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Original Research Article

Grading of Lymphocytic Thyroiditis Cytologically and Relationship to Hormonal Condition of the Thyroid

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Abstract

Background: The second most frequent thyroid lesion identified on FNAC after goitre is lymphocytic thyroiditis. Along with FNAC, other diagnostic factors include clinical characteristics, thyroid antibody titres, thyroid hormonal profile, and ultrasonography. The goal of the current study was to assess thyroid fine needle aspirates for the presence of lymphocytic thyroiditis, grade lymphocytic thyroiditis cases using predetermined cytological criteria, and determine the relationship between cytological grades and thyroid hormonal state.

Methods: From March to August 2019, this retrospective study was carried out at Department of Pathology, Darbhanga Medical College Laheriasarai, Bihar. According to Bhatia *et al*., cytological criteria were used to further categorise lymphocytic thyroiditis patients that had been reported using the Bethesda system. Where data were available, cytological grades were associated with thyroid hormonal status.

Results: According to the Bethesda method, a total of 162 instances of lymphocytic thyroiditis were documented in our study. Further grading revealed that grade II thyroiditis accounted for the majority of cases (104, 64.2%), followed by grade I (48, 29.6%), and grade III (10, 6.2%). Out of the 78 cases with accessible thyroid hormonal profiles, the majority of patients (42; 53.85%) were hypothyroid. Euthyroid (21; 26.92%) and hyperthyroid (15; 19.23%) individuals were next in line. With a P value greater than 0.05, there was no statistically significant correlation between grades and hormone status.

Conclusion: The "gold standard" test for diagnosing lymphocytic thyroiditis is still the FNAC. However, in our investigation, there is no statistically significant link between the cytological grades and thyroid hormonal condition.

Keywords: Lymphocytic thyroiditis, Cytological grading, Thyroid hormonal status

Introduction

With 42 million sufferers in India alone, thyroid disorders are among the most prevalent endocrine conditions globally [1]. The first line diagnostic method for assessing

thyroid lesions is fine needle aspiration cytology (FNAC), which is capable of efficiently identifying neoplastic and non-neoplastic lesions [2]. The majority of thyroid nodules are benign, and in about 60–70% of instances, the FNA results are interpreted as benign [3].

The second most frequent benign thyroid lesion identified by FNAC after goitre is chronic lymphocytic thyroiditis, which is also known as autoimmune thyroiditis. Hashimoto's thyroiditis (HT), also known as chronic lymphocytic thyroiditis or autoimmune thyroiditis, is more prevalent in women and has a prevalence rate of 1-4% and an incidence of 30-60/100000 population per year. FNA is highly sensitive in diagnosing HT, with a diaphrag In regions of the world where iodine is abundant, it is the most frequent cause of hypothyroidism [7] In addition to FNAC, clinical characteristics, thyroid antibody titres, thyroid hormonal profile, and ultrasonography are also helpful in its diagnosis [6-8].

The goal of the current study was to assess thyroid fine needle aspirates for the presence of lymphocytic thyroiditis, grade lymphocytic thyroiditis cases using predetermined cytological criteria, and determine the relationship between cytological grades and thyroid hormonal state.

Material and Methods

It was a retrospective study conducted in the Department of Pathology, Darbhanga Medical College, Laheriasarai, Bihar from March 2019 to August 2019. From our department's records, thyroid fine needle aspirates from individuals who presented with thyroid enlargement during this time period were found. These patients' stained smears with May-Grunwald-Giemsa (MGG) and Papanicolaou (PAP) were looked at under a light microscope.

According to the Bethesda System for Reporting Thyroid Cytopathology, the cases that were consisted of many polymorphic lymphoid cells along with benign thyroid follicular cells and/or Hurthle cells were classified as lymphocytic thyroiditis (LT). It was not necessary to have a certain quantity of Hurthle or follicular cells to make the diagnosis of lymphocytic thyroiditis [3].

