EDUCATIONAL COMMENTARY – BLOOD CELL ID: PERIPHERAL BLOOD CELLS IN A CASE OF ACUTE LYMPHOCYTIC (LYMPHOBLASTIC) LEUKEMIA

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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:

- discuss morphologic characteristics of normal peripheral blood leukocytes;
- identify morphologic features of immature leukocytes and erythrocytes; and
- describe normal platelet morphology.

Case Study

A CBC with differential was ordered for a 44 year old male. His CBC results are as follows: WBC=32.7 x 10^9/L, RBC=3.68 x 10^12/L, Hgb=11.7 g/dL, Hct=36%, MCV=97.8 fl, MCH=31.7, MCHC=32.4 g/dL, RDW=24.1%, Platelet=23 x 10^9/L.

Introduction

The images presented in this testing event are from the blood sample of a 44-year-old man diagnosed as having acute lymphocytic (lymphoblastic) leukemia (ALL). The cells selected for commentary represent normal mature cells as well as immature cells seen in his peripheral blood. A platelet abnormality is also present and will be discussed.

Educational Commentary

Image BCI-01 shows a segmented neutrophil. These cells are medium-sized and characterized by the shape of their nucleus, which typically displays two to five lobes. Generally, the lobes are separated by thin strands of chromatin. Although the lobes in this cell are not connected by chromatin threads, there are still three distinct lobes with at least two
joined by a constriction. Therefore, this cell should be classified as a segmented neutrophil. Also, note that the chromatin is dense and clumped, reflecting a mature cell. Segmented neutrophils feature numerous small cytoplasmic granules that usually stain light violet, pink, or tan. Sometimes it is difficult to appreciate distinct granules in images or with microscopy and the cytoplasm may only appear grainy.

The cell identified in Image BCI-02 is a nucleated red blood cell (RBC). Nucleated erythrocytes are immature and retain their nucleus. These cells are not usually seen in the peripheral blood of an adult. When present, nucleated RBCs may indicate abnormal or accelerated erythropoiesis. Nucleated RBCs vary in size, depending on stage of maturation. Generally, cells decrease in size as they mature. Likewise, the nucleus becomes smaller and the chromatin becomes clumped and dense until it is finally expelled from the cell. The chromatin in this particular cell, although primarily clumped, does show some lighter-staining areas. The slight indentation of the nucleus is likely an artifact of smear preparation and is not the characteristic round nucleus associated with most nucleated erythrocytes. During maturation, as the nucleus decreases in size, the cytoplasm becomes more abundant. The cytoplasm also transitions in color from a dark blue to pink as the cell matures, reflecting the amount of hemoglobin synthesized by the cell. The moderate amount of cytoplasm in this nucleated RBC appears blue-gray with just a hint of pink. The morphologic features of this nucleated erythrocyte indicate it is at a later stage of maturation. Although it is not necessary to identify the specific type of nucleated RBC, the presence and number seen must be reported.

Image BCI-03 shows a band neutrophil. As with the nucleated erythrocyte in Image BCI-02, the band is an immature cell. Though immature, as many as 6% of leukocytes in a normal peripheral blood smear may be band cells. Note this cell is medium-sized, similar to the segmented neutrophil in Image BCI-01. Band cells are distinguished by a nucleus shaped like the letter C or U. There is dense, clumped chromatin, but lighter areas of parachromatin may be evident, as in this cell. The lobes in a band are connected by a bridge of chromatin. As with a segmented neutrophil, the cytoplasm in a band contains numerous granules that stain light violet, pink, or tan.
The cell selected in Image BCI-04 is a monocyte. Note the large size of this cell. Monocytes are the largest cells normally seen in the peripheral blood. Nuclei in monocytes vary in shape. They may be round, oval, indented, lobated, or kidney-shaped. The chromatin usually stains a lighter purple and is generally fine, with minimal clumping. Compare the chromatin in this monocyte with that in the segmented and band neutrophils already discussed. Note that the lighter areas of parachromatin are less evident in the monocyte, reflecting a less dense chromatin structure. Monocytes typically have abundant blue or blue-gray cytoplasm. Vacuoles are often seen, as in this example. Monocytes also may have small pink or lilac granules, and some are present in this cell as well. Although these fine granules may be present, monocytes are not considered to be granulocytic cells such as the segmented and band neutrophils. However, the cytoplasm of monocytes appears rough or uneven and has been described as resembling ground glass or grains of sand.

