EDUCATIONAL COMMENTARY – MORPHOLOGIC ABNORMALITIES IN ERYTHROCYTES, LEUKOCYTES, AND PLATELETS

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Learning Objectives
Upon completion of this exercise participants will be able to:

- identify morphologic abnormalities in RBCs.
- describe the morphologic characteristics of mature and immature WBCs.
- identify morphologic abnormalities in platelets and platelet precursors.
- differentiate blood cells with similar morphologic features.

Photographs labeled BCI-01 through BCI-07 are microscopic images of blood smears from a Down syndrome newborn diagnosed with transient myeloproliferative disorder. These images include both normal and abnormal peripheral blood cells as well as cells that are not normally seen on a peripheral blood smear.

The cell identified in photograph BCI-01 is a polychromatophilic RBC. These cells also represent reticulocytes. The reticulocyte is the stage of erythrocyte development just prior to the mature RBC. Polychromatophilic erythrocytes have retained a small amount of RNA and will appear bluish when Wright stained. The term “polychromasia” may also be used to describe the presence of these cells on a peripheral blood smear. In addition to their grey-blue color, polychromatophilic RBCs are generally slightly larger than normal RBCs and often lack any area of central pallor. Their blue color distinguishes them from macrocytes. The presence of polychromasia indicates that the bone marrow is trying to replace erythrocytes that have been lost through acute blood loss or an anemia (hemolytic) in which RBC survival is shortened through intrinsic or extrinsic mechanisms. An increase in polychromatophilic RBCs is a normal finding in a newborn of this patient’s age; hematopoiesis is very accelerated in newborns.
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Photograph BCI-02 shows a nucleated RBC. As with polychromatophilic erythrocytes, nucleated RBCs may be seen normally in the peripheral blood of a newborn, but never in an adult. Nucleated RBCs are immature; they have not yet extruded their nuclei. Generally, even in a newborn, only the very late stages of nucleated erythrocytes are seen in the peripheral blood. This cell is typical of the stage of maturation that is usually present. Note the dense, nearly featureless chromatin and blue-pink cytoplasm. The amount of basophilia in the cytoplasm may vary, though these cells usually have their entire complement of hemoglobin. When nucleated RBCs appear in the peripheral blood, the stage of development does not need to be classified; however, they are quantitated and reported in the differential cell count.

A band neutrophil is pictured in photograph BCI-03. The band cell is the earliest precursor of neutrophil maturation that can normally be seen in the peripheral blood. The nuclei in bands are typically shaped like a band, a sausage, or the letters “C” or “U.” Note the dense and compact chromatin, which indicates the maturity of this cell. Also note that the lobes are connected by a bridge, with clearly evident areas of chromatin and parachromatin. The cytoplasm in a band cell contains numerous specific granules that stain pink, tan, or violet.

Photograph BCI-04 is a normal segmented neutrophil, also called polysegmented neutrophil, polymorphonuclear neutrophil, or simply “seg.” There are generally 2 to 5 nuclear lobes that are characteristically connected only by thin threads of chromatin, in contrast to the band cell shown in photograph BCI-03. Note, however, that both the band and the seg are similar in size, chromatin structure, and cytoplasmic features. Numerous pink, tan, or violet granules are visible in the cytoplasm of this segmented neutrophil.
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The platelet in photograph BCI-05 can be described as “giant.” Normally, platelets range in size from 1 to 4 µm. The term “giant” indicates that this platelet is larger than a normal RBC. Giant platelets often have areas of cytoplasmic clearing, as is evident in this example. The cytoplasmic margins may be frayed or smooth and even. Cytoplasmic color is variable, but it usually is slightly blue-gray. Purple or purple-red granules may be seen, but the cells may also appear agranular. It is not unexpected to see giant platelets in the peripheral blood smear of this patient. They are often associated with abnormal stem cell conditions such as the myeloproliferative disorders and represent disturbed megakaryopoiesis.

The cell identified in photograph BCI-06 is a promyelocyte. The characteristic morphologic feature is the presence of large, nonspecific or primary cytoplasmic granules; note their purple-red color. These granules often obscure a blue cytoplasm. The nucleus is generally round or oval with chromatin that is loose and open. Nucleoli may also be seen, though none are clearly visible in this example.

Photograph BCI-07 is likely an abnormal megakaryoblast. Nucleoli are present, and the chromatin is loose and open. The cytoplasm is moderately dark blue with budding or blebs, a feature often associated with megakaryoblasts. The cytoplasm is unevenly stained with light purple granulation. It is unusual to see granulation such as this in a megakaryoblast. However, this is not a normal megakaryoblast. Normal megakaryoblasts are round or oval cells. The nucleus is also round or oval. The scanty to moderate amount of blue cytoplasm is usually agranular; extensions of cytoplasm may be seen. Nucleoli may be evident in a coarse chromatin. Megakaryoblasts should not be seen in the peripheral blood. However, abnormal cells such as this example may be present in abnormalities like acute megakaryoblastic leukemia, chronic myeloproliferative disorders, and myelodysplastic syndromes.
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Chronic myeloproliferative disorders are clonal defects that originate in a bone marrow stem cell capable of differentiation. This group of hematologic malignancies includes several categories, but all show various degrees of peripheral blood and bone marrow involvement. Generally, an increase in one or more cell lineages may be seen with or without a decrease in other cellular components. The WBC count is variable, but often increased as in this case example. Blasts may be present in the peripheral blood. Likewise, the platelet count may be increased or decreased.

Abnormal cells such as the cell in photograph BCI-07 should not be confused with normal cells, such as lymphocytes. Although normal lymphocytes are variable in size, they are typically small with a scanty amount of blue cytoplasm. The nucleus may be round, oval, or slightly indented, but characteristically has dense clumped chromatin.

The morphologic abnormalities shown in these images are not unexpected in a patient with a myeloproliferative disorder. The differential count also included 47 blasts, which is a significant peripheral blood finding. Additional immunophenotyping indicated that these blasts expressed antigens associated with hematopoietic progenitors, myeloid precursors, and platelets/megakaryocytes. This testing event underscores the difficulty in using morphology alone to diagnose complex hematologic disorders, highlighting the critical role of ancillary testing in defining an abnormal condition.

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