NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Black and Blue with Love: A Case Study in Blood Clotting

by
Kendra S. Mell
Health Sciences Center, Texas Tech University, Lubbock, TX
and
Breanna N. Harris
Department of Biological Sciences, Texas Tech University, Lubbock, TX

Part I – Initial Office Visit

You are a nursing student and you have been given the opportunity to shadow Yasmin Gonzalez, a nurse practitioner. Today, Kelly Hunter brings in her 5-month-old son, Tristan, for an exam. Mrs. Hunter is anxious and concerned because she has recently noticed lots of bruises on Tristan and cannot figure out where they are coming from. Ms. Gonzalez looks over Tristan's body and sees visible bruises at different stages of healing along his arms. Upon further inspection, she finds bruises that are the size of half dollars that protrude along his rib cage. You and Ms. Gonzalez are concerned by the bruising and want to discuss this with the mother.

Questions

1. What do you think could be causing the bruising? Please list two possible explanations.

2. What are some important questions to ask the parent?

After talking with a tearful mom it is revealed that the parents had been trying for several years to become pregnant. Tristan sleeps no more than 20 minutes at a time even throughout the night. The mom says the baby's schedule "is tiring, but isn't that normal?" She has noticed the bruising over the past week and the bruises are getting bigger. She thinks they are coming from the excersaucer and jumpers that he plays in, but she is not sure. Tristan does not attend any daycare centers; he stays at home with his mom throughout the day. The mom verbalizes and physically shows that she loves her son and is concerned for his wellbeing.

Ms. Gonzalez calls a meeting with the medical team, which consists of the pediatrician, a social worker, a nurse, and you. The possible diagnoses discussed by the team include child abuse, leukemia, clotting disorders, nutritional deficiencies, and autoimmune diseases. Everyone on the team agrees that due to the location and sizes of the bruises, x-rays need to be taken to rule out broken ribs. X-rays are ordered for Tristan.

The x-rays return normal and show no broken bones. This result prompts the team to order a series of blood work. Tristan and his mother return to the hospital and blood is drawn. Ms. Gonzalez orders a complete blood count (CBC), a partial thromboplastin time (PTT), and a prothrombin time (PT) to evaluate Tristan's clotting time. She also orders a complete metabolic panel to get a comprehensive analysis of Tristan's blood work. The team meets again and you are curious as to what the blood tests are and why they are important in this situation. The pediatrician, Dr. Martavius Johnson, gives you a quick rundown of the tests.

Complete Blood Count

Used to measure: the number of red blood cells (RBC count), the number of white blood cells (WBC count), platelet count (PLT), breakdown of the white blood cells (granulocytes, lymphocytes, monocytes), the total amount of hemoglobin (HGB), and the percent of the blood sample composed of red blood cells (HCT). A CBC also tells us the average RBC size (MCV), hemoglobin amount per RBC (MCH), the amount of hemoglobin relative to size of the cell (hemoglobin concentration) per red blood cell (MCHC), and the RBC distribution width (measure of variability in RBC size). A CBC can be used to evaluate RBC production or destruction, test for infections, or detect clotting or blood disorders.

Comprehensive Metabolic Panel

A group of blood tests which provide information about body metabolism. This is usually performed to measure kidney function, acid/base balance, blood sugar, and electrolytes. For the metabolic panel, patients fast for 8h prior to having blood drawn. BUN (blood urea nitrogen) is determined to check function of kidneys. Creatinine is a breakdown product of creatine (from phosphocreatine – used to store ATP to fuel muscle activity), and is generally a measure of kidney function (high values indicate a kidney problem). Low levels of creatinine can be benign, or can mean a low-protein diet, pregnancy, or liver disease. Men tend to have higher creatinine levels than females due to higher muscle mass. eGFR = estimated glomerular filtration rate (based on creatinine and sodium clearance). BUN/creatinine ratio can be used to determine acute kidney injury or dehydration, both urea and creatinine are freely filtered by the glomerulus, but urea can be reabsorbed in the tubules whereas creatinine excretion remains fairly constant. Albumin is a blood protein made by the kidneys (it helps with the colloid pressure of the blood and keeps it from leaking out of the vessels; also carries other molecules). Globulin (proteins made by liver and immune system) can indicate blood disease. The ratio of albumin/globulin can indicate disease states (e.g., kidney disease, autoimmune disease, leukemias). Alkaline phosphatase is an enzyme and levels can indicate liver disease or bone problems. Bilirubin test checks for liver function. AST = asparate amino transferase, ALT = alanine amino transferase.

Partial Thromboplastin Time and Prothrombin Time

These blood tests measure how long it takes blood to clot. Blood is taken from the patient and kept in an airtight tube that contains certain chemicals. Then, additional chemicals are added to the blood and clotting (coagulation) time is measured (PTT is a measure of the intrinsic pathway and PT is a measure of the extrinsic pathway). For the PTT test, blood generally clots within 25 to 35 seconds, for the PT test it usually takes about 10 to 14 seconds. The coagulation cascade contains several clotting factors (XII, XI, IX, VIII, X, V, II [prothrombin], and I [fibrinogen]) and by performing PTT and PT together the health care provider can get an idea of what might be happening in the clotting process. These tests are performed when patients have a problem with bleeding or clotting. It can be used to help diagnose several disorders, including: factor XII or factor XI deficiency, hemophilia A, hemophilia B, hypofibrinogenemia, liver disease, vitamin K deficiency, or Von Willebrand's disease.