Image BCI-05 shows a normal lymphocyte. Lymphocytes vary in size, usually depending on the amount of cytoplasm seen in the individual cell. This lymphocyte has more cytoplasm than may be present in a small lymphocyte. However, when compared with the neutrophils and monocyte already discussed, this lymphocyte may be considered a smaller cell. Nuclei in normal lymphocytes are usually round, oval, or slightly indented, as in this cell. The nuclear chromatin is a deep purple with clumped and condensed chromatin. The cytoplasm in lymphocytes is blue. The clear area adjacent to the nucleus in this particular cell is uncharacteristic; however, this cell is not abnormal. The slight clearing area is not large enough to be representative of a Golgi body, as typically seen in a plasma cell. The cytoplasm is not a deep blue and the nuclear chromatin is not arranged as a "spoke-wheel" as might be seen in a plasma cell. Likewise, the size of the cell, uniform shape and dense chromatin of the nucleus, and scanty, blue cytoplasm are not characteristic features of a reactive lymphocyte. In addition, the uniform shape of the nucleus and lack of nuclear folding does not suggest a lymphoma cell. Small pink or lilac granules are sometimes also apparent in normal lymphocytes, and a few are evident in this cell.

At times, normal small lymphocytes and nucleated RBCs such as that seen in Image BCI-02, may be confused. Although these cells are similar in size, there are notable nuclear and cytoplasmic differences.
The chromatin pattern in the lymphocyte is generally uniformly clumped, with only minimal areas of lighter purple parachromatin. The chromatin in the nucleated erythrocyte may appear to be in patches. The cytoplasm in lymphocytes is a true blue, whereas the cytoplasm in nucleated RBCs may be a dull blue, blue-gray, or even pink, depending on how much hemoglobin the cell has synthesized. It is always important to evaluate all available morphologic features, including size, nucleus, and cytoplasm, when classifying blood cells.

The cell identified in Image BCI-06 is a blast. Blast cells are not normally seen in the peripheral blood. However, it is not unexpected to see one in a patient who has been diagnosed as having ALL. As with this cell, blasts are usually large with a high nuclear to cytoplasmic ratio resulting in a scanty amount of blue cytoplasm. The cells are generally round to oval with nuclei that are also typically round or oval. The unevenness and indentations in this cell most likely resulted from preparation of the blood smear. Some blasts have numerous and prominent nucleoli. This cell has a single, large nucleolus. When blasts are seen in the peripheral blood, their lineage is not easily determined. Blasts of different cell lines share similar morphologic features in size, nucleus, and cytoplasm. Therefore, additional laboratory studies must be performed to specifically classify blasts. Subsequent studies determined that this cell is a lymphoblast.

The last image in this testing event, Image BCI-07, shows a large, almost giant, platelet. The term “giant” is generally used to refer to a platelet that is larger than a normal red blood cell. Because the mean corpuscular volume is within the normal range, the average size of the RBCs in this picture is assumed to be normal. Although this platelet may not be larger than the surrounding erythrocytes, it is larger than a normal platelet. Platelets may be round or irregularly shaped. The cytoplasmic margins are usually even, but sometimes may appear frayed or scalloped. Platelets are typically light purple or blue-gray, although sometimes reddish-purple granules may be visible. The overall cytoplasm generally appears grainy. In this platelet, the granules are dispersed; in other platelets, the granules may form a central core encircled by a clearing. Large and giant platelets may be seen in ALL, representing impaired megakaryopoiesis associated with leukemia.
Acute Lymphocytic (Lymphoblastic) Leukemia

Acute lymphocytic (lymphoblastic) leukemia (ALL) is a malignant, uncontrolled proliferation of lymphoblasts originating in the bone marrow or other primary lymphoid tissue. There are two major types of lymphoblast: B cells and T cells. Once the presence of lymphoblasts has been confirmed, it is important to further classify them as either B or T cells. Treatment and prognosis vary depending on the type of lymphoblast as well as the subclassification of each blast type, which can also be determined. Most cases of ALL occur in children. Approximately 15% to 20% of ALL cases will be seen in adults, such as the patient presented in this testing event.

Hematologic abnormalities are common in ALL. As with this patient sample, the white blood cell count is elevated. Anemia and thrombocytopenia are usually present. The lymphoblasts overcrowd the bone marrow and limit the production of both normal erythrocytes and platelets. The anemia that develops in leukemia is generally normocytic and normochromic as reflected in this patient with normal RBC indices. Polychromasia, although not highlighted in this testing event, is evident in the images. Visible changes in RBC shape most likely represent poor areas of the smear or artifacts in slide preparation. No single RBC morphologic abnormality is consistent with ALL. However, a leukoerythroblastosis response may be seen in ALL and is noted in the cells selected for discussion in this educational commentary. The presence of immature granulocytes and nucleated RBCs characterizes this type of reaction. Peripheral blood leukoerythroblastosis also indicates that the bone marrow is stressed and overwhelmed by malignant lymphoblasts.

Summary

The patient presented in this testing event was diagnosed as having ALL. The images provided for evaluation represent both normal and abnormal peripheral blood cells that may be associated with this condition. Although additional laboratory testing defined this abnormality, the presence of immature cells such as nucleated RBCs and blasts was critical in the initial assessment of this patient’s disorder. Therefore, it is important that the laboratory professional carefully review any blood smear with suspected morphologic changes.

References


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