Piyush Gupta's

Learning Through

MCQs in PEDIATRICS

for MD and DM Students

Volume 1

General Pediatrics, Neonatology, Adolescent Health, and Social Pediatrics

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Volume 2

Systemic Pediatrics and Pediatric Subspecialities

Piyush Gupta

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Systemic Pediatrics and Pediatric Subspecialities

SECTION 16 GASTROENTEROLOGY

Section Editor: **Moinak Sen Sarma**

CHAPTER

18.8 Coagulation Disorders

Ritika Khurana, Purva Kanvinde, Sangeeta Mudaliar

1. A 2-year-old well child presented with recurrent epistaxis and easy bruisability since 7 months of age. His sibling at 3 years of age succumbed to massive hematemesis. Investigations revealed:

- Hemoglobin (Hb) 11 g/dL, white blood cell (WBC) count: 7,500/μL [absolute neutrophil count (ANC) 4,500 and absolute lymphocyte count (ALC) 3,500], platelet: 200×10^9/L
- *Platelet function studies:* Failure to aggregate with adenosine diphosphate (ADP) and epinephrine

How should we treat this condition?

A. Local measures for hemostasis and platelet transfusion may be required
B. Corticosteroids
C. Thrombopoietin (TPO) agonist like eltrombopag
D. Intravenous (IV) immunoglobulin

EXPLANATION

The child seems to be suffering from an inherited platelet type of disorder considering family history and early presentation of platelet type of bleeding (mucocutaneous).

Platelet function studies are suggestive of failure to aggregate in response to ADP, and epinephrine because they have a functional deficiency of platelet surface $\alpha IIb\beta_3$ receptors. This is diagnostic of Glanzmann's thrombasthenia.

The treatment recommended is local compression strategies, antifibrinolytic agents, and platelet transfusions as required.

Steroids, intravenous immunoglobulin (IVIG), TPO agonists, or other immunosuppressants have no role in this disorder.

Key: A

BOOST YOUR KNOWLEDGE

Glanzmann's thrombasthenia is a rare inherited autosomal recessive bleeding disorder due to a defect in the glycoprotein IIb/IIIa (Gp IIb-IIIa) platelet surface receptor. The hallmark of this is a failure of platelets to bind fibrinogen and aggregate after activation. Epistaxis and gastrointestinal bleeding are frequent issues in early childhood which often require intervention as well as iron supplementation.

Treatment options for mild bleeding are local compression strategies and antifibrinolytic agents. Moderate-to-severe bleeding requires platelet transfusion. Recombinant factor VIIa may be used in case of refractoriness to platelets.

REFERENCE/SOURCE

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2. A 5-year-old boy who is a known case of severe hemophilia A and is on regular prophylaxis is posted for appendicectomy. Choose the right preoperative plan for him.

A. Give appropriate factor VIII correction
B. Screen for inhibitors, if negative give appropriate factor correction preoperatively
C. 1 unit of cryoprecipitate per 10 kg body weight preoperatively
D. Must receive emicizumab 3 mg/kg preoperatively

EXPLANATION

Hemophilia patients on regular prophylaxis are prone to develop inhibitors post multiple exposures with factor therapy. They should be screened for the development of inhibitors by modified Bethesda assay before and after any surgery or invasive procedure. If negative for inhibitors, factor VIII should be given 80–100% preoperatively, followed by 60–80% postoperative Day 1–3; 40–60% Days 4–6, and 30–50% Days 7–14.

Cryoprecipitate is not the treatment of choice as it is not a specific treatment and is associated with the risk of viral transmitted infections. Emicizumab is used as prophylactic therapy and is not the choice of drug for surgery.

Key: B

BOOST YOUR KNOWLEDGE

The incidence of inhibitors is 33% in patients with severe hemophilia A, and 13% in mild-moderate hemophilia A.

Inhibitor screening is recommended by the modified Bethesda assay.

- Once every 5 exposure days till 20 exposure days, every 10 exposure days between 21 and 50 exposure days, at least two times a year till 150 exposure days, and later annually
- Before or after any surgery or invasive procedure
- Before or after a switch of products
- Bleeding episodes while on prophylaxis or suboptimal response to factor therapy during acute bleeding
- Low titer inhibitors have 0.6 to <5 Bethesda units (BU)/mL and high titer inhibitors have >5 BU/mL
- Low titer inhibitor will require higher doses of factor VIII. In the case of a high titer inhibitor, the treatment of choice is factor eight inhibitor bypassing agent (FEIBA) or recombinant factor VII or emicizumab.
- Emicizumab is a bispecific monoclonal antibody that binds factor IXa and X, resulting in the activation of factor X, thereby mimicking the actions of factor VIII.

