ADVANCED BLOOD CELL ID: MORPHOLOGIC CHARACTERISTICS OF HAIRY CELLS

Educational commentary is provided for participants enrolled in program #259-Advanced Blood Cell Identification. This virtual blood cell identification program includes case studies with more difficult challenges. 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. 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

After completion of this exercise, participants will be able to:

- discuss morphologic features of normal peripheral blood leukocytes.
- identify distinguishing morphologic characteristics of hairy cells.
- describe morphologic findings that are unique to peripheral blood artifacts.

Case History

A CBC with differential was ordered on a 69-year-old male patient complaining of weakness, fatigue, and weight loss. His CBC results are as follows: WBC=6.9 x 10^9/L, RBC=4.21 x 10^12/L, Hgb=11.9 g/dL, Hct=36%, MCV= 84.8 fl, MCH=28.3 pg, MCHC=33.3 g/dL, Platelet=123 x 10^9/L, RDW-CV=16.1 %.

Introduction

The patient presented in this testing event has been diagnosed with hairy cell leukemia. Several normal leukocytes, artifacts, and hairy cells have been annotated on the peripheral blood smear for identification and discussion.

Educational Commentary

The cell selected in ABI-15 is a segmented neutrophil. Neutrophils are medium-sized cells. They are characterized by a nucleus with 2-5 lobes connected by thin filaments of chromatin. The chromatin is dense and clumped and stains a dark purple. Segmented neutrophils have numerous cytoplasmic granules that appear pink or pink-violet.
ADVANCED BLOOD CELL ID: MORPHOLOGIC CHARACTERISTICS OF HAIRY CELLS

Another normal leukocyte has been chosen for ABI-16 and is a monocyte. Monocytes are the largest white blood cell seen on a normal peripheral blood smear. They are typically round. Monocyte nuclei may also be round, but can be oval, kidney-shaped, or lobulated, as shown in this cell. The nuclei stain a lighter purple, with minimal clumping of the chromatin. The cytoplasm in monocytes is generally abundant and blue-gray. Vacuoles as well as pink or lilac azurophilic granules may sometimes be seen. Neither vacuoles nor granules are seen in this cell. The cytoplasm often appears rough or as if grains of sand are present.

ABI-17 is a hairy cell, the abnormal lymphocyte characteristic of hairy cell leukemia. While these cells are variable in size, they are usually larger than normal, mature lymphocytes; note that this cell appears small because it is in a thicker area of the smear. Hairy cells are round or oval in shape, with nuclei that are also round or oval. Sometimes, slight indentations may be seen. Nuclear chromatin in hairy cells is finer than what is seen in normal lymphocytes and, at times, looks stippled. Nucleoli are typically single, small, and inconspicuous. However, no nucleolus is visible in this hairy cell. The cytoplasm is moderate to abundant and generally stains a light blue to blue-gray. The distinctive feature of the cytoplasm, and of the cell overall, is the frayed margins. The projections are irregular, fine, stringy, or hair-like, although sometimes they may appear thicker.

The cell annotated for ABI-18 is a normal lymphocyte. Lymphocytes are variable in size. This cell is a nice example of a small lymphocyte. The cell is characteristically round. Nuclei are round or oval. This particular cell has a slight indentation. The nuclear chromatin is condensed and clumped, in contrast to the hairy cell in ABI-17, which has a slightly more stippled chromatin pattern. This small lymphocyte has the usual scanty rim of blue cytoplasm.
ADVANCED BLOOD CELL ID: MORPHOLOGIC CHARACTERISTICS OF HAIRY CELLS

**ABI-19** is not really a cell at all but is a white blood cell artifact called a smudge or basket cell. The WBC has been damaged and distorted during the process of preparing the smear. The cells are fragile, typically lymphocytes. The damaged cell may appear as a mass or smudge of chromatin or more like a basket with strands of chromatin spreading out from a central, condensed nuclear remnant. In either artifact, the cytoplasm has been completely disrupted and stripped away when the slide was made. This particular artifact looks more like a smudge than a basket. Since there is no distinctive cytoplasm, it is not possible to identify the artifact as any specific white blood cell. Increased numbers of smudge or basket cells are commonly seen in chronic lymphocytic leukemia but a few may be associated with any hematologic malignancy. They are even sometimes seen on normal peripheral blood smears. Therefore, the appearance of a smudge or basket cell in this case of hairy cell leukemia is not unexpected.