These cases were further graded based on predefined cytological criteria as per Bhatia *et al* [8] as:

1. Grade 0- No lymphoid cells.
2. Grade I (Mild)- Few lymphoid cells infiltrating the follicles/increased number of lymphocytes in the background.
3. Grade II (Moderate)- Moderate lymphocytic infiltration or mild lymphocytic infiltration with Hurthle cell change/giant cells/anisonucleosis.
4. Grade III (Severe)- Florid lymphocytic inflammation with germinal center formation, very few follicular cells left.

Where available, the thyroid hormonal profile of these patients was examined. Based on the patients' serum TSH, T4 and T3 readings, the patients were categorised as euthyroid, hypothyroid, and hyperthyroid. Where available, cytological grades and thyroid hormonal status were compared. Fischer Exact test of significance was used to statistically evaluate the relationship between grades and hormonal status, and a P value < 0.05 was deemed statistically significant.

Results

According to the Bethesda method, a total of 162 instances of lymphocytic thyroiditis were documented in our study. The age categories of 21–30 years (36; 22.22%), 41–50 years (32; 19.75%), and 31–40 years (48; 29.63%) had the highest proportion of patients, respectively. With ages ranging from 7 to 80, the mean age was 35.99 years. The study's gender ratio was 9.125, with 146 (90.12%)

female participants and 16 (9.88%) male participants. These cases were then rated in accordance with Bhatia *et al*'s standards. Grade II thyroiditis had the most instances, followed by grade I and grade III (Table 1). (Figure 1, Figure 2, Figure 3).

Table 1: Distribution of lymphocytic thyroiditis cases into cytological grades

Lymphocytic Thyroiditis-cytological grading	No. of Cases	Percentage
Grade I (Mild)	48	29.6%
Grade II (Moderate)	104	64.2%
Grade III (Severe)	10	6.2%
Total	162	100.0%

Thyroid hormonal profiles were obtained for 78 out of 162 patients. The majority of patients (42; 53.85%) had hypothyroidism, which was followed by euthyroidism (21; 26.92%) and hyperthyroidism (15; 19.23%). Subclinical hypothyroidism was deemed to exist in cases with increased TSH but normal T4 and T3 levels (11; 14.10%).

As demonstrated in Table 2, cytological grades and thyroid hormonal state were compared. The majority of individuals with thyroiditis of grade II also had hypothyroidism. Grade II thyroiditis, grade I thyroiditis, and no cases of grade III thyroiditis were responsible for the majority of the euthyroid cases. There was no patient with grade III thyroiditis who had a normal hormonal status and a thyroid profile was available. The majority of the cases of lymphocytic thyroiditis associated with hyperthyroidism (Hashitoxicosis) had grade II thyroiditis (8 cases), followed by grade I thyroiditis (6 cases), with only 1 case having grade III thyroiditis (Table 2). However, there was no statistically significant correlation between the patients' thyroid hormonal status and cytological grades (P value = 0.21, greater than 0.05).

Table 2: Comparison of cytological grades with thyroid hormonal status

Cytological grade	Euthyroid	Hypothyroid	Hyperthyroid	Total
Grade I)	8	8	6	22
Grade II	13	32	8	53
Grade III	0	2	1	3
Total	21	42	15	78

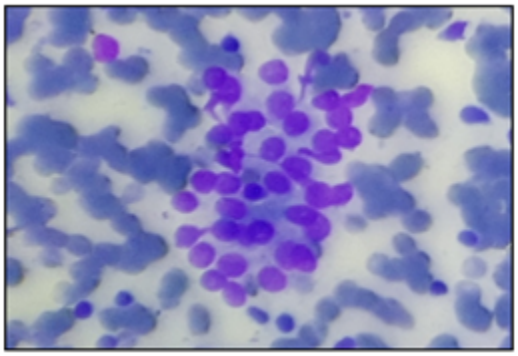

Figure 1: Photomicrograph from a case of grade I lymphocytic thyroiditis showing a cluster of thyroid follicular cells infiltrated by few lymphocytes (MGG 400X).

