Anemia and Leukocytosis Answers

Case #1 RBC abnormalities

History: A 19-year-old woman with anemia presents with a two day history of fever, joint pain, and left upper quadrant discomfort. She reports experiencing similar episodes 2-3 times/year that respond to hydration and pain medication. Her history is notable for avascular necrosis of the left femoral head at age 14. Examine the virtual slide and answer the following questions.

What are the major RBC abnormalities on the smear?

*Many sickle cells, polychromasia, occasional target cells. Also a few activated lymphs (? viral infection triggered sickle crisis)*

A diagnosis of the "process" is readily made by inspection of the smear in this case but what additional test(s) are needed to establish the specific cause (etiology)?

A patient with multiple sickle crises/year is likely to have a moderate-severe form of the disease and. most likely, would have been diagnosed in infancy or childhood. Hemoglobin electrophoresis establishes a diagnosis in most cases. In some instances, molecular studies (performed at specialized labs) are needed.

What additional morphologic abnormalities might you expect in some cases?

*Those associated with hemolytic anemias.*

What would you expect the red cell indices to show in this case?

*Generally normochromic and normocytic.*

If you just had the CBC and red blood cell indices, what other types of anemia would you consider?

*You would need to consider the differential diagnosis of a normochromic, normocytic anemia (see class notes or flow charts for anemia dx and ddx hemolytic anemia).*

How do the morphologic and biochemical abnormalities in this case produce symptoms, signs and complications in this disease?

*Sickled cells are stickier and stiffer than normal RBCs thus "adhere" to endothelium, to one another and to WBCs, particularly in post-capillary venules, producing thromboses. During "painful crises" (generally triggered by hypoxia, infection), sickled fraction increases resulting in thromboses in many microvascular beds. Ischemia and infarction ensues with cumulative organ damage in multiple organs (see class notes or pathophysiology SS).*
Case #2 RBC abnormalities

History: The patient is a 28-year-old woman in the second trimester of pregnancy with her first child. Her pregnancy has been uncomplicated but recently she has noticed that she tires easily and is short of breath from even the slightest exertion. She also has periods of light-headedness, though not to the point of fainting, an uncomfortable feeling in her legs that can only be relieved by movement. On examination, the patient has tachycardia at rest, pale gums and nail beds, and a swollen tongue. Examine the virtual slide and answer the following questions.

What are the major RBC abnormalities on the smear?

*Anisocytosis, poikilocytosis and hypochromia. Microcytosis as well but may be difficult to appreciate.*

The history and findings on blood smear strongly suggest a diagnosis but what additional tests are needed to confirm it and establish the specific cause?

*Serum ferritin and, if necessary, iron and iron-binding capacity to confirm IDA. If not iron deficiency (most likely dx with history given) then thalassemia and anemia of chronic disease are considerations.*

If IDA confirmed still need to establish cause. Insufficient intake most common cause in healthy pregnant women but want to rule out occult blood loss as a cause.

What would you expect the red cell indices to show in this case?

*Hypochromic, microcytic anemia. If early, may be normochromic, normochromic.*

If you just had the CBC and red blood cell indices, what other types of anemia would you consider?

*Hypochromic, microcytic anemia then thalassemia, anemia of chronic disease (see flow charts for anemia dx review iron deficiency anemia).*

How do the morphologic and biochemical abnormalities in this case produce symptoms, signs and complications in this disease?

*Principal symptoms and signs related to reduced oxygen carrying capacity. Fatigue, tachycardia, shortness of breath, pale gums and nail beds. Restless leg syndrome (described in history) and, occasionally, bizarre appetites for non-nutrients (termed Pica) occur (see review iron deficiency anemia)*
Case #3 WBC abnormalities

History: A previously fit 20 year old man was admitted with a three day history of fever, sore throat, dyspnea, and malaise. Ten days before admission he had fallen on to his left side with pain over the left chest wall. A chest radiograph did not show a fracture, but the pain had been sufficiently severe to warrant overnight observation. On admission he was feverish, with a temperature of 39.7°C, and had generalised lymphadenopathy, non-exudative pharyngitis, mild hepatomegaly, and splenomegaly of 2 cm below the costal margin. He looked pale but well, and his blood pressure was 115/95 mm Hg, with a pulse rate of 96 beats/min. He had mild left and right abdominal tenderness without guarding. Initial investigations showed a normal CBC except for an elevated percentage of lymphocytes (see smear).