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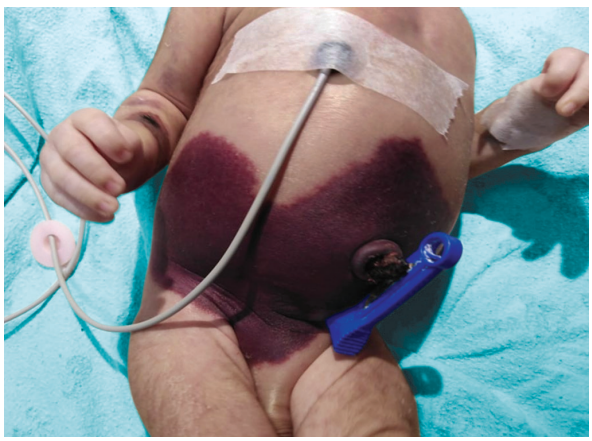
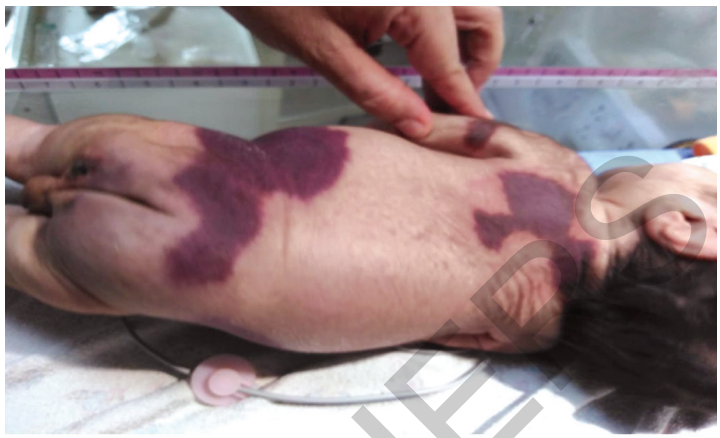
3. A 13-day-old child presented with complaints of (c/o) lethargy, decreased oral intake, and bluish discoloration of the skin.

- *C-reactive protein (CRP):* 1, *procalcitonin:* 0.1
- *Prothrombin time (PT):* 22 seconds (normal 12)
- *Activated partial thromboplastin time (APTT):* 62 seconds (normal 35)
- *International normalized ratio (INR):* 1.8

What is the most likely diagnosis?

A. Purpura fulminans due to protein C/protein S deficiency
B. Severe sepsis
C. Hyperhomocysteinemia
D. Toxic shock syndrome

EXPLANATION

Here, it is a neonate presenting with extensive skin discoloration and deranged PT/APTT suggestive of purpura fulminans.

It is a clinical term to describe intravascular thrombosis with extensive skin necrosis. It occurs usually due to severe protein C or protein S deficiency.

Sepsis or toxic shock syndrome appears unlikely as with severe disseminated intravascular coagulation (DIC), usually, sepsis markers such as CRP and procalcitonin are deranged.

Hyperhomocysteinemia may predispose to thrombosis but does not present like purpura fulminans.

Key: A

BOOST YOUR KNOWLEDGE

Purpura fulminans is a rare but life-threatening clinical condition caused by homozygous or compound heterozygous deficiency of protein C or protein S. These neonates present shortly after birth with severe skin necrosis caused by thrombosis of small or medium-sized dermal vessels. It may progress to thromboembolic phenomena or DIC if not treated promptly. A pretreatment citrate sample of plasma must be sent for protein C and S activity and compared with age-specific reference ranges. Genetic testing is considered confirmatory.

Causes of Purpura Fulminans

Congenital/inherited states:

- Homozygous protein C deficiency
- Homozygous protein S deficiency

Acquired causes:

- *Increased consumption:*
  - Infection, e.g., group B *Streptococcus* infection
  - DIC
  - Acute venous thrombosis
  - Antiphospholipid antibodies
  - Cardiac bypass
- *Decreased synthesis:*
  - Severe hepatic dysfunction
  - Galactosemia
  - Severe congenital heart disease
  - Warfarin therapy

