Neutrophil, segmented or band

<table>
<thead>
<tr>
<th>Identification</th>
<th>Referees</th>
<th>BCK Participants</th>
<th>BCP Participants</th>
<th>Performance Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil, segmented or band</td>
<td>15 93.8</td>
<td>3865 99.0</td>
<td>1715 99.5</td>
<td>Good</td>
</tr>
</tbody>
</table>

The arrowed cell is a segmented/band neutrophil and was correctly identified by 93.8% of referees and 99.1% of participants. Segmented neutrophils have condensed nuclear chromatin and segmented or lobated nuclei (2 to 5 lobes typically). Lobes are connected by a thin filament.
The arrowed cell is an eosinophil and was correctly identified by 100% of referees and 99.8% of participants. Eosinophils are typically easily recognized due to their characteristic coarse, orange-red granules of uniform size. These granules exhibit a refractile appearance and typically do not overlie the nucleus of the cell. The nucleus is usually segmented into two or more lobes separated by a thin filament, with lobes being of equal size and exhibit the same nuclear characteristics as neutrophilic leukocytes.
The arrowed cell is a monocyte and was correctly identified by 93.8% of referees and 97.6% of participants. Slightly larger than neutrophils, monocytes are usually round but may exhibit cytoplasmic extensions. The cytoplasm of monocytes is abundant and gray to gray-blue and may contain fine azurophilic granules or vacuoles. The nucleus is usually indented and often kidney-bean shaped with condensed chromatin, but less dense than that of a neutrophil or lymphocyte. Macrophages or histiocytes are found in tissues, rather than peripheral blood.
The arrowed cell is a lymphocyte and was correctly identified by 93.8% of referees and 96.8% of participants. A lymphocyte is a small, round to ovoid cell which may range in size from 7 to 15 μm with variable N:C ratios. While most lymphocytes are small with round to oval nuclei, some normal lymphocytes are medium-sized due to an increased amount of cytoplasm. Chromatin is diffusely dense or coarse and clumped. Nucleoli, if present, are small and inconspicuous. In contrast, 6.2% of referees and 0.3% of participants identified the arrowed cell as a nucleated red blood cell. Nucleated red blood cells have dense round nuclei and pink cytoplasm, rather than the basophilic cytoplasm present in the lymphocyte.
Blood Cell Identification – Graded

The arrowed cell is a lymphoma cell and was correctly identified by 37.5% of referees and 39.3% of participants. Lymphoma cells may show a variety of morphologic characteristics depending on the underlying type of lymphoma. In this case, the large size of the cell, moderate amount of deeply basophilic cytoplasm, angulated nuclei and prominent nucleoli suggest a large cell lymphoma. These cells can be easily confused with blasts, and additional studies may be necessary to make the correct diagnosis. An accurate clinical history can greatly aid the identification of these cells. In contrast, blast cells have a nucleus with finely reticulated chromatin. Myeloblasts may exhibit a few delicate granules or Auer rods, whereas lymphoblasts often have scant basophilic cytoplasm with nuclei containing finely dispersed chromatin or dense, but not clumped chromatin. See discussion on the following page regarding reactive lymphocytes versus lymphoma cells.

* Not graded due to lack of referee and participant consensus.
Discussion

Case History

The patient is a 58-year-old male with a history of diffuse large B-cell lymphoma treated 8 months previously, now thought clinically to be in relapse. Hemoglobin = 11.1 g/dL, WBC = 11.1 x 10^9/L, PLT = 383 x 10^9/L.

This case is an example of a patient with lymphoma, which now involves the peripheral blood. Lymphomas typically start in lymph nodes or extranodal tissues, spreading to adjacent lymph nodes and usually show a predilection for hematopoietic organs, including bone marrow and spleen. Blood involvement by lymphoma typically suggests that the bone marrow is involved by lymphoma. Components of the blood are produced in the bone marrow; therefore, when lymphoma is in the blood, that usually means it is in the bone marrow. Exceptions do exist, such as Sezary syndrome (lymphoma is in the blood, but not in the marrow), which will not be addressed in this discussion. Frequency of peripheral blood involvement by lymphoma depends on the underlying type of lymphoma (See Table 1 on page 14). In a recent study of lymphomas involving the bone marrow, the peripheral blood was involved in 29 percent of cases with available peripheral blood smears for review. In these cases, peripheral blood involvement by lymphoma was associated with higher white blood cell counts (12,000 vs. 5,480/μL, P = 0.0004 [probability or p value]), as well as higher absolute lymphocyte counts (6,840 vs. 1,180/μL; P = 0.0005) and higher percentage of lymphocytes (45 vs. 24%, P < 0.0001). Unlike acute leukemia, which typically presents with thrombocytopenia and marked anemia, lymphomatous involvement of the blood may minimally affect the hemoglobin and platelet counts, if at all. A bone marrow diagnosis of lymphoma should prompt a careful review of a concurrent peripheral blood smear. In this discussion, features distinguishing reactive lymphocytes from lymphoma cells will be discussed, as well as the morphologic features of lymphomas that commonly involve the peripheral blood.

