EDUCATIONAL COMMENTARY – BLOOD CELL ID: MORPHOLOGIC FINDINGS IN SICKLE CELL ANEMIA

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To view the blood cell images in more detail, click on the sample identification numbers underlined in the paragraphs below. This will open a virtual image of the selected cell and the surrounding fields. If the image opens in the same window as the commentary, saving the commentary PDF and opening it outside your browser will allow you to switch between the commentary and the images more easily. You will need Adobe Flash to use this feature. Click on this link for the API ImageViewer™ Instructions.

LEARNING OUTCOMES

On completion of this exercise, the participant should be able to:

• identify morphologic characteristics of normal peripheral blood leukocytes.
• describe morphologic features of sickle cells.
• distinguish giant platelets based on morphologic characteristics.
• discuss the pathophysiologic features of sickle cell anemia.

Case Study
The CBC from a 30 year old African American male is as follows: WBC=9.5 x 10^9/L, RBC=1.66 x 10^{12}/L, Hgb=5.0 g/dL, Hct=13.9%, MCV=83.7 fL, MCH=30.1 pg, MCHC=36.0 g/dL, RDW-CV=24.9%, MPV=9.6 fL, Platelet=326 x 10^9/L.

Educational Commentary
The patient in this testing event had severe anemia and classic red blood cell (RBC) findings distinctive for sickle cell anemia. Normal leukocytes and morphologically abnormal platelets were also present.

Image BCI-01 shows a normal eosinophil with abundant, vibrant, red-orange granules in the cytoplasm. These granules are typically larger than the granules seen in segmented neutrophils and are generally uniform in size. The overall cell size parallels that of segmented neutrophils, as does the densely clumped nuclear chromatin. The nucleus in this example appears to be bilobed, a typical finding in eosinophils.
The cell identified in Image BCI-02 is a typical monocyte. It is large (monocytes are the largest cells normally seen in the peripheral blood), with abundant cytoplasm. The blue-gray color and the vacuoles are characteristic. This monocyte has several pink or lilac (azurophilic) granules. The cytoplasm in this cell shows an even, smooth appearance, especially below and to the right of the nucleus, although this is unusual. More commonly, the cytoplasm looks rough and uneven. Likewise, the cellular margins are frequently not uniform, and cytoplasmic projections are sometimes present. Nuclei in monocytes are variable in shape and may be round, oval, lobulated, or kidney-shaped. The chromatin generally shows minimal clumping and stains lighter shades of purple.

Image BCI-03 represents a classic example of a sickle cell or drepanocyte. Sickle cells are characterized by two pointed ends, with no area of central pallor and an elongated crescent shape. Drepanocytes form when hemoglobin within the cells becomes deoxygenated. The hemoglobin produced in this disorder, HbS, is abnormal and has reduced solubility when deoxygenated. The molecules of deoxygenated HbS polymerize, and rods or filaments of HbS then distort the normal RBC (discocyte) into a sickle cell. The sickled RBC can revert to a discocyte when reoxygenated, but if deoxygenation occurs again, the cell will again sickle. This sickling/nonsickling process continues as the RBCs circulate. However, repeated sickling and nonsickling eventually deforms the cell permanently, so that it remains sickled even when reoxygenated.

Some of the other cells in this photograph appear to have an area of central pallor. These cells may be in transition from nonsickled to sickled. They should not be mistaken for elliptocytes (ovalocytes), which lack pointed or tapered ends and have parallel sides of equal lengths. Elliptocytes clearly have areas of central pallor with rounded ends.

Editor’s note: Some participants reported the cell shown in image BCI-03 as a schistocyte. Schistocytes are truly fragments of red blood cells and are variable in size and shape. Also, schistocytes usually have
more than two points, while sickle cells have only two points. When schistocytes are present, other fragments without specific shapes would also be seen on a blood smear, along with spherocytes and helmet cells. Additional examples of sickle cells can be found in each photograph and by scanning the virtual image of this patient’s blood smear using the ImageViewer™.

A normal segmented neutrophil is depicted in Image BCI-04. Segmented neutrophils typically have from two to five nuclear lobes connected by thin filaments of chromatin. The chromatin pattern is dense and clumped in appearance and stains a dark purple. Numerous pink, tan, or violet granules dot the cytoplasm.

