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

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Indolent B-Cell Non-Hodgkin Lymphoma

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Indolent B-Cell Non-Hodgkin Lymphoma

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INTRODUCTION AND CLASSIFICATION

Non-Hodgkin lymphomas (NHLs) are a heterogeneous group of lymphoproliferative disorders that involve neoplastic expansions of B cells, T cells, NK cells, or histiocytic/dendritic cells. Each has distinctive biological and clinical manifestations, making accurate diagnosis essential to management. Indolent lymphomas are generally considered incurable; however, with recent improvements in treatment, patients are living longer and often with preserved quality of life. The median survival was historically around 8 to 10 years; however, this likely represents an underestimation for patients diagnosed currently in the setting of improved treatment options. Patients may be asymptomatic for years prior to requiring treatment.

Indolent B-cell NHLs are best classified by correlation of morphologic, immunophenotypic, cytogenetic, and clinical features. An adequate tissue sample is vital to diagnosis and generally is best obtained by an excisional lymph node biopsy. The key characteristics are shown in Table 1. The current classification system is the 2008 World Health Organization (WHO) system.1

EPIDEMIOLOGY

NHL represents the sixth most common malignancy in both men and women annually in the United States. Over 65,000 new cases of NHL were diagnosed in 2010, and of these approximately 36% were indolent NHL.2,3 Over the past 30 years the overall incidence of NHL has been increasing around 2% to 3% per year in the Western world. In most cases the etiology for indolent NHL is unknown; however, associations have been made between indolent NHL and certain autoimmune disorders, immunodeficiency states, and infectious agents. One example is gastric MALT (extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue) lymphoma, which is strongly associated with Helicobacter pylori infection.

STAGING AND WORKUP

Following diagnosis, baseline complete blood count with differential, lactate dehydrogenase, chemistry panel, liver function tests, and β2-microglobulin are routinely obtained. Viral serological testing, including HIV and hepatitis B and C, should also be obtained. Imaging with a computed tomography (CT) scan of the neck, chest, abdomen and pelvis is important for staging. Positron emission tomography (PET) can be useful in staging and assessing response in some cases of indolent B-cell NHL, although according to the International Working Group criteria, PET scan is not routinely recommended.4 Bone marrow biopsy and aspirate should be obtained for staging of most patients. The Ann Arbor staging system is used for NHL (Table 2).5 Based on the treatment plan, baseline evaluation of cardiac and pulmonary function may be indicated.

INDOLENT B-CELL NHL SUBTYPES

FOLLICULAR LYMPHOMA

Follicular lymphoma (FL) is the most common indolent B-cell lymphoma, representing 20% of lymphomas in the United States and Europe. The median age at diagnosis is 59 years with a male-to-female ratio of 1:1.7.5 There are approximately 11,000 new cases per year in the United States, with an annual incidence of 3.2 cases per 100,000 persons per year. FL is more common in Caucasians compared to other ethnic groups.7 Treatment options and efficacy have improved significantly since the late 1990s with the introduction of the anti-CD20 monoclonal antibody rituximab, radioimmunotherapy, other novel agents, and a more effective use of stem cell transplantation.

FLs originate from germinal center B cells. The tumor demonstrates a follicular pattern of growth and is composed of small cleaved cells (centrocytes) and large cells (centroblasts). Nearly all cases of FL express the pan-B-cell antigens CD19, CD20, and CD79a. CD10

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