Chapter 11

MANAGEMENT OF ADVANCED STAGE HODGKIN’S LYMPHOMA

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1. INTRODUCTION

Hodgkin’s lymphoma (HL) is an uncommon malignancy of unknown etiology with an annual incidence in Western populations of 2-3 per 100,000 (1). On average there are 7000 new cases reported in the United States each year, distributed in a bimodal pattern with a first peak in the third decade and a second peak after the age of 50 (1, 2).

Although the trigger for malignant proliferation is poorly understood, it has become increasingly clear that most cases of HL represent a clonal proliferation of B cells (1, 3). As a result, the WHO has since classified “Hodgkin’s disease” as a lymphoma, allowing the two terms to be used interchangeably (4). According to this classification, two subtypes of HL with distinct immunohistochemical profiles, natural histories and prognoses have emerged: classical HL and nodular lymphocyte predominant HL. Pathologists further subdivided classical HL into nodular sclerosis, mixed cellularity, lymphocyte-rich and lymphocyte-depleted, however, these different entities have no known clinical significance and will be discussed only as classical HL (1).

Since the original discovery of HL in 1834, management of the disease has undergone a paradigm shift. By the 1960’s it had become apparent that, in most cases, extended field radiotherapy was curative in patients with
Localized disease at presentation. At that time, advanced HL was invariably fatal with a median survival of 2 years or less, and virtually no patient survived beyond 5 years. The development of combination chemotherapy with MOPP (nitrogen mustard, vincristine, procarbazine, prednisone) was a milestone, as this regimen demonstrated the curative potential of polychemotherapy in patients with advanced HL (5). The full impact of MOPP and the other drug regimens subsequently introduced was soon appreciated. Mortality data revealed that in 1950, HL accounted for 30% of the total lymphoma associated deaths, by the 1990’s it accounted for only 6% (6).

It soon became apparent that the principle factor dictating the success of the therapy introduced for HL was accurate staging of the patients underlying disease. From this observation, the Ann Arbor staging system emerged in 1971 (7). This system created a distinction between early stage (stage I-II) and advanced HL (stage III-IV) that has both prognostic and therapeutic implications. Current therapies for early stage HL result in long-term survival rates approximating 90%, compared with advanced disease where long-term survival rates are 50-60% (8).

Development of an accurate prognostic model was an important step in evaluating new therapies for advanced stage disease. Hasenclever et al. collected data on 5141 patients with advanced stage HL and identified seven adverse prognostic factors (Table 1) (9). The International Prognostic Score

Table 1: Prognostic factors in advanced stage Hodgkin’s lymphoma.

1. Male gender.
2. Age of 45 years or older.
3. Stage IV (according to the Ann Arbor classification).
4. Hemoglobin < 10.5g/dl.
5. Serum albumin < 4g/dl.
6. Leukocytosis (WBC > 15000/mm³).
7. Lymphocytopenia (ALC < 600/mm³ or lymphocyte count < 8% of WBC).

<table>
<thead>
<tr>
<th>No. of risk factors</th>
<th>Freedom from progression at 5 years</th>
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<tbody>
<tr>
<td>0</td>
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