Mechanisms of Human Disease
Small Group Sessions

Case Studies on Bleeding and Thrombotic Disorders

October 1, 2014
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The Bleeding Patient

Demonstrations:
1. Platelet Count
2. Platelet Aggregation

Case Studies:
1. 32 yo male with swollen and tender knee
2. 72 yo male with fever, dysuria
3. 42 yo male scheduled for surgery

October 1, 2014
EDUCATIONAL OBJECTIVES

BLEEDING PATIENT CASE STUDIES

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1. Identify platelets in a peripheral blood smear.
2. Interpret the hemogram data in relation to platelet number and distribution.
3. Describe the theory behind platelet aggregation and discuss its relevance to bleeding disorders.
4. Contrast the differences between the platelet count and platelet function tests, and describe the limitations of each test.
5. Identify the qualitative and quantitative platelet related disorders by examining blood smears and interpreting aggregation assays.
6. Discuss the role of platelets in the formation of the hemostatic plug to arrest bleeding.
7. Describe the coagulation factors responsible for bleeding complications (pathologic disorder vs. drug overdose).
8. Discuss how increased fibrinolytic activity can lead to bleeding (pathologic disorder vs. drug overdose).
9. Identify the screening tests for evaluating the coagulation system.
10. Describe the principle behind the prothrombin time (PT), activated partial thromboplastin time (APTT), and thrombin time assays. Identify what each test measures and discuss the relevance of each test to bleeding disorders.
11. Compare and contrast the clinical and laboratory aspects of hemophilia A and B.
12. Design a clinical work-up to differentiate between hemophilia A and von Willebrand’s disease (mild and severe cases) on the basis of patient’s history, physical exam, coagulation and platelet tests.
13. Recognize that von Willebrand’s disease is related to a platelet function defect and is not related to coagulation FVIII or FIX defects.
14. Recognize that DIC is associated with simultaneous bleeding and thrombosis.
15. Diagnose DIC by physical exam, medical history and lab tests.
16. Illustrate how clinical laboratory tests are used to differentiate patients with the following bleeding disorders:

<table>
<thead>
<tr>
<th>Factor deficiencies</th>
<th>Disseminated intravascular coagulation</th>
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<tbody>
<tr>
<td>Hemophilia A/B</td>
<td>Congenital platelet defects</td>
</tr>
<tr>
<td>Von Willebrand's disease</td>
<td>Drug-induced bleeding</td>
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17. Recognize that aspirin use may result in bleeding and describe the mechanism. Contrast this mechanism to that of bleeding induced by GP IIb/IIIa receptor antagonists and ADP receptor antagonists.
18. Utilize laboratory and clinical data to properly diagnose a bleeding disorder caused by a defect in primary hemostasis vs. a defect in a coagulation factor vs. a drug overdose.
History and Physical:

Patient: 32-year-old male.

Chief Complaint: This patient was a construction worker who had minor knee trauma while working on the basement of a new home. He presented to the emergency room with a swollen, tender left knee. An emergency room intern saw the patient and obtained an x-ray which showed only a fluid collection in the knee joint. The left knee was aspirated. The aspirate was bloody.

Medical History: The patient had a lifelong history of easy bruising that occasionally occurred spontaneously. In addition, he had a history of bleeding after dental extractions on several occasions. However, the patient was unable to provide detailed information regarding the quantity of blood loss after the dental procedures. The patient had not previously received transfusions or been hospitalized. The patient was taking no medication at the time of the accident.

Family History: There was no family history of bleeding problems.

QUESTIONS

1. What does the patient’s clinical presentation and medical history suggest?

2. What lab tests should be ordered for this patient to help identify a pathologic disorder as a first screening approach?

3. What specific lab tests would be useful to diagnose a patient with a bleeding disorder?

4. What is a mixing study and when is it used?

5. Determine the differential diagnosis of this patient from clinical exam, family history, and laboratory tests (will be provided).

6. Discuss the family history aspect of hereditary bleeding disorders in mild and severe cases.

7. Discuss the treatment of the three most common hereditary bleeding disorders.
History and Physical:

**Patient:** 72-year-old male.

**Chief Complaint:** This patient presented with low grade fever of 2 days duration and worsening urinary frequency, hesitancy, and dysuria. Significant physical findings on admission included a palpable midline abdominal mass and an enlarged, firm prostate on rectal examination.

**After Admission:** Upon admission to the hospital, an indwelling foley catheter was placed with the evacuation of 2000 ml of cloudy, foul-smelling urine and resolution of the abdominal mass. A urine culture was sent. The patient was started on ampicillin empirically for presumed urinary tract infection (UTI), with a plan to perform transurethral prostatectomy (TURP) after resolution of the infection.

The evening of admission, the patient developed spiking fevers and shaking chills. Blood cultures were sent. The following day (Day 2 in hospital), multiple petechiae were noted over his legs and buttocks and he was oozing blood from venipuncture sites and from around the indwelling catheter. Stools were heme positive.

Blood and urine culture results were obtained and revealed *E coli*, resistant to ampicillin. His antibiotic was switched to cephalosporin. With the administration of appropriate antibiotics, his bleeding diathesis resolved. The patient underwent TURP one week later without complications.

**QUESTIONS**

1. The symptoms on admission suggest what clinical problem? Should coagulation laboratory tests be ordered, and if so which ones?

2. On Day 2 the patient experienced bleeding and petechiae. Would you change the diagnosis you gave in Question #1? Are these symptoms due to a new disorder? Explain.

3. What coagulation lab tests should be ordered on Day 2? Discuss possible lab results that can be obtained.

4. Is this patient in a serious clinical state?

5. Provide examples of other clinical scenarios leading to a similar diagnosis.

6. Fibrinogen is an acute phase reactant. When would it be high or low in this patient?

7. Discuss the role of α₂-antiplasmin in bleeding disorders.

8. What is the primary treatment for this patient?
History and Physical:

**Patient:** 42-year-old male.

**Chief Complaint:** This patient has been diagnosed with a compressed lumbar disc. He is scheduled for lumbar laminectomy and discectomy.

**Medical History:** His only significant history is that of tension headaches occurring every few days, for which he ingests six Excedrin® tablets on the days of headache.

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**QUESTIONS**

1. Is further medical information needed on this patient prior to scheduling surgery?

2. Would laboratory tests provide any useful information? Discuss.

3. Would a factor VIII level give further information for a more accurate diagnosis?

4. Discuss platelet count lab results and their reliability in diagnosing bleeding disorders.

5. What useful information will the PT/APTT provide for this patient? Why?

6. Propose a course of action for this patient.

7. Formulate an action plan if emergency surgery such as surgery for acute appendicitis was required in this patient.

8. Suppose this was a patient with a history of angina, why would he be taking aspirin? Discuss other anti-platelet drugs in clinical practice.

9. Would there be any concern about giving heparin to a patient with angina (e.g., in cardiac surgery or for treatment of a myocardial infarction) if he has already ingested aspirin. Discuss in view of the mechanisms of both drugs types.