Therapy Effect
Impact on Bone Marrow Morphology

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KEYWORDS
• Bone marrow • Post-therapy and treatment effects • Hematologic malignancies

ABSTRACT

This article highlights the most common morphologic features identified in the bone marrow after chemotherapy for hematologic malignancies, growth-stimulating agents, and specific targeted therapies. The key is to be aware of these changes while reviewing post-therapeutic bone marrow biopsies and to not mistake reactive patterns for neoplastic processes. In addition, given the development and prevalent use of targeted therapy, such as tyrosine kinase inhibitors and immune modulators, knowledge of drug-specific morphologic changes is required for proper bone marrow interpretation and diagnosis.

OVERVIEW

This article highlights the morphologic changes in the bone marrow associated with various treatment modalities for hematologic malignancies. Because some of the morphologic findings can mimic residual disease or malignant neoplasms, pathologists must be aware of the distinguishing features between reactive and residual neoplastic processes. It is common to see a spectrum of morphologic changes in the bone marrow, and they are dependent on the type of therapy and/or the time frame in which a biopsy is performed. After an initial diagnostic bone marrow biopsy, the purpose of the subsequent biopsies is usually to assess residual disease, therapeutic efficacy, and/or marrow regeneration. Occasionally, there might be a change in a patient's clinical status or laboratory results, which also prompts a bone marrow biopsy to evaluate disease relapse. Knowledge of clinical history, including concurrent drug therapy in addition to chemotherapy, is the most important piece of information that can aid in the diagnostic process. This article reviews the most common bone marrow and/or peripheral blood findings associated with traditional therapy for hematologic malignancies and presents additional findings that have become important to recognize given the development and use of newer treatment modalities, including immune modulators and tyrosine kinase inhibitors. Morphologic changes that occur in the bone marrow after hematopoietic stem cell transplant are not included.

BONE MARROW POST MYELOABLATION

The most common traditional treatment modality for hematologic malignancies, especially in the setting of acute leukemias, is myeloablative chemotherapy. The intent of this systemic therapy is to eliminate the neoplastic population; however, it also indiscriminately destroys all proliferating normal hematopoietic elements.[1–3] Depending on the time in which the bone marrow biopsy is performed, a wide spectrum of morphologic changes can be seen. Some of these changes, subdivided into early and late, are presented in **Box 1** and demonstrated in **Figs. 1–6**.

FIBROSIS

Bone marrow fibrosis can be associated with a wide variety of malignant diseases, including leukemia, lymphoma, myeloid neoplasms, and metastatic carcinoma. It can also be seen in a postinduction chemotherapy bone marrow biopsy, most commonly in the form of mild reticulin fibrosis.[4] This fibrosis usually disappears or decreases after the treatment of the primary

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Box 1
Morphologic changes associated with myeloablative therapy

Early

- Prominent necrosis
- Edema
- Dilated sinuses
- Marrow aplasia
- Residual histiocytes, stromal cells, and plasma cells
- Mild reticulin fibrosis

Late

- Increased lobulated fat cells
- Foci of immature myeloid and erythroid precursors
- Gradual return of megakaryocytes
- Resolution of reticulin fibrosis
- Restoration of marrow cellularity

disorder.[5] It is important to be aware of this finding, especially in a patient with prior history of myeloproliferative neoplasm, and to not characterize the fibrosis as residual disease (**Figs. 7** and **8**).

NECROSIS

Bone marrow necrosis is most commonly associated with marrow involvement by malignancy, such as leukemias, non-Hodgkin and Hodgkin lymphomas, and metastatic carcinoma.[6] It is also common to see marrow necrosis after induction chemotherapy. Post-therapy marrow necrosis is usually characterized by complete replacement by so-called ghost cells with pyknotic nuclei and degenerative cytoplasm. Bone marrow aspirate smear may show an abundance of nonviable stripped nuclei. Depending on the time of the post-therapeutic biopsy, the bone marrow may show areas of normal regeneration or fibrosis. It is also important to exclude or document areas of residual viable tumor (**Fig. 9**).

SEROUS ATROPHY

Also known as gelatinous transformation, serous atrophy is characterized by increased gelatinous

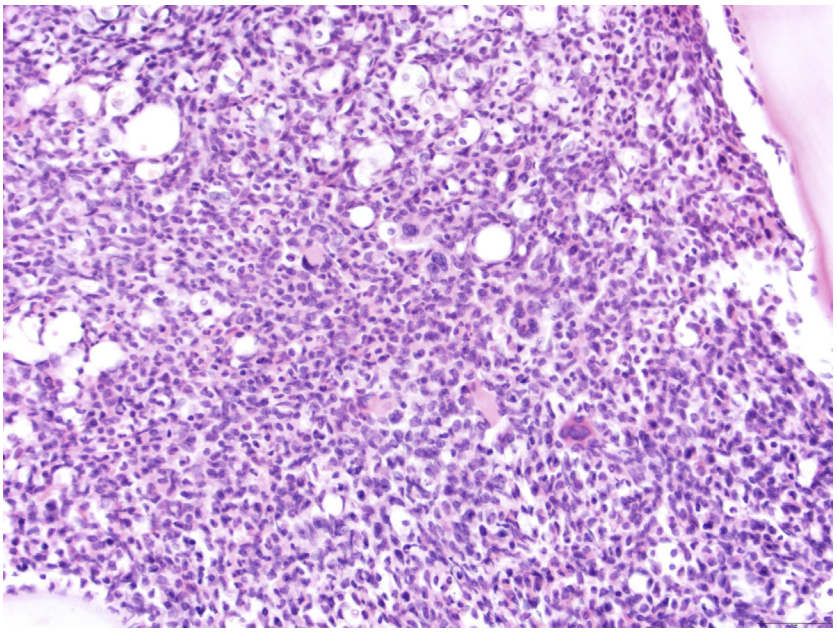

Fig. 1. Diagnostic bone marrow biopsy from a patient with AML demonstrating near 100% cellular marrow composed of mainly myeloid blasts (hematoxylin-eosin ×20).