EDUCATIONAL COMMENTARY – BLOOD CELL ID: IDENTIFYING COMMON PERIPHERAL BLOOD LEUKOCYTES AND ERYTHROCYTE CHANGES IN HEREDITARY SPHEROCYTOSIS

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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 new browser tab or window containing a virtual image of the selected cell and the surrounding fields. You will need Adobe Flash or the Microsoft Edge browser (included with Windows 10) to use this feature. Click on this link for the API ImageViewer™ Instructions.

Learning Outcomes

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

- describe morphologic features of normal peripheral blood granulocytes;
- discuss morphologic characteristics of normal peripheral blood lymphocytes and monocytes; and
- identify morphologic changes in erythrocytes associated with hereditary spherocytosis.

Case Study

A CBC with differential was ordered for a 3-year-old male. His CBC results are as follows: WBC=7.4 x 10^9/L, Hgb=9.7 g/dL, Hct=27.8%, MCV=76.5 fl, MCH=26.8, MCHC=35.0 g/dL, RDWSD=28.9, Platelet=573 x 10^9/L.

Educational Commentary

The young boy’s peripheral blood cells selected for identification and discussion in this testing event represent not only normal white blood cells, but also abnormalities in red blood cells that may be seen in hereditary spherocytosis.

The cell indicated in Image BCI-15 is a monocyte. Note the large size of this cell. Monocytes are the largest cells normally seen in the peripheral blood. This cell is a typical example of a monocyte. The cytoplasm in monocytes is usually abundant, often vacuolated, and blue-gray. Sometimes, fine lilac or purple granules may be seen. The cytoplasmic margins are frequently uneven and bulges or extensions are present. Likewise, the cytoplasm appears rough or sandy or, as it is sometimes described, like ground glass. Nuclei in monocytes
vary in shape and may be lobulated, reniform (kidney-shaped), oval, or round. The nuclear chromatin is fine with minimal clumping and stains lighter shades of purple.

The cell marked for identification in Image BCI-16 is a normal lymphocyte. Lymphocytes are variable in size; this example represents a smaller cell. The scanty amount of blue cytoplasm is characteristic. The nuclei are usually round, slightly oval, or barely indented. The nuclear chromatin in small lymphocytes is clumped, dense, and dark purple.

The cell indicated in Image BCI-17 is a segmented neutrophil. Segmented neutrophils are medium-sized cells. Note that this cell is smaller than the monocyte in Image BCI-15, but larger than the normal lymphocyte in Image BCI-16. The cytoplasm in segmented neutrophils contains numerous granules. These small granules are often tan, pink, or light violet. The granules in this particular cell have stained a darker color. A characteristic feature of segmented neutrophils is the nuclear shape, which usually shows two to five lobes. The lobes are separated by thin threads of chromatin. Sometimes the chromatin filaments are not easily distinguished if multiple folding of the lobes obscures the strands, as in this example. Cells such as this are still classified as the most mature form, a segmented neutrophil. Segmented neutrophils display nuclear chromatin that is dense and clumped.

Image BCI-18 shows an eosinophil. This cell is usually similar in size to the segmented neutrophil. In contrast to segmented neutrophils, however, the eosinophil has numerous large, uniformly round, red-orange cytoplasmic granules. This eosinophil appears to be bilobed, which is also characteristic. The purple nucleus has dense, clumped nuclear chromatin.
A basophil is selected in Image BCI-19. Basophils are often slightly smaller than their cousin granulocytes, segmented neutrophils and eosinophils. It is interesting that all the granulocytes appear in the peripheral blood of the patient in this test event, especially the basophil. It is often possible to evaluate 100 leukocytes on a stained peripheral blood smear and never see a basophil. Basophils feature deep purple or blue-black cytoplasmic granules. These granules are numerous, large, and generally round. Basophil granules are frequently so abundant that they obscure the nucleus. It is difficult to appreciate nuclear detail in this particular cell because of the granules.

