EDUCATIONAL COMMENTARY – PERIPHERAL BLOOD LEUKOCYTES AND ERYTHROCYTE ABNORMALITIES

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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. Click on this link for the API ImageViewer™ Instructions.

Learning Outcomes

On completion of this testing event, the participant should be able to

- describe morphologic features of normal peripheral blood leukocytes;
- discuss distinguishing morphologic characteristics of immature white blood cells and red blood cells; and
- identify morphologic abnormalities in erythrocytes.

Case Study

A CBC with differential was ordered on a 37 year old obstetric patient post-delivery. The patient developed separation of the placenta during delivery. Her CBC results are as follows: WBC=5.9 x 10^9/L, RBC=2.71 x 10^{12}/L, Hgb=8.1 g/dL, Hct=24%, MCV= 88.6 fL, MCH=29.9 pg, MCHC=33.8 g/dL, Platelet=112 x 10^9/L, RDW-CV 21.9%.

Introduction

The images selected for this exercise represent both normal and immature leukocytes as well as morphologic variations in red blood cells associated with a condition called microangiopathic hemolytic anemia (MAHA) initiated by an obstetric complication.

Image BCI-15 is a basophil. Basophils are medium-sized cells distinguished by their deep purple or blue-black cytoplasmic granules. These granules are numerous, large, and round, often obscuring the nucleus. When the nucleus is visible, the chromatin is dense and clumped. Note that basophilic granules are water soluble and may sometimes appear faded from the staining process.
The cell selected for **Image BCI-16** is a lymphocyte. Lymphocytes vary in size; this is an example of a smaller cell. Smaller lymphocytes characteristically have a thin rim of blue cytoplasm. The nucleus is usually round or oval, with condensed and clumped purple-staining nuclear chromatin.

**Image BCI-17** shows a monocyte. In contrast to the cells in Images BCI-15 and BCI-16, the monocyte is the largest cell that can normally be seen in the peripheral blood. The cytoplasm is abundant, and the vacuoles are characteristic. The cytoplasm’s blue-gray color is also typical, as is the uneven or grainy appearance. The nuclei in monocytes may be oval, round, indented, or lobulated, as in this example. The chromatin shows minimal clumping and is not as dense as the chromatin seen in small lymphocytes, such as the cell in Image BCI-16. The vacuolated and clear areas visible in the nucleus of this monocyte are not characteristically seen.

**Editor’s note:** Some participants identified this cell as a neutrophil. When determining the identification of a cell, the size, nuclear characteristics, and cytoplasmic appearance all need to be considered. For comparison, an example of a neutrophil is present in image BCI-19, adjacent to the targeted cell. Unlike BCI-17, this cell is smaller, the chromatin is dense with clear signs of segmentation, and the cytoplasm is pink with numerous secondary granules.

The cell identified in **Image BCI-18** is a metamyelocyte, a type of cell not normally seen in the peripheral blood. Metamyelocytes are medium-sized cells with pink, tan, or violet specific granules. There is only a hint of the pink granules visible here, and this particular cell has retained some bluish cytoplasm. The distinguishing feature of the metamyelocyte is the nuclear shape, which appears barely indented or like a kidney bean. Although it is an immature type of neutrophil, this metamyelocyte’s nuclear chromatin is beginning to appear condensed and clumped.
Editor's note: Some participants identified BCI-18 as a neutrophil, band (stab). Unlike a metamyelocyte, the indentation of the nucleus in a band (stab) neutrophil is greater than half the distance of a hypothetical round nucleus.

