

BLEEDING DISORDER

Slide75 (Types of clotting factors deficiency):

Today we will talk about public public factor deficiency it could be acquired or inherited , acquired diseases are more common and multiple factor deficiency .

The most common causes are :

1- Chronic liver diseases

The site of synthesis over 10 factors

2- Vitamin K deficiency

From its name K from coagulation , and this vitamin is important for the function of factors X,IX,VII and II (1972) . these factors are depend on vitamin K and if it is absent , they will not work so patient will have bleeding .

The same principle is Warfarin drug it is inhibit factors that depend on vitamin K so in over dose Warfarin cause bleeding by this mechanism.

3- Disseminated intravascular coagulation

We will talk about it at the end of the lecture . In this disease there will be a consumption of all clotting factors, so the patient will end up with bleeding .

4- Autoimmune diseases

Antibodies are formed against clotting factors .

We finished talking about acquired causes of bleeding disorders and we will talk about inherited causes

Slide 76 (Hemophilia A):

- It is an X-linked disease so it is more common in boys.
- Factor VIII is a cofactor for factor IX and factor IX activates factor X , so there is a deficiency in intrinsic pathway .
- Internal pathway is abnormal so there is a coinheritance in PTT (PTT is abnormal).
- This family history in 70 % of cases from mother and the patient have hemophilia .
- In 30 % it is a new mutation starts with person who pass it to the next generation .
- the level of factor VIII must be decrease to less than 1%to be a spontaneous bleeding , this is a severe case it has only 1% of normal level .
- most cases are milder they have a little amount help in , milder they have multiple mutation (the more the amount will loss , the severity will increase).

- In milder cases patients behave well until predisposing factors that activates the internal pathway so patients develop bleeding.
- 90% of cases there are a true deficiency , there is a low level of factor VIII.
- 10% the level is normal but the function is abnormal .

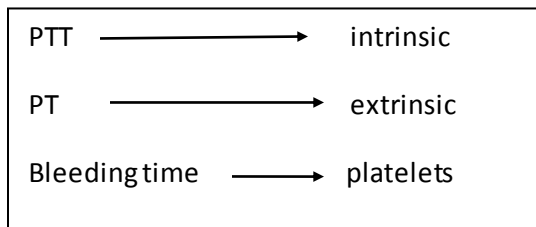
Slide 77 (Clinical features):

- Always clotting factors appear deep seated area in the body not in skin .
- Usually skin bleeding is controlled by platelets , small capillaries of skin need these platelets to be blunt to close (no deep seated here).
- Easily bruising specially in boys after circumcision there will be a prolong bleeding .
- The most common site of bleeding is skeletal system : joints and muscles so frequently patients have bone pain .
- Petechia differentiate clotting factor deficiency bleeding from platelets deficiency bleeding .
- Develop anemia as a result of blood loss .

Slide 78 (Tests) :

- Patient with PTT may be inherited or may be acquired.
- Mixing study to differentiate between acquired and inherited .

- In mixing study we get a normal serum with all clotting factors and we mix it with patient blood and we measure PTT again , so deficiency should be corrected because we mix patient serum with clotting factor VIII. So normal cell PTT normalized if it does not , that means the patient has auto antibodies against new factor VIII .(acquired has auto antibodies)
- PTT: partial thromboplastin time is measure the intrinsic pathway .
- Extrinsic has another pathway it is PT.
- Bleeding time third test measure the function of platelets (separate and know where is the defect exactly).



Slide 79 (Hemophilia B) :

- Same hemophilia A in abnormality and symptoms .
- Factor VIII is already a cofactor for IX if this one is absent ,any one is absent so will develop the symptom .
- It is correctable by mixing study .

Slide 80 and 81(Von Willibrand disease):

- It is more common than hemophilia .

- AD so affect both gender .
- vWF normally circulates in blood carries factor VIII to protect it from degradation by enzyme . they do not work until there is a stripping to endothelium (endothelial injury) so the cell expose to the below the endothelium . the environment is very thrombogenic to plug the damage usually by trauma . once epithelium is stripped the collagen is exposed or vWF attach to the collagen , once it is attached it attached platelets , platelets have receptor for glycoprotein 1 b that bind vWF . once it is bound the platelets start to adhere to each other with help of other factors and fibrinogen so it forms hemostatic plug .
- Hemostatic plug the first step of thrombosis .
- Hemostatic is a primary coagulation stage and it is platelets attached to vWF .
- In vWF deficiency no platelets adhesion and there is a permanent of bleeding .

