Peripheral Blood Blast Clearance as an Early Prognostic Marker for AML

A study published in Blood (2007;110:4172-4174) showed that, as in childhood acute lymphoblastic leukemia (ALL), the time to clearance of circulating blasts from peripheral blood also serves as an independent prognostic marker of relapse-free survival (RFS) and overall survival (OS) for acute myeloid leukemia (AML).

In an effort to evaluate the impact of time to peripheral blood blast (PBB) clearance on RFS and OS, researchers from the Mayo Clinic and Northwestern University retrospectively analyzed a cohort of 86 adult patients with AML (excluding acute promyelocytic leukemia) who received uniform induction and consolidation chemotherapy. Patients with PBBs at initiation of induction chemotherapy (n = 73) were separated into 2 groups based on whether blasts were cleared on or before day 5 (n = 45) or after day 5 (n = 28). Significant differences were observed with regard to different rates of relapse of 33% and 79% between the day 0 to 5 and day 6 or later subgroups, respectively. Significant differences in OS were also noted between these 2 subgroups.

The researchers also divided patients into 3 “blast risk groups” (good, intermediate, and poor) based on blast clearance on or before day 3, days 4 to 5, or day 6 or later. The good, intermediate, and poor risk groups had significantly different relapse rates of 12.5%, 47%, and 78%, respectively.

Univariate analysis of multiple variables at the time of diagnosis showed that only the day to blast clearance, number of induction cycles and the cytogenetic risk group had a significant impact on RFS. Multivariable analysis of these 3 variables showed that only the day of blast clearance or "blast-risk group" was an independent prognostic marker of RFS. Similar findings were noted with univariate analysis for OS in which only "blast-risk group" and number of induction cycles to achieve complete remission significantly impacted prognosis.

This study’s findings demonstrated that in AML patients achieving complete remission following standard chemotherapy, the time to PBB clearance had the strongest independent prognostic impact on RFS and OS. Additionally, the authors concluded that the time to PBB clearance, in acting as an early marker of in vivo chemosensitivity, potentially serves as a valuable measure of treatment response in AML patients.

At Saint Luke’s Hospital (SLH) the time to PBB clearance can be determined by a daily complete blood count (CBC) with a differential count, which is routinely performed on an automated analyzer in the hematology laboratory. Manual slide differential counts of one hundred cells are performed in all cases which are flagged by the analyzer due to immature granulocytes, including circulating blasts.

Infectious Mononucleosis Testing

The cardinal symptoms of infectious mononucleosis (IM) are the well-known triad of fever, pharyngitis, and peripheral lymphadenopathy, especially involving the posterior cervical nodes. About 5% of patients present with rash, especially if they are being treated with ampicillin for pharyngitis. Adults older than 40 years are less likely to present with lymphadenopathy and pharyngitis and more likely to have hepatitis, cholestasis, and hepatomegaly.

Monospot is a rapid latex agglutination test for the detection of IgM heterophile antibodies that are present in patients with infectious mononucleosis. Heterophile antibody recognizes cells from a different species, such as horse red blood cells. They do not recognize viral epitopes and appear to arise from the immunological chaos created by viral infection of B-lymphocytes. Heterophile antibodies usually appear within 1 week after infectious mononucleosis begins and peak during weeks 2 to 5. They are generally short-lived, but can persist at low levels for up to a year. About 10% of all patients with IM, especially children and older adults, have heterophile negative
disease that must be confirmed by ordering an EBV antibody panel.

More than 70% of patients with IM have an absolute lymphocytosis with values peaking during the second and third weeks of illness. Total WBCs usually range between 12,000 and 18,000 cells/μL, but may occasionally exceed 30,000 cells/μL. Typically 60 to 70% of the white blood cells are lymphocytes and monocytes. From 10 to 30% of all circulating lymphocytes may be atypical. Older patients are less likely to have significant lymphocytosis and atypical lymphocytes.

The final diagnosis of IM depends upon the combination of clinical, hematologic and serologic findings. A practical diagnostic approach to IM is shown in the following table.

<table>
<thead>
<tr>
<th>Atypical Lymph</th>
<th>Monospot</th>
<th>Diagnosis of IM</th>
<th>Further Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>Negative</td>
<td>Not confirmed</td>
<td>None</td>
</tr>
<tr>
<td>Present</td>
<td>Positive</td>
<td>Confirmed</td>
<td>None</td>
</tr>
<tr>
<td>Absent</td>
<td>Positive</td>
<td>Inconclusive</td>
<td>EBV Antibody Panel</td>
</tr>
<tr>
<td>Present</td>
<td>Negative</td>
<td>Suspicious</td>
<td>Repeat Monospot in 2 wk or EBV Panel</td>
</tr>
</tbody>
</table>

Patients with IM may have a negative Monospot test even though atypical lymphocytes are increased, because serological changes often lag behind peripheral blood changes. Most heterophile negative patients with EBV are young children. In this situation, the more sensitive EBV antibody panel can be ordered or the Monospot test can be repeated in two weeks. Other diseases, which can cause an IM-like syndrome, such as CMV, should also be considered. More rarely, the Monospot test may be positive, but atypical lymphocytes are not increased. This combination of results usually indicates a remote IM infection.

### Easier Evaluation of Iron Stores

A lot of confusion appears to exist concerning the ordering of laboratory tests for evaluation of iron stores. In order to alleviate this problem, a lab test order group entitled Iron Studies has been created that includes:
- Iron
- Transferrin
- Iron/Transferrin %Saturation
- TIBC
- Ferritin

This order set will become available in HOM on January 22.

### Troponin I Reference Range Change

The laboratory has become aware that too many patients without ischemic heart disease have Troponin I levels slightly elevated above the current cutoff point of 0.05 ng/mL. Accordingly, the cutoff points for Troponin I will be changed on January 16 to the following:

<table>
<thead>
<tr>
<th>Value</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00 – 0.07</td>
<td>Healthy</td>
</tr>
<tr>
<td>0.08 – 0.50</td>
<td>Increased cardiac risk</td>
</tr>
<tr>
<td>&gt;0.50</td>
<td>Myocardial infarction</td>
</tr>
</tbody>
</table>

### Informed Consent for Blood Transfusions

This is just a reminder that it is the physician’s responsibility to obtain Informed Consent with any order for Type and Screen, Type and Crossmatch or transfusion of any blood component. Documentation of the disclosure of the risks, benefits, and alternatives to transfusion must be documented in the Physician Progress Notes, Consent to Operation, Treatment, Transfusion or Other Procedures form (SLH.NSP.05.096) or on the Disclosure and Consent to Transfusion of Blood and/or Blood Products form (SLH.NSP.05.008). Current risks of transfusion can be found in the physician’s pocket calendar under “Transfusion Reactions.”

### Screening PSA Alert!

Medicare covers a screening PSA test for beneficiaries every twelve (12) months. If the interval between tests is less than a full 12 months, Medicare denies payment and holds the beneficiary responsible. Please consider alerting patients to this coverage issue and recommending they not schedule their annual physical until twelve months have elapsed.