What are the major WBC abnormalities on the smear?

An increased percentage of large, atypical lymphocytes with abundant, bluish cytoplasm and enlarged, irregular nuclei generally without nucleoli. Cell membrane frequently indented by surrounding red blood cells.

What additional test(s) are needed to establish a diagnosis?

In a young, previously healthy individual without evidence of bone marrow suppression on the CBC (e.g. marked anemia, thrombocytopenia or neutropenia), the most likely cause for atypical lymphocytes in the peripheral blood is a viral infection. Mononucleosis, is the viral illness most commonly associated with significant expansion of lymphoid tissues throughout the body, lymphocytosis and an increased percentage of atypical lymphocytes on the smear. The "classic" criterion-- at least 50% lymphocytes and at least 10% atypical lymphocytes in the presence of fever, pharyngitis and adenopathy--is useful but hardly specific. Serologic confirmation is required, most commonly a "monospot" (heterophile antibody) determination is sufficient for confirmation. If negative and index of suspicion is high then detection of EBV capsid antigens may be necessary (see reference for a useful chart showing predictive value of various symptoms and lab findings mononucleosis).

What other conditions should you consider?

If heterophile antibodies or viral capsid antigens are negative then, if not considered previously, streptococcal pharyngitis and other viral pharyngitides are consideration (one wouldn't expect the systemic lymphadenopathy and splenomegaly seen in this case). Acute cytomegalovirus infection, toxoplasmosis and acute HIV infections can produce systemic lymphoid tissue expansion; however, lymphopenia is more common than lymphocytosis. If the atypical lymphocytes were, infact, blast forms (a morphologic distinction that can be difficult in some cases) then precursor B-cell or T-
cell neoplasms would be considerations (usually associated with evidence of bone marrow suppression).

How are the morphologic abnormalities in the blood smear related to the symptoms, signs and complications in this disease?

The atypical lymphocytes in the peripheral blood are, primarily, virus-specific cytotoxic T-cells responding to the EBV infected B-cells. The EBV-infected B-cells are in the circulation as well (up to 20% of circulating Bs may contain virus during acute phase) but most are in the expanded lymphoid tissues. The lymphoid organ expansion is due to both the mitogenic action of the EBV virus on infected B-cells and the reactive T- and B-cells trying to clear infected cells. Splenic rupture is a rare complication of infectious mononucleosis.

Case #4 WBC abnormalities

History: After a several day prodrome of fever, chills, cough, and shortness of breath, an elderly patient presented to the emergency department (ED). In the ED, the subject was febrile, hypotensive and hypoxemic. The white count was elevated.

What are the major WBC abnormalities on the smear?

Leukocytosis, marked left shift with increased percentage of neutrophils, bands and occasional myeloid precursors (from marrow). Thrombocytosis (platelets are an acute phase reactant; will diminish if DIC develops).

What additional test(s) are needed to establish a diagnosis?

Sepsis is defined as the presence or presumed presence of an infection accompanied by evidence of a systemic response referred to as the "systemic inflammatory response syndrome" or SIRS. Effort to provide firm diagnostic criterion for SIRS and various degrees of sepsis underway but not a done deal (see article if interested: sepsis) However, tests aimed at diagnosing infection in organ/tissue and blood are always part of the workup. Evidence of infection, hemodynamic instability and organ disfunction then severe sepsis. Evidence of infection and refractory hypotension in the setting of sepsis then septic shock.

What other conditions should you consider?

When marked leukocytosis (leukemoid reaction), must differentiate from myeloid neoplasms like chronic myelogenous leukemia (CML) or chronic myelomonocytic leukemia (CMML).
How are the morphologic abnormalities in the blood smear related to the symptoms, signs and complications in this disease?

The changes in the blood smear indicate that the bone marrow is responding to a strong inflammatory stimulus (mediated by relevant cytokines and growth factors)