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Subject: Wbcs and platelets disorders

Q1. Write a note on Hodgkin lymphoma?

Answer:

Hodgkin lymphoma:

- This is based on the histological presence of Reed-Sternberg (RS) cells in Hodgkin's lymphoma.

Pathogenesis:

- Hodgkin's disease is a lymphoma in which RS cells are found in the disease tissue.
- The characteristic RS cells, and the associated abnormal mononuclear cells, are neoplastic whereas the infiltrating inflammatory cells are reactive.
- Immunoglobulin gene rearrangement studies suggest that the RS cell is of B-lymphoid lineage and that it is often derived from a B cell with a 'crippled' Immunoglobulin gene caused by the acquisition of mutations that prevent synthesis of full-length immunoglobulin.
- The Epstein-Barr virus (EBV) genome has been detected in 50% or more of cases in Hodgkin tissue but its role in the pathogenesis is unclear.

Clinical features:

- The disease can present at any age but is rare in children and has a peak incidence in young adults.
- There is 2: 1 male predominance.

Staging of Hodgkin's lymphoma:

- The selection of appropriate treatment depends on accurate staging of the extent of disease.
- Staging is performed by thorough clinical examination together with chest X-ray and CT scan to detect intrathoracic, intraabdominal or pelvic disease.
    - It is also used to monitor response to therapy.
    - MRI scanning may be needed for particular sites.
    - Bone marrow trephine is carried out in some centers and
    - Liver biopsy may also be needed in difficult cases.

Staging of Hodgkin's lymphoma:

Stage I: indicates node involvement in one lymph node area.

Stage II: indicates disease involving two or more lymph nodal areas confined to one side of the diaphragm.

Stage III: indicates disease involving lymph nodes above and below the diaphragm.

Stage IV: indicates involvement outside the lymph node areas and refers to diffuse or disseminated disease in the bone marrow, liver and other extra nodal sites.

The stage number in all cases is followed by the letter A or B indicating the absence (A) or presence (B) of one or more of the following:

Unexplained fever above 38°C, night sweats, or loss of more than 10% of body weight within 6 months.

Localized extra nodal extension from a mass of nodes does not advance the stage but is indicated by the subscript E.

Q2.What is Hemostasis, also explain steps and clotting factors?

Answer:

Hemostasis:

Definition:

- The procedure in which the body stop bleeding.
- Spontaneous arrest or prevention of bleeding form injured \ damage vessel by the physiological process.
- Hemostasis is a precisely orchestrated process involving platelets, clotting factor, and endothelium that occurs at the site of vascular injury and culminates in the formation of the blood clot, which serves to prevent or limit the extent of bleeding.

Steps:

Three steps involve in hemostasis….

I) Vasoconstriction

ii) Hemostastic plug\ platelet plug formation

iii) Coagulation of blood

1) Vasoconstriction:

Vasoconstriction is a result of increased Ca ion concentration in smooth muscles.

Hormonal components:

- Circulating epinephrine and activation of sympathetic nervous system

- Interact with cell surface adrenergic receptors signal transduction
- Increased intercellular Ca from sarcoplasmic reticulum, Ca-calmodulin complex

- Activates myosin light-chain kinase
- Stimulate cross bridge cycle

2) Hemostastic plug\ platelet plug formation:

- Here platelets perform 2 functions
- Release other two chemicals like (thromboxane and ADP adenosine diphosphate)
- fill the gap (injured areas)
- Thromboxane and ADP help in platelets aggregations
- Von wile brand (glycoprotein) act as an adhesive protein
- Also localize some factors to sites of platelets plug.

3) Coagulation of blood:

- Major haemostatic function responsible for preventing and termination of bleeding
- The process by which a blood clot is formed.
- Coagulation system consist of
- 13 clotting factors that help in different coagulation pathways
- There are 13 factors that help in coagulation but factor vi presence not proved (still missing)
- Clotting Factors:
- fibrinogen
- Prothrombin
- Thromboplastin (tissue factor)
- calcium
- Labile facto
- Presence not proved
- Stable factor
- Antihemophilic
- Christmas
- Stuart power factor
- Plasma Thromboplastin or antecedent
- Hageman
- Fibrin stabilizing factors

Q3.Explain Hemophilia its types, symptoms, and lab diagnosis?

Answer:

Hemophilia:

Hemophilia A and B are similar in both clinical and pathological features, the difference Being in the deficient factor. Both are sex-linked recessive disorders resulting in Inherited deficiency of the clotting factor or synthesis of a defective clotting factor. Males are effected and females are carriers.

Types of hemophilia:

Hemophilia A (factor VIII deficiency):

• Hemophilia A is the most common hereditary X- linked recessive disease with a Reduction in the amount or activity of factor VIII. About 30% of hemophiliacs have no Family history and may be due to acquired mutations.

