EDUCATIONAL COMMENTARY – BLOOD CELL ID: IDENTIFYING ABNORMALITIES TYPICAL OF MULTIPLE MYELOMA

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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

On completion of this activity, the participant should be able to:

- identify morphologic characteristics of peripheral blood leukocytes and erythrocytes; and
- describe morphologic abnormalities in leukocytes and erythrocytes associated with multiple myeloma.

Case Study

A 65 year old male complained of fatigue during a routine physical. His CBC results are as follows:

WBC=3.9 x 10^9/L, RBC=2.48 x 10^{12}/L, Hgb=8.2 g/dL, Hct=24.7%, MCV=99.5 fL, MCH=32.9, MCHC=33.0 g/dL, RDW=19.8%, Platelet=28 x 10^9/L.

Educational Commentary

The patient presented in the case study for this testing event has been diagnosed as having multiple myeloma. The images for review represent both normal leukocytes and abnormalities in white blood cells and red blood cells that may be seen in the peripheral blood in this condition.

Image BCI-08 illustrates a normal segmented neutrophil. Typically, these cells have a nucleus with 2 to 5 lobes connected by thin strands of chromatin. The chromatin is dense and clumped, with lighter areas of parachromatin usually visible. The cells are generally of medium size. Segmented neutrophils have numerous fine cytoplasmic granules that appear tan, pink, or violet. Individual granules are difficult to visualize in this particular cell, but the cytoplasm still has an underlying pinkish color.
Note that although the cell in this image has only two nuclear lobes, it is not a Pelger-Huet cell. The nucleus of a typical Pelger-Huet neutrophil has two round or almost round lobes connected by a single thin chromatin filament. Sometimes this is referred to as a “pince-nez” morphology (resembling eyeglasses). The chromatin in classic Pelger-Huet cells may also be more dense and clumped than that of normal segmented neutrophils. Likewise, this cell is not a pseudo-Pelger-Huet (or false Pelger-Huet) cell that is often associated with myelodysplastic syndromes. These dysplastic neutrophils may lack granules, but the nuclear lobes in these abnormal cells are usually not round, of equal size, or symmetrical. In some cases, dysplastic neutrophils have only a single, round nucleus.

When trying to identify peripheral blood cells, it is also important to consider other cells seen on the smear as well as any additional laboratory information. True Pelger-Huet anomaly is an inherited but benign condition that does not affect the function of the neutrophils or result in any other unusual hematologic findings. While pseudo-Pelger-Huet cells, as may be seen in myelodysplastic syndromes, can be associated with other hematologic abnormalities (such as anemia), the other white cell and red cell morphologic changes evident in this case study patient do not suggest dysplasia is present.

*Image BCI-09* shows the stage of neutrophil maturation immediately before the segmented neutrophil, which is the band neutrophil. Although the overall cell size and cytoplasmic features of the band are similar to the mature segmented neutrophil, the nuclear shape is different. Band cells characteristically have a nucleus shaped like the letters C or U. Early scientists also thought this nuclear shape, with contrasting clumped chromatin and areas of lighter parachromatin, resembled a sausage. The two nuclear lobes in a band cell are connected by a bridge of nuclear material with chromatin and parachromatin visible. Band neutrophils, although immature, may constitute approximately 2% to 6% of the number of cells normally seen in a differential leukocyte count.
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The cell in Image BCI-10 is a monocyte. The first feature to note is the large cell size. Monocytes are the largest cells normally seen in the peripheral blood. Nuclei in monocytes may appear oval, lobulated, round, or kidney-shaped. The chromatin stains lighter shades of purple (especially in contrast to the segmented and band neutrophils), is finer, and shows minimal clumping. Sometimes convolutions or folds are apparent. Nucleoli are not visible. The cytoplasm in monocytes is generally abundant and blue-gray, although some monocytes may have a pink cytoplasm similar to neutrophils. The cytoplasm is not smooth and even, but may appear rough or sometimes as if small grains of sand were present. This is why all morphologic characteristics are used to properly identify. Cytoplasmic protrusions resembling pseudopods are often seen. The pseudopods are generally clear and therefore do not have a grains of sand appearance. Vacuoles may be present in the cytoplasm as well.

