Cytological Features of Hashimoto's Thyroiditis (Chronic Lymphocytic Thyroiditis): A Literature Review

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Introduction

Hashimoto's thyroiditis (HT), also known as chronic lymphocytic thyroiditis (CLT) or autoimmune thyroiditis, is the most common inflammatory disease of the thyroid gland and the leading cause of hypothyroidism in iodine-sufficient regions [7, 8]. It is a chronic, organ-specific autoimmune disorder marked by immune-mediated destruction of thyroid follicular cells, initiated by activation of $CD4^+$ T helper cells that stimulate production of autoantibodies directed against thyroid-specific antigens, notably thyroid peroxidase (TPO) and thyroglobulin (Tg) [7]. Clinically, HT often presents as painless thyroid enlargement, though many patients remain euthyroid at diagnosis and functional deterioration develops gradually over time [10].

Fine-needle aspiration cytology (FNAC) is a rapid, cost-effective, and minimally invasive procedure that provides essential morphological information for the diagnosis of HT [7, 10]. According to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), lymphocytic (Hashimoto) thyroiditis is classified under Category II (Benign) when reported "in the proper clinical context" [9, 16]. The diagnostic accuracy of FNAC for HT is well-established, but cytodiagnostic sensitivity has been reported as low as 57% in some series, reflecting the overlapping morphological features with other thyroid pathologies [8].

The most consistent cytological hallmarks of HT observed on FNA smears include a lymphocyte-rich background, lymphocytic infiltration into follicular epithelial cell clusters, and the presence of Hürthle cells (oncocytic metaplasia) [4, 7, 10, 11]. A comprehensive review of 110 cases of thyroiditis reported the following frequencies of cytological features in HT: increased background lymphocytes in 100% of cases, lymphocytic infiltration of follicular cell clusters in 79%, Hürthle cells in 64%, mild anisonucleosis in 19%, few giant cells in 18%, histiocytes in 12%, scanty colloid in 8%, epithelioid cells in 6%, plasma cells in 5%, and fire flares in 3% [11]. The

lymphoid:epithelial ratio in HT cytology ranges from 2:1 to 10:1, reflecting the severity of lymphocytic infiltration [15].

Cytologically, lymphocytic thyroiditis typically presents in two main patterns corresponding to different stages of disease activity: (1) the classic pattern, characterized by prominent background lymphocytes and lymphocytic infiltration of follicular cell clusters, and (2) the florid lymphoid pattern, dominated by mature and maturing lymphoid cells, suggestive of a more advanced immunological response [10]. Large "blast-like" lymphocytes may be seen on smears with dense lymphoid cells, and cellular lymphoplasmacytes infiltrating follicular and oncocytic cells are diagnostic features of CLT on FNAC [4].

Hürthle cells (oncocytes) are a hallmark of HT and represent metaplastic transformation of follicular epithelial cells. They are characterized by abundant eosinophilic granular cytoplasm, enlarged nuclei, and prominent nucleoli [13]. Hürthle cells can be binucleated, with variable nuclear size and often prominent nucleoli [13]. Importantly, benign Hürthle cells in HT are usually cohesive and typically do not show the marked nuclear atypia or macronucleoli seen in Hürthle cell neoplasms [13]. The nuclear chromatin of Askanazy cells (Hürthle cells) in Hashimoto's thyroiditis is typically bland and even, whereas neoplastic Hürthle cells display finely granular, coarsely granular, or irregularly clumped chromatin, and macronucleoli are present in Hürthle cell tumors but not in the Askanazy cells of Hashimoto's thyroiditis [13]. Occasional follicular or Hürthle cells may display focal chromatin clearing and nuclear grooves, but these changes are mild and focal [13].