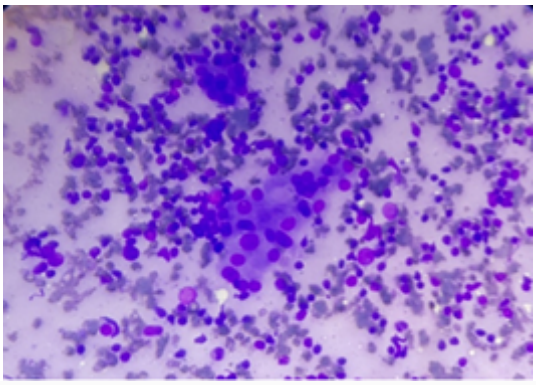

Figure 2: Photomicrograph from a case of grade II lymphocytic thyroiditis showing mild lymphocytic infiltration with Hurthle cell change, anisonucleosis and increased lymphocytes in the background (MGG 400X).

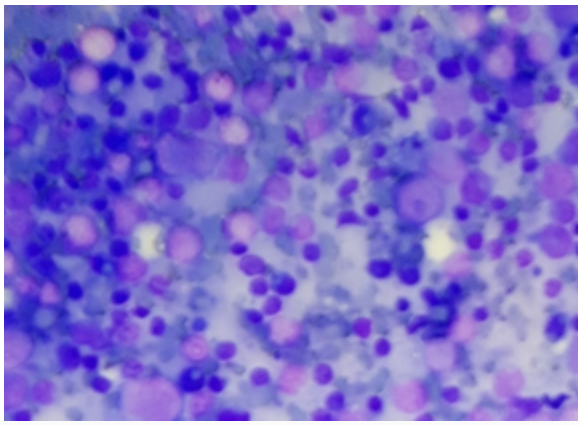

Figure 3: Photomicrograph from a case of grade III lymphocytic thyroiditis showing florid inflammation comprising of polymorphic lymphoid cells, and few scattered follicular cells (MGG 400X).

Discussion

Hakaru Hashimoto, who bears his name, described the struma lymphomatosa, the first case of chronic thyroiditis [8]. An autoimmune condition called Hashimoto's thyroiditis causes thyroid gland damage as well as gradual and increasing thyroid failure [7]. The prevalence of HT appears to be rising recently. Ten times as many people now experience it as they did in the early 1990s. A high iodine diet, especially in coastal locations, has been related to this rise in incidence [9,10].

Characteristic cytological findings include the presence of lymphoid cells in the background and lymphoid cell infiltration of follicular cells. Hurthle cells, plasma cells, epithelioid cell granulomas, and multinucleated giant cells are examples of variable characteristics [11]. Hypothyroidism typically comes on gradually. It may be preceded in some patients by temporary thyrotoxicosis, characterised by a decrease in TSH and an increase in free T4 and T3 levels. T4 and T3 levels drop as hypothyroidism progresses, and TSH levels rise as a result [7].

According to the Bethesda approach, thyroid fine needle aspirates were examined for cytological signs of lymphocytic thyroiditis, and 162 cases were identified as such in the current study. Our study's most prevalent age

range for these individuals was 31 to 40 years old, which is consistent with research by Bhatia *et al* [8]. Anila *et al* [6] and Shetty *et al* [12] In contrast to a western study, where the median age of the individuals was 58 years old, these Indian studies demonstrate a younger age at which lymphocytic thyroiditis is diagnosed in the Indian population [13] Female preponderance was comparable to that of the majority of research in the literature in the current investigation [5-12].

The majority of patients in our study had grade II thyroiditis, which was followed by grade I thyroiditis, while grade III thyroiditis affected the fewest patients. Studies by Bhatia *et al*.[8] and Shetty *et al*. [12] are comparable to this one. However, the majority of patients in a study by Anila *et al*.[6] had grade I thyroiditis, whereas the majority of cases in a study by Sood *et al*.5 were grade III thyroiditis.

