Aggressive B-Cell Non-Hodgkin Lymphoma

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INTRODUCTION

Non-Hodgkin lymphoma (NHL) comprises a wide variety of malignant hematologic disorders with varying clinical and biologic features. The more than 60 separate NHL disorders can be classified according to cell of origin (B cell versus T cell), anatomical location (orbital, testicular, bone), clinical behavior (indolent versus aggressive), or histological features. Although various NHL classification schemes have been utilized over the years, the World Health Organization (WHO) classification is now widely accepted as the definitive pathologic classification system for lymphoproliferative disorders, incorporating morphologic, immunohistochemical, flow cytometric, cytogenetic, and molecular features. While the pathologic subclassification of NHL has become increasingly refined in recent years, from a management standpoint, classification based on clinical behavior remains very useful. This approach separates NHL subtypes into indolent versus aggressive categories. Whereas indolent NHLs may remain clinically insignificant for months to years, aggressive B-cell NHLs generally become life-threatening within weeks to months without treatment.

STAGING AND WORKUP

Tissue biopsy is essential in the diagnosis and management of NHL. The most significant disadvantage of fine-needle aspiration cytology is the lack of histologic architecture. The optimal specimen is an excisional biopsy; in a situation where this cannot be performed, a core biopsy is the next best choice. The following baseline tests are appropriate for all histologies once the diagnosis is made:

1) A complete blood count with differential and peripheral smear
2) Evaluation of renal and hepatic function
3) Measurement of serum lactate dehydrogenase (LDH), a prognostic marker
4) Bone marrow biopsy and aspiration
5) HIV serologies (systemic NHL is an AIDS-defining malignancy)
6) Hepatitis B and C serology. Each of these has been associated with increased risk of NHL. In addition, there is a risk of hepatitis B reactivation following certain NHL therapies.

Epidemiology

Data from cancer registries show a steady, unexplainable increase in the incidence of NHL during the second half of the 20th century; the incidence has subsequently plateaued. There was also a significant increase in NHL between 1970 and 1995, which has been attributed partly to the HIV epidemic. Over 65,000 new cases of NHL were diagnosed in the United States in 2009, compared with approximately 8000 cases of Hodgkin lymphoma, making NHL the sixth most common cancer in adult men and fifth in adult women. NHL appears to occur more frequently in Western countries than in Asian populations.

Various factors associated with increased risk for B-cell NHL have been identified over the years, including occupational and environmental exposure to certain pesticides and herbicides, immunosuppression associated with HIV infection, autoimmune disorders (e.g., rheumatoid arthritis, systemic lupus erythematosus, Sjögren syndrome, and Hashimoto thyroiditis), iatrogenically induced immune suppression in the post-transplant setting, family history of NHL, and personal history of a prior cancer, including NHL. Epstein-Barr virus (EBV) has a clear pathogenic role in Burkitt lymphoma, in many cases of post-transplant lymphoproliferative disorders, and in some cases of HIV-related aggressive B-cell lymphoma. Hepatitis B may have a causal relationship with NHL. There is also epidemiologic evidence supporting the association between hepatitis C and NHL. There are reports suggesting a possible causative association between psittacosis (Chlamydia psittaci) and ocular adnexal lymphoma. Associations have also been suggested but are largely null for simian virus (SV40). Despite these associations, a specific cause cannot be identified for most patients diagnosed with aggressive B-cell NHL.