EDUCATIONAL COMMENTARY – BLOOD CELL ID: PERIPHERAL BLOOD FINDINGS IN A CASE OF PELGER HUËT ANOMALY

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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 exercise, the participant should be able to

• discuss the morphologic features of normal peripheral blood leukocytes;
• describe characteristic morphologic findings in Pelger-Huët cells; and
• differentiate Pelger-Huët cells from other neutrophils in a peripheral blood smear.

Case History: A 30 year old female had a routine CBC performed as part of a physical examination. Her CBC results are as follows: WBC=5.9 x 10^9/L, RBC=4.53 x 10^12/L, Hgb=13.6 g/dL, Hct=40%, MCV=88.3 fl, MCH=29.7 pg, MCHC=32.9 g/dL, Platelet=184 x 10^9/L.

Introduction

The images presented in this testing event represent normal white blood cells as well as several types of neutrophils that may be seen in the peripheral blood when a patient has the Pelger-Huët anomaly. Pelger-Huët is a benign, inherited abnormality in which the nuclei in neutrophils fail to completely segment. This condition is most often seen as a heterozygous state; homozygosity is quite rare.

Commentary

The cell identified in Image BCI-08 is a hyposegmented neutrophil and is an example of the classic type of leukocyte associated with the Pelger-Huët anomaly. The medium size of this cell is typical for a neutrophil. The numerous tan, pink, or purple cytoplasmic granules are also characteristic. However, note that the nucleus has only two lobes, which are connected by a thin strand of chromatin. These lobes are round or nearly round, approximately the same size, and have dense and clumped chromatin. The single filament of chromatin connecting the two lobes in this conformation has been described as resembling pince-nez eyeglasses.
(spectacles with only a nose clip instead of earpieces). Sometimes the wisp of chromatin connecting the lobes is not present and the nuclei appear shaped like a dumbbell or peanut. Cells with bilobed nuclei such as this example are most often seen in the heterozygous form of Pelger-Huët, although unilobed (nonsegmented) and dumbbell nuclear forms may be present. The nuclei in homozygous Pelger-Huët are characteristically unilobed or monolobated (no segmentations; only a single, round nucleus).

**Image BCI-09** shows an eosinophil. Eosinophils are medium-sized cells, approximately the same size as neutrophils. Eosinophils are distinguished from neutrophils and other leukocytes by their bright, red-orange cytoplasmic granules. These characteristic granules are large, numerous, and uniform in size. Generally, the nucleus in an eosinophil is bilobed; however, in this particular cell, it is difficult to appreciate more than one lobe. The chromatin is clumped and condensed.

**Image BCI-10** shows a band neutrophil. This cell is about the same size as the eosinophil and the mature neutrophil. Bands are the earliest stage in neutrophil maturation that may be seen normally in the peripheral blood and represent the precursor seen immediately before the mature neutrophil. The cytoplasm of band neutrophils also has numerous fine purple, pink, or tan cytoplasmic granules. The nucleus in a band cell may look like a band, sausage, or the letters C or U. The lobes are connected by a wide bridge of clumped and dense chromatin. The indentation of the nucleus is greater than half the diameter of a hypothetically round nucleus.

The cell selected for **Image BCI-11** is a monocyte. Monocytes are the largest cells that can normally be seen in the peripheral blood, and this example clearly shows how large these cells may appear. Note the abundant, blue-gray cytoplasm. The unevenly stained and rough appearance of the cytoplasm is characteristic, as are the several vacuoles. Sometimes, a few purple-red azurophilic granules may be visible. Likewise, cytoplasmic projections may be prominent. Monocyte nuclei vary in shape and may look indented, kidney-shaped,
lobulated, oval, or round. The nuclear chromatin usually shows minimal clumping and stains slightly lighter shades of purple.

The cell identified in Image BCI-12 is a normal lymphocyte. Normal lymphocytes vary in size; this is a nice example of a small cell. The cytoplasm in lymphocytes is characteristically blue and, in small lymphocytes, scanty, often barely rimming the nucleus. Nuclei in normal lymphocytes are typically round, oval, or may be slightly indented. The nuclear chromatin is condensed and clumped. This particular lymphocyte demonstrates a clear zone, or hof, adjacent to the nucleus, which is an occasional finding.

Image BCI-13 is another hyposegmented neutrophil. The size is similar to the neutrophil in Image BCI-08, the eosinophil in Image BCI-09, and the band in Image BCI-10. The purple, pink, or tan cytoplasmic granules are also like those seen in the cytoplasm of the neutrophil and the band. However, several features of the nucleus distinguish it as hyposegmented and not a band cell. The lobes of the nucleus are nearly the same size and are symmetrically oval. Although it may appear that these lobes are connected by a bridge of chromatin, parachromatin is also evident, suggesting more of a filament rather than a bridge. Finally, the nuclear chromatin appears more uniformly dense in the hyposegmented neutrophil than in the band neutrophil.