The next cell selected for annotation and discussion, **ABI-20**, is a platelet but it is situated overlying a red blood cell. When reviewing a peripheral blood smear for possible abnormalities in cells, it can be helpful to scan several more fields to determine if the same morphologic finding is visible in or between additional cells. In this case, the platelet superimposed on an RBC is similar to other platelets on the slide. This platelet is typical in its morphology. Platelets are small, round, or oval, and stain a light purple, light blue, or blue-gray. They often have a central granular core with a surrounding clearer area; although, the clear zone is not evident in this platelet. Note that the clear area in a platelet still retains some bluish color. When platelets are superimposed on red blood cells, there is usually a different type of clear area, one that is white and resembles a halo. A halo surrounding an overlying platelet is a unique feature seen in this situation. Another useful technique when using a microscope, that helps distinguish platelets superimposed on erythrocytes from true red cell inclusions, is careful focusing. An actual inclusion will be in the same focal plane as the cell, whereas platelets overlying the RBC will focus separately from the red cell. Also, if inclusions are really present in erythrocytes, they will likely be seen in other cells and noticed when the smear is reviewed. It is
interesting to note that, at about 2:00, on the virtual slide, there is another platelet superimposed on an RBC, with the halo. It is unusual to see two such cells in one field of view.

The last cell chosen for discussion in this testing event, ABI-21, is another hairy cell. However, this hairy cell differs from the one seen in ABI-17. Hairy cells can be variable in size and may have abundant cytoplasm. This particular cell has a larger nucleus with more open chromatin than is usual. It is possible for the cytoplasmic projections in hairy cells to also be thick and blunted, as in this example. More typical filamentous fraying can be seen on the left side of the cell. This cell is considered a hairy cell based on the appearance of numerous other hairy cells on the slide and the possibility that especially fragile lymphocytes are susceptible to distortion during the process of blood smear preparation.

Hairy Cell Leukemia

Hairy cell leukemia is a B cell lymphoproliferative condition. It is not common and is seen more often in middle-aged to older men. It is characterized not only by the unique morphology of the lymphocytes, but also by pancytopenia. Although the patient in this exercise has a normal WBC count, he does have slight anemia as well as thrombocytopenia. Typically, the number of hairy cells is low. But, in this case, there appear to be numerous hairy cells when the entire virtual slide is scanned (using 60x).

Despite the characteristic morphology, hairy cell leukemia can be confused with other lymphoproliferative disorders that sometimes express similar lymphocytic features. One condition of note is splenic marginal zone lymphoma but prolymphocytic leukemia, T cell large granular lymphocytic leukemia, and the hairy cell leukemia variant may also be included in the differential diagnosis. When clinical presentation, complete blood count results, and lymphocyte morphology suggest hairy cell leukemia or another possible lymphoproliferative disorder, a final diagnosis is confirmed based on immunophenotyping. Hairy cells express primarily surface immunoglobulin, CD 19, CD 20, CD 22, CD 79a, CD 103, CD 11c, CD 25, CD 123, cyclin D1, and annexin A1. Hairy cells are also tartrate resistant acid phosphatase (TRAP) positive, a cytochemical stain traditionally used to confirm hairy cells, but is no longer often performed.
ADVANCED BLOOD CELL ID: MORPHOLOGIC CHARACTERISTICS OF HAIRY CELLS

Cytogenetic procedures have been utilized more recently in defining hairy cell leukemia. The BRAF V600E mutation has been identified in the majority of patients with hairy cell leukemia. An accurate diagnosis is important as, fortunately, hairy cell leukemia responds well to treatment protocols.

Summary

The morphologic evaluation of peripheral blood cells is an important procedure in determining a diagnosis of hematologic malignancies, such as hairy cell leukemia. This testing event demonstrates key characteristics of normal and abnormal cells and artifacts that can be seen in this condition.

Bibliography