— *Information from NIH Medline*

Part II – Blood Work

Tristan's blood work comes back and the results are listed below. Please use this information to answer the questions below.

CBC Panel – T. Hunter

Measure	Value	Normal Range
White Blood Cells (WBC) (K/ul)	14.3	5.0–19.5
Red Blood Cells (RBC) (M/ul)	4.07	3.1–4.5
Hemoglobin (HGB) (g/ul)	9.4	10.0–14.0
Hematocrit (HCT) (%)	26.7	28–42
Platelets (PLT) (K/ul)	513	150–400
Mean Corpuscular Volume (MCV) (FL)	65.6	77–110
Mean Corpuscular Hemoglobin (MCH) (PG)	23.0	26–35
Mean Corpuscular Hemoglobin Concentration (MCHC) (g/dl)	35.0	33–36
Red Cell Distribution Width (RDW) (%)	14.8	11.5–14.5
Mean Platelet Volume (MPV) (FL)	7.8	7.4–10.4
RBC morphology	normal	normal-abnormal
WBC morphology	normal	normal-abnormal

Comprehensive Metabolic Panel – T. Hunter

Measure	Value	Normal Range
Glucose (mg/dl)	92	60–100
Sodium (Mmol/l)	137	139–146
Potassium (Mmol/l)	4.6	3.7–5.6
BUN (mg/dl)	6	5–17
Creatinine (mg/dl)	0.2	0.3–0.6
Chloride (Mmol/l)	104	98–108
CO2 (Mmol/l)	22	20–28
Calcium (mg/dl)	10.4	8.7–9.8
Protein, total (Gm/dl)	6.0	5.9–7.0
Albumin (mg/dl)	4.0	2.1–4.5
Bilirubin, total (mg/dl)	0.5	0.6–1.4
AST (u/l)	51	20–60
ALT (u/l)	36	6–50
ALK phosphatase (u/l)	234	145–320
Globulin (u/l)	2.0	2–4

PTT and PT tests – T. Hunter

Measure	Value	Normal
PTT Average (sec)	107.2	23.3–37.1
Prothrombin average (sec)	10.2	9.9–12.3
INR	0.94	See below

Historically, a PTT prolongation of 1.5–2.5 times the median of the normal range is considered to be the therapeutic level. However, many clinical factors may alter the therapeutic range.

International normalized ratio (INR) therapeutic values: anticoagulant therapy = 2.0–3.0; Prosthetic heart valve = 2.5–3.5

Questions

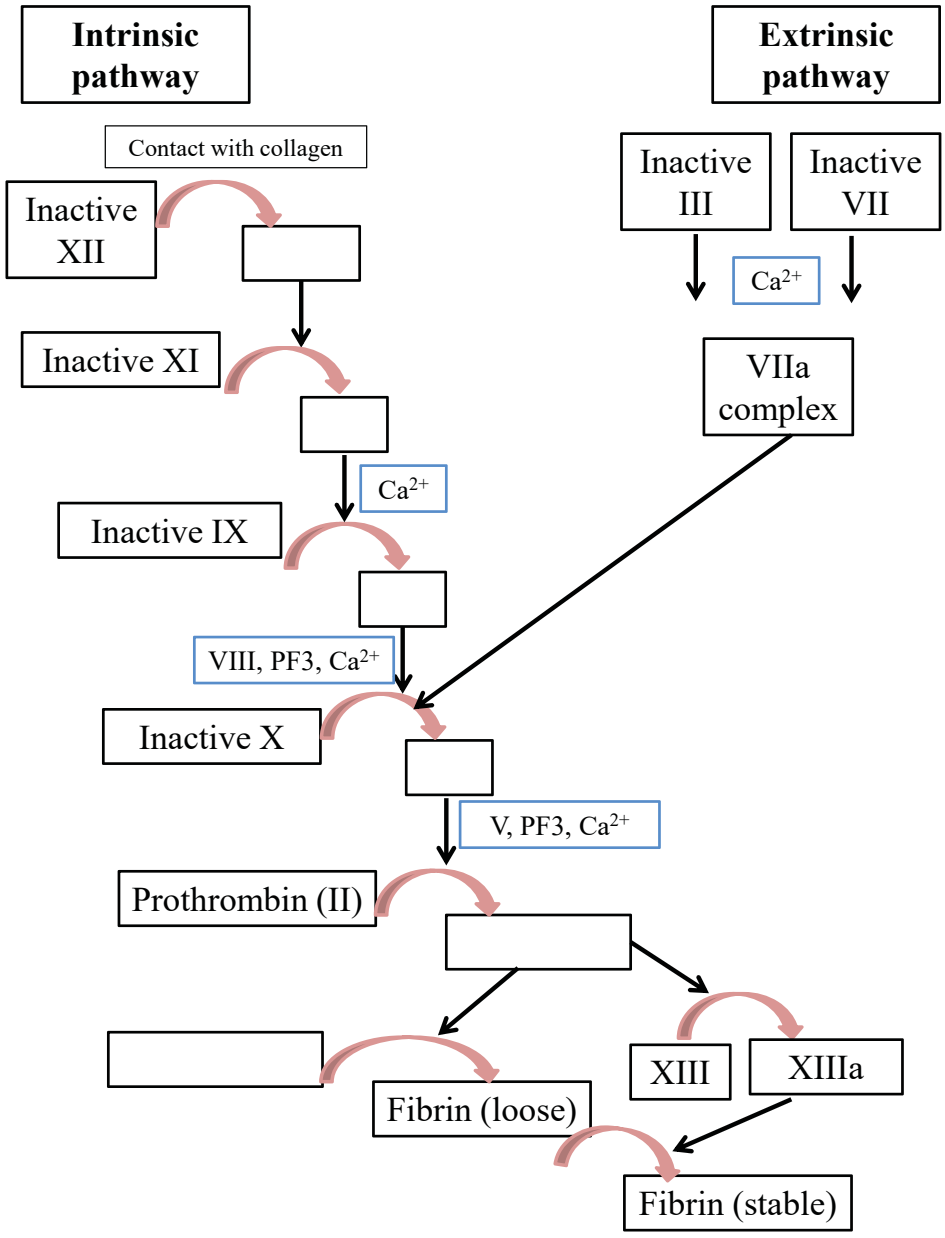
3. What results came back abnormal?

