Introduction

Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal hematopoietic stem cell disorders characterized by dysplastic hematopoiesis, peripheral cytopenias, and risk of progression to acute myeloid leukemia (AML).1-3 MDS are primarily diseases of the elderly with the median age of diagnosis being 76 years in the United States.4 Overall, 10,000 individuals are diagnosed with MDS annually in the United States.4 MDS are primarily diseases of the elderly with the median age of diagnosis being 76 years in the United States.4

Objective

To educate advanced practitioners about the importance of the BM examination for patients with suspected MDS, including:
- The use of BM in MDS diagnosis, classification, and risk stratification
- Overview and utility of the BM examination
- What constitutes an adequate BM sample
- Practical considerations for the BM procedure

Practical Guide to BM Sampling

Diagnosis and Classification of MDS

MDS are among the most challenging of the myeloid neoplasms to diagnose and classify.
- MDS are diagnosed and classified into 7 subtypes by World Health Organization criteria based on percentage of blasts in the BM and peripheral blood.
- Morphological, cytogenetic, and molecular studies have a major role in the evaluation of patients with MDS.
- Clonal cytogenetic abnormalities are observed in >50% of MDS cases.5
- BM examination is required to assess BM blast percentage and morphology for diagnosis and accurate classification.

Risk Stratification of MDS

The International Prognostic Scoring System (IPSS)6-8 for risk stratification of patients with MDS was revised in 2012 (IPSS-R; http://www.ipss-r.com).8

- BM examination is required to assess BM blast percentage and morphology for diagnosis and accurate classification.
- IPSS-R stratifies patients into 5 risk groups with significantly different median overall survival and time to acute myeloid leukemia (AML) evolution.8

Table 1. IPSS-R Classification of MDS

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Very Poor</th>
<th>Poor</th>
<th>intermediate</th>
<th>Good</th>
<th>Very Good</th>
</tr>
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<tbody>
<tr>
<td>Prognostic Score Value</td>
<td>&gt; 6</td>
<td>3-6</td>
<td>1-2</td>
<td>≤ 1</td>
<td>≤ 0.5</td>
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<tr>
<td>ANS, × 10^9/L</td>
<td>&gt; 10</td>
<td>&gt; 2-&lt; 5</td>
<td>5-10</td>
<td>≤ 2</td>
<td>≤ 1</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>≥ 10</td>
<td>&gt; 9-&lt; 10</td>
<td>≤ 9</td>
<td>≤ 9</td>
<td>≤ 8</td>
</tr>
<tr>
<td>BM blasts, %</td>
<td>&gt; 10</td>
<td>&gt; 5-&lt; 10</td>
<td>≤ 5</td>
<td>≤ 1</td>
<td>≤ 0.5</td>
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- BM examination is essential for diagnosis, classification, and risk stratification of MDS.
- Proficiency in this procedure is critical to obtain high-quality BM specimens to facilitate accurate diagnoses, and minimize patient discomfort and risk.

Overview and Utility of the BM Examination

The BM examination obtains 2 interrelated specimens:
- The BM aspirate (BMA, Figure 2A)
- The BM trephine biopsy (BMTB, Figure 2B)

- Combined examination of the BMA and BMTB allows the most thorough assessment
- BM aspirate provides cellularity, morphological, cytogenetic, and immunophenotypic characterization important for diagnosis.
- Pathologists review:
  - A cytological smear of the BM to evaluate cell morphology and a count of marrow elements, including blasts (Figure 2A).
  - Additionally, pathologists review a peripheral blood smear for abnormal cellular morphology and count of blasts (Figure 2C).
  - Sections of the BM trephine to describe overall cellularity (the ratio of hematopoietic tissue to fat), topography, stromal elements, and the proportion and maturation of hematopoietic cells (Figure 2B).

- Metaphase cytogenetics of BM to identify clonal chromosome abnormalities (Figure 3).

What Constitutes an Adequate BM Sample

- BMA samples should be evaluated for the presence of spicules to ensure proper BM sampling:
  - If BMA cannot be obtained due to fibrosis or cellular packing, touch preparations of the BMF can provide valuable cytogenetic information.
  - An adequate BMTB specimen must be ≥ 1.5 cm in length to allow evaluation of ≥ 5 partially preserved metaphases.4

- In aggressive MDS, there may be aggregates (3-8 cells) or clusters (>5 cells) of blasts, usually localized to the central portion of the BM, away from the vascular stroma and areas of the bone trabeculae, demonstrating the need for an adequate BMTB specimen.

Figure 4. Examples of Adequate (A and B) and Poor (C) BM Biopsy Core Specimens

Figure 2. Aspirate Smear from Patient With RAEB-2 MDS (A), Hypercellular BM Biopsy Section (B), and Peripheral Blood Smear with Dysplastic WBC (C).

Figure 3. Metaphase Cytogenetics From a Patient With MDS

Table 2. Practical Considerations for the BM Procedure

<table>
<thead>
<tr>
<th>Practical Considerations</th>
<th>Details</th>
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</table>
| Patient preparation | Patients should be positioned prone or in the right/left lateral decubitus position.
- The site is prepared with sterile technique and the patient is draped.
- The posterior iliac crest (PIC) is the preferred site for the procedure.2
- The anesthesiologist should be present in the room to monitor the patient and provide anesthetic care.
- Following the procedure, firm pressure is applied to the site for 5 minutes for adequate hemostasis.

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