PathMD™: Board Review Letter

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Case #1 The diagram shown for this question illustrates initial platelet adhesion and aggregation. The substance highlighted by the red box best represents?

D. Fibrinogen

Answer: D. The highlight red box represents fibrinogen which is responsible for the initial aggregation of platelets mediated via the GPIIb/IIIa receptors. Von Willebrand's factor links to expose collagen to platelets via the GPIb receptor. (Goodnight, pages 3-19)

Case #2 The diagram shown for this case represents a platelet control and the patient's platelets is tested for aggregation in the presence of low dose and high-dose ristocetin. In addition, electrophoresis showed decreased large molecular weight von Willebrand's multimers. Mixing the patient's plasma with random donor platelets resulted in the same platelet arrogation findings with high and low dose ristocetin. Based on this information, the best diagnosis is:

D. von Willebrand's disease, type 2B

Answer: D. This case illustrates an example of font Willebrand's disease, type 2B. vWD type 2B is characterized by a gain of function mutations in the vWF which leads to spontaneous binding of platelets and rapid clearance of high molecular weight multimers. Pseudo-von Willebrand's disease is also in the differential diagnosis and is characterized by a gain of function of the GPIb receptor. Given that is a defect of the platelet, mixing the patient's plasma with random donor platelets would expect to correct the abnormal aggregation study with low and high-dose ristocetin, which does not happen in this case. (Goodnight, pages 115-125)

Question #1 A young patient is diagnosed with a pulmonary embolism, and is found to have a large DVT. No acquired risk factors for hypercoagability are found, and genetic etiologies are suspected. The patient is still in the ER and has not yet received anticoagulation. Which of the following tests can be performed to evaluate possible hypercoaguable states:

A. PT20210
B. Protein C and S
C. Factor V Leiden
D. A and C are correct

Answer: D. In the acute state of a thrombosis, only genetic based tests should be done. Plasma tests for “levels” are not helpful in the setting of an acute thrombus or anticoagulation because they will be affected. These include: protein C and S, antithrombin III, factor VIII. Genetic tests including Factor V Leiden and PT20210 (PCR based testing) can both be performed acutely or while on anticoagulation therapy.

Question #2 All of the following may result in a prolonged thrombin clotting time (TCT) EXCEPT:

A. Factor II deficiency

Answer: A. The thrombin clotting time (TCT) measures the conversion of fibrinogen to fibrin. The test supplies thrombin (factor II) to start this process. Heparin contamination, abnormal fibrinogen (i.e. dysfibrinogenemia), low fibrinogen levels (usually < 100), fibrin degradation products, and high concentrations of immunoglobulin (especially IgM – stays intravascular) can cause prolongation of the TCT. (Kitchens, page 19)

Question #3 Of extracellular matrix constituents, which is the most important pro-thrombotic component?

A. Collagen

Answer: A. Collagen is the most important pro-thrombotic component of the extra cellular matrix. Von Willebrand's factor acts as a bridge between collagen and platelets.

Question #4 A 46 y/o woman is found to have a prolonged aPTT with a normal PT. A mixing study was performed, and the aPTT corrected into the high normal range. Clinically, the patient does not have any evidence of bleeding or bleeding tendencies. Further questioning reveals the patient has been noted to have a prolonged aPTT during a routine physical exam 5 years ago. He was referred to a hematologist at that time who told him he was fine and not to worry. Based on these findings, which of the following is the most likely etiology of the patients prolonged aPTT?

C. Factor XII deficiency

Answer: C. In vitro factor XII is required to bind to glass beads to activate the intrinsic clotting pathway. This factor is not required to activate the clotting cascade in vivo, and patients with deficiencies of factor XII, high molecular weight kininogen, or prekallikrein do not have a bleeding diathesis clinically. A mild hemophilia A might be a reasonable answer, but the patient is a woman, and hemophilia A follows an X-linked inheritance pattern. Lupus anticoagulant and factor V inhibitors would not result in a corrected mixing study. (Kitchens, page 17)

Question #5 An acquired inhibitor to factor X can be caused by which of the following?

B. Amyloidosis

Answer: B. Amyloidosis is a cause of an acquired inhibitor to factor X. Hemophilia A patients may develop Factor VIII inhibitors, and Hemophilia B patients may develop inhibitors to factor IX. Use of bovine thrombin in vascular surgery is associated with development of factor V inhibitors.

Question #6 Which of the following has the greatest effect in inhibiting both factors V and VIII?

B. Thrombomodulin

Answer: B. Thrombomodulin acts on thrombin to activate Protein C (with Protein S as a cofactor) to cause proteolysis of factors V and VIII. Anti-thrombin III inhibits activity of thrombin and factors XIIa, XIa, Xa, and IXa. It is potentiated by heparin. Factor XIII is platelet stabilizing factor. Thromboplastin is another name for tissue factor, and tissue factor pathway inhibitor complexes with factor Xa and VIIa.

Question #7 Heparin induced thrombocytopenia is caused by heparin interacting with:

B. Platelet factor 4

Answer: B. HIT is caused by platelet factor 4 interactions with heparin.

Question #8 All of the following are symptoms of type 1 von Willebrand's disease EXCEPT:

B. Joint bleeding

Answer: B. Joint bleeding is characteristic of Hemophilia A (Factor VIII deficiency). Type 2N is characterized by abnormal binding of vWF to Factor VIII, which results in a hemophilia A-like picture.

References:

Disorders of Hemostasis and Thrombosis. Goodnight SH, Hathaway WE. Second Edition. 2001.

Consultative Hemostasis and Thrombosis. Kitchens, CS, et al. 2002.

Notes for question set:[1]

[1] PathMD strives for the highest quality and accuracy. However, the *PathMD: Board Review Letter* is for review purposes and not meant for clinical decision making. It should not be used in place of review of primary reference texts and the current medical literature. If inaccuracies are identified, please notify us so that a correction may be published. (info@PathMD.com)

