EDUCATIONAL COMMENTARY – IDENTIFYING ABNORMALITIES IN PERIPHERAL BLOOD CELLS

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Learning Outcomes
Upon completion of this exercise, participants will be able to:

- describe the morphologic features of normal peripheral blood leukocytes.
- identify abnormalities in red blood cells (RBCs) that are characteristic of hereditary spherocytosis.
- discuss the pathophysiology of hereditary spherocytosis.

An 8 year old female was seen in the pediatric hematology clinic. Laboratory findings included: WBC= 13.6 x 10^9/L, RBC= 2.63 x 10^{12}/L, Hgb= 8.5 g/dL, Hct= 22%, MCV= 85.0 fl, MCH= 32.4 pg, MCHC= 38.1 g/dL, RDW= 21.4%, and Platelets= 897 x 10^9/L.

This patient has been diagnosed with hereditary spherocytosis. Normal leukocytes and abnormalities in erythrocytes that may be seen in this condition are presented in the images.

BCI-01 shows an eosinophil. Eosinophils characteristically have large, red-orange cytoplasmic granules. These granules are numerous and uniform in size. The nucleus of an eosinophil is often bilobed, although in this image, it is round. The chromatin is generally dense and clumped.
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The cell identified in BCI-02 is a segmented neutrophil. Neutrophils usually have 2 to 5 nuclear lobes connected by thin filaments of chromatin. The chromatin is coarse and densely clumped. In contrast to the eosinophil shown in BCI-01, segmented neutrophils have numerous small granules that normally stain light-violet or pink.

Editor’s note: To compare and contrast this segmented neutrophil (BCI-02) with a photograph of a hypersegmented segmented neutrophil, you can go to the 2010 3rd Test Event discussion in the ASCP Educational Commentary library. Look on the left side of the screen, under Continuing Education, then click on Educational Commentaries. Click on Hematology, then choose “Blood Cell ID: Peripheral Blood Cell Morphologic Changes (2010)” and look for the photograph labeled BCI-21.

BCI-03 illustrates an abnormal RBC called a “polychromatophilic erythrocyte.” Note that other polychromatophilic erythrocytes are present in this image as well as in other images.

Polychromasia is the condition associated with the appearance of these cells on a peripheral blood smear. Polychromatophilic erythrocytes are the stage of RBC maturation just before the mature erythrocyte, also called the reticulocyte. Reticulocytes have lost their nucleus, but have retained residual RNA. Therefore, the cell appears blue-gray when Wright stain is used.
Sometimes, reticulocytes look larger than normal RBCs, although that is not the case in this example. Reticulocytes usually mature for approximately 48 hours in the bone marrow and another 24 hours after their release into circulation. The presence of polychromatophilic cells in the peripheral blood suggests enhanced bone marrow activity in response to a decrease in oxygen reaching the cells and tissues of the body. The patient has hereditary spherocytosis, a specific type of hemolytic anemia. “Hemolytic anemia” describes any decrease in oxygen-carrying capacity that is related to shortened RBC survival or increased erythrocyte destruction. So the appearance of polychromatophilic erythrocytes in this patient is not unexpected, especially given the low RBC count, and low hemoglobin and hematocrit values.

The cell depicted in BCI-04 is a spherocyte. Spherocytes are smaller than normal RBCs. They form when cellular membrane is lost resulting in a decreased surface-to-volume ratio. Spherocytes are dense and lack any area of central pallor. This decrease in surface-to-volume ratio is reflected in an elevated mean corpuscular hemoglobin concentration (MCHC). An increased MCHC can be a useful parameter to evaluate the peripheral blood smear for possible spherocytes.

Hereditary spherocytosis is a condition associated with intrinsic defects in membrane proteins that provide stability to the RBC. The defect that most often causes this unstable membrane is a deficiency of spectrin, though a dysfunctional spectrin molecule or decreases in other proteins may also occur. The unsupported membrane allows microscopic vesicles to form. The spleen removes these bulges, causing loss of membrane and the formation of spherocytes.

Hereditary spherocytosis is the most common hemolytic anemia in persons of northern European descent. Diagnosis can occur at any age. Patients who have the condition may have no symptoms and no apparent anemia or they may display a moderately severe hemolytic state with signs of anemia. Characteristically, variable numbers of spherocytes and polychromasia are seen on the peripheral blood smear.
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**BCI-05** shows a monocyte. Monocytes are large cells. They have abundant, blue-gray cytoplasm that is often vacuolated. The cytoplasm also appears uneven and rough. Sometimes, fine lilac or purple granules may be seen in the cytoplasm. A hint of these granules can be seen in the upper left area in this image. Cellular margins in monocytes are frequently not uniform, and sometimes cytoplasmic bulging may be seen. The nuclei in monocytes vary in shape and can be round, oval, kidney-shaped, or lobulated. The nuclear chromatin is fine, with little clumping, and generally stains a lighter purple or pink. No nucleoli should be visible.

**Editor’s note:** Another photograph of a monocyte may be found in the 2010 1st Test Event discussion in the ASCP Educational Commentary library. On the left side of the screen, under Continuing Education, click on Educational Commentaries. Click on Hematology and then choose "Blood Cell ID: Malaria and Morphologic Look-Alikes (2010)." Look for the photograph labeled BCI-02.

A stomatocyte is pictured in **BCI-06**. The area of central pallor is slightly curved, like a slit or a mouth, instead of being round. Stomatocytes can result from defects in membrane proteins, but more often they are artifactual, produced during smear preparation.
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The cell identified in BCI-07 is a hypochromic erythrocyte. Normal RBCs have an area of central pallor that is about 1/3 of the diameter of the cell. Cells that have a larger area are called hypochromic, and the condition associated with increased central pallor is called hypochromasia or hypochromia. The mean corpuscular hemoglobin (MCH) is a useful indicator of hypochromasia. However, the MCH represents an average value, so it may not be decreased if hypochromic cells are not prevalent. Such is the case in this test situation.

Summary

The patient has hereditary spherocytosis. Classic morphologic findings in this condition include spherocytes and polychromasia, both prominent in the peripheral blood images presented for evaluation. Hereditary spherocytosis results in a hemolytic anemia because spherocytes are removed more readily by the spleen than normal erythrocytes. The recognition and reporting of spherocytes by laboratorians is important to the diagnosis and subsequent management of this disorder.

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