ADVANCED BLOOD CELL ID: EXPECTED AND UNEXPECTED PERIPHERAL BLOOD CELLS IN A CASE OF CHRONIC LYMPHOCYTIC LEUKEMIA

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

Learning Outcomes

After completing this exercise, participants should be able to:

- Describe morphologic characteristics of mature and immature lymphoid cells.
- Differentiate red blood cells with similar morphologic features.
- Identify selected WBC and platelet artifacts that can be confused with abnormalities.

Case Study

A 61 year old male was seen by his physician during a routine physical. His CBC results are as follows: WBC=447.7 x 10^9/L, RBC=5.37 10^12/L, Hgb=15.0 g/dL, Hct=46.9%, MCV=87 fl, MCH=28 pg, MCHC=32 g/dL, RDW=15.9%, Platelet=209 x 10^9/L, MPV=9.4.

Educational Commentary

The patient presented in the case study was diagnosed with chronic lymphocytic leukemia (CLL). The cells and artifacts chosen for discussion represent both common findings associated with CLL as well as unexpected morphologic features.

Cell [ABI-15](#) is a lymphocyte. Seeing what appears as mature, normal lymphocytes is not surprising in a case of CLL. There are numerous other similar lymphocytes distributed throughout the blood smear. The automated differential for this patient showed 55.8% lymphocytes. Although these cells are morphologically indistinguishable from mature, normal lymphocytes, they are malignant and dysfunctional. Morphologic characteristics of mature lymphocytes include a round to ovoid shape with round to ovoid nucleus that is dark purple; the chromatin is dense and clumped. The cytoplasm is blue and often scanty, barely rimming the nucleus.

The cell selected for [ABI-16](#) is a prolymphocyte. Notice the larger size of this cell when compared to the lymphocyte in ABI-15. The prolymphocyte is also a round cell, though it may appear oval. This particular cell has been distorted because of the high WBC count and crowding of all the cells. The nucleus is round or oval as well. The nucleus still appears condensed, though the chromatin is slightly more open or
loose than in the small lymphocyte. A distinguishing feature of prolymphocytes is the presence of a single, prominent nucleolus. The nucleolus in this cell is not as distinct as usual, but can still be seen at about the eleven o’clock position in the nucleus. Prolymphocytes have a moderate amount of blue cytoplasm. Cells similar to this prolymphocyte can be seen in other areas of this digital slide and are recognized if contrasted with the more mature-appearing small lymphocytes. It is not surprising to see some prolymphocytes on this smear of a CLL patient. Prolymphocytes are abnormal in the peripheral blood. However, in a classic case of CLL such as this, less than ten percent of the cells may be prolymphocytes.

**ABI-17** is not a cell at all but is an artifact described as a smudge or basket cell. This distorted WBC has no cytoplasm and is merely a smear of nuclear chromatin. The chromatin may appear a dark purple or, sometimes, red-purple. It forms from a fragile cell during the process of blood smear preparation. The cytoplasm falls apart and the nucleus smudges. Most often the frail cell is a lymphocyte, so smudge cells are commonly visible in the peripheral blood of patients with CLL. A review of the digital slide will show numerous smudge cells. These “cells” are not counted, but should be reported. It is possible the automated differential included smudge cells in the count of 40.2% large unidentified cells (LUCs). Smudge cells can sometimes hinder the morphologic review of WBCs on a peripheral blood smear. Smudging can be eliminated by adding one drop of 22% bovine serum albumin to four to five drops of blood prior to slide preparation. However, note that a smear without albumin should still be used to evaluate RBC and platelet morphology since albumin can induce artifactual changes in erythrocytes, such as stomatocytosis.

Cell **ABI-18** is an echinocyte, also called burr or crenated cell. This spiculed cell usually has 10-30 short, blunt, evenly spaced projections surrounding the cell. The cells are generally the same size as normal erythrocytes and characteristically still retain their area of central pallor. Echinocytes are a common artifactual variation of RBCs caused by slow drying of the blood smear, blood smears that are prepared too thick, or old blood. The echinocytes seen in this virtual slide are most likely artifacts from the smear preparation. The markedly elevated WBC has distorted many of the RBCs.

In contrast, the cell identified in **ABI-19** is an acanthocyte or spur cell. Note that this cell has 3-12 spicules that are unevenly spaced around the periphery of the RBC. The projections are also longer than those seen in the echinocyte. Likewise, there is no area of central pallor. Also in contrast to echinocytes, acanthocytes are abnormal findings in the peripheral blood. They result from changes in the lipid content of erythrocytes that are not completely understood. However, a rare acanthocyte can be seen even in a normal blood smear. These cells are inconsistently present on this slide and it is unclear why an occasional acanthocyte is seen.
ABI-20 is a giant platelet. The term giant is used to describe platelets that are larger than normal red blood cells. Giant platelets are variable in shape and may be round, oval, or irregular. The cell’s edges may be even and smooth or ruffled. The cytoplasm is usually the same color as a normal platelet, that is, light blue, blue-gray, or light purple. Giant platelets generally have numerous granules, either dispersed or clumped within the cytoplasm.

Note that this giant platelet should not be confused with the smudge cell seen in ABI-17. Smudge cells are usually as large as or larger than WBCs, though they have no definite size or shape. These artifacts have no granules and stain a dark purple or sometimes red-purple.

The last cell selected for this testing event, ABI-21, is a platelet, but it is superimposed on a red blood cell. Platelets are small, round, or oval in shape, and stain a light blue, blue-gray, or light purple. It is important to distinguish such superimposed platelets from any type of possible RBC inclusion. Any inclusion will lie within the same focal plane as the cell. Platelets overlying the erythrocyte will focus separately from the cell. It is also helpful to view other cells on the slide when considering that inclusions may be present. If there are truly inclusions in RBCs, they will likely be seen in other cells.

Chronic Lymphocytic Leukemia

Chronic lymphocytic leukemia (CLL) is a common malignancy of middle-aged and elderly individuals, with males more predominantly affected. The clinical presentation for CLL is often made “accidentally” when patients seek routine medical attention. Most cases of CLL represent a B lymphocyte malignancy. The clinical course of the disease is variable. Many patients have long lives without major symptoms. Other patients may experience a more aggressive progression of the disorder and only live 1 to 2 years.

Summary

The virtual peripheral blood slide presented in this testing event illustrates typical lymphocyte morphology associated with many cases of CLL. The numerous, small, round lymphocytes with scanty blue cytoplasm and clumped nuclear chromatin are classic features of this disorder. The occasional prolymphocyte is also an expected finding. The changes in RBCs and platelets are not characteristics common in CLL, but highlight the importance of carefully reviewing any peripheral blood smear.

References
