Limited-Stage Hodgkin Lymphoma

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**INTRODUCTION**

Hodgkin lymphoma, previously known as Hodgkin’s disease, is a B-cell malignancy with unique pathological and epidemiological features for which highly effective therapies exist. The disease is characterized by the presence of mononuclear and multinucleate giant cells called Hodgkin and Reed-Sternberg (HRS) cells. Hodgkin lymphoma is unique compared to other B-cell lymphomas because of the scarcity of the malignant cells in the tumor tissue. The HRS cells usually account for only 0.1% to 10% of the cells in the affected tissues, and the HRS cells induce accumulation of nonmalignant lymphocytes, macrophages, granulocytes, eosinophils, plasma cells, and histiocytes, which constitute more than 90% of tumor cellularity. Although the disease was first described by Sir Thomas Hodgkin in 1832, in part because of this unique histopathology, not until 1991 was it conclusively demonstrated that HRS cells are in fact monoclonal germinal center–derived B-cells. This article reviews management and frontline treatment options for limited-stage classical Hodgkin lymphoma and nodular lymphocyte predominant Hodgkin lymphoma. Treatment of advanced-stage and relapsed/refractory Hodgkin lymphoma will be discussed in a separate article (Hospital Physician Hematology Board Review Manual, Volume 7, Part 4).

**ETIOLOGY/PATHOGENESIS**

The cause of Hodgkin lymphoma is unknown. Epstein-Barr virus (EBV) infection is present in up to 40% of Hodgkin lymphoma cases, suggesting a role of this virus in the pathogenesis of some cases. The risk of EBV-positive Hodgkin lymphoma was found to be higher following an episode of infectious mononucleosis, while the risk of EBV-negative Hodgkin lymphoma remained unchanged. The incidence of Hodgkin lymphoma is 5 to 14 times higher in HIV-infected patients than in noninfected patients. It is not considered an AIDS-defining illness, but has become more frequent with the growth and aging of the AIDS population. Hodgkin lymphoma patients with HIV typically have CD4 lymphocyte counts greater than 200 cells/µL, with the incidence of Hodgkin lymphoma declining with lower CD4 lymphocyte counts. HIV-related Hodgkin lymphoma tends to have an aggressive course, with high rates of EBV positivity. Positive socioeconomic status gradients in Hodgkin lymphoma incidence were observed in young adults with nodular sclerosis Hodgkin lymphoma and older adult white and Hispanic males with mixed cellularity Hodgkin lymphoma. The incidence of Hodgkin lymphoma is somewhat higher among smokers, and the risk appears to increase with duration of smoking.

The cell of origin of Hodgkin lymphoma, while long suspected to be the HRS cell, remained unproven until the 1990s when microdissection and single-cell polymerase chain reaction techniques allowed for confirmation that the HRS cell was in fact a monoclonal germinal center B-cell. These HRS cells lack immunoglobulin due to defective transcription regulation and not due to crippling mutations.