Image BCI-11 identifies a dacryocyte or teardrop-shaped red blood cell. Note the tapered or tear-like end of this cell. Dacryocytes are classically elongated at one end and may or may not have an area of central pallor. The tapered end may be long or short, blunt or pointed, or barely visible. Teardrop formation occurs when splenic macrophages slow the passage of erythrocytes with inclusions and the cell is stretched abnormally. Dacryocytes can also form when the bone marrow is obstructed or packed with abnormal or malignant cells. These cells hinder the normal movement of red blood cells and cause the cells to elongate as they exit the marrow. It is most likely that this mechanism has resulted in the teardrop cells seen in the case study patient’s peripheral blood. Malignant myeloma cells are increased in the bone marrow and impede the maturation and movement of normal cells. For reasons unknown, but perhaps because the teardrop cell’s membrane has been too severely damaged or misshapen too long, the dacryocyte cannot return to a normal biconcave shape.
Image BCI-12 shows red blood cells in rouleaux. This morphologic feature reminded early microscopists of a stack of coins. Rouleaux is defined as 4 or more erythrocytes arranged in a linear pattern. However, it is important to recognize that artifactual rouleaux can be seen in the thick section of almost any peripheral blood smear. Clinically significant rouleaux is seen in the thin areas of the blood slide. The rouleaux shown here is in an acceptable location on the blood film and is consistent with a diagnosis of multiple myeloma. In this condition, excessive amounts of protein produced by malignant plasma cells coat the surface of red blood cells and allow the cells to stack on top of each other like a stack of coins or uniform chains. This pattern is called rouleaux formation. Normally, erythrocytes are repelled by negative charges. It is important not to confuse the distribution pattern of rouleaux with agglutination. In agglutination, red blood cells clump or form a network that is not as orderly or defined as rouleaux. In addition, agglutination forms through a different mechanism, when antibodies attach to antigenic sites on red blood cells and form bridges between adjacent red blood cells.

Image BCI-13 shows a plasma cell. These cells are medium in size and generally round to oval. The nucleus is also round or oval and characteristically eccentrically located in the cytoplasm. The nuclear chromatin is clumped, although this particular cell is not as dense as is usually seen in mature plasma cells. However, the deep blue cytoplasm and prominent perinuclear halo, or hof, is a classic morphologic feature of plasma cells. This clear zone adjacent to the nucleus represents the Golgi body, a cellular constituent that packages protein for cells, in this case, immunoglobulin. Multiple myeloma is associated with an increased proliferation of plasma cells. Usually this overproduction is most evident in the bone marrow, where normally less than 1% of leukocytes will be plasma cells. It is never normal to see plasma cells in the peripheral blood.

The large size, roundish shape of the cell and its nucleus, and deep blue cytoplasm of this cell may suggest some type of blast. However, the chromatin is not as fine or open as seen in blasts. What may appear to be nucleoli are most likely only lighter staining areas, as the chromatin is a darker purple and more dense. The cytoplasmic clearing or hof also indicates this is not a blast cell. Even immunoblasts (immature plasma cells) have an indistinct hof, but lacy chromatin. Likewise, this cell is not an immature
granulocyte such as a promyelocyte or myelocyte as it lacks any evidence of primary or secondary granulation that characterizes these cells.

The final cell identified in this testing event, Image BCI-14, is a plasmacytoid lymphocyte. This cell is transitioning from a lymphocyte to a plasma cell. Mature lymphocytes have a very dense chromatin; this cell’s chromatin pattern is less dense. If a rare plasmacytoid lymphocyte is seen in the peripheral blood, it is generally not significant and represents only a “reactive” lymphocyte (one responding to an antigenic stimulus). However, in the context of a red blood cell abnormality such as rouleaux and the presence of plasma cells, seeing such a cell in the peripheral blood contributes to the abnormal findings suggestive of multiple myeloma. Plasmacytoid lymphocytes vary in size. They may be round or oval in shape with a round or oval nucleus. In contrast to the plasma cell, however, the nucleus is generally centrically located within the cell. Likewise, the perinuclear clearing typical of plasma cells is generally not evident or is minimal. The nuclear chromatin may not appear as dense as that of the plasma cell. The cytoplasm in a plasmacytoid lymphocyte may still be a deep blue. Plasmacytoid lymphocytes are often difficult to distinguish from plasma cells because of the close resemblance between the two cell types.

The chromatin pattern, though less dense than a mature lymphocyte, is still not as loose and open as the chromatin seen in blasts. Again, the apparent nucleoli are probably only lighter staining areas in the nucleus. This dark purple nucleus is morphologically similar to the nucleus in the cell in image BCI-13. Blasts may also be variable in size, but this cell is also smaller than would be expected in a blast. The high nuclear to cytoplasmic ratio and lack of any cytoplasmic blebbing suggest this cell is not a megakaryoblast or immature megakaryocyte. Promyelocytes and myelocytes have granules, so these cells should be excluded as possible choices for the identity of this cell. Hairy cells are lymphoid in origin; however, the cytoplasm is usually more moderate in amount with typically frayed or stringy margins. Once again, it is helpful to view other cells seen in the peripheral blood as well as consider general hematologic parameters when trying to classify white blood cells.

Summary

Multiple myeloma is a disorder that originates in the bone marrow and is characterized by the overproduction of immunoglobulin associated with the autonomous proliferation of a single clone of malignant plasma cells. Both plasma cells and the increase in immunoglobulin contribute to the abnormal
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Peripheral blood findings seen in this condition. A complete blood cell count with differential count, as performed by a medical laboratory professional, is a key procedure that aids in the diagnosis and evaluation of multiple myeloma.

References


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