EDUCATIONAL COMMENTARY – PERIPHERAL BLOOD CELLS IN A CASE OF INFECTIOUS MONONUCLEOSIS

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To view the blood cell images in more detail, participants enrolled in program #224 or 225 for Blood Cell Identification can click on the sample identification numbers underlined in the paragraphs below. After logging on with a Paperless Proficiency Testing user name and password, you will see 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. To avoid the need to log in for each image, use the online tool to choose the cell you want to view. Click on this link for the API ImageViewer Instructions.

Learning Outcomes

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

- describe morphologic characteristics of normal peripheral blood leukocytes and platelets;
- identify morphologic features of reactive lymphocytes; and
- compare and contrast morphologic characteristics of a lymphocyte, monocyte, and reactive lymphocyte.

Case History

A CBC with differential was ordered on a 22 year old female patient with unexplained fevers, fatigue, and sore throat. Her CBC results are as follows: WBC=9.3x10^9/L, RBC=4.79x10^12/L, Hgb=14.4 g/dL, Hct=43.1%, MCV=89.9 fL, MCH=30.1 pg, MCHC=33.4 g/dL, Platelet=126x10^9/L, RDW-CV 26.1 %.

Introduction

The young woman whose blood smear is presented in this testing event was diagnosed with infectious mononucleosis. The cells selected for identification and discussion include white blood cells and platelets that may be seen as a result of this infection.
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Educational Commentary

**Image BCI-06** is an eosinophil. Eosinophils are medium-sized cells and are round or oval. Eosinophils are unique because they have numerous, red-orange cytoplasmic granules. These granules are large and generally uniform in size. The nuclei in eosinophils are usually bilobed, with dense and clumped chromatin.

The cell in **Image BCI-07** is a lymphocyte. Lymphocytes are variable in size. Although this cell is smaller than the eosinophil in **Image BCI-06**, it is medium-sized for a lymphocyte. Lymphocytes are usually round or oval and their nuclei are typically round or oval too; although, they are sometimes slightly indented. The cytoplasm is blue and scanty. The chromatin in lymphocytes is generally clumped, condensed, and a deep purple. Note that this particular cell has some areas of parachromatin as well as a clearer area resembling a nucleolus that are also visible.

**Image BCI-08** shows a monocyte. Monocytes are the largest cells that can normally be seen in the peripheral blood. Monocytes are typically round or oval but may also have cytoplasmic protrusions or sprawling cytoplasmic margins. However, the edges often “push” cells away rather than form contours around these cells. The cytoplasm is characteristically abundant, blue-gray, and may appear rough and uneven, similar to fine grains of sand; it is difficult to appreciate any graininess in this monocyte. There are often vacuoles visible in the cytoplasm, as in this example. Nuclei in monocytes may be round, oval, indented, lobulated, or horseshoe-shaped. Sometimes folds or convolutions are evident. The nuclear chromatin shows minimal clumping and stains a lighter purple. Mature monocytes have no nucleoli. The clear-staining areas in the nucleus of this cell are uncharacteristic.
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**Image BCI-09** illustrates platelets that are clumped. Clumps of platelets indicate that the blood sample was clotted or in the process of clotting when the smear was made. Note that in this image (especially above the clumped platelets) other individual platelets are still dispersed throughout the smear. It is important to evaluate the entire slide when clumped platelets are seen to ensure that adequate platelet numbers are present and that there is not more widespread clotting. If individual platelets are not observed elsewhere on the smear and large platelet clumps are present near the feathered edge of the slide, a new blood smear should be prepared. It is also important to verify that the original collection tube does not contain clotted blood. If it does, a new sample must be obtained from the patient. It is possible that isolated platelet clumps on a peripheral blood smear could be associated with delayed mixing of the tube after the specimen is collected. When platelet clumps are seen, the platelets within the group morphologically resemble those platelets that are individually dispersed. They appear the same in regard to size, color, and granularity, as with the platelets in this image. Typical features of platelets include small size (although some platelets in the clump are slightly larger), round or oval shape, blue-gray color, and granularity. Widespread platelet clumping can falsely decrease the total platelet count provided by automated cell counting instruments. The platelet estimate from a review of the blood smear should correlate with the automated platelet count. The automated platelet count for this patient was reported as 126 × 10⁹/L.

