Acute Myeloid Leukemia; Decided Victories, Disappointments, and Detente: An Historical Perspective

Martin S. Tallman

John Hughes Bennett (1812-1875) was only 33 years old and Rudolf Virchow (1821-1902) only 24 in 1845 when each described patients at autopsy with two common features: an enlarged spleen and a change in the color and consistency of the blood. Although Bennett believed the blood contained purulent material, Virchow was not convinced. He described the finding as white blood or "leukemia," a term attributed to him in 1847. It was Nobel Laureate Paul Ehrlich (1854-1915) in 1891 who introduced new methods for staining blood cells and as a result confirmed that granulocytes were the predominant cell type in the myeloid form of leukemia.

The ability to transfuse platelets (1963) was a major, and today perhaps unappreciated, victory. The French-American-British (FAB) classification published in 1976 was another important accomplishment that has provided the foundation for a universal language among hematopathologists and hematologists for more than 30 years. Since then, the heterogeneity of acute myeloid leukemia (AML) has become increasingly clear as advances in cytogenetics, immunophenotyping, molecular genetics and most recently, gene expression profiling (2004), have taken place.

Paralleling rapid progress in the understanding of AML cell biology, clinical trials have brought about modest, but successive clinical gains. These have led to a relatively standard induction regimen using an anthracycline and ara-C (1982) followed by repetitive cycles of intensive consolidation chemotherapy, usually with higher doses of ara-C. Such treatment is curative for many patients with favorable-risk and some with intermediate-risk cytogenetics, but for very few older adults and those with unfavorable-risk cytogenetics.

Heinrich Lissauer (1861-1891) first reported the benefit of arsenic for a patient with CML. The drug was revisited in 1931 as a component of Fowler's solution to treat patients successfully with advanced CML. Today, arsenic is the most effective agent for patients with acute promyelocytic leukemia (APL), the most highly curable subtype of AML. The treatment of APL is arguably the most decided victory in the field of AML. In the 1990s-2000s, targeted drug therapy has emerged as the new and most exciting treatment paradigm. Unfortunately, as single agents, drugs such as FLT3 inhibitors, farnesyltransferase inhibitors, histone deacetylase inhibitors, and gemtuzumab ozogamicin have been disappointing. They have important biologic effects, but generally only modest clinical benefits. Studies evaluating combinations of such agents, perhaps with cytotoxic chemotherapy, will fill the agendas of many clinical investigators for the next several decades.

The first communication in the literature describing human marrow transplantation occurred in 1957, the year before the first meeting of the American Society of Hematology. As discussed elsewhere in this volume, transplantation has increased in importance as a curative strategy since it was first reported to be effective for patients with AML in first complete remission (1979).

Because of the heterogeneity and rarity of AML, future advances will require détente. Increased collaboration among investigators, pharmaceutical companies, cooperative oncology groups, and international colleagues will be necessary if major progress in therapy is to continue in this fascinating disease first described by our blood brothers more than 150 years ago.

See the related ASH 50th Anniversary Review articles under the ACUTE AND CHRONIC LEUKEMIAS section of the publication ASH 50th Anniversary Reviews: A Salute to the American Society of Hematology.