- *Initial treatment:*
  - *Fresh frozen plasma (FFP):* 10–20 mL/kg every 12 hourly
- *Definitive treatment:*
  - *Protein C concentrates (if available):* 100 units/kg followed by 50 units/kg every 6 hourly. The dose should be titrated to achieve protein C activity through levels of 50 units/dL. Low molecular weight heparin (LMWH) is also started.
- *Curative treatment:* Liver transplant

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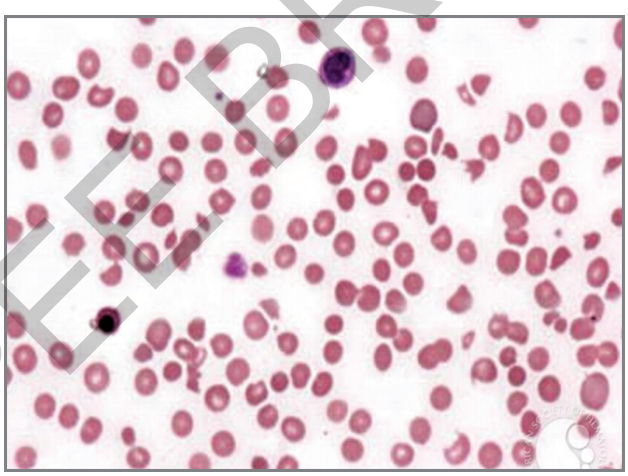
4. An 11-year-old female presented with acute onset of hematuria, severe headache, and confusion. She also developed a fever in the last few days.

Complete blood count (CBC):

- *Hb:* 9 g/dL
- *Mean corpuscular volume (MCV):* 75
- *WBC:* 4,500/mm^3
- *Platelets:* 11,000/µL



Peripheral smear picture

Pick up the most appropriate statement for this condition.

A. History and peripheral smear are suggestive of autoimmune hemolytic anemia, glucocorticoids are the treatment of choice
B. Thrombotic thrombocytopenia is the likely diagnosis, ADAMST13 activity should be checked, and plasma exchange initiated
C. Acute intravascular hemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficiency
D. The main pathogenesis in TTP is persistently raised low molecular weight von Willebrand multimers

EXPLANATION

Acute onset bleeding manifestations with fever, neurological symptoms, thrombocytopenia, and evidence of microangiopathic anemia [schistocytes or fragmented red blood cells (RBCs)] are suggestive of

thrombotic thrombocytopenic purpura (TTP). Autoimmune hemolytic anemia (AIHA) is an important differential, but it usually has very high MCV, and peripheral smear will have features of hemolysis, such as polychromasia and nucleated RBCs, and will show RBCs in clumps (in cold AIHA) or spherocytes (in warm AIHA). Thrombocytopenia and neurological symptoms are unusual in G6PD deficiency.

Key: B

BOOST YOUR KNOWLEDGE

Thrombotic thrombocytopenic purpura is a thrombotic microangiopathy caused by reduced activity of the vWF-cleaving protease ADAMTS13. TTP can be acquired, due to autoantibody inhibitors, or hereditary, due to homozygous or compound heterozygous ADAMTS13 mutations.

Plasma exchange is the treatment of choice to which 50–80% of patients respond.

Under conditions of sheer stress, ultra-large vWF (UL-vWF) multimers increase as they act more efficiently than other multimers. In a deficiency of ADAMTS13, cleaving of these UL multimers does not happen which leads to prothrombotic condition. Patients with Upshaw–Schulman syndrome, or congenital TTP have unusually large vWF multimers causing uncontrolled platelet aggregation and microvascular thrombosis.

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- Orkin SH, Nathan DG, Ginsburg D, Look AT, Fisher DE, Lux S. Nathan & Oski's Hematology and Oncology of Infancy and Childhood, 8th edition. Philadelphia: Saunders; 2014. 1092-1094.

5. A 13-year-old well female with a history of menorrhagia since 2 months and occasional fatigue. No organomegaly/lymphadenopathy.

- *CBC:*
  - *Hb:* 11 g/dL
  - *WBC:* 5,500/µL, neutrophil (N) 40, leukocyte (L) 56, and eosinophil (E) 4
  - *Platelet count:* 5×10^9/L
  - *Immature platelet fraction (IPF):* 22

Diagnosis of immune thrombocytopenic purpura (ITP) was made. Choose the right approach for this patient.

