

A Three-Year Retrospective Study Assessment of the Cytological Grading of Lymphocytic Thyroiditis and its Correlation with Thyroid Hormonal Status

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Abstract

Aim: The aim of the present study was to evaluate thyroid fine needle aspirates for cytological features of lymphocytic thyroiditis; to grade lymphocytic thyroiditis cases based on predefined cytological criteria and to correlate cytological grades with thyroid hormonal status.

Material & Methods: A three-year retrospective study conducted in the Department of Pathology, Thyroid fine needle aspirates from 100 patients presenting with thyroid swelling during this period were retrieved from the archives of our department. May Grunwald-Giemsa (MGG) and Papanicolaou (PAP) stained smears from these patients were examined under light microscopy.

Results: In the study, 88 (88%) were female participants and 12 (12%) male participants. The age categories of 21–30 years (25%), 41–50 years (20%), and 31–40 years (30%) had the highest proportion of patients, respectively. With ages ranging from 7 to 80, the mean age was 35.99 years. Grading revealed that grade II thyroiditis accounted for the majority of cases (65%), followed by grade I (30%), and grade III (5%). Thyroid hormonal profiles were obtained for 48 out of 100 patients. The majority of patients (25; 52.08%) had hypothyroidism, which was followed by euthyroidism (13; 27.08%) and hyperthyroidism (10; 20.84%). 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 (4 cases), followed by grade I thyroiditis (6 cases), with only 1 case having grade III thyroiditis.

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

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Introduction

Thyroid disorders are the most common endocrine disorders affecting about 42 million people in India. [1] Among all the disorders LT is the second most common thyroid lesion diagnosed on cytology next to goiter. [2] Struma thyroiditis a chronic disorder of the thyroid gland is characterized by diffuse lymphocytic infiltration, fibrosis, parenchymal atrophy and eosinophilic changes in some of the acinar cells (Hurthle cell change). The word LT is used synonymously with Hashimoto's thyroiditis or autoimmune thyroiditis is more common in women and has prevalence rate of 1–4% and incidence of

30–60/100000 population per year [3] which is again subclassified as atrophic and non-goitrous thyroiditis on histopathology. [4] LT typically presents with painless enlargement of thyroid gland, hypothyroidism, or both; 90% of LT patients also have High Anti Thyroid Peroxidase (TPO) and anti-Thyroglobulin (Tg) antibodies. [5] Fine needle aspiration cytology (FNAC) is the first line diagnostic procedure for evaluating thyroid lesions and can effectively distinguish between neoplastic and non-neoplastic lesions. [2] Most thyroid nodules are benign and a benign result is the most common

FNA interpretation (approximately 60-70% of all cases). On histopathology, the hallmark finding is lymphocytic infiltration of thyroid follicles resulting in glandular destruction, formation of lymphoid follicles and Hurthle cell changes. [6] Fine Needle Aspiration Cytology (FNAC) of thyroid provides a safe and accurate method for diagnosis with a sensitivity of 92% in predicting LT. [7]

On cytology presence of lymphocytic impingement of thyroid follicular cells, presence of a mixed population of mature and transformed lymphocytes, Hurthle cells, follicular cells with fine chromatin, an iso-nucleosis, multinucleated giant cells, scanty or absence of colloid on aspirated smears are the hallmark of LT. [7] Hurthle cells appears as large cells forming small syncytial aggregates having well defined abundant finely granular eosinophilic cytoplasm and large nucleus. [8]

Chronic lymphocytic thyroiditis is the second most common benign thyroid FNA diagnosis next to benign follicular nodule, [2, 9] and also overall the second most common thyroid lesion diagnosed on FNAC after goitre. [10] FNA is highly sensitive in diagnosing HT, with a diagnostic accuracy rate of 92%. [11] Most patients present with painless enlargement of thyroid, usually symmetric and diffuse. It is the most common cause of hypothyroidism in iodine sufficient areas of the world. [12]

Cytomorphological diagnosis may be superior in the initial stages of LT as antibody production may be confined to only intrathyroidal lymphocytes or localised areas without spillover into the blood. [5,13,14] Thus, there exists a wide range of values of TSH and variability of presence of ATPO making early diagnosis of LT difficult clinically and biochemically. However, a combination of cytomorphological, clinical and biochemical features helps in making a better diagnosis than using individual features alone. Besides FNAC, clinical features, thyroid antibody titres, thyroid hormonal profile, and ultrasonography also help in its diagnosis. [11,15]

Hence the present study was carried out to evaluate thyroid fine needle aspirates for cytological features of lymphocytic thyroiditis; to grade lymphocytic thyroiditis cases based on predefined cytological

criteria and to correlate cytological grades with thyroid hormonal status.

Material & Methods

A three year retrospective study conducted in the Department of Pathology, Nalanda Medical College and Hospital, Patna, Bihar, India for one year. Thyroid fine needle aspirates from 100 patients presenting with thyroid swelling during this period were retrieved from the archives of our department. May Grunwald-Giemsa (MGG) and Papanicolaou (PAP) stained smears from these patients were examined under light microscopy.

