Follicular lymphoma

Liron Pantanowitz, MD;
Lester D.R. Thompson, MD, FASCP

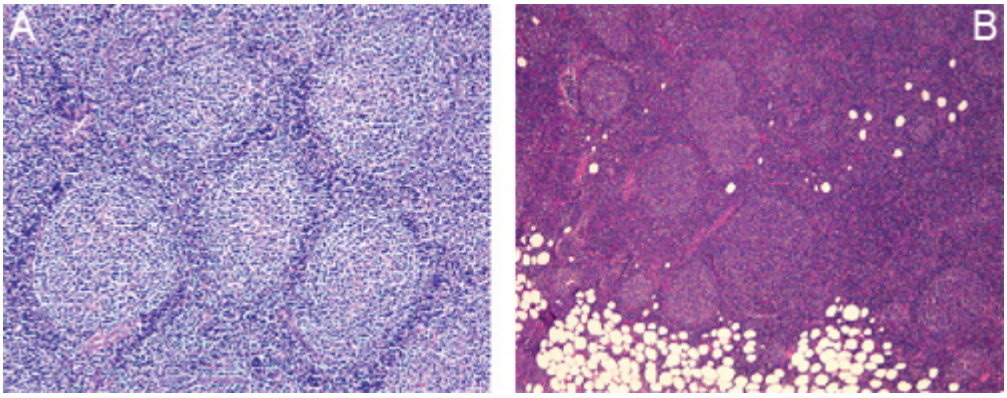

Figure. ***A:*** *Neoplastic lymphoid follicles are packed closely together. They lack a mantle zone, and they have no central germinal center.* ***B:*** *Follicular lymphoma extends beyond the lymph node capsule and into extranodal adipose tissue.*

Follicular lymphoma is defined as a neoplasm of follicle center B lymphocytes (centrocytes and centroblasts) that has at least a partially follicular growth pattern. It is a low-grade lymphoma, and its course is indolent. Most patients present during the sixth decade of life; the neoplasm is very rare in patients younger than 20 years of age. The female-to-male ratio is 1.7:1. Lymph node enlargement is the usual presentation; only about 20% of patients have B symptoms (i.e., fever, chills, night sweats, and weight loss). The disease is usually systemic at presentation (stage III or IV). In the head and neck region, follicular lymphoma may involve lymph nodes, Waldeyer's ring, and/or skin.

Histologically, the characteristic finding is the presence of uniform neoplastic lymphoid follicles packed closely together (figure, A), usually effacing the nodal architecture and often extending out into the extranodal fat (figure, B). Neoplastic follicles are poorly defined; they lack a mantle zone and polarization; they have few mitotic figures; and they tend to lack tingible-body macrophages. The neoplastic cells vary from small to large, showing folding and cleaving of the nuclei, resembling centrocytes (small- to medium-sized cleaved cells with inconspicuous nucleoli) and centroblasts (large noncleaved cells with vesicular chromatin and several peripheral nucleoli).

There are several histologic variants of follicular lymphoma: signet ring cell type, plasmacytoid type, marginal zone type, floral variant with amorphous extracellular material, and diffuse type.

Lymphomas require immunophenotypic evaluation (immunohistochemistry and/or flow cytometry) to confirm the diagnosis. While there is tumor individuality, the neoplastic cells usually show a B cell phenotype (CD19, CD20, CD22, CD79a) with coexpression of CD10 and CD43; they also express bcl-2 and bcl-6 and demonstrate light-chain (kappa or lambda) restriction. Approximately 85% of patients with follicular lymphoma have a t(14;18) translocation in which the bcl-2 oncogene is translocated from chromosome 18 to the immunoglobulin heavy-chain locus on chromosome 14. This results in overexpression of bcl-2, which confers a survival advantage to the malignant B cells by preventing apoptosis.

There is a complex grading system for follicular lymphoma that is based on the proportion of centroblasts in 10 representative neoplastic follicles:

- Grade 1: ≤5 centroblasts per high-power field (HPF)
- Grade 2: 6 to 15 centroblasts/HPF
- Grade 3: ≥16 centroblasts/HPF.

Grade 1 and grade 2 follicular lymphomas, which account for 80% of all cases, are indolent and incurable, whereas grade 3 neoplasms, while more aggressive, are potentially curable. Transformation to a high-grade lymphoma occurs in 25 to 35% of patients. The treatment of choice is chemotherapy, which usually includes cyclophosphamide, vincristine, and prednisone. There is potential for a better overall response when these agents are combined with monoclonal antibody therapy (e.g., rituximab).

Suggested reading

Jaffe ES, Harris NL, Stein H, Vardiman JW, eds. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. Lyon, France: IARC Press, 2001.
Kipps TJ. Advances in classification and therapy of indolent B-cell malignancies. Semin Oncol 2002;29(suppl 2):98-104.