

Kaplan USMLE Step 1: Which factor is involved in the pathogenesis?

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If you're preparing for the United States Medical Licensing Examination[®] (USMLE[®]) Step 1 exam, you might want to know which questions are most often missed by test-prep takers. Check out this example from Kaplan Medical, and read an expert explanation of the answer. Also check out all posts in this series.

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This month's stumper

A 48-year-old woman comes to the emergency department because of a 16-hour history of confusion, dizziness, and fatigue. The patient has a history of HIV and is currently on antiretroviral therapy. Her temperature is 38.3°C (101.0°F), pulse is 98 beats per minute, respirations are 20 breaths a minute, and blood pressure is 110/72 mm Hg. Physical examination shows petechiae on her lower extremities. Laboratory studies show:

- Leukocyte count: 13,000/mm³.
- Hemoglobin: 8.1 g/dL.
- Platelet count: 75,000/mm³.
- Haptoglobin: 38 mg/dL.
- Lactate dehydrogenase (LDH): 305 U/L.
- Activated partial thromboplastin time (aPTT): 35 seconds.
- Prothrombin time (PT): 14 seconds
- Blood urea nitrogen: 29 mg/dL.

Peripheral blood smear shows multiple schistocytes. Which of the following factors is most likely involved in the pathogenesis of this patient's diagnosis?

- A.** Factor VIII.
- B.** Fibrinogen.
- C.** Glycoprotein Ib.
- D.** Glycoprotein IIb/IIIa.
- E.** Von Willebrand factor.

The correct answer is E.

Kaplan Medical explains why

Thrombotic thrombocytopenic purpura (TTP) is a rare idiopathic disorder of platelet consumption. Patients with HIV are at higher risk for developing TTP. TTP is caused by deficiency of von Willebrand factor (vWF) metalloproteinase (ADAMTS-13), leading to accumulation of large vWF multimers that trigger platelet aggregation and thrombosis. TTP is characterized by thrombocytopenia (due to platelet consumption), microangiopathic hemolytic anemia, acute kidney injury, fever, and fluctuating transient neurologic signs (including altered mental status and hemiplegia). TTP is on a disease spectrum with hemolytic uremic syndrome (HUS), but HUS generally occurs in children with recent dysentery due to *Escherichia coli* O157:H7. HUS is also not associated with neurologic changes.

Petechiae is a hallmark finding of platelet disorders such as TTP. Bleeding time is increased, while coagulation studies (aPTT and PT) are normal, unlike disseminated intravascular coagulation (DIC), which is associated with coagulopathy. Increased serum LDH levels, decreased serum haptoglobin levels, and schistocytes on blood smear are all consistent with microangiopathic hemolytic anemia. Microthrombi of the renal vasculature commonly leads to acute kidney injury in TTP. Accumulation of large vWF multimers in TTP causes thrombosis, as vWF facilitates platelet adhesion and aggregation at sites of endothelial injury. Exposed subendothelial collagen binds vWF, which in turn interacts with glycoprotein Ib on the surface of platelets, anchoring platelets to the site of vessel injury.

Why the other answers are wrong

Choice A: Factor VIII is a clotting factor that circulates bound to vWF in its inactive form and is released from vWF upon activation by thrombin. Hemophilia A is an inherited factor VIII deficiency characterized by increased aPTT without neurologic symptoms, anemia, thrombocytopenia, or acute kidney injury.

Choice B: Fibrinogen is another clotting factor that is converted into fibrin by thrombin. Fibrin molecules are cross-linked to form a fibrin mesh that stabilizes and reinforces the hemostatic plug. Fibrinogen is not involved in the pathogenesis of TTP.

Choice C: Glycoprotein Ib is a surface molecule that allows platelet adhesion to sites of endothelial injury via vWF, which anchors the platelet to exposed subendothelial collagen. Bernard-Soulier

disease is associated with an inherited deficiency of glycoprotein Ib, which causes thrombocytopenia, but it would not present with neurologic changes, anemia, or renal insufficiency.

Choice D: Glycoprotein IIb/IIIa is a surface molecule that is important for platelet aggregation. Fibrinogen links two platelets together by binding glycoprotein IIb/IIIa and forming a fibrin mesh. Glanzmann thrombasthenia is an inherited deficiency of glycoprotein IIb/IIIa that is not associated with neurologic symptoms, anemia, thrombocytopenia, or acute kidney injury.

Tips to remember

- | Thrombotic thrombocytopenic purpura (TTP) is caused by a deficiency of vWF metalloproteinase (ADAMTS-13), leading to the accumulation of large vWF multimers resulting in thrombosis.
- | TTP is characterized by thrombocytopenia, microangiopathic hemolytic anemia, acute kidney injury, fever, and neurologic changes.
- | Bleeding time is increased, while coagulation studies (aPTT and PT) are normal in TTP, unlike DIC, which is associated with coagulopathy.

For more prep questions on USMLE Steps 1, 2 and 3, view other posts in this series.