Advanced-Stage and Relapsed/Refractory Hodgkin Lymphoma

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Table of Contents

Introduction ........................................... 2
Presentation, Initial Evaluation, and Prognosis . 2
Treatment ............................................. 3
Summary ............................................. 10
References ............................................. 10
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INTRODUCTION

Hodgkin’s lymphoma, previously known as Hodgkin’s disease, is a B-cell lymphoproliferative disease characterized by a unique set of pathological and epidemiological features. The disease is characterized by the presence of multinucleate giant cells called Hodgkin Reed-Sternberg (HRS) cells. HL is unique compared to other B-cell lymphomas because of the relative rarity of the malignant cells within affected tissues. The HRS cells usually account for only 0.1% to 10% of the cells, and these HRS cells induce accumulation of non-malignant lymphocytes, macrophages, granulocytes, eosinophils, plasma cells, and histiocytes which then constitute the majority of tumor cellularity. Despite the disease first being described by Sir Thomas Hodgkin in 1832, in part because of this unique histopathology, it was not until the 1990s that it was conclusively demonstrated that HRS cells are in fact monoclonal germinal center–derived B cells. Due to the development of highly effective therapies, cure is a reasonable goal for most patients. Because of the high cure rate, late complications of therapy must be considered when selecting treatment. This article, the second in a 2-part series on management of Hodgkin lymphoma, reviews the clinical features and treatment options for advanced-stage and relapsed/refractory Hodgkin lymphoma. The initial article in this series reviewed the epidemiology, etiology/pathogenesis, pathologic classification, initial workup, and staging evaluation of Hodgkin lymphoma, as well as the prognostic stratification and treatment of patients with limited-stage Hodgkin lymphoma.

PRESENTATION, INITIAL EVALUATION, AND PROGNOSIS

Overall, classical Hodgkin lymphoma (cHL) usually presents with asymptomatic mediastinal or cervical lymphadenopathy. At least 50% of patients will have stage I or II disease. A mediastinal mass is seen in most patients with nodular sclerosis cHL, at times showing the characteristics of “bulky” (>10 cm) disease. Constitutional, or “B,” symptoms (fever, night sweats, and weight loss) are present in approximately 25% of all patients with cHL, but 50% of advanced-stage patients. Between 10% and 15% of patients will have extranodal disease, most commonly involving lung, bone, and liver. Lymphocyte-predominant Hodgkin lymphoma (LPHL) is a rare histological subtype of Hodgkin lymphoma that is differentiated from cHL by distinct clinicopathological features. The clinical course and treatment approach for LPHL are dependent upon the stage of disease. The clinicopathological features of LPHL are discussed in the limited-stage Hodgkin lymphoma article.

For the purposes of prognosis and selection of treatment, Hodgkin lymphoma is commonly classified as early favorable, early unfavorable, and advanced stage. It should be noted that in the German Hodgkin Study Group (GHSG), only stage III/IV patients are considered advanced stage, while in North American clinical trials (until recent years), stage I/II patients with bulky mediastinal disease have generally been enrolled on advanced-stage Hodgkin lymphoma protocols.

The prognosis of advanced-stage Hodgkin lymphoma patients can be refined using a prognostic index commonly referred to as the International Prognostic Score (IPS). This index consists of 7 factors: male gender, age ≥45 years, stage IV disease, hemoglobin <10.5 g/dL, white blood cell (WBC) count >15,000/µL, lymphopenia (absolute lymphocyte count of <600 cells/µL or lymphocytes <8% of WBC count), and serum albumin <4 g/dL. In the original study by Hasenclever and Diehl, the 5-year freedom from progression (FFP) ranged from 42% to 84% and the 5-year overall survival (OS) ranged from 56% to 90%, depending on the number of factors present. This scoring system, however, was developed using a patient population treated prior to 1992. Using a more recently treated patient population, the British Columbia Cancer Agency