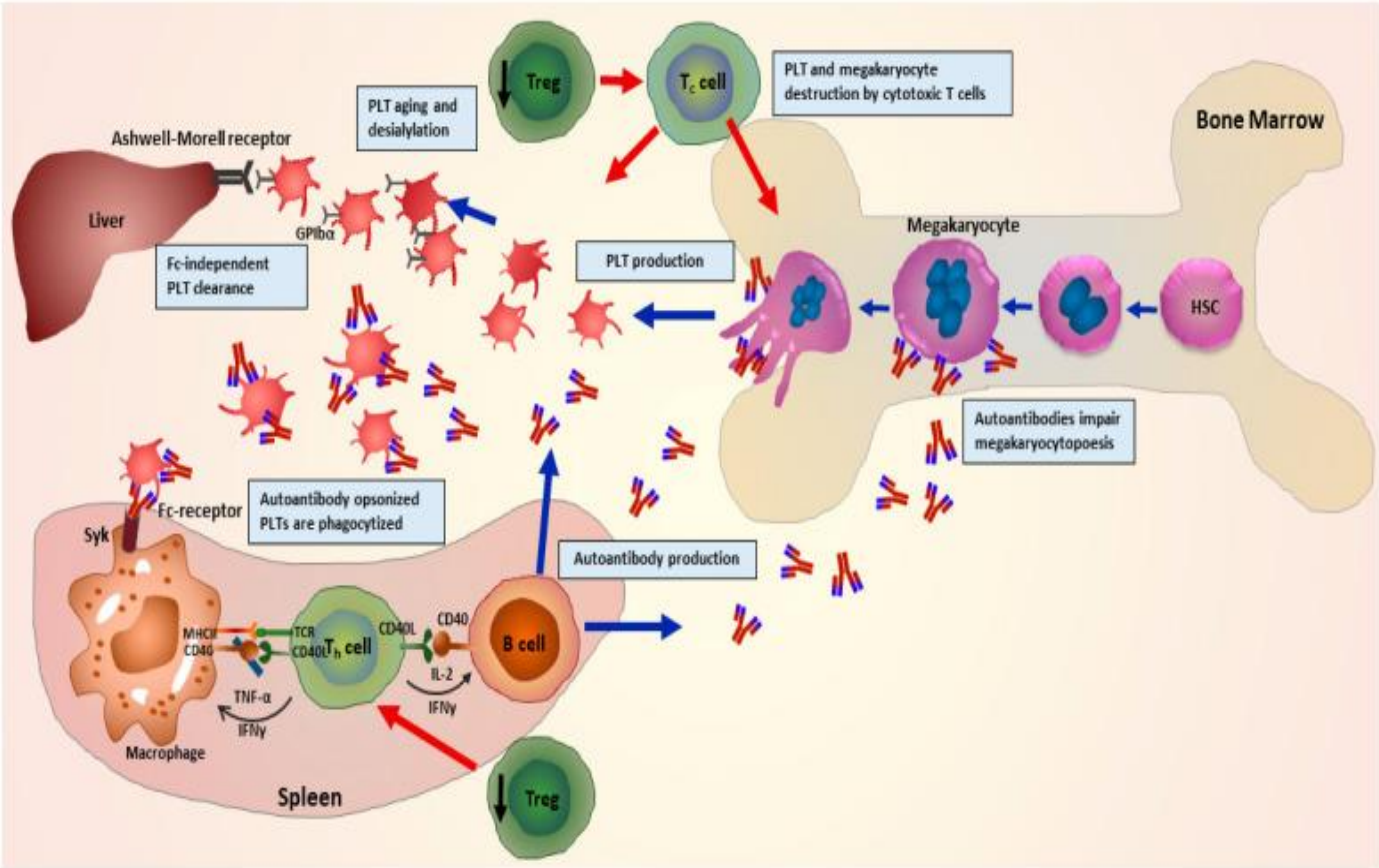
PREDICTORS OF CHRONIC ITP

- A recent systematic review and meta-analysis identified following predictors of chronic ITP in children:
- older age, insidious onset, no preceding infection or vaccination, mild bleeding, and higher platelet counts at presentation (> 20 x 109/L)
- two genetic biomarkers have been suggested as predictors of chronic disease: overexpression of vanin-1 (VNN-1), an oxidative stress sensor, and the Q63R missense variant of the gene encoding the cannabinoid receptor type 2

