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Original Research Article

Cytomorphological Study of Chronic Lymphocytic Thyroiditis

Shailesh Patel[1], Deepika Modi[2], Rippal Kumar Bhimani[3], Anandkumar A.Kanasagara[4], Jayesh Modi[5]

[1,2,4]Associate Professor, Department of Pathology, Banas Medical College and Research Institute, Palanpur, Gujarat

[3]Professor, Department of Pathology, Banas Medical College and Research Institute, Palanpur, Gujarat

[5]Professor, Department of General Surgery, Banas Medical College and Research Institute, Palanpur, Gujarat

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Corresponding author: Dr. Anandkumar A. Kanasagara

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Abstract

Background and Aim: Chronic lymphocytic thyroiditis is a frequently encountered cause of acquired hypothyroidism. The clinical management of thyroid nodules, whether or not accompanied by chronic lymphocytic thyroiditis, primarily relies on clinical data, ultrasonography, and fine-needle aspiration cytology (FNAC). FNAC is considered the most reliable method for diagnosing thyroid nodules prior to surgery. Our study sought to assess the range of cytomorphological features observed in lymphocytic thyroiditis and examine its correlation with clinical factors, thyroid hormone levels, and ultrasound results.

Material and Methods: The study was conducted in two stages. All patients with goitre who presented to the department of pathology and underwent FNA cytology were included in Step 1 of the study. This served as the sampling frame for identifying study participants for this study. In the next phase of the study, all patients who were diagnosed with lymphocytic thyroiditis on cytology were included for further evaluation. An analysis was conducted on the demographic characteristics, clinical features, biochemical, and radiology findings of the patients.

Results: During the study period, 200 individuals were referred for fine-needle aspiration (FNA) of the thyroid gland. Lymphocytic thyroiditis was diagnosed in 50 patients based on cytological findings. In 4 (8%) cases, there were associated features of pain in the neck. Out of the patients experiencing pain, there were two individuals with hypothyroidism, one with euthyroidism, and one with hyperthyroidism. Two patients were found to have cervical lymphadenopathy. Reactive hyperplasia was observed in the cytology of these. The most common cytomorphological finding was Grade II thyroiditis, which was observed in 40 (80%) of cases. Grade I was found in 8 (16%) cases, while Grade III was seen in 2 (4%) cases.

Conclusion: The correlation between cytological grading of thyroiditis and clinical, biochemical, and ultrasonographic findings is quite poor. Our patients show strong serological evidence of autoimmunity through the presence of TPO antibody, which also has a strong correlation with cytology.

Keywords: Chronic Lymphocytic Thyroiditis. Chronic Autoimmune Thyroiditis, Cytomorphological Study, Fine-Needle Aspiration Cytology.

Introduction

Chronic lymphocytic thyroiditis is another term for autoimmune thyroiditis, which encompasses both Hashimoto's thyroiditis (goitrous thyroiditis) and nongoitrous atrophic thyroiditis. Women are most commonly affected by this disorder, and it can manifest in various ways, from a noticeable enlargement of the thyroid gland (either diffuse or nodular) to a shrunken gland, normal thyroid function, underactive thyroid, and in rare cases, overactive thyroid. There are significant pathological changes observed in the thyroid, such as a high presence of lymphocytes infiltrating the gland and the formation of germinal centres. Additionally, there is atrophy of the thyroid follicles accompanied by oxyphil metaplasia, absence of colloid, and mild to moderate fibrosis. Autoimmune thyroiditis is characterised by the presence of thyroid peroxidase (TPO) antibody. The hyperthyroid variant is closely associated with Graves' disease in terms of its gross examination and microscopic appearance. In such cases, the diagnosis of Graves' disease can be confirmed by the presence of thyroid stimulating hormone (TSH) receptor antibodies. [1] Clinical examination, hormonal

profile, and ultrasonography (USG) of the thyroid gland are frequently utilised to evaluate both diffuse and solitary thyroid swellings. However, fine-needle aspiration cytology (FNAC) has emerged as the preferred method in outpatient departments for diagnosing thyroidal nodules, whether accompanied by chronic lymphocytic thyroiditis or not. In addition to FNAC, the non-aspiration technique for cytology is gaining popularity as a method for evaluating thyroid nodules.

