Pathology of Lymphoma of the Thyroid

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The thyroid may be involved secondarily by lymphoma from other sites in the body or by leukemic infiltrates [1–3]. Most primary thyroidal lymphomas are B-cell types, but both Hodgkin's lymphoma [1, 3] and T-cell lymphoma [4] may occur.

From an epidemiologic viewpoint, almost all primary thyroid lymphomas arise on a background of severe chronic lymphocytic thyroiditis [1–3]. Clinically, women are more commonly affected. These patients often have a history of a goiter with hypothyroidism. Rapid growth of a mass lesion is noted.

Gross examination reveals homogeneous, pale, and firm tissue that has replaced the thyroid irregularly. If advanced autoimmune thyroiditis is also present, the lymphoma probably cannot be distinguished from the inflammatory infiltrate without histologic examination. Microscopically, the regions of autoimmune thyroiditis reveal either the usual benign lymphoplasmacytic infiltrates or the common alterations of the follicular epithelial cells (e.g., oxyphilic cell metaplasia) [1, 5].

The lymphoma usually consists of a monotonous infiltrate of abnormal lymphoid cells which replace the thyroid parenchyma, fill and distend some thyroid follicles (Figs. 92.1 and 92.2), and permeate the walls of some of the larger vessels [1]. Extra-glandular extension into perithyroidal fat and skeletal muscle is very often present [1, 6]. Cytokeratin antibodies can demonstrate displaced and distorted follicular epithelium; lymphoepithelial lesions characteristic of so-called mucosa-associated lymphoid tissue (MALT) lymphoma are seen [6–8]. Cervical lymph nodes may be involved.

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Smears from the aspirates may show predominantly chronic lymphocytic thyroiditis, and it is necessary to perform multiple aspirates until the lymphomatous regions are sampled [9, 10]. The latter show a monotonous lymphoid population, readily observed mitotic figures, and a conspicuous absence of follicular epithelial cells. There is controversy about the wisdom of making a primary cytological diagnosis of malignant lymphoma without addition of ancillary techniques such as flow cytometry or gene rearrangement studies [11, 12].

Sometimes in order to make a diagnosis of a specific subtype of lymphoma, an open surgical wedge biopsy of the mass may be needed.

The lymphoma may be diffuse or follicular (nodular). Separating the lymphoma from an adjacent infiltrate of autoimmune thyroiditis requires careful appraisal of the abnormal cells in the routine histologic sections and the use of immunohistochemical stains. In large cell malignant lymphoma, this is usually confirmatory and the histologic diagnosis is obvious; in cases of small cell lymphoma, special studies are warranted and needed to make the diagnosis [13].

Some thyroid lymphomas present as aggressive neoplasms, often in the elderly. A considerable number of thyroid lymphomas are of intermediate or low grade. Cases of this type have led to the concept that a thyroid involved with autoimmune disease is comparable to mucosa-associated lymphoid tissue (MALT), such as the Peyer's patches of the intestine [13, 14]. Thus, it has been suggested that the majority of thyroidal lymphomas are MALT lymphomas [14]. These lymphomas may tend to be localized for extended periods of time, possibly explaining why some thyroid lymphomas have been cured by surgery alone. Thyroid lymphomas may spread to other sites of MALT (e.g., small bowel); in some patients, extranodal MALT lymphoma of the lung or bowel may precede the development of thyroid lymphoma. Some of these tumors may show plasmacytic differentiation [1, 3]. Such

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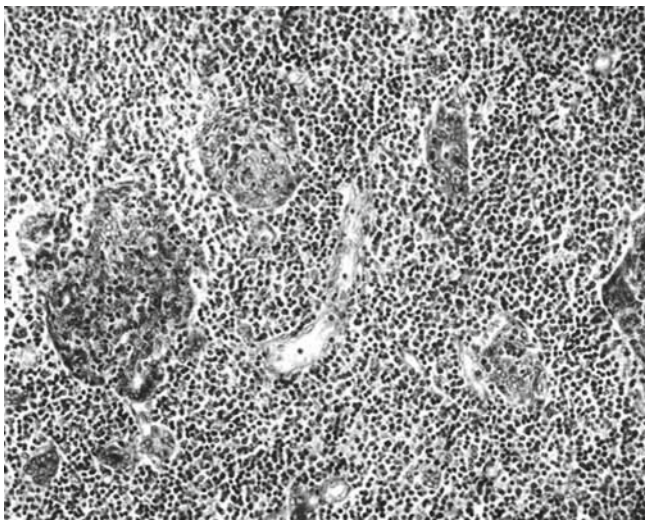

Fig. 92.1 Malignant lymphoma. A number of thyroid follicles are formed by metaplastic epithelial cells, presumably because of previous Hashimoto's thyroiditis. Both the interstitial tissue and the altered follicles are extensively infiltrated by the lymphoma (H&E stain)