A. Screen for antinuclear antibodies (ANA), antidouble-stranded deoxyribonucleic acid (dsDNA), and viral markers and then initiate steroids
B. Bone marrow examination should be considered in adolescent patients suspected of ITP
C. There is no rationale for doing bone marrow or any blood investigations as it is suggestive of a typical ITP
D. The goal of treatment should be to achieve a platelet count of at least 50,000/L

EXPLANATION

Isolated thrombocytopenia in a well child, without any signs or symptoms of an underlying malignancy, etc., and a high IPF is suggestive of peripheral destruction due to ITP. ITP typically affects preschool toddlers aged 2–6 years.

In children <1 year of age, underlying immunodeficiency should be ruled out and autoimmune diseases, such as systemic lupus erythematosus (SLE) should be ruled out in adolescents; especially in females with additional symptoms, such as rash, photosensitivity, arthralgias, and fatigue.

Bone marrow examination is not mandatory if clinical signs and symptoms are typical of ITP and other cell lines are unaffected.

Key: A

BOOST YOUR KNOWLEDGE

Immune thrombocytopenic purpura now called immune Thrombocytopenia is an autoimmune disorder characterized by reduced peripheral blood platelet count due to a combination of premature platelet destruction and inadequate platelet production.

Patients with ITP have activated platelets, autoreactive B- and T-cells, and cytokine imbalance suggestive of peripheral intolerance.

Steroids or IVIG are the mainstay of treatment in acute ITP. TPO agonists (eltrombopag and romiplostim) are now widely used for persistent and chronic ITP with good results. Dapsone, rituximab, etc., are next-line drugs. Splenectomy is now rarely indicated.

The goal of treatment is to prevent life-threatening bleeding and to ensure a good quality of life, rather than chasing the platelet counts.

REFERENCES/SOURCES

- Gupta P, Menon PSN, Lodha R, Ramji S. PG Textbook of Pediatrics, 3rd edition. New Delhi: Jaypee Brothers Medical Publishers; 2022. 1916-8.
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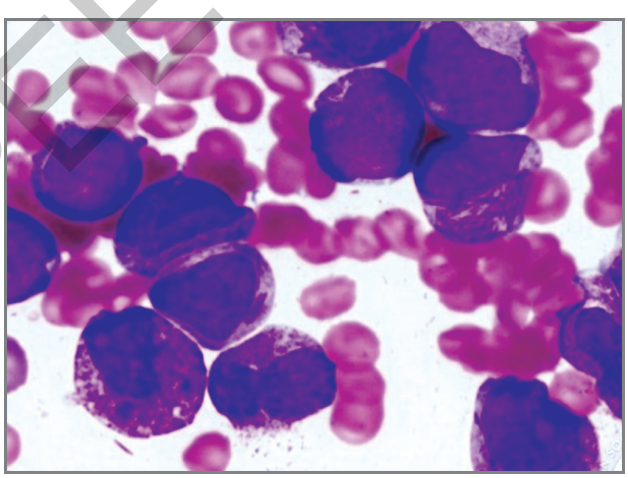
6. A 10-year-old male child presented with fever since 3 days, pallor, and multiple ecchymotic patches. There has been hemiparesis and altered sensorium since morning.

- *CBC:*
  - *Hb:* 3 g/dL
  - *WBC:* 90,000/mm^3
  - *Platelets:* 4,000/µL
  - *PT:* 28(14)
  - *APTT:* 69(36)
  - *INR:* 2



Peripheral blood smear

You are the registrar on call, what steps will you take?

A. Initiate unfractionated heparin (UFH) as soon as possible along with platelet and FFP transfusions
B. Give all-trans retinoic acid (ATRA) as soon as possible @45 mg/kg/day along with heparin
C. Give ATRA @25 mg/m^2/day and maintain platelets above 50,000 and fibrinogen >100
D. Plan bone marrow aspiration, depending on flow cytometry report start definitive treatment

EXPLANATION

Peripheral smear findings of leukemic promyelocytes with abundant, irregularly appearing primary azurophilic granules should raise suspicion of acute promyelocytic leukemia (APL). If APL is suspected, ATRA should be started immediately to rapidly ameliorate coagulopathy.

The International Consortium on Childhood APL (ICC APL-01) protocol (NCT01226303) recommends maintaining platelets >50 × 10^9/L and fibrinogen >1.5–2.0 g/L. Although heparin partially inhibits coagulation in DIC, a retrospective study comparing heparin with antifibrinolytic agents in the pre-ATRA era showed no benefit of heparin in APL-induced coagulopathy.

Complications such as pseudotumor cerebri and differentiation syndrome are more common in children, and many pediatric studies have shown that ATRA remains effective at 25 mg/m^2/day, with a lower incidence of side effects.

