Factor VIII or Factor IX Deficiency (Hemophilia A or B)

Factor VIII and factor IX deficiencies are the most common severe inherited bleeding disorders

GENETICS AND CLASSIFICATION

- **Hemophilia occurs in approximately 1:5,000 males, with 85% having factor VIII deficiency and 10–15% having factor IX deficiency.**
- **Hemophilia shows no apparent racial predilection**
- **The severity of hemophilia is classified on the basis of the patient's baseline level of factor VIII or factor IX with 1 unit of each factor defined as the amount in 1mL of normal plasma.**
- **Severe hemophilia is characterized by having <1.0U/dL (<1%) of the specific clotting factor.**
- **Moderate hemophilia patients have 1–5U/dL,**
- **mild hemophilia patients have levels >5U/dL.**
- **The hemostatic level for factor VIII is >30–40U/dL and >25–30U/dL for factor IX.**
- **The genes for both factors are carried on the X chromosome**
- **Approximately 45–50% of patients with severe hemophilia A have gene mutation**

CLINICAL MANIFESTATIONS

- **Neither factor VIII nor factor IX crosses the placenta; thus, bleeding symptoms may be present from birth.**
- **only about 30% of affected male infants with hemophilia bleed with circumcision.**
- **easy bruising, intramuscular hematomas, and hemarthroses.**

- **Bleeding from the mouth may persist for hours or days**
- **Patients may lose large volumes of blood into the iliopsoas muscle and verge on hypovolemic shock with only a vague area of referred pain in the groin.**
- **Life-threatening bleeding in the hemophilic patient is caused by bleeding into vital structures (CNS, upper airway,gastrointestinal)**
- Repeated bleeding episodes into the same joint in a patient with severe hemophilia may become a “target” joint.

Investigations

- the APTT is usually (2) to (3) times the upper limits of normal of the APTT.
- Unless the patient has an inhibitor to factor VIII, the mixing of normal plasma with patient plasma results in correction of the PTT.
- (platelet count, bleeding time, prothrombin time, and thrombin time) are normal.
- The specific assay for factor VIII and factor IX will confirm the diagnosis of hemophilia.
- Bethesda assay for detecting the inhibitors

TREATMENT.

SUPPORTIVE CARE

- The prevention of trauma is important to the care of the child with hemophilia
- avoide **Aspirin** and other nonsteroidal anti-inflammatory drugs that affect platelet function

- the infant should be immunized against hepatitis B virus in case plasma-derived products are used with future bleeds.
- Patients should be periodically screened for hepatitis and abnormalities in liver function.

DRUGS

- With mild factor VIII hemophilia, the patient's endogenously produced factor VIII can be released by the administration of desmopressin acetate (DDAVP). A concentrated intranasal form of desmopressin acetate, The dose is 150 µg (1 puff) for children weighing <50 kg and 300 µg (2 puffs) for children and young adults weighing >50 kg.
- In patients with moderate or severe factor VIII deficiency, we use factor VIII
- **Dose of FVIII(units,U) = (u/dL(%)desired rise in plasma FVIII)X Body W.t(Kg) X0.5**
- **Dose of FIX (units,U) = (u/dL(%)desired rise in plasma FIX)X Body W.t(Kg) X1.4**
- **When bleeding occurs, the factor VIII level must be raised to hemostatic levels (35–50%) or for life-threatening or major bleeds to 100% (100U/dL)**

PROPHYLAXIS

prophylaxis should be considered optimal therapy for children with severe hemophilia .

Treatment is usually provided every 2-3 days to maintain a measurable plasma level of clotting factor (1-2%) when assayed just before the next infusion

primary prophylaxis

secondary prophylaxis

CHRONIC COMPLICATIONS

- chronic arthropathy. As further hemorrhages occur into the same joint, the patient is said to have developed a “target” joint for future bleeds.
- risk of transfusion-transmitted infectious diseases, including HIV and hepatitis C or B,
- the development of an inhibitor to either factor VIII or factor IX. Inhibitors are suspected clinically when patients who have responded well to replacement therapy suddenly become less responsive
- Those develop a higher titer with subsequent infusions and may need to go through desensitization programs, in which high doses of factor VIII or factor IX are infused in an attempt to saturate the antibody and to permit the body to develop tolerance. If desensitization fails, these patients are treated with either activated prothrombin complex concentrates or factor VIIa

Von Willebrand Disease

von Willebrand disease (VWD) is the most common inherited bleeding disorder

VWD is caused by a defect in von Willebrand factor (VWF). VWF has several functions in coagulation

1. VWF serves to tether platelets to injured subendothelium via binding sites for platelets and for collagen.
2. VWF serves as a carrier protein for factor VIII (FVIII), protecting FVIII from degradation in plasma

- von Willebrand disease is inherited autosomally, but most centers report more women than men. Since menorrhagia is a major symptom, it may cause more women to seek diagnosis.

CLASSIFICATION

- quantitatively reduced but not absent (type 1),
- qualitatively abnormal (type 2),

- absent (type 3)

Clinical manifestations

- mucocutaneous hemorrhage, including excessive bruising, epistaxis,
- menorrhagia
- Surgical bleeding, particularly with dental extractions or adenotonsillectomy

LABORATORY FINDINGS

- long bleeding time
- long PTT.
- vWf antigen, vWf activity

GENETICS.

- Chromosome 12 contains the gene for vWf.

TREATMENT

- Desmopressin, which increases the amount of circulating VWF by release from storage. thus use for treatment of type 1 ..it can be given either I.V or IN in a dose 1 spray IN (<50 kg) 2 sprays IN (>50 kg)
- von Willebrand factor concentrates is used for type 2 and type 3
- Antifibrinolytics : Aminocaproic acid or Tranexamic acid:

Source of the lecture

Nelson textbook of pediatrics

Further reading

Illustrated textbook of pediatrics