

A ten month old male child presented with the history of multiple bluish swellings off and on in the skin for last 4 months.

Objectives:

1. Obtain the history to unravel the symptoms suggestive of the haemopoietic and lymphoid system disorders and other symptoms secondary or related to that system.
2. Perform physical examination to elicit signs pertaining to the haemopoietic system disorders.
3. Relate the presenting signs and symptoms associated to altered structure and function.
4. Generate differential diagnosis based on signs, symptoms, and laboratory and data.
5. Identify laboratory investigations required to screen and confirm the differential diagnosis.

Key points in the clinical evaluation of a child with bleeding disorder

History:

Full medical history with special emphasis on the following points:

Age and sex, family history, consanguinity of marriage, drugs ingested by mother

Onset: Age, rapid or slow, preceding viral or bacterial infection, drugs,

Site of bleeding: Haematuria, malena, convulsion, skin lesions, epistaxis, gum bleeding, hematemesis.

Alimentary system: Jaundice, distension of abdomen, abdominal pain.

Skin: large area, pin point, saeborrhoea, skin elasticity,

Skeletal: Bone pain, arthritis, swellings.

Past history: Blood transfusion, previous treatment, investigations, umbilical or other areas bleeding.

Examination:

Nutritional status, anaemia, jaundice, tachycardia, oedema, hypertension, mental status.

Superficial lymphnodes, bony tenderness, status of joints, tourniquet test.

Skin: Petechiae, ecchymosis, dermatitis, other rash, telangiectasia, vascular malformations.

Eyes: Conjunctival haemorrhage, proptosis, fundus

Mouth: oral cavity bleeding, gum hypertrophy.

Abdomen: Hepatosplenomegaly, tenderness, mass, ascitis

Chest: Cardiac murmurs, lung sounds, effusions.

CNS: Focal neurological signs, state of consciousness.

Signs and Symptoms of Haematological Disorders

Symptoms Signs

Symptoms	Signs
1. Easy fatiguability	1. Pallor
2. Easy bruising	2. Jaundice
3. Bleeding	3. Koilonychia
4. Loss of appetite/weight	4. Glossitis
5. Failure to thrive	5. Angular stomatitis
6. Bone pain	6. Leg ulcers
7. Joint swelling	7. Petechiae
8. Neck swelling	8. Purpura
9. Abdominal swelling	9. Ecchymosis
10. Pruritus	10. Haematoma
	11. Haemarthrosis
	12. Capillary fragility
	13. Lymphadenopathy
	14. Hepatomegaly
	15. Splenomegaly
	16. Bone tenderness
	17. Bony or skeletal deformity
	18. Signs of heart failure
	19. Functional murmur

The presence of multiple bluish coloured swellings in the skin which disappears on its own is indicative of haemorrhage in the skin. For a hemorrhagic condition the history should determine the site or sites of bleeding, the severity and duration of hemorrhage, and the age of symptom onset. Bleeding from a platelet disorder is usually localized to superficial sites such as the skin and mucous membranes. In contrast, bleeding from secondary hemostatic or plasma coagulation defects occurs hours or days after injury. Such bleeding most often occurs in deep subcutaneous tissues, muscles, joints, or body cavities. Since bleeding can be mild, lack of a family history of bleeding does not exclude an inherited hemostatic disorder. One should determine if symptoms correlate with the degree of injury or trauma. Does bruising occur spontaneously? Are there lumps with

bruises for which there is minimal trauma? If there has been previous surgery or significant dental procedures, was there any increased bleeding from umbilicus? The physical examination should focus on whether symptoms are primarily associated with the mucous membranes or skin (mucocutaneous bleeding) or the muscles and joints (deep bleeding). The most common site to observe bleeding is in the skin and mucous membranes. Collections of blood in the skin are called *purpura* and may be subdivided on the basis of the site of bleeding in the skin. Small pinpoint hemorrhages into the dermis due to the leakage of red cells through capillaries are called *petechiae* and are characteristic of platelet disorders—in particular, severe thrombocytopenia. Larger subcutaneous collections of blood due to leakage of blood from small arterioles and venules are called *ecchymoses* (common bruises) or, if somewhat deeper and palpable, *hematomas*.

The examination should determine the presence of petechiae, ecchymoses, hematomas, hemarthroses, or mucous membrane bleeding. Patients with defects in platelet-blood vessel wall interaction (von Willebrand disease or platelet function defects) usually have mucous membrane bleeding (epistaxis, hematuria, gastrointestinal bleeding); petechiae on the skin and mucous membranes; and small, ecchymotic lesions of the skin sometimes associated with hematomas. Individuals with a clotting factor deficiency such as factor VIII or factor IX deficiency have symptoms of deep bleeding into muscles and joints with much more extensive ecchymoses and hematoma formation. For unclear reasons, hemarthroses are much less common in patients with other plasma coagulation defects. Patients with mild von Willebrand disease or other mild bleeding disorders may have no abnormal findings on physical examination.