Key: C

BOOST YOUR KNOWLEDGE

Childhood APL is a medical emergency, and aggressive blood product support guided by frequent coagulation studies should commence promptly.

The presence of Auer rods and hypergranular promyelocyte blast cells is typical of APL. Frequently, the bone marrow classical morphology reveals promyelocytes with abundant Auer rods in multiple clusters (the so-called "faggot cells").

The classical hallmark of APL is the cytogenetic translocation t(15;17) (PML:RARA) present in 95–98% of cases, other translocations are also seen which may be resistant to ATRA.

All-trans retinoic acid acts as a differentiating agent for promyelocytic blasts whereas arsenic trioxide (ATO) induces apoptosis in blast cells. A combination of ATRA and ATO is now the preferred induction treatment in many centers, with the addition of anthracyclines in patients with WBC >10,000.

REFERENCES/SOURCES

- Abla O, Ribeiro RC. How I treat children and adolescents with acute promyelocytic leukaemia. Br J Haematol. 2014;164(1):24-38.
- De Botton S, Coiteux V, Chevret S, Rayon C, Vilmer E, Sanz M, et al. Outcome of childhood acute promyelocytic leukemia with all-trans-retinoic acid and chemotherapy. J Clin Oncol. 2004;22(8):1404-12.
- Tallman MS, Altman JK. How I treat acute promyelocytic leukemia. Blood. 2009;114(25):5126-35.
- Yilmaz M, Kantarjian H, Ravandi F. Acute promyelocytic leukemia current treatment algorithms. Blood Cancer J. 2021;11:123.

7. Direct oral anticoagulants (DOACs) have been approved for use in children with thrombosis in recent years. Which of the following will be the right candidate for putting on rivaroxaban?

A. A 5-year-old male with sickle cell disease and right middle cerebral artery (MCA) infarct
B. A 6-month-old female with cholestasis and Budd–Chiari syndrome
C. A 32-week neonate with cerebral venous sinus thrombosis
D. A 7-year-old child with Pott's spine and common femoral vein thrombosis

EXPLANATION

Two trials—EINSTEIN-Jr and DIVERSITY evaluated rivaroxaban and dabigatran for use in pediatric patients. They were found to be equally efficacious as LMWH and have an advantage of oral administration with the least side effects.

Till date, their use is approved for limited situations, restricting their use to venous thrombosis in children beyond 37 weeks of age, with normal liver and kidney function tests, following 4–5 days of unfractionated or LMWH. Budd–Chiari syndrome in the options given is associated with direct hyperbilirubinemia (cholestasis), hence not recommended.

Key: D

BOOST YOUR KNOWLEDGE

- DOACs exert their anticoagulant properties by affecting the common pathway in the coagulation cascade, with the two major oral medication classes being direct factor Xa inhibitors (DFXaI) and direct thrombin inhibitors (DTIs).
- An advantage of DOACs is their selective binding to their target factors (FXa for DFXaI and thrombin for DTIs) without the need for a cofactor.

Description of DOACs that have been studied in children

Drug	*Mechanism of action*	*Onset of action*	*Duration of action*	*Monitoring*	*Side effects*	*Available formulations in India*	*Reversal agent*	*Contra-indications*
Rivaroxaban	Direct factor Xa inhibitor	3–4 hours	24 hours	Requires no laboratory monitoring of PT or aPTT	Bleeding, dyspepsia, abdominal pain, pyrexia, fatigue, and headache	2.5, 10, 15, and 20 mg tabs	Andexanet alfa	Hepatic and renal impairment
Dabigatran	Reversibly blocks the catalytic site of thrombin	2 hours	24 hours	Though oral bioavailability is low, the anticoagulant effect is consistent, and no laboratory monitoring is required	Bleeding, dyspepsia, abdominal pain, pyrexia, fatigue, and headache	75, 110, and 150 mg caps	Idarucizumab	Renal impairment

Limitations for use of DOAC

- Due to the limited experience on DOACs long-term data on safety in children are lacking.
- DOACs need to be avoided in severe renal failure and rivaroxaban needs to be avoided in severe hepatic failure.
- DOACs have not been studied in neonates <37 weeks and birth weight <2.6 kg.
- In patients with arterial thrombus some studies have shown that warfarin is more beneficial. Hence the use in arterial thrombus is still not established.

REFERENCES/SOURCES

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- Whitworth H, Raffini L. Practical considerations for use of direct oral anticoagulants in children. Front Pediatr. 2022;10:860369.