**Editor’s note:** Some participants reported the cell shown in image BCI-04 as a neutrophil with toxic granulation. Toxic neutrophils contain large purple or dark blue cytoplasmic granules. They also often include Döhle bodies and vacuoles. In contrast, the normal segmented neutrophil shown in this image has small pink granules.

Image BCI-05 shows a normal lymphocyte. Lymphocytes vary in size and this is an example of a small lymphocyte. The nucleus is dense, clumped, and a deep purple. Small lymphocytes characteristically have a scanty rim of blue cytoplasm, as seen in this cell.

Image BCI-06 shows another example of a sickle cell. Again, note the tapered ends and general lack of central pallor. There are several drepanocytes in other images as well. Numerous drepanocytes can also be found while scanning this smear using the ImageViewer™. Many of these other sickle cells are not classically shaped but resemble boats, holly leaves, splinters, or envelopes. The typical crescent-shaped
drepanocyte with pointed ends results from repeated sickling events and represents an irreversibly sickled cell. Cells that are less classically shaped, with a less pronounced curvature, tapering ends, and a broader center are reversibly sickled. These cells are capable of reverting back to discocytes or near-normal RBC shape when reoxygenated.

Sickle cell anemia and sickle cell disease are severe disorders that result when individuals are homozygous for the condition. Because they inherit two abnormal genes that code for the production of HbS, persons with sickle cell anemia or sickle cell disease form no normal hemoglobin. A heterozygous state occurs when one abnormal gene is inherited and some normal hemoglobin is produced. People who inherit one abnormal gene have sickle cell trait. It is rare to see sickle cells in the peripheral blood of a patient with sickle cell trait. People with sickle cell trait are asymptomatic.

Patients with sickle cell anemia, however, experience symptoms related to severe anemia as well as other abnormal manifestations. The hemoglobin and hematocrit levels of the current patient were critically low, 5.0 g/dL and 13.9%, respectively.

Because of their abnormal shapes, sickle cells do not circulate freely. They are rigid and aggregate in vessels, eventually occluding the microvasculature. The blockage that results prevents normal RBCs from passing through the vessels and triggers additional deoxygenation. Lack of oxygen exacerbates sickle cell formation and also causes tissue death. Therefore, most symptoms experienced by patients with sickle cell anemia occur because of the lysis of RBCs, obstruction of the microvasculature, and subsequent tissue necrosis.

Other peripheral blood findings that may be seen in a patient with sickle cell anemia, and which were seen in the current patient, are target cells, polychromasia, and Howell-Jolly bodies. Slight eosinophilia is sometimes seen (this patient had 5% eosinophils on a differential cell count), as well as leukocytosis and thrombocytosis, neither of which was noted in the current patient.

Finally, sickle cells may be seen in combined disorders, such as HbS-thalassemia, and in patients who are also doubly heterozygous for two qualitative defects, such as sickle cell C and sickle cell D diseases.
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The arrow in Image BCI-07 identifies a giant platelet. The descriptor giant is used to classify a platelet that is larger than a normal RBC. This platelet has no nucleus and therefore it should not be confused for any type of leukocyte. In this example, the periphery is generally even and smooth, although it sometimes appears ruffled or scalloped in platelets of this size. Giant platelets often display light and dark areas in the cytoplasm, as well as either finely dispersed or aggregated granules. The platelet in this photo appears to be agranular or have very few granules, which may be typical in giant platelets, specifically in sickle cell anemia. The overall staining color of the cell is usually a light blue or blue-gray. The vacuoles in this giant platelet are not characteristic and most likely represent an artifact of smear preparation or an aged blood sample. Also, the more-granular cytoplasm, zoning with clear areas, and color that is more blue-gray helps distinguish giant platelets from polychromatophilic RBCs.

Editor’s note: Additional examples of both large and giant platelets can be seen by scanning the virtual image using the ImageViewer™. To see one of these examples, click “Additional giant platelet” here or while viewing BCI-01, -02, -03, or -06.

Summary

The patient described in this testing event had sickle cell anemia. Several classic and reversibly sickled cells can be identified in the images and on the smear that are diagnostic for this disorder. Because these cells are diagnostic, the laboratory professional contributes significantly to the quality of patient care by identifying and reporting sickle cells from an evaluation of a stained peripheral blood smear.