Cytomorphological features were assessed as per Bethesda system and the cases that were composed of many polymorphic lymphoid cells associated with benign thyroid follicular cells and/or Hurthle cells were reported as lymphocytic thyroiditis (LT) as per The Bethesda System for Reporting Thyroid Cytopathology. A minimum number of follicular or Hurthle cells for adequacy were not required for diagnosis of lymphocytic thyroiditis. ³ These cases were further graded based on predefined cytological criteria as per Bhatia et al. [15] 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.

Thyroid hormonal profile of these patients, wherever available, was evaluated. The patients were classified as euthyroid, hypothyroid and hyperthyroid based on their serum TSH, T4 and T3 values. Cytological grades were compared with thyroid hormonal status wherever available.

Statistical Analysis

Statistically, the association of grades with hormonal status was assessed using Fischer Exact test of significance and P value < 0.05 was considered as statistically significant.

Results

Table 1: Demographic data

Gender	N%
Male	12 (12)
Female	88 (88)
Age group in years	
21-30 years	25 (25)
31-40 years	30 (30)
41-50 years	20 (20)
>50 years	25 (25)

In the study, 88 (88%) were female participants and 12 (12%) male participants. The age categories of 21–30 years (25%), 41–50 years (20%), and 31–40 years (30%) had the highest proportion of patients, respectively. With ages ranging from 7 to 80, the mean age was 35.99 years.

Table 2: Distribution of lymphocytic thyroiditis cases into cytological grades

Lymphocytic Thyroiditis-cytological grading	No. of Cases	Percentage
Grade I (Mild)	30	30
Grade II (Moderate)	65	65
Grade III (Severe)	5	5
Total	100	100

Grading revealed that grade II thyroiditis accounted for the majority of cases (65%), followed by grade I (30%), and grade III (5%).

Table 3: Comparison of cytological grades with thyroid hormonal status

Cytological grade	Euthyroid	Hypothyroid	Hyperthyroid	Total
Grade I	4	4	6	14
Grade II	9	20	3	32
Grade III	0	1	1	2
Total	13	25	10	48

Thyroid hormonal profiles were obtained for 48 out of 100 patients. The majority of patients (25; 52.08%) had hypothyroidism, which was followed by euthyroidism (13; 27.08%) and hyperthyroidism (10; 20.84%). 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 (4 cases), followed by grade I thyroiditis (6 cases), with only 1 case having grade III thyroiditis.

Discussion

The first report of chronic thyroiditis, struma lymphomatosa was described by Hakaru Hashimoto in 1912, which bears his name. [15] Hashimoto's thyroiditis is an autoimmune disease that results in destruction of thyroid gland and gradual and progressive thyroid failure. [12] The incidence of HT seems to be increasing in the recent times. It has become 10 times more common than it was until the early 1990s. This increase in incidence has been linked to excess iodine intake, particularly in coastal areas. [7,16] Cytological findings of lymphoid cells in the background and infiltration of follicular cells by lymphoid cells are characteristic. Variable features include Hurthle cells, plasma cells, epithelioid cell granulomas and multinucleated giant cells. [17]

In the study, 88 (88%) were female participants and 12 (12%) male participants. The age categories of 21–30 years (25%), 41–50 years (20%), and 31–40

years (30%) had the highest proportion of patients, respectively. With ages ranging from 7 to 80, the mean age was 35.99 years which was consistent with research by Bhatia et al [15], Anila et al [11] and Shetty et al. [18] 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. [19]

Grading revealed that grade II thyroiditis accounted for the majority of cases (65%), followed by grade I (30%), and grade III (5%). Thyroid hormonal profiles were obtained for 48 out of 100 patients. The majority of patients (25; 52.08%) had hypothyroidism, which was followed by euthyroidism (13; 27.08%) and hyperthyroidism (10; 20.84%). 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 (4 cases), followed by grade I thyroiditis (6 cases), with only 1 case having grade III thyroiditis. However, in a study by Sood et al [2] Grade 3 lymphocytic infiltration has statistical correlation with TPO and TSH together or TSH alone. In a study by Kumar et al [20] the association between hormonal status and lymphocytic infiltration was statistically significant (P- 0.02). Among cases with moderate to heavy infiltration, the ratio of hypothyroidism (44%) was greater than hyperthyroidism (6%), but no statistically significant association was noted for hypo- or

euthyroidism (P- 0.36; P- 0.29). Among cases with minimal infiltration the proportion of hyperthyroid cases was greatest (47%) and statistically significant (P- 0.0006). In a study by Megalamane et al [21] there was a statistical significance between the cytological grades of LT and TSH (p-value <0.001). While poorly coordinated and cohesive cell clusters support neoplasia, Hurthle cells in flat sheets encourage thyroiditis. [17] The likelihood of lymphoma may increase if lymphoid components predominate, as in grade III thyroiditis. [18]

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. However, in our investigation, there is no statistically significant link between the cytological grades and thyroid hormonal condition.

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