Conquering Blood Diseases –
From Research to Patient Care

Clinical Challenges in Hodgkin Lymphoma: An Historical Perspective

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For the past 50 years, Hodgkin lymphoma has been at the center of the development of modern oncologic therapeutics, and investigation into the fundamental biology of Hodgkin lymphoma has consistently demonstrated the unique power of novel molecular biologic investigatory techniques. This lymphoma has served as a model for development of (1) combined modality treatment planning with input from hematology, medical and radiation oncology, hematopathology, diagnostic imaging and oncologic nursing; (2) radiologic assessment based on novel techniques such as lymphangiography, computerized tomography and functional positron emission tomographic imaging; (3) multi-agent chemotherapy protocols; (4) image guided, computerized radiation, delivered using modern linear accelerators; (5) regional, national and international cooperative oncology groups to conduct large-scale clinical trials; (6) randomized prospective clinical trials and population-based validation studies to demonstrate therapeutic effectiveness; (7) studies demonstrating the effectiveness of high-dose chemo-radiotherapy and hematopoietic stem cell transplantation to cure otherwise treatment-resistant recurrent disease; and (8) long-term follow-up studies providing the data necessary to seek a balance between treatment effectiveness and avoidance of late gonadal, cardiac and secondary neoplastic toxicity.

In parallel with these therapeutic advances, elegant laboratory-based studies have employed cutting edge science to explore the basic biology of Hodgkin lymphoma, verifying the power of these techniques to yield major insights into neoplastic biology. Laser-capture single-cell dissection followed by demonstration of monoclonal immunoglobulin gene rearrangement and stable p53 gene mutational status in primary and relapsed specimens clarified both the neoplastic and B-cell origin of Hodgkin lymphoma. Immunophenotyping with internationally validated cluster designation markers separated Hodgkin lymphoma into classic and nodular lymphocyte predominant subtypes. Epidemiologic and virologic studies combined to provide novel insights into the basic and neoplastic biology of Epstein-Barr virus. Characterization of the interconnected signaling pathways within Hodgkin cells and between Hodgkin cells and their microenvironment, with their distortions of normal antigen feedback loops and inappropriate blockage of apoptosis and evasion of immunologically mediated cell destruction, has illuminated our thinking about oncogene expression, cytokine action, immunologic regulation, and immune cell networks.

Hodgkin lymphoma has evolved from frequently fatal to imminently curable in the practice lifetime of many still active hematologists. As a medical student, I helped care for a patient dying of her first recurrence. As an oncology fellow, I warned patients they had to choose between being cured and fathering children. Today patients who required treatment through two relapses bring me pictures of their children and grandchildren. These extraordinary changes characterize the recent history of Hodgkin lymphoma, a history in which hematologists have played a major role.

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