The cytomorphological grading of HT was first proposed by Bhatia et al., offering a framework to evaluate disease severity based on FNAC findings and improving clinicopathological correlation [7, 12]. This grading system categorizes the disease based on cytomorphological features observed in FNA smears, ranging from mild lymphocytic infiltration to extensive inflammation with germinal center formation [10, 12]. Cytological grading via FNAC typically shows Grade I (mild) in approximately 60% of cases, Grade II (moderate) in about 24%, and Grade III (severe) in approximately 16% of cases [7]. A significant correlation has been observed between cytological grade and anti-thyroid peroxidase (ATPO) antibody levels, with higher grades consistently associated with higher antibody levels [7, 10]

Despite its diagnostic utility, FNAC has certain limitations in accurately identifying lymphocytic thyroiditis. In some cases, smears may predominantly exhibit cytological features suggestive of follicular hyperplasia, as seen in Graves' disease, or contain abundant colloid, potentially leading to a missed diagnosis of HT [10]. Moreover,

distinguishing between the toxic phase of HT and classical Graves' disease based solely on cytological findings can be challenging [10].

A major diagnostic pitfall in HT cytology is the presence of follicular cells exhibiting features that overlap with papillary thyroid carcinoma (PTC). Follicular cells in Hashimoto's thyroiditis may display some of the features of papillary carcinoma, including powdery chromatin, occasional nuclear grooves or holes, and intranuclear cytoplasmic inclusions, leading to a diagnostic pitfall and potential overdiagnosis of PTC [2, 14]. Features leading to overdiagnosis of papillary carcinoma include powdery chromatin, occasional nuclear grooves or holes, and paucity of background lymphocytes [14]. One feature that differentiates Hashimoto's/lymphocytic thyroiditis from neoplasm is the presence of lymphocytes infiltrating follicular groups, which is noted in most cases; in contrast, true papillary carcinomas display characteristic features including frequent nuclear grooves, intranuclear cytoplasmic inclusions, and psammoma bodies [14].

Another important diagnostic consideration is the coexistence of HT with thyroid neoplasms. The incidence of HT coexisting with thyroid neoplasia ranges from 3 to 14%, and papillary carcinoma is the most commonly associated neoplastic lesion [8]. Hashimoto's thyroiditis without any associated lesions is diagnosed histopathologically in only about 45.5% of cases, highlighting the importance of careful evaluation for coexisting lesions [8]. If suspicious foci are not sampled on FNAC, Hashimoto's thyroiditis with papillary carcinoma is often missed; therefore, FNAC from multiple sites or image-guided aspiration can reveal coexisting hidden neoplastic lesions and minimize discordance rates [8].

Additionally, focal nodular Hürthle cell hyperplasia in Hashimoto's thyroiditis can present as a diagnostic dilemma on FNA, mimicking a follicular neoplasm [2]. A careful search for lymphocytes in Hürthle cell sheets, multiple aspirates, associated clinical findings, and ancillary techniques reduce the diagnostic pitfall and avoid unnecessary surgery [2]. The presence of hyperplastic follicular cells on FNAB samples from HT may also mimic a follicular neoplasm and result in a false positive interpretation [2]

The Bethesda System for Reporting Thyroid Cytopathology classifies lymphocytic (Hashimoto) thyroiditis under Category II (Benign), alongside benign follicular nodules and granulomatous (subacute) thyroiditis [9, 16]. This category carries a very low risk of malignancy and is managed with clinical and ultrasound follow-up [16]. In cytology practice, HT accounted for 24.2% of Category II diagnoses in one large cytohistological study, and autoimmune thyroiditis (encompassing Hashimoto's thyroiditis and

lymphocytic thyroiditis) has been reported to account for up to 46% of all cases in some series [16].

Conclusion

Hashimoto's thyroiditis has well-established and characteristic cytomorphological features on FNAC, including a lymphocyte-rich background, lymphocytic infiltration of follicular cell clusters, and Hürthle cell metaplasia. The cytological grading system proposed by Bhatia et al. provides a valuable framework for assessing disease severity and correlates with serological markers such as ATPO antibodies. However, the cytological diagnosis of HT is not without pitfalls, particularly the overlapping nuclear features with papillary thyroid carcinoma and the potential for missing coexisting neoplastic lesions. A comprehensive diagnostic approach integrating clinical assessment, thyroid function tests, serological markers, and careful cytomorphological evaluation—with attention to the presence of lymphocytes infiltrating follicular groups—remains essential for accurate diagnosis and appropriate patient management.