The last cell for identification in this testing event, Image BCI-14, is a second normal lymphocyte. This lymphocyte demonstrates the variability in size and morphology that can be seen in these cells. Most normal peripheral blood lymphocytes are like the one shown in Image BCI-12, but up to approximately 15% of normal circulating lymphocytes may be larger, with more cytoplasm and distinct azurophilic granules. These cells may also be described as large granular lymphocytes and actually represent a subset of lymphocytes called natural killer cells. The abundant, pale blue cytoplasm is characteristic as are the coarse lilac or pink (azurophilic) granules. The nucleus is round or slightly oval, and the nuclear chromatin is clumped.
and condensed, as seen in a normal small lymphocyte. Large granular lymphocytes are normal cells and are reported as normal lymphocytes in a differential cell count unless their numbers are greatly increased, which may occur in some disease conditions.

This type of normal lymphocyte, the large granular lymphocyte, should not be confused with a reactive lymphocyte. The variety in morphologic appearance of cells within the peripheral blood smear is greater for reactive lymphocytes than for normal lymphocytes. Reactive lymphocytes are usually large cells with abundant cytoplasm. The cytoplasm may be gray, pale blue, or a deep blue, with even darker patches of blue where the cell interfaces other cells such as erythrocytes. The nuclear shape varies in reactive lymphocytes and may be round or oval, but also folded, indented, or lobulated. Reactive lymphocytes show variability in nuclear chromatin structure as well. The chromatin may appear more open and fine, with distinct areas of parachromatin visible.

Pelger-Huët Anomaly

The Pelger-Huët anomaly is an inherited autosomal dominant condition in which the nuclear lobes in mature neutrophils fail to completely segment. Estimates vary, but this anomaly may affect as many as 1 in 5000 individuals. Fortunately, the hyposegmentation has no effect on neutrophil function, and the disorder is considered benign. However, Pelger-Huët anomaly may be confused with a neutrophilic left shift (increase in immature neutrophils) that is frequently associated with bacterial infection. A careful review of the peripheral blood smear is important in differentiating a neutrophilic left shift from a true Pelger-Huët anomaly. In an apparent left shift, the overall white blood cell count is often elevated. Note that in the patient’s blood sample presented for review in this testing event, the total WBC was normal at 5.9 x 10^9/L. Immature cells such as bands and metamyelocytes generally have nuclear chromatin that is not as condensed and clumped as in mature neutrophils, including those in the Pelger-Huët anomaly. In cases of infection, morphologic changes in neutrophils such as toxic granulation and Döhle bodies may be seen; these reactions are not evident in Pelger-Huët cells. Finally, a variety of neutrophils, both immature and mature, are seen in infectious processes. In cases of Pelger-Huët, the vast majority of the neutrophils will be hyposegmented. In fact, generally less than 10% of neutrophils will have three or more lobes in a Pelger-Huët blood smear. Most of the neutrophils in the blood from a patient with an infection, however, will display three or more nuclear lobes and there is also the potential to see immature granulocytes, such as band cells and metamyelocytes.

Pelger-Huët–like neutrophils may also be seen in certain acquired abnormalities and are called pseudo–Pelger-Huët cells. The conditions associated with pseudo–Pelger-Huët neutrophils include myelodysplastic syndromes, myeloproliferative neoplasms, and leukemias. Pseudo–Pelger-Huët cells often have single, round nuclei with extremely dense chromatin. If the nuclei are bilobed, the nuclear
lobes are generally not of equal size and frequently are not round or uniform in shape. In cases of pseudo–Pelger-Huët, the presence of completely segmented neutrophils (3-5 lobes) is common. Some conditions, such as myelodysplastic syndromes, result in neutrophils that are also hypogranular. Abnormalities in red blood cells and platelets may be seen as well. True Pelger-Huët anomaly is not linked to neutrophil cytoplasmic changes or to changes in other cell lines.

Summary

The images in this testing event are from a patient who presented with a Pelger-Huët anomaly. Normal peripheral blood leukocytes as well as cells demonstrating the classic morphologic features of this condition were selected for identification. The diagnosis of Pelger-Huët depends on recognition and differentiation of the hyposegmented neutrophils. The laboratory professional provides a significant contribution to quality patient care by distinguishing benign Pelger-Huët neutrophils from cells that may indicate an infection or other abnormality.

References


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