Reactive Lymphocytes versus Lymphoma

Distinguishing reactive lymphocytes from lymphoma cells can be challenging, but a number of key features should be kept in mind. First, age of the patient is essential. Many of the lymphomas which involve peripheral blood are much more common in middle aged to elderly adults than children or infants. For example, certain lymphomas (i.e., Burkitt) are more commonly seen in children. Second, accurate clinical history can be critical, since any prior diagnosis of lymphoma can aid in the identification of these cells. Third, a well-prepared and stained peripheral blood smear can be your greatest friend. Old blood and ill prepared samples can lead to misdiagnoses or simply ‘misses.’ Once you are looking at the peripheral smear, perform a scan at 10X examining the overall slide before going to higher magnification. Reactive lymphocytosis will show a wide range of cellular sizes and shapes. The classic example is infectious mononucleosis (Epstein-Barr viral infection) in which a variety of lymphocytes are seen, ranging from small lymphocytes with round nuclei and condensed chromatin to reactive lymphocytes with abundant pale blue cytoplasm, round to oval nuclei and moderately condensed chromatin. (Images 1 and 2 of reactive lymphs from cases of infectious mononucleosis are seen on the following page.) The cytoplasm of these reactive lymphocytes may hug adjacent red cells and show a basophilic rim at their margins. Immunoblasts are often
frequently present, being large lymphocytes with round to oval nuclei containing one or more prominent nucleoli. The cytoplasm of an immunoblast is abundant and deeply basophilic. Plasmacytoid lymphocytes may also be seen. In contrast, while reactive lymphocytes are heterogenous, lymphoma cells tend to be homogenous. A peripheral blood smear may contain a subset of lymphoma cells amidst a background of small lymphocytes, but those lymphoma cells will resemble one another. Lymphoma cells can exhibit a variety of morphologic appearances depending on the underlying type of lymphoma, as discussed below. Lymphoma cells can show various sizes and shapes, ranging from 8 to 30 μm in size and nuclear:cytoplasm ratios from 3:1 to 7:1, again depending on the type of lymphoma.

Splenic Marginal Zone Lymphoma
The World Health Organization (WHO) recognizes 3 types of marginal zone lymphomas: splenic, nodal and extranodal. A high frequency of blood involvement by splenic marginal zone lymphoma is well described.¹⁻³ Splenomegaly, often with anemia or thrombocytopenia, is often accompanied by peripheral blood containing lymphoma cells with ‘villous lymphocytes,’ in which bipolar cytoplasmic projections are present. These lymphoma cells are larger than typical lymphocytes with abundant pale blue or blue-grey cytoplasm, round to oval nuclei containing condensed chromatin with usually a single nucleolus. (See Image 3: Splenic marginal zone lymphoma on the following page.) However, not all cases of splenic marginal zone lymphoma in the blood will contain lymphoma cells with prominent ‘villi’. These morphologic features often overlap with hairy cell leukemia. Hairy cells, in contrast have homogenous chromatin and lack nucleoli, with spiky cytoplasmic projections extending from the entire periphery of the cell. (See Image 4: Hairy cell on the following page.) Immunophenotyping is often necessary to distinguish these two disorders.
Mantle Cell Lymphoma

The high frequency of peripheral blood involvement by mantle cell lymphoma is now being recognized.\textsuperscript{4-6} Frequencies as high as 77 percent peripheral blood involvement have been reported.\textsuperscript{4} In mantle cell lymphoma, lymphoid cells may range from small to intermediate sized lymphoid cells with irregular nuclear contours to large blast-like cells resembling acute leukemia. Typical mantle cell lymphoma cells are larger than lymphocytes with folded nuclei and a small amount of basophilic cytoplasm. (See Image 5: Mantle cell lymphoma below.) Nuclei, while condensed contain more reticular chromatin, and may contain a single prominent nucleolus resembling prolymphocytes. Blastic or blastoid variants of mantle cell lymphoma are the size of large cell lymphoma cells (20 to 30 μm) and have moderate amount of basophilic cytoplasm, and nuclei while round to oval, may be indented or convoluted. (See Image 6: Mantle cell lymphoma blastic variant below.) Chromatin is less condensed, resembling blastic chromatin, although these lymphoma cells are typically more variable than blasts seen in acute leukemia.