The cell indicated in Image BCI-20 is a microspherocyte (spherocyte), an abnormal red blood cell. Two morphologic characteristics define spherocytes: they are smaller than normal red blood cells and they are dense, lacking any area of central pallor. Spherocytes form when cellular membrane is lost. Therefore, they have a decreased surface to volume ratio. Spherocytes have reduced surface, but the same volume of cytoplasm, resulting in the features that morphologically distinguish these cells.

Spherocytes often appear microcytic, although the mean corpuscular volume (MCV) varies related to the degree of reticulocytosis that may be present. They are sometimes called microspherocytes, although some references suggest that spherocytes are not microcytic, as indicated by a normal MCV. Likewise, true microcytes generally display some area of central pallor. The MCV in this case study patient is in the low-normal range, probably because of a minimal relative reticulocyte response combined with several smaller spherocytes.

Spherocytes are the only red blood cells in which the mean corpuscular hemoglobin concentration (MCHC) is elevated (35 to 38 g/dL or more, depending on each laboratory’s normal range). Therefore, spherocytes are truly hyperchromic, with a constant volume packed into a cell that has lost surface membrane. Consequently, these cells appear dense with no area of central pallor.
The final cell for identification, in Image BCI-21, is a polychromatophilic red blood cell. Polychromatophilic erythrocytes are reticulocytes, the precursor stage of erythrocyte maturation just before the mature red blood cell. Normally, reticulocytes mature in the bone marrow for approximately 48 hours and then develop for another 24 hours after their release into circulation. Polychromasia is the condition associated with the presence of these cells on a peripheral blood smear. Polychromatophilic red blood cells have no nuclei, but have retained a small amount of ribonucleic acid (RNA) and will appear bluish when Wright stained. The darker, blue-gray cytoplasm in this cell is characteristic of a polychromatophilic erythrocyte. Likewise, the larger size of this cell suggests that it is more like a normal red blood cell and is not a spherocyte. In fact, polychromatophilic cells are often slightly larger than normal erythrocytes as they represent immature red blood cells. Polychromatophilic red blood cells usually have no area of central pallor. It is not unusual to see polychromasia in a patient diagnosed as having hereditary spherocytosis. Hereditary spherocytosis results in red blood cells with shortened survival. Erythropoietic activity increases in the bone marrow in response to the loss of circulating red blood cells, releasing reticulocytes into the peripheral blood as a compensatory mechanism.

Hereditary Spherocytosis

Hereditary spherocytosis is a disorder caused by an intrinsic defect in erythrocyte proteins that provide stability to the membrane. The condition is heterogeneous in that several different membrane proteins may be deficient or defective. Because hereditary spherocytosis varies in etiology and pathophysiology, there are ranges in clinical severity as well. Similarly, the number of spherocytes seen on a stained peripheral blood smear varies, with some patients having few prominent spherocytes.

Spherocytes are less deformable and flexible than normal red blood cells. They have difficulty negotiating the small passageways of the spleen and are easily trapped and removed. Sometimes the unstable membrane allows microscopic vesicles to form on the surface of the red blood cell. The spleen also pits these bulges, causing further loss of membrane and the formation of additional spherocytes. Regardless, spherocytes are eventually destroyed or removed from circulation, resulting in a hemolytic anemia. Individuals who are able to compensate for the loss of erythrocytes are generally asymptomatic.
Summary

The boy presented in this testing event was diagnosed as having hereditary spherocytosis. Although several normal peripheral blood leukocytes were selected for identification, the classic morphologic features of this condition include spherocytes and polychromasia. Spherocytes may also be seen in immune-mediated and microangiopathic hemolytic anemias. Diagnosis of hereditary spherocytosis as well as of these other disorders depends on recognition of spherocytes and other erythrocyte abnormalities on the peripheral blood smear. Appropriate identification of abnormal cells provides key information to help define various conditions.

References


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