Bone Marrow Cellularity Determination: Comparison of the Biopsy, Aspirate, and Buffy Coat

By Ralph A. Gruppo, Beatrice C. Lampkin, and Suzanne Granger

Bone marrow biopsies (244) performed with a Jamshidi needle were evaluated in 53 children with leukemia or aplastic anemia. Adequate specimens were obtained in 85%. Results of cellularity estimated by biopsy were compared to the cellularity of the aspirate versus volumetric determination of the myeloid-erythroid layer (buffy coat). A wide discrepancy was noted between marrow cellularity confirmed by biopsy versus the aspirate or buffy coat. The greatest variance was seen in the hypercellular or normocellular marrows, as estimated by biopsy, in which 39% were misinterpreted as moderately or severely hypocellular by aspirate. Volumetric measurement of buffy coat was least acceptable for estimating cellularity. Thus the biopsy has proved to be an important and reliable indicator of bone marrow cellularity.

THE ESTIMATE OF CELLULARITY OF THE BONE MARROW in patients with leukemia and aplastic anemia is important in following the clinical course of these diseases and in evaluating their responses to therapy. Cellularity of marrow has routinely been estimated by a variety of means. Examination of aspirate “smears” or measurement of the myeloid-erythroid layer (buffy coat) as a percentage of the total volume (volumetric method) are the most widely used methods. Both of these methods have the disadvantage that aspirated material is a mixture of marrow and sinusoidal blood and thus may not accurately reflect true cellularity of the marrow. The introduction of a new biopsy needle by Jamshidi and Swaim has provided an instrument capable of easily obtaining bone marrow biopsies with little or no more discomfort than a routine aspiration. In addition, with this needle, a sample of marrow of adequate size and minimal destruction of structure can be obtained, which allows an accurate interpretation of the cellularity of the marrow and architectural characteristics. A comparison of the cellularity by this needle biopsy versus the aspirate (“fleck”) and buffy coat has not heretofore been recorded. The purpose of this report is to compare these three methods of determining marrow cellularity in children with leukemia or aplastic anemia.

MATERIALS AND METHODS

The biopsy needle used was a 12- or 14-gauge Jamshidi bone marrow needle (Kormed).* The posterior iliac crest was routinely employed for marrow procedures. Approximately 0.5 to

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1.0 ml of marrow was initially aspirated and immediately discharged into a petri dish. Marrow "flecks" or spicules were selected for making cover glass smear preparations and stained with Wright's stain. A second syringe was used to aspirate 2.0 ml of marrow into 0.5 ml of 4% EDTA for volumetric determination, which was recorded as a percentage of the total volume. Following aspiration for smears and buffy coat, a fresh biopsy needle was inserted, and the procedure used was similar to that described by Jamshidi and Swaim. The biopsy specimen was immediately fixed in a mixture of 90% Zenker's solution and 10% glacial acetic acid for 24 hr, and followed by routine histologic processing and staining with hematoxylin and eosin. Cellularity of the biopsy and aspirate were independently and blindly graded by the author (R.G.) according to the following grading system: 3+, definite hypercellularity; 2+, normal cellularity; 1+, moderate hypocellularity; 0, severe hypocellularity.

An estimate of the cellularity of the aspirate was based upon examination of at least two cover slips with particular reference to the quality of the bone marrow flecks. Most marrow aspirates and biopsies were performed by the Pediatric Hematology-Oncology Fellows, after obtaining appropriate consent.

RESULTS

Consecutive bone marrow biopsies (244) were evaluated in 53 patients (113 biopsies) with acute lymphoblastic leukemia, 19 patients (113 biopsies) with acute myelo-, myelomonocytic, or monoblastic leukemia, 3 patients (15 biopsies) with chronic myelogenous leukemia, and 1 patient (3 biopsies) with aplastic anemia. Most patients were followed serially during the clinical course of their disease. Thirty-seven biopsies were considered inadequate for assessment, representing a total of 15%. Adequate specimens were more consistently obtained by those individuals with greater experience in performing biopsies. One hundred seventy-eight of the adequate specimens had aspirates of the marrow available for review of cellularity and form the basis of this report. Buffy coats were measured by the volumetric technique in 62 of the patients.

As noted in Table 1, there was a wide discrepancy between cellularity of the marrow as estimated by biopsy versus aspirate or buffy coat. The greatest variance was seen in the hypercellular or normocellular marrows as estimated by biopsy in which 44 of 113 (39%) were interpreted as moderately or severely hypocellular by aspirate. Volumetric measurements of buffy coat were least acceptable for estimating cellularity. Of those marrows judged hypercellular by biopsy, the mean buffy coat was 3.2% (range, trace to 11%), of those judged normocellular, the mean buffy coat was 2.7% (range, trace to 10%), of those

<table>
<thead>
<tr>
<th>Bone Marrow Biopsy</th>
<th>Aspirate Cellularity (No.)</th>
<th>Buffy Coat</th>
<th>N</th>
<th>X</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercellular, 3+</td>
<td>4 (5.7%)</td>
<td>21 (30.4%)</td>
<td>40 (57.9%)</td>
<td>29</td>
<td>3.2%</td>
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<td>(N = 69)</td>
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<tr>
<td>Normocellular, 2+</td>
<td>4 (9.0%)</td>
<td>15 (34.0%)</td>
<td>16 (36.3%)</td>
<td>9</td>
<td>2.7%</td>
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<td></td>
<td>(N = 44)</td>
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<tr>
<td>Moderately</td>
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<tr>
<td>hypocellular, 1+</td>
<td>21 (36.8%)</td>
<td>32 (56.1%)</td>
<td>4 (7.0%)</td>
<td>0</td>
<td>0.5%</td>
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<td></td>
<td>(N = 57)</td>
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<td>Severely</td>
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<tr>
<td>hypocellular, 0</td>
<td>4 (50.0%)</td>
<td>3 (37.5%)</td>
<td>1 (12.5%)</td>
<td>0</td>
<td>0.6%</td>
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<td></td>
<td>(N = 8)</td>
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judged moderately hypocellular, the mean buffy coat was 0.5% (range, trace to 1.5%) and of those judged severely hypocellular, the mean buffy coat was 0.6% (range, trace to 2%). In many of the biopsy-proven hypercellular marrows, the aspirate was obtained only with difficulty ("dry tap"). In patients in whom there were dry taps, the biopsy specimen was used for making touch preparations on a dry slide which were then stained with Wright’s stain. Thus a rapid assessment of cellularity and differential count of the marrow were obtained.

DISCUSSION

An important limitation of marrow examination obtained by aspirate is the admixing of marrow and sinusoidal blood, which may not allow for reliable estimates of marrow cellularity. The use of the biopsy needle of Jamshidi and Swaim allows adequate marrow specimens with well-preserved architecture, permitting better evaluation of cellularity. This evaluation is of particular importance in the hypercellular marrow which yields a "dry tap" or only dilute sinusoidal blood.

The use of the biopsy avoids misinterpretation of cellularity by smears or buffy coat in 39% of patients in whom the biopsy confirmed a normal or hypercellular marrow.

REFERENCES

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