**Image BCI-10** is a reactive lymphocyte. This type of cell is also sometimes called a *variant* or *atypical lymphocyte*. Reactive lymphocytes are most often present in viral infections. Therefore, it is not surprising to observe this cell in the case study patient, who was diagnosed with infectious mononucleosis. Reactive lymphocytes represent cells that have been stimulated by antigen and are responding to this challenge. Because lymphocytes can react in many ways to the antigenic stimulus, there are a variety of morphologic features associated with these cells. Although there are no typical characteristics seen in reactive lymphocytes, certain morphologic features are distinctive. Reactive lymphocytes are generally large cells. They may be round, oval, or irregular in shape. The cell’s cytoplasm may skirt or mold around adjacent red blood cells. Sometimes the cytoplasmic edge closest to the red blood cells may be darker blue than the remainder of the cytoplasm. The cytoplasm in reactive lymphocytes is typically abundant and may be
pale blue, deep blue, gray, or gray-blue. It is possible to see lighter and darker colors within the same cell as well as clear areas within the cytoplasm. Cytoplasmic vacuoles and/or azurophilic granules may also be seen. There is variability too in the nucleus of reactive lymphocytes. Nuclei are generally large and may be round, oval, indented, lobulated, or folded. The nuclear chromatin may be fine or moderately clumped and the parachromatin is sometimes distinct. Nucleoli may also be visible. Note, however, that the presence of nucleoli does not indicate the cell is immature, only that it is reacting appropriately to antigenic stimulation.

Usually, small lymphocytes are not confused with other cells, such as reactive lymphocytes and monocytes. Larger lymphocytes may sometimes be mistaken for reactive lymphocytes or monocytes, but the cytoplasm is generally not as abundant as in other cells, is a more consistent blue color, and does not tend to sprawl around or push up against nearby erythrocytes. In larger lymphocytes, the nucleus is also usually round or oval with more clumped chromatin and may be large when compared to the amount of cytoplasm. Nucleoli and parachromatin are generally absent. However, monocytes and reactive lymphocytes are sometimes confused. Both cells are large with abundant cytoplasm but cytoplasmic and nuclear differences can help differentiate the two cells. The cytoplasm in monocytes is frequently blue-gray, appears grainy, and often contains vacuoles. In addition, the cellular margins typically do not mold around adjacent red blood cells, although there may still be cytoplasmic extensions. Reactive lymphocytes, in contrast, may have intensely blue, light blue, or blue-gray cytoplasm but it does not usually appear rough or granular. Darker blue cytoplasmic edges may be seen at the interface of cytoplasmic margins and surrounding erythrocytes. Vacuoles and azurophilic granules are not seen as often in reactive lymphocytes as in monocytes. The nuclei also vary between monocytes and reactive lymphocytes. In monocytes, the nuclei are typically round, oval, indented, lobulated, or horseshoe-shaped. The chromatin in monocytes shows minimal clumping and no nucleoli are evident. In reactive lymphocytes, the nuclear shape is frequently more irregular than in monocytes, although it too may be round, oval, indented, lobulated, or folded. The nuclear chromatin structure is also more variable in reactive lymphocytes than in monocytes and may be loose and open or moderately clumped. Likewise, nucleoli and parachromatin are more often seen in reactive lymphocytes than in monocytes.

**Infectious Mononucleosis**

A reactive lymphocytosis is associated with many disorders including infectious mononucleosis (IM). The causative agent of IM is the Epstein-Barr virus, which infects B lymphocytes. However, most reactive cells seen in the peripheral blood are cytotoxic T lymphocytes. These T lymphocytes respond in an acute immune reaction to the Epstein-Barr virus. Infectious mononucleosis is a benign condition, although complications are sometimes seen. Because there are numerous other disorders in which reactive
lymphocytes are produced, patients with suspected IM should be evaluated with additional laboratory analyses, such as a rapid test for the heterophile antibody.

**Summary**

The images provided in this testing event represent several types of peripheral blood cells observed in a patient with IM. The reactive lymphocyte, in particular (Image BCI-10), is a significant and classic finding in this condition. It is also important to note the morphologic characteristics of reactive lymphocytes that distinguish them from larger lymphocytes and monocytes. Laboratory professionals provide key diagnostic information through a careful and accurate evaluation of a peripheral blood smear.

**Bibliography**


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