The most important screening tests of the primary hemostatic system are (1) a *bleeding time* (a sensitive measure of platelet function), and (2) a *platelet count*. The normal platelet count is 150,000 to 450,000/uL of blood. As long as the count is >100,000/uL, patients are usually not symptomatic and the bleeding time remains normal. Platelet counts of 50,000 to 100,000/uL cause mild prolongation of the bleeding time; bleeding occurs only from severe trauma or other stress. Patients with platelet counts <50,000/uL have easy bruising, manifested by skin purpura after minor trauma and bleeding after mucous membrane surgery. Plasma coagulation function is readily assessed with the PTT, prothrombin time (PT), thrombin time (TT), and quantitative fibrinogen determination. Prothrombin time assesses the extrinsic and common pathways (V, VII, X, prothrombin and fibrinogen). The PTT screens the intrinsic limb of the coagulation system and tests for the adequacy of factors XII, XI, IX, and VIII. The PT screens the extrinsic or tissue factor-dependent pathway.

Following conditions are associated with large haemorrhage in the skin without having *petechiae*. Most of this type of disorders are coagulation defects.

Factor II or prothrombin deficiency

This deficiency is caused either by a markedly reduced prothrombin level (hypoprothrombinemia) or by a functionally abnormal prothrombin (dysprothrombinemia). Laboratory testing in homozygous patients demonstrates a

prolonged PT and PTT. Factor II or prothrombin assays demonstrate the markedly reduced prothrombin level.

Deficiency of factor V

The deficiency of factor V, also known as labile factor, is an autosomal recessive, mild to moderate bleeding disorder that has also been termed parahemophilia. Hemarthroses occur rarely; mucocutaneous bleeding and hematomas are the most common symptoms.. Laboratory evaluation demonstrates a prolonged PTT and PT. Rarely, one encounters the patient with a negative family history of bleeding who has an acquired antibody to factor V. Often, these patients do not bleed because the factor V in platelets prevents excessive bleeding

Factor VII deficiency

Factor VII deficiency is a rare bleeding disorder that is usually detected only in the homozygous state. Individuals with this deficiency may have spontaneous intracranial hemorrhage and frequent mucocutaneous bleeding. They will have a markedly prolonged PT but a normal PTT. This is a rare autosomal disorder that results in mucocutaneous and post-traumatic bleeding. This deficiency is the result of either a quantitative deficiency or a dysfunctional molecule. A reduced factor X level is associated with a prolongation of both the PT and the PTT. Although rarely a problem in pediatric patients, systemic amyloidosis may be associated with factor X deficiency

Factor VIII , factor IX deficiency

Neither factor VIII nor factor IX crosses the placenta; thus, bleeding symptoms may be present from birth or occur in the fetus. Surprisingly, only about 30% of affected male infants with hemophilia bleed with circumcision. Thus, if the family history does not alert the physician to be suspicious for its presence, hemophilia may go undiagnosed in the newborn. It is only when a child begins to crawl and walk that mobility causes the initiation of easy bruising, intramuscular hematomas, and hemarthroses. Patients with mild hemophilia who have factor VIII activities greater than 5% usually do not have spontaneous hemorrhaging.

Factor XIII deficiency

Since factor XIII is responsible for the cross linking of fibrin or the stabilization of fibrin clot, symptoms of delayed hemorrhage are secondary to poor maintenance of hemostasis. Typically, patients will have trauma one day and then develop a bruise or hematoma on the following day. Clinical symptoms include mild bruising, delayed separation of the umbilical stump beyond 4wk.

von Willebrand disease

Patients with von Willebrand disease usually have symptoms of mucocutaneous hemorrhage, including excessive bruising, epistaxis, menorrhagia, and postoperative hemorrhage, particularly after mucosal surgery such as tonsillectomy or wisdom tooth extraction. Patients with von Willebrand disease are said to have a long bleeding time and a long PTT.

Congenital afibrinogenemia

Congenital afibrinogenemia is a rare autosomal recessive disorder in which there is an absence of fibrinogen. Interestingly, these patients do not bleed as frequently as hemophilia patients and rarely have hemarthroses. Affected patients may present in the neonatal period with gastrointestinal hemorrhage or hematomas following vaginal delivery.

Antifibrinolytic deficiency

Deficiency of antifibrinolytic proteins results in increased plasmin generation and the premature lysis of fibrin clots. Patients have mucocutaneous bleeding but rarely have joint hemorrhages. Since the usual hemostatic tests are normal, further work-up of a patient with a positive bleeding history should include the euglobulin clot lysis time that measures fibrinolytic activity and is shortened in the presence of these deficiencies.

Storage disorders

Easy bruising and epistaxis are common and are associated with a prolonged bleeding time as a result of impaired platelet aggregation and adhesion in Glycogen storage disorder.

In this patient the normal platelet count nearly rules out the conditions associated with the thrombocytopenia. Although the platelet dysfunctions can not be ruled out, with the absence of purpuric spots, disease associated with platelet abnormality is unlikely. Other conditions with normal bleeding time and coagulation time are coagulation factors deficiency. The severity of clinical symptoms and abnormality in the laboratory test in coagulation disorder mainly depends upon the percentage deficiency of the clotting factors. Usually these symptoms could be present in the neonatal period or beyond neonatal period when the infant begins to sit, crawl or walk because of trivial injuries. In this child the lesion could be due the deficiency of: factor V, Factor VIII , factor IX, factor XIII, and antifibrinolytic proteins. The further work up which will be helpful to make a diagnosi in this child is coagulation screening.

