

MORNING REPORT

Thrombocytopenia in a Traveler

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A 33-year-old woman of Thai origin presents to urgent care for a one-day history of diarrhea and black stools. She currently lives in Denver, CO, and returned from a trip to Thailand five days prior. She was in her usual state of health until five days prior to presentation when she developed flu-like symptoms. She then noted three days of fever (up to 102°F) associated with nausea, vomiting, chills, severe abdominal pain, decreased appetite, and headache. The vomitus was blood-tinged, and the patient had an episode of epistaxis. These symptoms slowly improved but then returned one day prior to presentation with recurrence of flu-like symptoms in addition to her diarrhea and black stools. Her menstrual cycle was heavier than normal. She denied any respiratory symptoms. At urgent care, she was found to have severe thrombocytopenia and a positive stool guaiac test; she was transferred to the hospital for inpatient management. She has no significant past medical history or known bleeding issues. She denies any family history for hematologic disorders. She is not on any regular medications and denies any illicit drug use. In Thailand, she was prescribed an unknown antiemetic and antibiotic for gastroenteritis two weeks prior.

The causes of thrombocytopenia are varied and usually fit into two broad categories: decreased production or increased destruction/consumption. Decreased production includes hematologic malignancies, congenital thrombocytopenia, a drug reaction, infection, radiation, or any infiltrative bone marrow issue. Increased destruction/consumption includes broad categories of immune-mediated processes, lytic

processes, and sequestration: idiopathic thrombocytopenic purpura (ITP), autoimmune disease, medications such as heparin or antibiotics, infection with subsequent disseminated intravascular coagulation (DIC) or sepsis, thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS), cardiac valve lysis, or sequestration into the spleen.

However, the first issue to address is the clinical stability of the patient. Without knowing her actual platelet count, she may have internal hemorrhage. With platelet counts less than 10 K/mm³, patients are at increased risk for spontaneous bleeding and may need platelet or blood transfusions for supportive care. In this patient presenting with epistaxis, hematemesis, menorrhagia, and melena, evaluating for spontaneous bleeding is a priority. This patient's physical exam should look for signs of active bleeding, signs of rash or bites, pulmonary findings, lymphadenopathy, cardiac murmurs, splenomegaly, or signs of jaundice. Once the patient is clinically assessed and stabilized, a deeper evaluation of the cause of thrombocytopenia can continue.

On presentation, her temperature is 96.4°F, blood pressure is 113/64 mm Hg, heart rate is 52 beats per minute, respiratory rate is 16 breaths per minute, and oxygen saturation is 97% on room air. Mental status is intact with no focal findings. Physical exam is notable for evidence of blood clots in the nostrils. Cardiovascular exam shows no tachycardia, regular rhythm, no murmurs, rubs, or gallops. Her pulmonary exam is clear to auscultation without any crackles or rales. Skin exam shows no rash, ecchymosis, petechiae, or bites. No

lymphadenopathy is noted, and the spleen is not enlarged. Digital rectal exam shows no evidence of frank blood, and stool is scant but brown. The remainder of the exam is unremarkable.

The patient is noted to be clinically stable according to her vital signs and exam. Now I would obtain more history and more thorough exam and laboratory information to narrow down the differential, as the patient just returned from Thailand. In addition, the physical exam could be repeated to verify any insect bites or signs of jaundice. The history should include where she visited in Thailand (a rural area or large city), if she traveled to other countries, if she was exposed to any sick contacts, and what drugs were given when she had gastroenteritis. Important laboratory values should include the complete blood cell count with differential and peripheral smear, an electrolyte panel including kidney function, liver function, a urinalysis, and a DIC panel. Another consideration includes a urine pregnancy test.

In Thailand, she reports that she had an episode of food poisoning. She does not know what medications she received, but she did recover from this episode of gastroenteritis without issue. She mentions that she was mostly in Bangkok but did travel to the coast. She denies swimming in water; however, she does mention that numerous mosquitoes bit her. At that time, there were floods sweeping across Thailand, which prompted her to leave the country and travel back to Colorado. No other findings are noted on a more in-depth physical exam to suggest a cause for the thrombocytopenia.

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Initial laboratory studies show platelets are 7 K/mm³ (150-400 K/mm³), her hemoglobin is 14.3 g/dL (12.1-16.3 g/dL), and white blood cell counts and differential are normal. Her sodium is 130 mEq/L (133-145 mEq/L), and creatinine is normal. Prothrombin time is 12.8 seconds (12.2-15.0 seconds), activated partial thromboplastin time is 41.9 seconds (23.4-34.8 seconds), thrombin time is 26.5 seconds (15.8-18.3 seconds), D-dimer is 2210 FEU (0-500 FEU), and her LDH is 636 U/L (98-192 U/L). Her AST is 228 U/L (0-47 U/L), her ALT is 120 U/L (0-47 U/L), and total bilirubin is 1.1 mg/dL (0-1.3 mg/dL). Urine pregnancy test is negative. Her urinalysis shows a high number of red blood cells but no signs of infection or casts. Her peripheral smear is negative for any schistocytes. Due to her low platelet count, one pack of platelets is transfused. The patient is admitted to the general medicine floor for further evaluation of her thrombocytopenia.