8. A 3-month-old well boy, born of third-degree consanguinity presented with hematoma at the vaccine site. On investigation:

- *PT/APTT/INR:* 28/14, 95/42, *INR:* 2
- Fresh frozen plasma transfusion and vitamin K were given, after which the coagulation profile normalized. 10 days later child developed melena.

PT	26/14
APTT	65/40
INR	2
Protein induced by vitamin K absence (PIVKA)	40,000
Liver function tests	Normal

Which tests will clinch the diagnosis?

A. vWF assay
B. Coagulation factor levels, clinical exome
C. Coagulation factor levels and mixing studies
D. D dimer, fibrinogen, and thrombin time

EXPLANATION

Deranged PT/APTT/INR and increased PIVKAs are suggestive of vitamin K deficiency. It is commonly acquired but since this child is born of consanguinity and getting repeated symptoms. Congenital vitamin K deficiency should be ruled out.

Factor levels will show a reduced amount of vitamin K dependent factor II, VII, IX, and X. Clinical exome sequencing with clinch the diagnosis.

von Willebrand disease will not have such a grossly deranged coagulation profile and PIVKAs will not be high. Also unlikely to be hemophilia as both PT/APTT are deranged.

Key: B

BOOST YOUR KNOWLEDGE

Combined deficiency of vitamin K-dependent factors is usually acquired secondary to no administration of vitamin K at birth, liver disease, warfarin therapy, sepsis, etc.

Although rare, an inherited form of vitamin K deficiency also exists which leads to decreased levels of coagulation factors II, VII, IX, and X as well as natural anticoagulants protein C and protein S.

Vitamin K-dependent clotting factor deficiency (VKCFD) is an autosomal recessive disorder caused by mutations in the genes of either γ-glutamyl carboxylase or vitamin K2,3-epoxide reductase complex. VKCFD1, which is associated with point mutations in the γ-glutamyl carboxylase gene (*GGCX*), and *VKCFD2*, which results from point mutations in the vitamin K epoxide reductase gene (*VKOR*).

Bleeding manifestation ranges from mild to severe with onset in the neonatal period in severe cases.

Vitamin K administration is the mainstay of therapy in VKCFD; however, during surgery or severe bleeding episodes, FFP supplementation will be needed.

REFERENCES/SOURCES

- Bhattacharyya J, Dutta P, Mishra P, Dixit A, Srinivas U, K Meghanathan, et al. Congenital vitamin K-dependent coagulation factor deficiency: a case report. Blood Coagul Fibrinolysis. 2005;16(7):525-7.
- Napolitano M, Mariani G, Lapecorella M. Hereditary combined deficiency of the vitamin K-dependent clotting factors. Orphanet J Rare Dis. 2010;5:21.

9. A full-term baby born by normal vaginal delivery developed convulsion on Day 2 of life, a magnetic resonance imaging (MRI) brain was suggestive of intracranial hemorrhage.

- *CBC:*
  - *Hb:* 11 g/dL
  - *WBC:* 13,000
  - *Platelet count:* 12,000 and *PT/APTT/INR:* normal
  - *CRP:* Negative, *D-dimer:* negative, and *fibrinogen:* 250

Pick up the right diagnostic and management approach.

A. Neonatal alloimmune thrombocytopenia (NAIT) is the likely diagnosis. Screen for human platelet antigen (HPA)/human leukocyte antigen (HLA) antibody, administer platelet transfusion and IVIG
B. Child appears to be in DIC, administer FFP and platelet transfusion immediately
C. ITP is likely, to perform bone marrow studies and administer steroids
D. NAIT is likely, long-term monitoring and regular courses of IVIG are warranted

EXPLANATION

Neonatal alloimmune thrombocytopenia is caused by the placental transfer of maternal alloantibodies directed against paternally inherited antigens present on fetal platelets.

NAIT is suspected in patients with isolated thrombocytopenia in a term, otherwise, clinically well baby, in whom causes such as sepsis, are ruled out. ITP is extremely uncommon in this age group.

In all suspected cases of NAIT, HPA, and HLA antibody screening should be considered to confirm diagnosis as well as guide in subsequent pregnancies.

It is a transient disease, with resolution of thrombocytopenia by 2–3 weeks, when antibodies wean off.

