ADVANCED BLOOD CELL ID: MORPHOLOGIC CHARACTERISTICS OF IMMATURE GRANULOCYTES

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. You will need Adobe Flash to use this feature. Click on this link for the API ImageViewer™ Instructions.

Learning Outcomes
After completing this exercise, participants should be able to:

- identify morphologic features of normal peripheral blood leukocytes.
- describe morphologic characteristics of immature granulocytes.

Case Study
A 64 year old female was seen by her physician for weakness, fatigue, and weight loss. Her CBC results are as follows: WBC=131.0 x 10^9/L, RBC=2.75 10^{12}/L, Hgb=9.8 g/dL, Hct=29.1%, MCV=106 fl, MCH=35.8 pg, MCHC=33.9 g/dL, RDW=14.9%, Platelet=229 x 10^9/L.

Educational Commentary
The patient presented in the case study for this Advanced Blood Cell Identification testing event was diagnosed with Chronic Myelogenous Leukemia (CML). The images chosen for this virtual educational activity are primarily immature granulocytes (neutrophils), but some normal peripheral blood cells have also been selected.

CML is a disease characterized by the presence of immature granulocytes, in all stages of maturation, in the peripheral blood and bone marrow. The condition is defined by three phases: chronic, accelerated, and blast crisis. In the initial chronic stage, a spectrum of mature and maturing neutrophils will be observed. Most of the cells will be myelocytes and neutrophils, but other stages as well as an increase in eosinophils and basophils may be seen. Blasts are generally less than 5% of all the white blood cells. Given the variety of neutrophils and increase in other granulocytes present, this patient was most likely diagnosed with CML in the chronic phase. In the accelerated phase, the blast count increases, though it is still less than 20%, and the basophil relative number may be as high as 20% or more. The terminal phase is blast crisis, in which blasts represent 20% or more of the white blood cells. The blasts are generally myeloid in origin (70% of cases), but sometimes lymphoblasts predominate. The peripheral blood and bone marrow of a patient in blast crisis may appear indistinguishable from acute leukemia.
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Image **ABI-01** is a band neutrophil. Although this cell is an immature granulocyte, it is the earliest precursor that can be seen normally in the peripheral blood. However, given the variety of other immature neutrophils seen, it is clear that this cell must be considered abnormal in this context. Note the nucleus that is characteristically shaped like the letter “C” or “U”. If the nucleus is hypothetically viewed as round, the indentation in this band cell is greater than half of the distance across this hypothetically round nucleus. The lobes are connected by a thick bridge of chromatin that is also mostly dense and clumped. The cytoplasm contains numerous, small specific granules that give the cell a pinkish color.

The cell selected for **ABI-02** is a metamyelocyte. In contrast to the band, if the nucleus of this cell is viewed as hypothetically round, the indentation is less than half of the distance across the possible round nucleus. Metamyelocytes characteristically have nuclei that are only slightly indented, or shaped like a kidney bean. As with the band, the metamyelocyte is a post-mitotic cell, so the nuclear chromatin is generally condensed, though some lighter purple areas indicate that the cell is still immature. Also like the band, the cytoplasm contains many fine pink or tan specific granules. Sometimes, a few dark purple primary or nonspecific granules may be seen in the cytoplasm, although none are apparent in this example.

Image **ABI-03** is a myelocyte, the stage in neutrophil maturation immediately preceding the metamyelocyte. The myelocyte is important as it is the last cell capable of mitosis and the first in which the secondary, specific granules can be seen. As with the metamyelocyte, darker purple nonspecific or primary granules are retained and may be visible. Because the pink specific granules are also present, the cytoplasm may appear pinkish-blue. The nucleus of a myelocyte is usually round or oval and eccentrically located in the cell. Sometimes an area of clearing, or hof, is adjacent to the nucleus and represents the Golgi organelle. The hof is not apparent in this example. Even though the myelocyte is immature, distinct nucleoli are generally not seen. Parachromatin may still be evident within mostly clumped and condensed nuclear chromatin.

The cell identified in image **ABI-04** is a promyelocyte. Promyelocytes are large cells with a large nucleus and relatively less cytoplasm than has been seen in the other stages of neutrophil maturation. The nucleus in promyelocytes is purple and is also more open and loose; nucleoli are often visible. The cytoplasm stains blue or blue-gray. The key distinguishing features of the promyelocyte, however, are the coarse, larger nonspecific or primary cytoplasmic granules. These granules appear a dark purple or reddish purple.
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The cell selected for **ABI-05** is a blast. Note the cell is large, with a scanty amount of dark blue, agranular cytoplasm. The nuclear chromatin pattern is open and fine. At least two nucleoli are present. The large, roundish-shaped nucleus is typical. The multiple, distinct nucleoli and overall large cell size suggest a myeloblast. However, it can be difficult to identify the cell lineage of blasts based only on Wright-stained morphology because blasts of different cell lines are so similar in appearance. Therefore, this cell would be reported simply as a “blast” and additional techniques would be needed to define cell type.

Image **ABI-06** is a basophil. Basophils characteristically have dark purple or blue-black cytoplasmic granules. However, these granules are also water soluble and often wash out and fade during the staining process, as occurred in this example. Note that the granules that are present are larger and darker than the primary granules seen in the promyelocyte previously described. Also, the visible cytoplasm is not blue and the nuclear chromatin is dense and clumped, indicative of a mature cell. Basophils are particularly significant when increased in CML as this signals a transition to the next phase of the disease.

The last cell selected for identification in this testing event, **ABI-07**, is a normal monocyte. Several features of this cell are in morphologic contrast to the immature neutrophils. While this monocyte is large and many of the maturing granulocytes are also large, important differences can be seen in the cytoplasm and the nucleus. The cytoplasm in monocytes is characteristically abundant and blue-gray. It often appears rough or uneven and may have vacuoles, as in this cell. Sometimes faint pink azurophilic (primary granules) are visible, but these are always less numerous and not as prominent as those seen in immature granulocytes. The nuclei in monocytes are purple and vary in shape to be oval, round, lobulated or indented. The chromatin pattern is finer than in mature cells, with no visible nucleoli. Sometimes nuclear folds or convolutions can be seen.

**Summary**

The blood smear for this testing event is from a patient with CML. A spectrum of immature granulocytes is typical in the initial stages of this condition. The medical laboratory professional plays a key role in identifying and reporting these cells and contributing to an accurate clinical diagnosis.

**References**