When thyroid hormone status was evaluated, the majority of individuals were hypothyroid, which is consistent with many other studies [8,12,14]. In our investigation, there were 11 (14.1%) patients with subclinical hypothyroidism. Shetty *et al* study [12] found that, greater than in our study, 39.6% of the cases had subclinical hypothyroidism. No statistically significant link was identified in our study when cytological grades were further correlated with patients' thyroid hormonal status, which is similar with many other studies in the literature [6,8,12].

Grade 3 lymphocytic infiltration does, however, statistically correlate with either TPO and TSH together or TSH alone, according to a research by Sood *et al*. In a research by Kumar *et al*., [15] there was statistically significant correlation between hormonal state and lymphocytic infiltration (P- 0.02). The ratio of hypothyroidism (44%) was higher than hyperthyroidism (6%), however neither condition was statistically associated with cases of moderate to heavy infiltration (P- 0.36; P- 0.29). The proportion of hyperthyroid patients was highest (47%) and statistically significant among those with little infiltration (P- 0.0006). The statistical relevance between the cytological grades of LT and TSH was found in a study by Megalamane *et al*.16 (p-value< 0.001).

Clinical, radiographic, and hormonal criteria are overlapped in Hashimoto's thyroiditis and other thyroid pathologies, making them ineffective [15]. However, due to local antibody generation by intrathyroidal lymphocytes without spillover into the blood, around 7 to 33% of cases of Hashimoto's thyroiditis are antibody negative, particularly in the early stages of the disease. Therefore, FNAC is preferred as well as more economical than antibody screening to detect Hashimoto's thyroiditis, [10,17] especially in the early stages of the disease and if antibody testing facilities are not accessible, such as in our institution, or are prohibitively expensive [15].

However, there are certain difficulties with using FNAC to diagnose lymphocytic thyroiditis. Smears with cytological signs of hyperplasia, such as in Grave's disease or copious colloid, are prone to miss the diagnosis of Hashimoto's thyroiditis [9]. It may not be able to differentiate between pure Grave's disease and Hashimoto's thyroiditis in the toxic phase, or Hashitoxicosis, based solely on cytological findings; this requires comparison with clinical information and hormonal profile [11].

Adenomatous/colloid/hyperplastic goitre is the primary differential diagnosis in I2 deficient regions when smears demonstrate hyperplastic follicular cells, Hurthle cells, a small population of background lymphocytes, and the absence of lymphocytes in epithelial groups [15].

Selective sampling from a hyperplastic nodule with a predominance of Hurthle cells and little to no lymphocytic infiltrate in the

early stages of Hashimoto thyroiditis raises the possibility of a Hurthle cell tumour [3]. While poorly coordinated and cohesive cell clusters support neoplasia, Hurthle cells in flat sheets encourage thyroiditis [11]. The likelihood of lymphoma may increase if lymphoid components predominate, as in grade III thyroiditis [12]. Approximately 75% of thyroid gland primary lymphomas develop against a background of Hashimoto's thyroiditis [11]. It is possible to distinguish these patients from Non-Hodgkin lymphoma thanks to the polymorphic lymphoid population [3,8].

In cases when the diagnosis is unclear morphologically, immunophenotyping tests are critical to support the diagnosis. There is evidence that the incidence of cancer in HT can range from 0.4% to 28%. The likelihood of papillary cancer should be slightly increased since the follicular or Hurthle cells in LT occasionally exhibit modest atypia, nuclear expansion, grooves, and chromatin clearance [3,12].

As a result, some of the potential pitfalls and uncertainties can be reduced, and the value of FNAC in the diagnosis of lymphocytic thyroiditis can be increased. This is because it is important to be aware of how cytological features of one thyroid pathology may overlap with those of another, and by using an integrated approach with clinicopathologic correlation.

Conclusion

Although the diagnosis of lymphocytic thyroiditis is aided by a combination of cytomorphology, clinical characteristics, thyroid hormone profile, antibody testing, and ultrasonographic features, particularly in cytologically ambiguous patients, FNAC continues to be the "gold standard" investigation [5-8,10,12,14]. However, in our investigation, there is no statistically significant link between the cytological grades and thyroid hormonal condition.

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