Image 3: Splenic marginal zone lymphoma

Image 4: Hairy Cell leukemia; “hairy cell” is to the left, while a reactive lymphocyte is seen at right.

Image 5: Mantle cell lymphoma

Image 6: Mantle cell lymphoma, blastic variant
Burkitt Lymphoma
Burkitt or Burkitt-like lymphoma cells are morphologically identical to the cells seen in Burkitt leukemia. The distinction rests on whether there is less than or greater than 25 percent bone marrow involvement, respectively. The Burkitt cell is moderate in size (10 to 25 μm) with an oval to round nucleus, moderately coarse chromatin, and 1-3 prominent nucleoli. (See Image 7: Burkitt cell below.) A moderate amount of deeply basophilic cytoplasm is present and typically contains multiple small vacuoles. Burkitt-like lymphoma resembles Burkitt lymphoma, but is accompanied by greater pleomorphism in cell size and shape.

Image 7: Burkitt cell

Diffuse Large B-cell Lymphoma
Surprisingly, a relatively high rate (32 percent) of diffuse large B-cell lymphoma in the blood may be seen, although this is likely underrecognized.1,7 Large cell lymphomas show some of the most abnormal morphology of the lymphomas. In the past, these lymphomas have been called ‘histiocytic lymphoma’ or ‘reticulum cell sarcoma,’ but now are simply termed large cell lymphoma. Immunophenotypic studies are necessary to classify whether these lymphomas are of B-, T- or NK-cell origin. They may resemble a proliferation of immunoblasts with 1-2 prominent nucleoli, or in other cases present with deep convolutions with occasional nucleoli. These cells are large with small to moderate amounts of deeply basophilic cytoplasm, occasionally vacuolated, and often show angulated and folded nuclear contours. (See blood cell images BCK/BCP-11 through 15.) While these cells can be confused with blasts, large cell lymphoma cells vary in size more than blasts and lack the smooth, even chromatin found in blasts. Additional studies such as flow cytometry immunophenotyping or bone marrow biopsy may be necessary for correct identification.

Follicular Lymphoma
Follicular lymphoma, when it involves the blood, shows a characteristic morphology. These lymphoma cells are slightly bigger than normal lymphocytes with a clefted appearance and moderately coarse chromatin. (See Image 8: Follicular lymphoma on the following page.) Cytoplasm is typically scant, but may be moderate, and the majority of nuclei show folds and convolutions. Nucleoli may be present. Other types of lymphoma cells also show angulated nuclei, including mantle cell lymphoma and Sézary cells. Mantle cell lymphoma cells lack the coarse chromatin of follicular lymphoma and are usually larger in size with gentle
nuclear folds, not the deep clefts and possible lobes of follicular lymphoma. Sezary cells show convoluted nuclear membranes with a cerebriform appearance and contain dark, hyperchromatic chromatin lacking nucleoli typically. (See Image 9: Sezary cell below.) The distinction among the lymphoma types typically requires immunophenotyping.

Table 1. Frequency of Peripheral Blood Involvement by Bone Marrow Lymphoma (adapted from ¹)

<table>
<thead>
<tr>
<th>Type of lymphoma</th>
<th>PB disease /total samples</th>
<th>Percentage of PB involvement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marginal zone lymphoma⁰</td>
<td>8/10</td>
<td>80</td>
</tr>
<tr>
<td>High grade lymphoma, NOS⁰</td>
<td>1/2</td>
<td>50</td>
</tr>
<tr>
<td>Mantle cell lymphoma</td>
<td>11/23</td>
<td>48</td>
</tr>
<tr>
<td>Burkitt lymphoma</td>
<td>2/5</td>
<td>40</td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma</td>
<td>12/38</td>
<td>32</td>
</tr>
<tr>
<td>Mature T-cell &amp; NK-cell lymphomas</td>
<td>6/20</td>
<td>30</td>
</tr>
<tr>
<td>Low grade B-cell lymphoma, NOS⁰</td>
<td>5/18</td>
<td>28</td>
</tr>
<tr>
<td>Follicular lymphoma</td>
<td>9/46</td>
<td>20</td>
</tr>
<tr>
<td>Lymphoplasmacytic lymphoma</td>
<td>2/21</td>
<td>10</td>
</tr>
<tr>
<td>Small lymphocytic lymphoma ³</td>
<td>1/10</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>57/197</td>
<td>29</td>
</tr>
</tbody>
</table>