The history, physical exam, and laboratory values do help narrow down the differential diagnosis for her thrombocytopenia. Decreased production or an intrinsic bone marrow issue is less likely as the presentation is so acute. She has no family history for hematologic cancers, and she personally had no symptoms prior to her trip overseas. Additionally, all of her cell lines are not decreased. Some type of cardiac lytic process is also less likely as the patient has no murmur. Splenic sequestration is also less likely as she does not have any organomegaly. TTP or HUS is less likely in the absence neurological findings, renal dysfunction, or schistocytes on peripheral smear.

A drug reaction, infection, or autoimmune process is most likely. The

patient was given two unknown drugs when she had food poisoning. Additionally, she was in Thailand where she could have been exposed to a viral or bacterial infection, HIV, or a vector-borne infection like malaria or dengue. She does have some evidence of DIC as her partial thromboplastin time, thrombin time, and d-dimer are elevated. She has a mild increase in her liver function testing. This could be from mild DIC or systemic inflammatory response syndrome (SIRS). An autoimmune process remains in the differential as she is a young female and could have ITP or new onset connective tissue disease.

The next step would be to continue to monitor how the patient is doing clinically, specifically looking for ongoing signs of bleeding. Additionally, serial blood counts should be monitored. If her platelets remain less than 10,000 K/mm³ or she has evidence of active bleeding, she should be further transfused. Now that the patient is stabilized, additional laboratory testing is warranted including blood cultures, acute viral hepatitis serologies, HIV testing, a smear looking for malaria, and dengue antibodies. A hematology and infectious disease consult should be considered to help determine the cause of the illness.

The patient remains clinically stable after one pack of platelets without signs of bleeding. Platelet counts are monitored twice daily. The hematology service is consulted given her clinical symptoms and profound thrombocytopenia. They find the clinical picture consistent with DIC (elevated thrombin time, d-dimer, no elevations in fibrinogen). ITP is also considered but less likely as the clinical picture does not fit and other eti-

ologies seem more likely. The hematology service suspects an immune mediated process from a viral syndrome and recommends starting prednisone at 1mg/kg per day.

The infectious disease service is consulted. Her recent travel history to Thailand, an endemic area for many tropical diseases, is a concern. The infectious disease team suspects a possible bacterial infection with her history of gastroenteritis, vector-borne disease with her history of mosquito bites, or a viral infection. Possible etiologies include salmonella, typhoid, leptospirosis, malaria, dengue, or acute HIV. Acute hepatitis serologies, HIV, and dengue antibodies are ordered.

The patient improves clinically within two days. Acute hepatitis serologies and HIV are negative. Her platelet count trends upwards with a value of 52 K/mm³ without additional steroids. Further serological test results come back after she is discharged. The IgG and IgM against dengue virus are both positive with values at 19.84 IV and 14.68 IV, respectively. (Values above 2.85 IV are considered positive.)

Dengue virus is a mosquito-borne infection that is endemic in more than 100 countries with reports of more than 50 million cases yearly. Infection can range from a flu-like syndrome to a potentially lethal disease causing internal bleeding, DIC, sepsis, and even death. The World Health Organization (WHO) classifies patients with either dengue or severe dengue. The category of dengue is classified further into those with and without warning signs. Those with severe dengue must show signs of shock with respiratory distress, liver failure, heart

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failure, and impaired consciousness. Our patient has dengue with warning signs. Diagnosis is made clinically and with laboratory confirmation (PCR testing and serologies such as antibodies). Treatment is largely supportive (fluids, transfusions, intubation), and no antiviral therapy has been shown to be effective. Although our patient did receive steroids, this treatment has not been shown to improve survival or achieve higher platelet counts in acute infection.

Take Home Points

1. The causes of thrombocytopenia generally fit into two broad categories: decreased production or increased destruction/consumption.
2. Dengue should be considered in the differential diagnosis for

patients with thrombocytopenia if they have recently traveled to an endemic area.

3. The severity of dengue ranges from a flu-like syndrome to a potentially lethal systemic disease. Treatment is largely supportive.

Suggested Reading

Dengue: Guidelines for treatment, prevention and control. Geneva: World Health Organization, 2009.

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