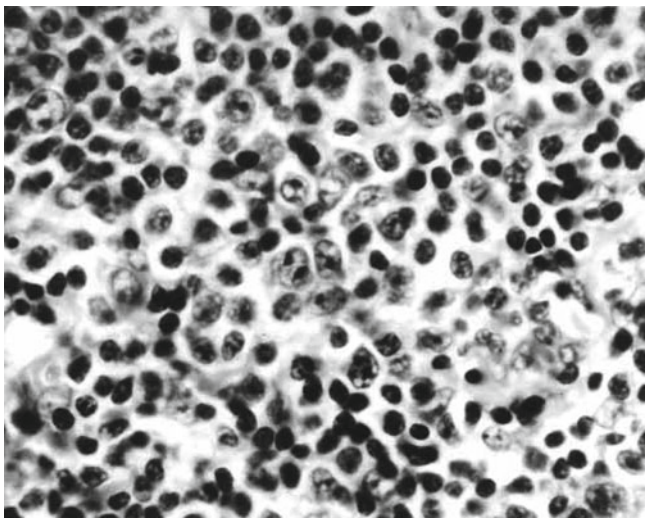

Fig. 92.2 Malignant lymphoma. Many abnormal lymphoid cells are visible. The smallest cells are likely normal lymphocytes that accompany the malignant infiltrate (H&E stain)

cells are usually monotypic with immunoglobulin light-chain restriction. The lymphoma cells may extend into the reactive lymphoid follicles of the autoimmune thyroiditis, thereby explaining the follicular (nodular) pattern of some lymphomas [15]. Also, persisting lymphoid follicles have been reported in the rare plasmacytomas of the thyroid [16], possibly supporting the theory that plasmacytomas of the thyroid are mature MALT lymphomas. When a high-grade lymphoma is present, there is often evidence that it has arisen from a low-grade MALT lymphoma [17].

References

1. Kossev P, Livolsi V. Lymphoid lesions of the thyroid: review in light of the revised European-American lymphoma classification and upcoming World Health Organization classification. Thyroid. 1999;9:1273–80.
2. Kebapcilar L, Alacacioglu I, Comlekci A, Ozcan MA, Piskin O, Kargi A, Undar B, Yesil S. Primary thyroid lymphoma: case series with literature review. J BUON. 2009;14:295–9.
3. Lam KY, Lo CY, Kwong DL, Lee J, Srivastava G. Malignant lymphoma of the thyroid. A 30-year clinicopathologic experience and an evaluation of the presence of Epstein-Barr virus. Am J Clin Pathol. 1999;112:263–70.
4. Kim NR, Ko YH, Lee YD. Primary T-cell lymphoma of the thyroid associated with Hashimoto's thyroiditis, histologically mimicking MALT-lymphoma. J Korean Med Sci. 2010;25:481–4.
5. Hamburger JI, Miller JM, Kini SR. Lymphoma of the thyroid. Ann Intern Med. 1983;99:685–93.
6. Derringer GA, Thompson LD, Frommelt RA, Bijwaard KE, Heffess CS, Abbondanzo SL. Malignant lymphoma of the thyroid gland: a clinicopathologic study of 108 cases. Am J Surg Pathol. 2000;24:623–39.
7. Sun TQ, Zhu XL, Wang ZY, Wang CF, Zhou XY, Ji QH, Wu Y. Characteristics and prognosis of primary thyroid non-Hodgkin's lymphoma in Chinese patients. J Surg Oncol. 2010;101:545–50.
8. Thieblemont C, Mayer A, Dumontet C, Barbier Y, Callet-Bauchu E, Felman P, Berger F, Ducottet X, Martin C, Salles G, Orgiazzi J, Coiffier B. Primary thyroid lymphoma is a heterogeneous disease. J Clin Endocrinol Metab. 2002;87:105–11.
9. Babu N, Dey P. Fine needle aspiration cytology of non-Hodgkin's lymphoma of thyroid. Cytopathology. 2002;13:188.
10. Lu JY, Lin CW, Chang TC, Chen YC. Diagnostic pitfalls of fine-needle aspiration cytology and prognostic impact of chemotherapy in thyroid lymphoma. J Formos Med Assoc. 2001;100:519–25.
11. Cha C, Chen H, Westra WH, Udelsman R. Primary thyroid lymphoma: can the diagnosis be made solely by fine- needle aspiration? Ann Surg Oncol. 2002;9:298–302.
12. Takano T, Miyauchi A, Matsuzuka F, Yoshida H, Kuma K, Amino N. Diagnosis of thyroid malignant lymphoma by reverse transcription- polymerase chain reaction detecting the monoclonality of immunoglobulin heavy chain messenger ribonucleic acid. J Clin Endocrinol Metab. 2000;85:671–5.
13. Straus DJ. Primary thyroid lymphoma, a rare disease with a good treatment outcome. J Surg Oncol. 2010;101:543–4.
14. Sarinah B, Hisham AN. Primary lymphoma of the thyroid: diagnostic and therapeutic considerations. Asian J Surg. 2010;33:20–4.
15. Isaacson PG, Androulakis-Papachristou A, Diss TC, Pan L, Wright DH. Follicular colonization in thyroid lymphoma. Am J Pathol. 1992;141:43–52.
16. Ohshima M, Momiyama T, Souda S, Kuratani T, Toda K, Hiasa Y. Primary plasmacytoma of the thyroid: a case report and comparative literature study between western nations and Japan. Pathol Int. 1994;44:645–51.
17. Pedersen RK, Pedersen NT. Primary non-Hodgkin's lymphoma of the thyroid gland: a population based study. Histopathology. 1996;28:25–32.