PB = peripheral blood.

a. 8 of 9 cases of splenic marginal zone lymphoma showed PB involvement.

b. A small number of cases with limited material were classified as high-grade, not otherwise specified and low-grade, not otherwise specified.

c. Not meeting criteria for chronic lymphocytic leukemia.


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Hematology and Clinical Microscopy Committee
The arrowed cell is a blast (or myeloblast). Myeloblasts are the most immature cells in the myeloid series. The myeloblast is a large cell, 15-20 millimicrons in diameter with a high nuclear to cytoplasmic (N:C ratio), generally round nuclear membranes, a distinct nucleolus and basophilic cytoplasm. The blasts are normally confined to the bone marrow, but may be released into the peripheral blood in malignant and reactive states.
The promyelocyte is a round to oval cell that usually is slightly larger than a myeloblast; 12-24 millimicrons in diameter. Promyelocytes have nuclear to cytoplasmic ratios in the range of 5:1 to 3:1, with fine nuclear chromatin and a single prominent nucleolus. In the basophilic cytoplasm, distinct azurophilic (primary) granules are present. Promyelocytes are confined to the bone marrow, except in pathologic states.
The arrowed cell is a myelocyte. Myelocytes are smaller in diameter than the earlier precursors with round to oval nuclei, no nucleoli and chromatin clumping. The cytoplasm is amphophilic with both azurophilic and specific granules present.
The leukocytes in the slide are neutrophils/neutrophils with toxic granulation. Neutrophils generally constitute 5-10% of peripheral blood leukocytes. Neutrophils have a nuclear to cytoplasmic ratio of 1:3 with dense nuclear chromatin. The nucleus is segmented or lobated with pale cytoplasm which contains specific granules. Toxic granulation is the presence of large purple or dark blue cytoplasmic granules representing primary granules in the cytoplasm of neutrophils. Toxic changes in neutrophils may be seen in response to infection, burns, trauma or other acute stimuli.
### Neutrophil, toxic (to include toxic granulation and/or Döhle bodies, and/or toxic vacuolization)

- **Referees**
  - No.: 16
  - %: 100.0

- **BCK Participants**
  - No.: 2906
  - %: 77.2

- **BCP Participants**
  - No.: 1157
  - %: 69.7

**Evaluation**: Educational

The arrowed cell is a neutrophil with a Döhle body. Neutrophils with cytoplasmic Döhle bodies may be seen as a response to various toxic stimuli. Döhle bodies are single or multiple blue or gray-blue cytoplasmic inclusions of variable size and shape. They may be seen in neutrophils, bands, or metamyelocytes. Döhle bodies may be seen in association with neutrophilic toxic granulation or toxic vacuolization.

### Neutrophil, segmented or band

- **Referees**
  - No.: -
  - %: -

- **BCK Participants**
  - No.: 434
  - %: 11.5

- **BCP Participants**
  - No.: 312
  - %: 18.8

**Evaluation**: Educational

### Neutrophil with Pelger-Huët nucleus (acquired or congenital)

- **Referees**
  - No.: -
  - %: -

- **BCK Participants**
  - No.: 369
  - %: 9.8

- **BCP Participants**
  - No.: 152
  - %: 9.2

**Evaluation**: Educational
Discussion

Case History

The patient is a 71-year-old Hispanic female with breast cancer. The patient was recently treated and also received G-CSF that was discontinued a couple of days before the blood smear was obtained.

Additional laboratory data reveals:
- White blood cell count = 15.2 x 10^9/L
- Hemoglobin = 10.0 g/dL
- Platelets = 325 x 10^9/L

This case demonstrates the peripheral blood cell count and morphologic changes that can be seen in patients who receive recombinant hematopoietic growth factors. Hematopoietic growth factors are proteins that bind to receptors on the cell surface with the primary result of activating cellular proliferation and promoting differentiation and maturation of hematopoietic progenitors. These growth factors are naturally made in the body. Recombinant DNA technology has allowed production of synthetic growth factors, which are now available for use in patients with cytopenias. While different growth factors have varied affects on different cell systems, in general they stimulate lymphocytic, hematopoietic and non-hematopoietic cell lineages.