An abnormally shaped erythrocyte, called a schistocyte, is seen in Image BCI-19. Schistocytes are irregular fragments of red blood cells that vary in size and shape, although most are small. This schistocyte is atypical in that an area of central pallor is visible. Physiologic changes or mechanical damage to red blood cells that can occur in several disease states and clinical conditions can lead to the formation of schistocytes. One such condition is a microangiopathic hemolytic anemia (MAHA), the diagnosis identified in the patient presented for this testing event. Microangiopathic hemolytic anemias cause fibrin to be deposited in small blood vessels, which in turn obstructs the flow of red blood cells. Erythrocytes pass through vessels under high speed and pressure. As they flow, they may become hinged or draped around a fibrin strand, shearing into various fragments. The membranes may reseal, but the cells remain damaged and fragmented. Schistocytes are a significant finding on a peripheral blood smear and must be reported. These cells have decreased survival in the circulation and contribute to the anemia present in this case study patient.

Image BCI-20 is an erythrocyte with basophilic stippling. These inclusions generally appear small, numerous, and deep blue or blue-gray. They are either fine or coarse and are evenly dispersed in the red blood cell cytoplasm. Basophilic stippling results from one of two possible mechanisms. Fine stippling represents an artifact associated with the slow drying of the peripheral blood smear after preparation. Fine basophilic stippling is commonly seen in polychromatophilic red blood cells and is usually not clinically significant. Coarse basophilic stippling consists of abnormal aggregates of ribosomes and polyribosomes formed from dysfunctional RNA degradation. The presence of coarse stippling is a clinically significant finding. The granules in this cell are an example of fine basophilic stippling.

The final image in this testing event, Image BCI-21, is a nucleated red blood cell. Nucleated erythrocytes are immature cells not normally visible in the peripheral blood of an adult. Their presence in this case study patient suggests accelerated erythropoiesis in response to the anemia. This particular nucleated
red blood cell is a smaller cell. Nucleated red blood cells are typically round or slightly oval. The abundant cytoplasm is a dull blue-gray, although it sometimes may appear more pink or pink-gray, depending on how much hemoglobin has been synthesized by the cell. The nucleus is round and is often eccentrically located, as in this example. Nucleoli are absent. Frequently, a perinuclear halo is visible, as can be seen in this nucleated red blood cell. The nuclear chromatin is dense and clumped, with distinct areas of parachromatin.

Sometimes nucleated RBCs and small lymphocytes, as seen in Image BCI-16, may be confused. Although the cells in Images BCI-16 and BCI-21 are similar in size, differences in cytoplasmic and nuclear characteristics are apparent. The cytoplasm in the nucleated erythrocyte is abundant and blue-gray, whereas in the lymphocyte, the cytoplasm is scanty and more of a “true” blue. The nuclear chromatin in both cells is condensed and clumped, with visible areas of parachromatin. However, the nucleus in the erythrocyte is smaller, eccentrically situated, and surrounded by a rim of clear cytoplasm.

**Microangiopathic Hemolytic Anemia**

Microangiopathic hemolytic anemias result when erythrocytes become fragmented in small blood vessels. Although red blood cells are flexible and deformable, they are not indestructible. As discussed above, when obstructions, such as fibrin strands, impede their flow in the circulation, the cells are randomly “caught” or hinged on the fibrin. The mass of cells and pressure of the flowing cells eventually shear the erythrocytes into variously shaped fragments. Cells with torn membranes that can reseal continue circulating, although they will ultimately be removed by the spleen.

Pathologic deposition of fibrin in the vessels occurs in several clinical conditions, including disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome. Each of these conditions has precipitating events or origins. It is possible that the obstetric complication experienced by the patient presented in this testing event caused an imbalance in the hemostatic system, leading to disseminated intravascular coagulation.

Other mechanisms in addition to occlusion of blood vessels by fibrin, can cause erythrocyte fragmentation. For example, schistocytes may appear in the blood of patients who experience severe burns, as the red blood cells fragment when exposed to high temperatures.
Summary

The images provided in this exercise represent normal and immature leukocytes and erythrocytes as well as morphologic abnormalities in red blood cells. A careful review of the blood smear is important when evaluating a patient with anemia. Observing significant morphologic changes in cells, such as schistocytes, can suggest a mechanism for the development of the anemia that can be further defined by additional laboratory testing.

References


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