• Factor VIII serves as a cofactor for factor IX in the activation of factor X in the Coagulation cascade (Fig. 33.2). Reduced amount or activity of factor VIII is associated With life threating bleeding. Bleeding is due to both inadequate coagulation and Inappropriate clot removal (fibrinolysis).

Hemophilia B (Christmas disease, Factor IX Deficiency):

Both factor VIII and IX together activate factor X in coagulation cascade. Thus, severe Factor IX deficiency is clinically indistinguishable from hemophilia A. It is also inherited as an X-linked recessive trait and presents with variable clinical severity. Assay of factor IX should be done to diagnose Christmas disease (named after the first patient). Recombinant factor IX is used for treatment.

Symptoms of hemophilia:

- Sudden pain, swelling and warmth in large joints
- painful, prolonged headache
- repeated vomiting
- extreme fatigue
- neck pain
- double vision

Lab Diagnosis:

• Bleeding time: Normal.

• Clotting time: Prolonged.

• Platelet count: Normal.

• Prothrombin time: Normal.

• Activated partial Thromboplastin time (APTT): Increased (normal 30-40 seconds) Prolongation of APTT is dependent upon the severity of deficiency of factor VIII.

Q4 .Describe Von Willebrand disease?

Answer:

INTRODUCTION:

- Von willebrand disease:
- Von Willebrand disease (vWD) was first described in 1926 by a Finnish physician named Dr. Erik von Willebrand.
- Von Willebrand disease is estimated to affect 1 in 100 individuals.
- Most researchers agree that von Willebrand disease is the most common genetic bleeding disorder.
- Glycoprotein and composed of 2050 amino acid
- It is a autosomal dominant inheritance disease pattern
- Males and females are affected equally

Physiology of willebrand disease:

- **Location:** The majority of vWF is circulating in the blood plasma.
- Synthesis: vWF is synthesized as a monomer that is subsequently made into multimers that are secreted alpha granules of platelets and endothelial cells of blood vessels
- Store: mainly in weibal palate bodies of endothelial cells
- **Receptors:** A1 and C1 domain for pelts, A3 domain for collagen and D3 for FVIII
- Cytogenetic Location: 12p13.3, which is the short (p) arm of chromosome 12 at position 13.3
- Also called coagulation factor VIII or F8VWF.

Function of willebrand disease:

- **Mainly have two roles:**
    1. Von Willebrand factor's primary function is binding to particular factor VIII and Factor VIII is bound to vWF while inactive in circulation; factor VIII degrades rapidly when not bound to vWF. Factor VIII is released from vWF by the action of thrombin
    - It is important in platelet adhesion to wound sites. vWF binds to collagen, e.g., when it is exposed in endothelial cells due to damage occurring to the blood vessel.

Clinical Features:

- Most cases are of mild bleeding
- Spontaneous bleeding from mucous membranes (e.g. epistaxis)
- Excessive bleeding from wounds
- Menses bleeding increase
- In severe cases, similar to hemophilia A.

Lab diagnosis:

- CBC
- Hemoglobin N/
- Hematocrit N/
- Platelet count Normal and Low in type 2b
- Prothrombin time Normal
- Activated partial Thromboplastin time increase
- Fibrinogen Normal
- Collagen binding factors: to find out the binding ability of vwf with collagen
- Bleeding time: prolonged
- Clotting time: prolonged
- Thrombin time Normal
- Factor VIII decrease

Q5.Explain Hemolytic uremic syndrome and its types?

Answer:

Hemolytic uremic syndrome:

- Hemolytic uremic syndrome (HUS) is a condition that results from the abnormal premature destruction of red blood cells.
- Once this process begins, the damaged red blood cells start to clog the filtering system in the kidneys, which may eventually cause the life-threatening kidney failure associated with hemolytic uremic syndrome.
- Most cases of hemolytic uremic syndrome develop in children after two to 14 days of diarrhea-- often blood-- due to infection with a certain strain of Escherichia coli (E. coli).
- Adults also may develop hemolytic uremic syndrome after an E. coli infection, but the cause also may be certain medications, other types of infections, pregnancy or it may be unknown.

Types of hemolytic uremic syndrome:

There are two types of hemolytic uremic syndrome.

I. Typical:

- Infection by Shiga toxin-producing bacteria *E coli* serotype O157:H7 is the cause
- Mostly with diarrhea often bloody diarrhea (D+HUS).

II. Atypical:

- Atypical HUS (non–Stx-Hemolytic Uremic Syndrome) is rare.
- As the name implies, infection by Stx-producing bacteria is not the cause, and disease may occur year-round without diarrhea (D__ Hemolytic Uremic Syndrome).
- The familial form is associated with genetic abnormalities.

Signs and symptoms:

- Bloody diarrhea & Vomiting
- Abdominal pain
- Pale skin
- Fatigue and irritability
- Fever, usually not high and may not be present at all
- Blood in the urine
- Decreased urination or blood in the urine
- Swelling of the face, hands, feet or entire body.

The end