The following is a list of the growth factors that are most commonly used clinically:
- Granulocyte/colony stimulating factor (G-CSF)
- Granulocyte/monocyte colony stimulating factor (GM-CSF)
- Interleukin (IL-3)
- Erythropoietin
- Thrombopoietin

Granulocyte colony stimulating factor (G-CSF) regulates the proliferation and maturation of neutrophilic granulocytic progenitors by binding to receptors on committed granulocyte precursors. G-CSF also increases the functionality of granulocytes by enhancing granulocytic, monocyctic and macrophage cells involved in antigen presentation and cell-mediated immunity. The maturation time of myeloid progenitors in the bone marrow is shortened from 5 days to as little as one day. The gene for G-CSF is located on chromosome 17 (17q11-23).

Granulocyte/monocyte colony stimulating factor (GM-CSF) is a potent stimulus for the growth of granulocytic, erythrocytic, macrophage and megakaryocytic progenitors. The GM-CSF receptor is expressed on granulocyte, erythrocyte, megakaryocyte and macrophage progenitor cells, as well as mature neutrophils, monocytes, macrophages, dendritic cells, plasma cells, certain T-lymphocytes, and vascular endothelial cells. Although GM-CSF has greater activity on immature progenitors than does G-CSF, its proliferative effects are less significant than those of interleukin 3 (IL-3). GM-CSF also enhances the function of mature granulocytic cells and monocytes. The gene for GM-CSF is located on chromosome 5 (5q23-31).
Interleukin-3 also known as multi-CSF stimulates the bone marrow stem cells and thereby the growth of granulocytes and monocytes, and to a lesser degree megakaryocytic and erythroid precursors. The gene for IL-3 is located on the long arm of chromosome 5.

Erythropoietin (EPO) is the primary regulator for erythropoiesis. EPO stimulates and induces maturation of colony forming units erythroid (CFU-E) and a subset of the burst-forming units erythroid (BFU-E). The gene for EPO is located on chromosome 7.

Thrombopoietin is a primary stimulator of megakaryocytic proliferation, causing a significant rise in the platelet count.

All of the growth factors work by interacting with specific receptors on target cells. For example:

- EPO binds to EPO receptors on committed red blood cell precursors
- GM-CSF and IL-3 bind to receptors on early granulocyte precursors
- G-CSF binds to receptors on slightly more mature committed granulocytic precursors

Due to the diversity in the clinical indications for using hematopoietic growth factors, it is important for laboratory professionals and pathologists to recognize the peripheral blood and bone marrow findings in patients on such factors. Although there is some variability in the peripheral blood findings related to which growth factor the patient has received, peripheral neutrophilia is expected. The growth factors utilize three mechanisms that lead to the increase in neutrophils. These include:

- demargination of neutrophils from the marginated pool
- mobilization of the maturation-storage bone marrow compartment
- increased neutrophil production

As a response, the granulocytic series is frequently left-shifted with myeloid elements including blasts, promyelocytes, myelocytes and metamyelocytes present. Challenges BCK/BCP-16, BCK/BCP-17 and BCK/BCP-18 demonstrate a blast (myeloblast), promyelocyte and myelocyte, respectively, which were identified in the peripheral blood of this patient.

In addition to the increased number of mature and immature granulocytic elements, toxic changes are frequently seen. Toxic granulation, Döhle bodies and toxic vacuoles, all changes more commonly associated with infection, can be seen as a response to hematopoietic growth factors. Challenges BCK/BCP-19 and BCK/BCP-20 exhibit a neutrophil with toxic granulation and a neutrophil with a Döhle body, respectively.

The two major differential diagnostic categories of a peripheral blood granulocytosis include reactive neutrophilia and neoplastic neutrophilia (myeloproliferative disorders). Reactive neutrophilia may be due to an infectious process; as a response to drug or hormonal therapy; in patients with burns, acute trauma or myocardial infarction; in inflammatory disorders such as collagen vascular or other autoimmune disorders; as a response to stress or severe exercise; in pregnancy; in uremic patients; and in patients with acute hemorrhage or hemolysis. In the myeloproliferative disorders the white blood cell count is usually more pronounced than in reactive processes. Chronic myelogenous leukemia (CML) is the most common
myeloproliferative disorder, with essential thrombocythemia, polycythemia vera, myelofibrosis and chronic myeloproliferative disorder, non-specified completing the list.

