SwedishAmerican Health System Experience with Acute Promyelocytic Leukemia

By Harvey E. Einhorn, MD

Although advances are constantly being made in cancer treatment, only a handful of conditions can we say we have changed the course of a malignancy substantially. Acute promyelocytic leukemia (APL) is probably the best example of miraculously overcoming a formerly fatal illness with now over a 90 percent cure rate for most patients diagnosed with this malignancy.

APL is a clinically and biologically distinct form of acute myelogenous leukemia. There are approximately 6,000 to 800 new cases per year in the United States. The median age in the United States is approximately 40 years old. The French-American-British (FAB) classification is M3 and it is characterized as a t(15:17) translocation involving the PML gene on chromosome 15, linking it to the retinoic acid receptor alpha (17). This is easily identified by cytogenetic studies and can be rapidly identified within 24 hours using FISH. Pathologic features include atypical promyelocytes, often described as bilobed or folded, which can be seen in the peripheral blood and bone marrow, often with densely packed dark purple granules and Auer rods. Flow cytometry reveals characteristic cellular markers. APL frequently is associated with a coagulopathy with a significant predisposition to bleeding, and for this reason is regarded as a medical emergency.

The use of all-trans-retinoic acid (ATRA), a vitamin is crucial for successful treatment of the disease. Most authorities agree that if APL is suspected, and there are no contraindications, ATRA should be started and may be discontinued if the diagnosis is a different disease. The high doses of this vitamin contribute to differentiation of the promyelocytes to mature neutrophils and significantly improve the coagulopathy. Induction therapy involves ATRA and also utilizes chemotherapy, particularly an anthracycline. Various consolidation regimens and maintenance programs have been utilized, typically containing all-trans-retinoic acid and often employing oral chemotherapy methotrexate and 6-mercaptopurine. Arsenic, which had been used in the past for relapsed APL, appears to offer improvement in outcomes selected groups of patients when used in consolidation.

According to cumulative data noted by UpToDate, with modern therapy the three-year relapse free survival for acute promyelocytic leukemia is:

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<thead>
<tr>
<th>Risk Level</th>
<th>White Blood Cells (WBC)</th>
<th>Platelets</th>
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<tbody>
<tr>
<td>Low Risk</td>
<td>less than or equal to 10,000</td>
<td>more than 40,000</td>
</tr>
<tr>
<td>Intermediate Risk</td>
<td>less than or equal to 10,000</td>
<td>less than or equal to 40,000</td>
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High Risk  
WBC greater than 10,000  
77%  
Platelets less than 40,000

SwedishAmerican Regional Cancer Center’s experience with APL between 1994 and 2011 compares favorably with national standards. Twelve new cases initially were diagnosed and treated. All had the 15,17 translocation and all received ATRA with induction consolidation and maintenance. The last five patients (which were diagnosed after 2009) received arsenic, methotrexate, 6-MP along with ATRA. One of the patients was heavily pretreated for large cell lymphoma, receiving multiple chemotherapy agents and radiation therapy years before diagnosis of APL. The median age for the 11 de novo APL patients was 41 years. There were no early deaths. There was one death approximately three years after diagnosis, which occurred in the oldest patient of the group who was 58 years old. Ninety-two percent of our patients remain free of disease.

Two other special cases were successfully treated, including a Jehovah’s Witness diagnosed in 2005. During treatment his hemoglobin was as low as 2.7. No blood products were used and the patient is doing well, without evidence of disease. His treatment consisted of daunorubicin and ATRA induction, Mylotarg and ATRA consolidation, and ATRA maintenance for one year. In addition, he also received Procrit. A second unusual case involved a patient with HIV. Diagnosed with APL in 2008, this patient also was successfully treated. Our center also had a patient initially treated at a major university medical center who was 78 years old and received arsenic and ATRA induction with no chemotherapy. He subsequently went into remission with chemotherapy and ATRA but died of relapsed disease about a year later.

Our first patient treated in 1994 went on to have several successful pregnancies. We are proud of results in the treatment of Acute Promyelocytic leukemia. This is a disease that, when properly treated, can be highly curable.