Key: D

BOOST YOUR KNOWLEDGE

In Caucasians, the most commonly implicated alloantigen is HPA-1a, whereas in Asians HPA-4 is most common (80%). Antibodies to HLA class 1 antigen are also found as a cause of NAIT in a few patients. The degree of thrombocytopenia in neonates at risk for NAIT (mother immunized against HPA-1a) can be quite variable. The most serious complication of NAIT is intracranial hemorrhage, which occurs in 10–20% of symptomatic infants. Up to 80% of these bleeds occur prenatally. Flow cytometry using secondary probes specific for immunoglobulin G (IgG) and immunoglobulin M (IgM) immunoglobulin isotypes provides a rapid and sensitive means of detecting platelet reactive antibodies.

Irradiated maternal platelet transfusion is the treatment of choice in case of significant bleeding. If it is not feasible, then random donor platelets can be given. IVIG therapy should also be given at 1–2 g/kg/day for 2–4 days to deplete the formed antibodies.

REFERENCES/SOURCES

- Orkin SH, Nathan DG, Ginsburg D, Look AT, Fisher DE, Lux S. Nathan & Oski's Hematology and Oncology of Infancy and Childhood, 8th edition. Philadelphia: Saunders; 2014. pp. 1088-9.
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10. A 9-year-old boy with acute lymphoblastic leukemia (ALL) on induction chemotherapy, presented with induration and edema of the right upper limb. Ultrasonography (USG) Doppler is suggestive of right basilic vein thrombosis. He has a peripherally inserted central catheter (PICC) line in the same limb.

Choose the right statement for the management of line-associated thrombosis.

A. Port is associated with a higher risk of thrombosis compared to external devices like PICC line
B. Inherited thrombophilia work up is warranted in such situations
C. PICC line removal must be done and initiate enoxaparin
D. Initiate enoxaparin, and reassess after 6 weeks; the line can be salvaged in most situations

EXPLANATION

An internal device (port) has a lesser risk of thrombosis than an external tunneled device (Hickman or Broviac catheter). Amongst external devices, tunneled lines are less prone to thrombosis than PICC lines.

Since the child has conditions like malignancy, therapy involving steroids and L-asparaginase, and a line in-situ; all of which predispose to thrombosis, extensive thrombophilia workup is not warranted at this point.

If the line is necessary, is well positioned, and functioning well, needs not to be removed.

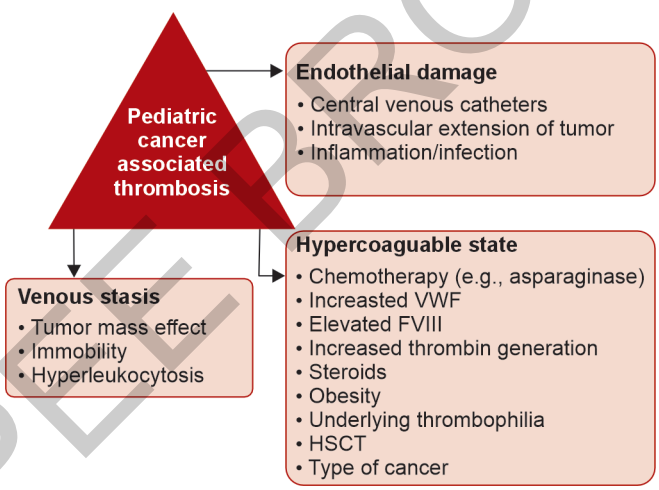
Enoxaparin in the dose of 1 mg/kg/dose 12 hourly is the treatment of choice. Reassessment scans should be done post 6 weeks of enoxaparin and if improving, it should be continued for another 6 weeks and then stopped. In case, the line is not required further or nonfunctional, it should be removed after 3–5 days of enoxaparin therapy to prevent embolization at the time of removal.

Key: D

BOOST YOUR KNOWLEDGE

Central venous access devices (CVADs) predispose patients to venous thrombosis because they impact each component of Virchow's triad: Stasis, hypercoagulability, and endothelial injury. CVAD insertion results in local vessel wall injury, activating coagulation and proinflammatory cascades.

Risk factors for thrombosis in cancer patients are listed in the given figure.



Cancer-associated thrombosis

Traditionally, UFH and LMWH have been the standard of care in pediatric oncology patients. Oral anticoagulants such as warfarin were typically avoided due to multiple food and drug interactions. However, with the EINSTEIN Jr and DIVERSITY trials demonstrating the safety and efficacy of DOACs such as rivaroxaban and dabigatran respectively; they are now extensively used.

For a child on chemotherapy, care should be taken to keep platelet count above 50,000 during anti-coagulation or reduce the dose of the drug when platelets are between 25,000 and 50,000 and withhold the drug when below 25,000.