In some patients a peripheral monocytosis and circulating nucleated red blood cells are also identified as a response to growth factors. Less commonly, dyspoietic myeloid elements are seen as a response to the synthetic growth factors. The dyspoietic features can include cells, which exhibit nuclear-cytoplasmic dyssynchrony and nuclear segmentation defects.

In patients with a known diagnosis of acute myeloid leukemia receiving chemotherapy, the distinction of persistent or relapsed leukemia from regenerating bone marrow related to growth factors can be quite challenging. The findings of blasts with Auer rods, the presence of more differentiated myeloid elements, and the presence of erythroid or megakaryocytic elements as would be expected in regeneration, can be helpful in this distinction. However, sometimes ancillary studies, to include cytogenetic analysis and flow cytometric analysis may be necessary to confirm the absence of leukemic blasts.

In patients with a known diagnosis of the myelodysplastic syndrome, administration of synthetic growth factor may lead to a left-shift in the myeloid series, raising the concern of transformation of the myelodysplastic syndrome into acute leukemia. Close attention to morphologic details, in conjunction with cytogenetic analysis and flow cytometric analysis may be necessary to make this distinction.

Examination of the bone marrow of the patient receiving growth factors reveals panhyperplasia, involving all three cell lines. However, myeloid hyperplasia is most pronounced and can be significantly left-shifted. As the duration of therapy persists, the left-shifted myelopoiesis becomes less pronounced and the myeloid to erythroid ratio typically normalizes.

Clinical indications for use of the hematopoietic growth factors have been an area of intense study since their discovery in the mid 1990’s. In addition to reviewing patient’s peripheral blood and bone marrow responses to the growth factors, the incidence of neutropenic fever, rate of infections, duration of hospitalization, morbidity and mortality have all been outcomes, which have been reviewed in patients receiving growth factors. In 1994 the American Society of Clinical Oncology issued recommendations for the use of hematopoietic colony-stimulating factors. These clinical practice guidelines have been reviewed with the most recent guidelines released in November 2003. The current recommendations are that colony stimulating factors are recommended in some situations:

1. To reduce the likelihood of febrile neutropenia when the expected incidence is >40 percent
2. After documented febrile neutropenia in a prior chemotherapy cycle to avoid infectious complications
3. To maintain dose intensity in subsequent treatment cycles when chemotherapy dose reduction is not appropriate
4. After high-dose chemotherapy with autologous progenitor cell transplantation
It is not recommended, based on current evidence, that colony stimulating factors should routinely be used in patients with neutropenia who are afebrile. The therapeutic use of CSF in addition to antibiotics at the onset of febrile neutropenia should be reserved for patients at high risk for septic complications. It is not recommended that CSF be used concurrently with chemotherapy and radiation therapy. The clinical indications for use of CSF in the pediatric population are similar. While it is recognized that administering growth factors can significantly shorten the duration of severe neutropenia, however, this does not always lead to shortened hospital stays or decreased rate of infection.

Recombinant erythropoietin (epoetin) is recommended in patients with chronic anemias to enhance erythrocyte production. Epoetin is recommended for patients with a chemotherapy-associated anemia who have a hemoglobin < 10.0 g/dL. In some chemotherapy patients, epoetin may be given when the anemia is less severe (< 12.0 but > 10.0 g/dL). Epoetin is also recommended for patients with chronic renal disease or other chronic disease causing significant anemia.

The side effects, adverse reactions, complications of growth factors are generally mild and the drugs are well tolerated. Diarrhea and fluid retention may be seen as a side effect in patients receiving erythropoietin. GM-CSF has a risk of fever, headaches, skin rash, pericardial effusions and medullary bone pain. Medullary bone pain is the most common acute adverse reaction seen in the pediatric population. Bone pain, skin rash, allergic reactions and splenomegaly may be seen in patients receiving G-CSF.

Summary

As hematopoietic growth factors are frequently used in patients receiving chemotherapy, in patients with the myelodysplastic syndrome, and in patients with chronic anemias, it is important for those in laboratory medicine to recognize the peripheral blood and bone marrow findings related to these agents.


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