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The Hospital Physician Oncology Board Review Manual is a study guide for fellows and practicing physicians preparing for board examinations in oncology. Each quarterly manual reviews a topic essential to the current practice of oncology.

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Hodgkin’s Disease

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Cover illustration by Christie Grams
Hodgkin’s Disease

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I. INTRODUCTION

A. Definition. Hodgkin’s disease is a lymphoproliferative disorder that is defined histologically by characteristic Reed-Sternberg (RS) cells. A hallmark of this neoplasm is a paucity of malignant cells surrounded by abundant “bystander” cells, including eosinophils, lymphocytes, histiocytes, and neutrophils.

B. Incidence. Age-specific incidence rates suggest a bimodal distribution, with one peak occurring between ages 15 to 34 years (increasing in part due to an association with HIV) and a second peak occurring after age 50 years. Approximately 7500 patients are diagnosed with Hodgkin’s disease in the United States each year.1

C. There are several patterns of presentation, but the disease generally involves lymph nodes, is unicentric in origin, progresses in a predictable manner, and is fatal without therapy.

D. Although the majority of patients with Hodgkin’s disease are cured, significant limitations to therapy remain. Treatment-related morbidity, including a rising incidence of secondary malignancies, mandates improved staging and minimization of toxic therapy as important future goals for patients with a favorable prognosis.

E. Patients with advanced-stage disease who relapse early after standard therapy, who achieve only a partial initial remission, or who relapse with clinically high-risk features represent a poor prognostic group. Even with aggressive approaches, the long-term overall survival of these patients is less than 50%.2,3

II. BIOLOGY AND PATHOLOGY

A. The etiology of Hodgkin’s disease is unknown; however, epidemiologic studies, including case-clustering, familial associations, and relationship to infectious mononucleosis, support the role of viral infection in its pathogenesis.4

B. Biology

1. Molecular studies have determined that diagnostic RS cells are clonal populations of transformed germinal-center B-cells with immunoglobulin gene mutations.5

2. Diagnostic RS cells contain Epstein-Barr virus (EBV) DNA in a subset of patients.6 These EBV genomes have been shown to be monoclonal in origin, suggesting that defective immune control of EBV-infected cells may contribute to Hodgkin’s disease.

a. Patients with Hodgkin’s disease that contains EBV or specifically expresses the EBV antigen LMP1 have a more favorable response to primary therapy and improved disease-free survival rates compared to patients with EBV-negative Hodgkin’s disease.7

b. Moreover, RS cells have been shown to express viral antigens in vitro, and they can be lysed by EBV-specific cytotoxic T-lymphocytes that have been isolated from patients with Hodgkin’s disease.8

3. CD30, a member of the tumor necrosis factor receptor family, is present in the majority of RS cells.

C. Pathology. In all cases, the malignant RS cells and variants are the minority of cells in the specimen, which consists of a rich inflammatory infiltrate of lymphocytes, eosinophils, neutrophils, histiocytes, and plasma cells. It is critical for specimens to be reviewed by an experienced hematopathologist to confirm the diagnosis.

1. Nodular sclerosis (Figure 1) is the most common subtype of Hodgkin’s disease in the United States. Diagnosis requires a nodular growth pattern, bands of fibrosis, and “lacunar” RS cells, with abundant cytoplasm. The disease usually presents in young adults, and anterior mediastinal involvement is very common.

2. Mixed cellularity subtype is associated with diffuse architectural effacement and classic RS cells with prominent inclusion-like nucleoli.