REFERENCES/SOURCES

- Rajasekhar A, Streiff MB. How I treat central venous access device-related upper extremity deep vein thrombosis. Blood. 2017;129(20):2727-36.
- Samji N, Bhatt MD, Kulkarni K. Challenges in management of VTE in children with cancer: risk factors and treatment options. Front Pediatr. 2022;10:855162.

11. A 4-year-old girl was brought to the pediatric outpatient department (OPD) with a history of (H/O) easy bruisability noticed since the past 6 months. Bruises occurred episodically, usually observed a day after trivial trauma. On detailed history mother mentioned about similar episodes since early infancy. On examination, she had a large ecchymotic patch over the flank. No organomegaly/lymphadenopathy. History did not give any evidence of physical abuse.

Investigations:

- *Hb:* 10.8 g/dL
- *WBC count:* 6.4×10^9/L
- *Platelets:* 328×10^9/L
- *Peripheral smear:* Normal
- *Coagulation profile:* Normal
- *Platelet function tests:* Normal

What is the most likely diagnosis?

A. Factor XII deficiency
B. Factor V and VIII combined deficiency
C. Factor XIII deficiency
D. Factor X deficiency

EXPLANATION

History of episodic bruising with or without a history of umbilical cord bleeding with a normal coagulation profile and platelets are suggestive of factor XIII deficiency. Factor XII deficiency usually presents with incidentally found abnormal APTT in an asymptomatic child. Combined deficiency of factor V and VIII as well as factor X deficiency will have both PT and APTT deranged.

Key: C

BOOST YOUR KNOWLEDGE

Factor XIII is responsible for clot stability and crosslinking of fibrin polymer, protecting it from fibrinolysis, and hence factor 13 deficiency leads to delayed bleeding. Typically, the patient develops trauma, and a bruise or hematoma will be observed the next day. Other common symptoms are delayed umbilical cord hemorrhage, delayed umbilical cord separation, poor wound healing, or spontaneous abortion.

For a child with such bleeding manifestations and normal screening tests, factor XIII assay, and urea clot lysis test should be done.

12. A 7-year-old child with Marfan's syndrome undergoes cardiac surgery for severe aortic stenosis with valve replacement. He was initiated with UFH drip in the perioperative period. On the night of surgery, the child develops swelling and induration in the left upper limb near intravascular catheter insertion.

Investigations:

- *Hb:* 11 g/dL
- *WBC:* 9.3×10^9/L
- *Platelets:* 32×10^9/L
- *PT:* Normal and *APTT:* 62/34

You are the registrar on call that night, what are your thoughts on planning management of this patient?

A. Child has developed DIC, prompt FFP, and platelet transfusions should be initiated
B. Unlikely to be heparin-induced thrombocytopenia (HIT) as it occurs after 5 days of heparin infusion
C. Child has developed immune-mediated thrombocytopenia due to heparin, switch to LMWH
D. HIT is likely, stop heparin infusion and consider switching to lepirudin

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Piyush Gupta MD FAMS FRCPCH is a renowned Academician, Teacher, Researcher, Author, and Editor. He has published more than 300 papers, 450 book chapters, and edited/authored 50 books including the *UG Textbook and PG Textbook (3 Vols) of Pediatrics*. He has served as an Editor-in-Chief of "Indian Pediatrics", for 6 years. He has been conferred fellowships by the Royal College of Paediatrics and Child Health (RCPCH), UK; Indian Academy of Pediatrics (IAP); National Neonatology Forum (NNF); and National Academy of Medical Sciences, India, and awarded by the American Academy of Pediatrics (AAP). His major initiatives include workshops on thesis and scientific paper writing and increasing awareness for practicing rational management of diarrhea and pneumonia in children. He has served as Technical Expert/Advisor to the Government of India, WHO, UNICEF, and ICMR. He has delivered 40 orations, including the prestigious KL Wig Oration in the field of medical education in India. He has served as the Joint Secretary of South Asia Pediatrics Association. He has been awarded the National Teacher of Excellence by the Vice-President of India. In 2021, he served as the National President of the Indian Academy of Pediatrics. During his presidential year, he conceptualized and facilitated framing of *105 IAP Guidelines on Parental Education* and initiated a nationwide campaign on *Nurturing Care for Early Childhood Development*, supported by WHO and UNICEF. In 2022, he was awarded the "Outstanding Asian Pediatrician Award" by the Asia Pacific Pediatric Association (APPA). His thrust areas are nutrition, child survival, and medical education.

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