4. One of the largest lab abnormalities is Tristan's PTT (partial thromboplastin time). What does the PTT measure? What diseases/disorders could this abnormal test result indicate?

Part III – Clotting and Factor VIII

Question

5. What are the steps involved in blood clotting? Fill in the figure of the clotting cascade (use "a" to designate the activated form of the factor). What happens if there is a break in the cascade (i.e., what if one part does not function properly)?



Ms. Gonzalez and the team look over the results from Tristan's bloodwork and discuss the possible outcomes. The extended PTT values, combined with the elevated platelets, make the team decide to call in the local hematology/oncology specialist. Upon viewing the results the hematologist requests a factor VIII assay. Again you are curious as to what a factor VIII test is, and Dr. Johnson explains.

Factor VIII Assay

This is a blood test that measures the activity of factor VIII. Factor VIII or factor 8 is a large protein that is important to the clotting cascade. It accelerates the activation of factor X. Factor VIII is not an enzyme, but it plays a large role in the activation of factor X. The factor VIII assay measures the percentage of factor VIII present in the blood. Results are represented as a percentage of factor VIII needed to from a clot. Normal levels range from 50–200%. When results are low, this test can be used to diagnose hemophilia A, Von Willebrand's disease, and presence of factor VIII inhibitor (an antibody). For hemophilia A, levels less than 1% constitute severe hemophilia, 1–5% signifies moderate hemophilia, and values of 6–49% are diagnostic of mild hemophilia. When values are too high, this test can be used to diagnose/as a marker for diabetes, liver disease, inflammation, obesity, or pregnancy.

Results from Tristan's test are listed below.

Factor VIII Assay Results – T. Hunter

Measure	Value	Normal
Factor VIII	0.27%	50–200%

Questions

6. What is factor VIII? Why would having a decreased/absent amount of factor VIII be problematic?

7. What can an abnormal factor VIII test result mean? Do any of these conditions overlap with the possible outcomes from the PTT test? Based on the combined results, what is the most likely diagnosis?

Part IV – The Diagnosis

Ms. Gonzalez and her team meet with the hematologist and determine that Tristan has severe hemophilia A. Use the information provided by the National Hemophilia Foundation (http://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A) and the National Institutes of Health (http://www.nlm.nih.gov/medlineplus/ency/article/000538.htm; http://ghr.nlm.nih.gov/condition/hemophilia) to answer the following questions about hemophilia A.

Questions

8. What is hemophilia A? What is the incidence of hemophilia A (i.e., how often does it occur)?

9. What genes are affected in hemophilia A?

10. What are symptoms of hemophilia A?

11. What treatments are used to help manage hemophilia A?

12. What are the three severity levels of hemophilia A? What are the differences/criteria for diagnosis?

13. How would you explain this diagnosis to the parents?

Part V – Hemophilia A Inheritance

Questions

14. How is hemophilia A passed from parent to child? If a mother is a carrier, what is the likelihood that she'll pass that gene on to a son? To a daughter?

15. If the mother has hemophilia A what is the likelihood that her offspring will get a copy of the mutated gene (X)? It might be helpful to draw out a family tree or Punnett square to answer this question.

16. Will Tristan's sons and daughters have hemophilia A? Why or why not?