RATES OF SPONTANEOUS REMISSION IN CHILDREN AND ADULTS WITH ITP

- Time point (mo) Children (%) Adults (%)
- 6 1559/2233 (70) 145/324 (45)
- 12 1160/1639 (71) 133/271 (49)
- 24 744/1045 (71) 111/197 (56)
- Data are from the PARC-ITP study.6 Numbers at each time point included only those prospectively enrolled patients withdata available at the specified time point and did not includepatient lost to follow-up

physiopathology


Treg
T_c cell
PLT and megakaryocyte destruction by cytotoxic T cells
PLT aging and desialylation
Ashwell-Morell receptor
Liver
GPIbα
Fc-independent PLT clearance
Bone Marrow
Megakaryocyte
PLT production
HSC
Autoantibodies impair megakaryocytopoesis
Fc-receptor
Syk
Autoantibody opsonized PLTs are phagocytized
Autoantibody production
MHCII
CD40
TCR
CD40L
T_h cell
CD40L
CD40
B cell
IL-2
IFNγ
TNF-α
IFNγ
Macrophage
Spleen
Treg

Diagnosis

Physical Exam

CBC

PBS

Others?

BONE MARROW ASPIRATION

the international consensus guidelines published in 2010 recommend consideration of bone marrow examination only for patients aged >60 years old, prior to splenectomy, or in other atypical circumstances (ie, relapse following remission or first-line treatment failure •

Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115(2):168-186

BONE MARROW ASPIRATION

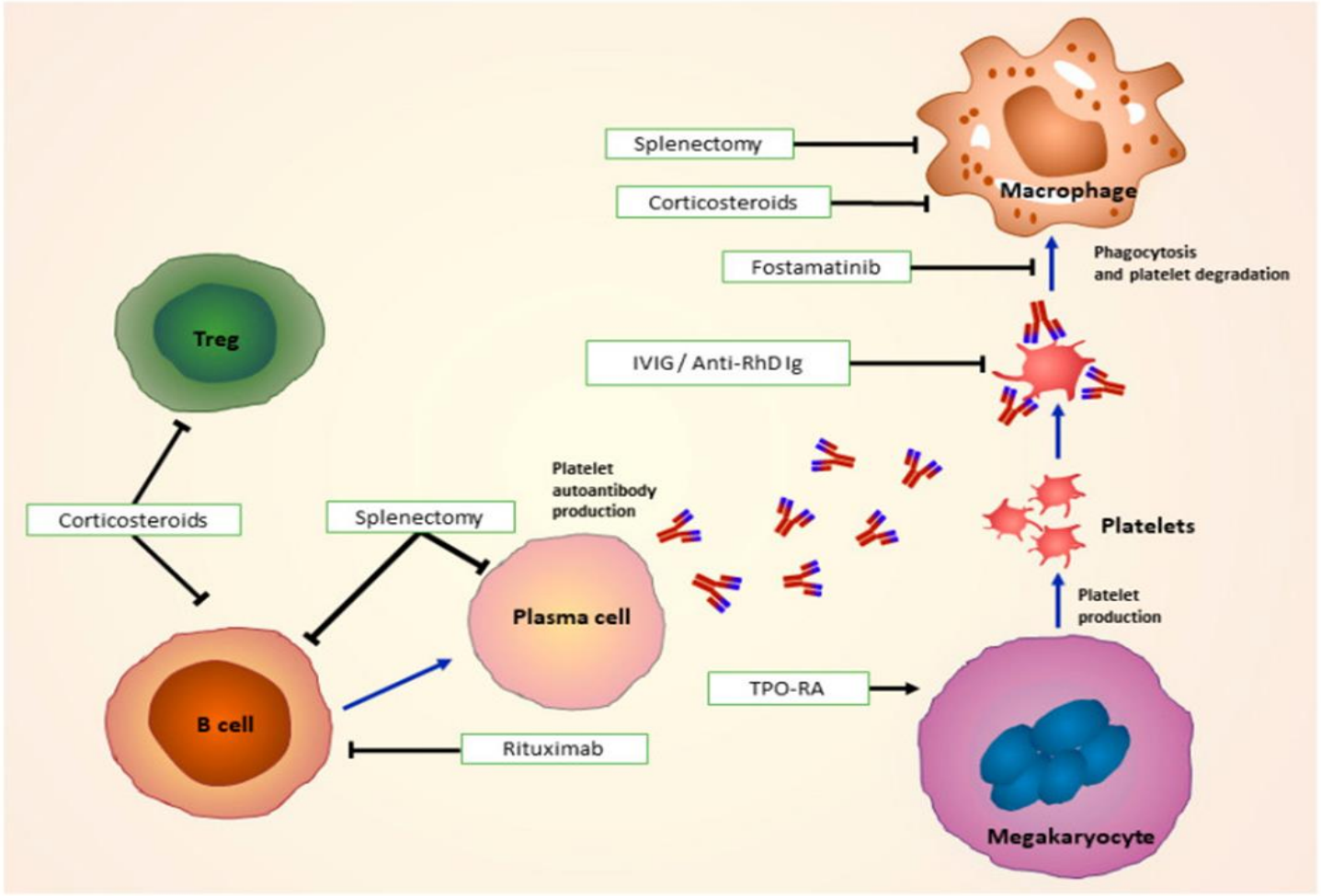
- the most recent ASH evidence-based practice guidelines for ITP recommend against routine bone marrow examination in children (even prior to corticosteroid therapy or splenectomy) and adults (irrespective of age) with typical features of ITP •

Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA.; American Society of Hematology. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117(16):4190-4207.

Management

Watchful waiting

Treatment


Splenectomy
Corticosteroids
Macrophage
Fostamatinib
Phagocytosis
and platelet degradation
Treg
IVIG / Anti-RhD Ig
Platelet
autoantibody
production
Corticosteroids
Splenectomy
Platelets
Plasma cell
Platelet
production
TPO-RA
B cell
Rituximab
Megakaryocyte

TREATMENT

- Children with ITP have an excellent chance of recovery with or without treatment.
- Typically, bleeding signs subside within weeks, and the platelet count returns to normal in a few weeks to months.
- Overall, 70% to 80% of children diagnosed with ITP will go into complete remission within a few months .
- Remission rate of 87%, achieved by watchful waiting without specific therapy 6 months after initial presentation

WATCHFUL WAITING

- The self-limited nature of childhood ITP and very low incidence of severe bleeding is the basis of a non-interventional strategy.
- Pharmacotherapy has proven to be mostly effective in raising the platelet count in a short period of time
- it has never been demonstrated that the fast platelet response is of clinical significance
- ASH practice guidelines recommend that children with no bleeding or mild bleeding (defined as skin manifestations only), be managed with observation alone regardless of platelet count
.
- This “watch and see” strategy is now accepted by many experts

- ITP treatment may be conceptually divided into rescue therapy and maintenance therapy

. • The objective of rescue therapy is a swift rise in platelet count in a patient with active hemorrhage, a high risk for bleeding, or need for a critical procedure.

- In selecting rescue therapy, a premium is placed on rapidity of response with relatively less regard for durability of response, patient convenience, or safety and tolerability with long-term use.

- Maintenance therapy, in contrast, is given with the goal of achieving a sustained platelet response while minimizing short- and long-term treatment-related toxicity

NEW DRUGS UNDER INVESTIGATION

Rozanolixizumab

Bortezomib

Efgartigimod

Decitabine