References

1. Rana S, Aziz N, Trisal M, Jalal N, Khetrapal S, Jairajpuri ZS, Sharma A. Cytomorphological spectrum of lymphocytic thyroiditis: correlation with thyroid hormones and antibodies in a South Delhi Tertiary Care Center. MGM Journal of Medical Sciences. 2025;12(3):422-429. https://doi.org/10.4103/mgmj.mgmj_146_25
2. Revathi G, Vimal M, Ivan EA. Role of cytology in diagnosis of thyroiditis and possible pitfalls – An experience from a South Indian Institute. Journal of Dr. NTR University of Health Sciences. 2023;12(2):141-145. https://doi.org/10.4103/jdrntruhs.jdrntruhs_131_22
3. Bhatia A, Rajwanshi A, Dash RJ, Mittal BR, Saxena AK. Lymphocytic thyroiditis – is cytological grading significant? A correlation of grades with clinical, biochemical, ultrasonographic and radionuclide parameters. Cytojournal. 2007;4:10. https://doi.org/10.1186/1742-6413-4-10
4. Cytomorphological Spectrum of Thyroiditis: A Review of 110 Cases. Journal of Thyroid Research. 2018;2018:5246516. https://doi.org/10.1155/2018/5246516
5. Jasim S, Dean DS, Gharib H. Fine-Needle Aspiration of the Thyroid Gland. In: Feingold KR, Adler RA, Ahmed SF, et al., editors. Endotext [Internet]. South

Dartmouth (MA): MDText.com, Inc.; 2000-. Updated 2023 Mar 23. Available from: https://www.ncbi.nlm.nih.gov/books/NBK285544/
6. Diagnostic pitfalls of Hashimoto's/lymphocytic thyroiditis on fine-needle aspirations and strategies to avoid overdiagnosis. Acta Cytologica. 2012;56(4):352-360. https://doi.org/10.1159/000338738
7. Fine needle aspiration biopsy of Hashimoto's thyroiditis. Sources of diagnostic error. Acta Cytologica. 1999;43(3):400-406. https://doi.org/10.1159/000331088
8. A focal nodular Hürthle cell hyperplasia in Hashimoto's thyroiditis: A diagnostic dilemma on fine needle aspiration. Journal of Cytology. 2021;38(3):167-169. https://doi.org/10.4103/JOC.JOC_32_20
9. Diagnostic pitfalls in the evaluation of fine needle aspiration cytology of the thyroid: correlation with histopathology in 260 cases. Cytopathology. 2009;20(2):103-108. https://doi.org/10.1111/j.1365-2303.2008.00552.x
10. Cibas ES, Ali SZ. The Bethesda System for Reporting Thyroid Cytopathology. Thyroid. 2009;19(11):1159-1165. https://doi.org/10.1089/thy.2009.0274
11. Chronic lymphocytic (Hashimoto's) thyroiditis. In: Eurocytology [Internet]. Available from: https://win.eurocytology.eu
12. Hashimoto Disease – Chronic Lymphocytic (Hashimoto) Thyroiditis. In: ScienceDirect [Internet]. Available from: https://www.sciencedirect.com
13. Cytological Grading of Lymphocytic Thyroiditis and Its Correlation With Biochemical Parameters: An Experience From a Tertiary Care Center in North India. Cureus. 2024;16(4):e58712. https://doi.org/10.7759/cureus.58712
14. Cytomorphological variations in Hashimoto's thyroiditis: A study of 164 cases. Indian Journal of Pathology and Oncology. 2025;12(2):145-150. https://doi.org/10.18231/j.ijpo.2025.028
15. Lymphocytic (Hashimoto) thyroiditis. In: Papanicolaou Society of Cytopathology [Internet]. Available from: https://www.papsociety.org
16. The Bethesda System for Reporting Thyroid Cytopathology: Recommended Diagnostic Categories. In: NCBI Bookshelf [Internet]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK285544/table/tyd-aspiration-biops.T.the_bethesda_syst/