Slide 82 (vWF deficiency):

- Type 1 : multiquantitive true deficiency .
- Type 2: abnormal protein (abnormal shape).as a result of mutation this abnormal one has activity does not need collagen so the enzyme decrease this abnormal protein and causes deficiency .

- Type 2 from type 1 that 2 has platelets deficiency (thrombocytopenia that causes bleeding).
- Bleeding in both types as a result of no adhesion of platelets .
- Secondary factor VIII deficiency as a result of factor VIII cleavage by the enzyme so they are not protected.
- Bleeding more pronounced in deep area .
- VWF usually milder than hemophilia .
- PTT is prolonged as a result of lost factor VIII
- Anemia because of blood loss.
- Secondary hemophilia.
- Low platelets .

We finished clotting factors deficiency disorders . Let's go to platelets disorders .

Slide 84 (ITP) :

- **Immune mediated so it is acquired.**
- **Antibodies bind normal platelets .**
- **Autoantibody IgG binds platelets proteins GP IIb/IIIa a normal protein important in platelets adherence .**
- **Patients will have thrombocytopenia .**
- **Ig's are synthesized in spleen cell . itself it is not known well now but patients with splenectomy have correction of disease . (removing spleen is treatment)**

- **Acute:** after cold and flu may the child has bleeding ,we test the platelets which they are low (thrombocytopenia)
- **Chronic :-** common as a part of autoimmune disease
 - Common in middle aged female (usually autoimmune disease more common in woman).
 - Correction by splenectomy .
- RBC's are normal
- Only platelets are low then they are immature and they are larger than ordinary platelets .
- **BM:** normal hematopoiesis(like in hemolytic anemia)
- Skin bleeding is common also they have deep organs bleeding .
- There is a bleeding in critical organ like brain that kills patient .

Slide 85 (TTP):

- Immature platelets (it is big when it released then it will be damaged).
- Thrombopoietin increases production .
- Totally different disease
- Part of microangiopathic hemolytic anemia .
- Clinically (5 symptoms):
 - Fever
 - Anemia (hemolytic, schestocytes)

- Thrombocytopenia
- Neurologic symptoms
- Renal failure
- Renal failure is more prominent in hemolytic uremic syndrome than in TTP.
- Neurological symptoms more obviously in TTP than in hemolytic uremic syndrome.

Slide 86 (pathogenesis) :

- VWF normally has a big precursor .
- Deficiency with ADAMTS 13 ends up with big number of multimers .
- In normal situation these multimers do not prolong because they are a potent aggregator of platelets (acts by itself without any activation).
- In deficiency activemultimer causes platelates aggregation everywhere so thrombosis are found all over the body in this disease .
- Causes of ADAMTS 13 deficiency either inherited (less common) or acquired (more common).
- In acquired cases autoantibodies are formed against the ADAMTS enzyme the multimer activates and the platelets aggregates and thrombosis everywhere in body .
- PT and PTT are normal.

- Thrombocytopenia because the consumption of platelets in thrombosis which formed everywhere .
- Bleeding time is prolonged .

Slide 87 (DIC) :

- Systemic activation of clotting factor (activation everywhere in the body as a result of different factors).
- Next stage anticlotting factor start to work remove thrombi that are formed everywhere end up with bleeding and no platelets different factor activates tissue factors that activate coagulation cascade this one release in high amount certain situation like in :
 - 1-sepsis (septicemia) : bacteria release endotoxin which activate monocyte that release tissue factors in high amount in the body so it is end with DIC.
 - 2- circulation activates thrombosis . myosin in cancer cells when they do invasion and open circulation sometimes malignant cell lysis release myosin that trigger coagulation cascade end up with DIC.
 - 3- in delivery sometimes complication make to death as a result of DIC .
 - 4 – in head trauma(brain) part of the tissue released in circulation and activate the cascade .

Slide 89 (pathogenesis):

- Second mechanism there is a wide spread endothelial damage in the body following different situation .
- Snake venom does wide spread endothelial damage that lead to systemic lupus erythematosus (SLE)
- In some autoimmune disease like SLE autoantibodies are deposited in blood and cause endothelia damage .

In general all microangiopathic disease are emergency patients can bleed to death in few moments there is no thing to prevent or stop the bleeding in the body. thrombocytopenia in peripheral blood most important in microangiopathic

PT and PTT are normal in TTP while they are prolong in DIC

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Sorry for any mistake

Shaima Al-Haj

