Educational Commentary – Blood Cell ID: Distinguishing Fragmented Erythrocytes

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Learning Outcomes

After completion of this exercise, participants will be able to

- discuss the morphologic characteristics of normal peripheral blood leukocytes and platelets.
- identify the morphologic abnormalities on a peripheral blood smear that are associated with disseminated intravascular coagulation.

Commentary

The patient presented in this testing event was diagnosed as having metastatic breast cancer. Her condition was further complicated by disseminated intravascular coagulation (DIC). The images provided show both normal and abnormal cells in the peripheral blood that are characteristic of this condition.

**Image BCI-15** shows a normal polysegmented neutrophil (polymorphonuclear neutrophil, poly, segmented neutrophil, seg, or neutrophil). Neutrophils typically have a nucleus with two to five lobes connected by threads of chromatin. The chromatin is coarsely clumped and dense. Segmented neutrophils also have numerous small tan, pink, or violet-pink cytoplasmic granules. Sometimes the individual granules are difficult to differentiate, but their presence gives the cytoplasm an overall pink color and grainy appearance. This cell should not be mistaken for a hypersegmented neutrophil. Hypersegmentation should be considered when a cell has six or more nuclear lobes or when three or more five-lobed segmented neutrophils are counted per 100 leukocytes. Hypersegmented neutrophils are most commonly associated with megaloblastic anemias caused by folate and vitamin B₁₂ deficiencies. In these conditions, red blood cells (RBCs) may appear as macro-ovalocytes, a peripheral blood picture much different than what is seen in this case study. While it appears that this cell may have five lobes, the segmentation on the left side of the cytoplasm is probably one large lobe; no thin strands of chromatin or tapering are present to suggest that there is another segment.
The cell in Image BCI-16 is a nucleated RBC (NRBC). NRBCs are immature erythrocytes that have not yet expelled their nuclei. Except in newborns and infants, NRBCs are seen only in bone marrow samples and not in peripheral blood smears. Their presence in the peripheral blood of an adult suggests abnormal or accelerated erythropoiesis. NRBCs represent specific stages in erythrocyte maturation, but the particular stage does not need to be identified. However, it is important to count and report them. Several morphologic features distinguish the later stages of NRBCs, as are typically seen in the peripheral blood. Note the round nucleus, with clumped and dense chromatin. Nucleoli are not evident. The cytoplasm may be variably blue-gray to pink-gray, depending on how much hemoglobin the cell has synthesized.

In contrast, a prorubricyte or a rubriblast would be larger than a rubricyte or metarubricyte; nuclei would be open and lacy, without any clumping; and the cytoplasm would be more blue with a hint of gray in the prorubricyte.

Image BCI-17 identifies a band or stab neutrophil. These cells are the earliest precursors of neutrophil maturation that can normally be seen in the peripheral blood. Bands feature a nucleus that is shaped like the letters “C” or “U.” In contrast to the segmented neutrophil shown in Image BCI-15, the lobes in a band neutrophil are connected by a bridge rather than thin filaments of chromatin. The nuclear chromatin is clumped and dense, as is usual for a mature cell. The cytoplasm in these cells is similar to that in segmented neutrophils and contains numerous granules that stain tan, pink, or violet-pink.
Image BCI-18 depicts a normal monocyte. Monocytes are large cells, and characteristically have abundant, blue-gray cytoplasm. Vacuoles are often visible, and the cytoplasm appears rough and uneven. The nuclei in monocytes are variable in shape and may be round, kidney-shaped, oval, or lobulated. This cell has folds, or lobulations. The chromatin is usually a lighter pink or purple color and is generally fine, with minimal clumping.

Image BCI-19 shows a normal platelet. Platelets technically are not cells, because they have no nuclei. However, they originate from nucleated bone marrow cells called megakaryocytes and represent fragments of cytoplasm from these cells. Platelets are small in size, usually 1 to 4 μm in diameter. They vary in shape but are usually round or oval. Platelets stain purple or blue-gray and often appear grainy. The platelet in this image is not typical. It appears more pink than purple or blue-gray. However, its very small size and round, uniform shape distinguishes it from the fragmented RBCs that are also present.

Image BCI-20 is a specific and abnormally shaped RBC called an acanthocyte. Acanthocytes characteristically have three to twelve spiny projections unevenly spaced around the cell. These protrusions are most often sharp, but may sometimes appear blunt. Acanthocytes have no area of central pallor and are often smaller than normal erythrocytes. They are most often associated with defects in lipid metabolism, such
as abetalipoproteinemia. However, small numbers may be present in microangiopathic hemolytic anemias such as DIC.

The cell in image BCI-20 could also be considered a schistocyte. Schistocytes typically have 3 or more points, so it is possible this cell could be classified as such. In addition, some cells represent transitional forms between acanthocytes and echinocytes. These hybrids sometimes have areas of central pallor, though that is not seen in this particular example. The irregular size and shape of the projections as well as uneven distribution suggests a cell in transition.

The cell shown in Image BCI-21 is a fragmented erythrocyte, or schistocyte. As with acanthocytes, schistocytes have no area of central pallor. However, schistocytes are more irregular, with shapes resembling helmets, commas, or triangles. Schistocytes also lack the spikes typically seen in acanthocytes. The presence of schistocytes indicates that the RBCs have survived physical or mechanical trauma. The intravascular fibrin formation that occurs in DIC is an important mechanism in schistocyte formation. DIC is also associated with the consumption of platelets and peripheral blood thrombocytopenia. Therefore, a low platelet estimate and the presence of schistocytes are significant peripheral blood findings that can be some of the first indicators of an abnormal hemolytic event such as DIC.

Several other acceptable responses can be considered for image BCI-21, in addition to schistocyte. “Helmet cell” is actually just a specific name used to characterize the shape of fragment. Likewise, this cell could be considered an acanthocyte since the projections are uneven, pointed, and there is no area of central pallor.

**Summary**

A careful review of a peripheral blood smear can provide important clues in the evaluation of a patient with DIC. The appearance of schistocytes, in particular, suggests that the process causing RBC hemolysis results from conditions associated with intravascular obstruction.

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