The cytological grading system proposed by Bhatia et al. is widely accepted for reporting chronic lymphocytic thyroiditis. Grade 1 in this system is classified as mild and is characterised by a small number of lymphoid cells infiltrating the follicles, along with an increased number of lymphocytes in the background and a few Hurthle cells (follicular-derived epithelial cells with oncocytic cytology). In Grade 2, there is lymphocytic infiltration or mild lymphocytic infiltration with the presence of Hurthle cell clusters, giant cells, or anisonucleosis. This particular grade, known as grade 3 or florid, is characterised by inflammation of lymphocytes and the formation of germinal centres. On a smear, there are very few identifiable follicular cells, specifically Hurthle cells. [2]

Chronic lymphocytic thyroiditis is characterised by an increase in thyroid-stimulating hormone (TSH) levels, a decrease in free T4 (FT4) levels, and lower levels of free T3 (FT3). During the later stages, around 25% of cases might show normal FT3 levels. There is a correlation between the concentration of TPO antibodies and the level of lymphocytic infiltration in lymphocytic thyroiditis.

For primary diagnosis of thyroid swellings, fine needle aspiration (FNA) is the preferred method. It is a trustworthy and affordable method for diagnosing and grading lymphocytic thyroiditis. Studies conducted in India revealed that a significant number of young girls and schoolchildren in the country have been diagnosed with juvenile autoimmune thyroiditis. The prevalence of this condition was found to be 7.5% among goitrous healthy young girls aged 10-18 years, and 6.02% among schoolchildren aged 6-18 years. [3,4]

According to studies conducted in hospitals, the occurrence of lymphocytic thyroiditis in patients with thyroid swelling who underwent FNA ranged from 7.6% to 15.3%. [5-7] Our research was conducted in a medical college situated in the picturesque Kangra Valley of India, an area known for its high prevalence of goitre and iodine deficiency. In 1956, a study conducted in the district of Kangra in Himachal Pradesh reported a goitre prevalence of 55%. During the postiodization phase, there has been a significant decrease in goitre prevalence in the region. However, it is still persisting to some extent. In 1999, the district saw a decrease in the prevalence of goitre, with rates dropping to 12.1%. [8] In 2004, the total goitre rate was still at 19.8%, despite the efforts made through the universal iodisation program to address this issue. [9] Our study aimed to assess the range of cytomorphological features seen in lymphocytic thyroiditis and explore its relationship with clinical factors, thyroid hormone levels, and ultrasound results.

Material and Methods

The study took place in a tertiary care referral hospital in India. The study was conducted in two phases. All patients with goitre who presented to the department of pathology and underwent FNA cytology were included in Step 1 of the study. This served as the sampling frame for identifying study participants for this study. In the next phase of the study, all patients who were diagnosed with lymphocytic thyroiditis on cytology were included for further evaluation. The slides were carefully analysed by two highly experienced senior pathologists who have collaborated on this study. All patient data, including demographic, clinical, biochemical, and radiology information, was meticulously recorded using a structured pro forma. Thyroid function tests (T3, T4, and TSH) and thyroid peroxidase antibody were analyzed using a chemiluminescent immunoassay.

The condition is characterised by the presence of lymphocytes and plasma cells in the thyroid follicles, along with an increased number of lymphocytes in the background. Other possible features include Hurthle cell change, multinucleated giant cells, epithelioid cell clusters, anisonucleosis, or interlobular fibrosis, which refers to the presence of fibrous tissue or scattered fibroblasts in the aspirate. [10] The grading of lymphocytic thyroiditis was classified into three categories: mild, moderate, and severe, based on the criteria established by Bhatia et al. [10]

The assessment of thyroid function was based on TSH levels. A positive TPO was indicated when the antibody level reached or exceeded 30 U/ml.

Statistical analysis

The data was compiled and entered into a spreadsheet computer program (Microsoft Excel 2019) before being exported to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). The quantitative variables were presented using either means or standard deviations or median and interquartile range, depending on their distribution. The data on qualitative variables were displayed as counts and percentages. Confidence level and level of significance were set at 95% and 5% respectively for all tests.

Results

During the study period, a total of 200 individuals underwent FNA of the thyroid gland. Lymphocytic thyroiditis was diagnosed in 50 patients based on cytological findings. The patients' ages spanned from 10 to 80 years, with an average age of 38.5 ± 12.7 years. The majority of patients were female, accounting for 86% of the total. All the patients presented with goitre as a clinical symptom. Furthermore, 4 (8%) cases exhibited associated features of neck pain. Out of the patients experiencing pain, two had hypothyroidism, while one had normal thyroid function and another had hyperthyroidism. Two patients were found to have cervical lymphadenopathy. Reactive hyperplasia was observed in the cytology of these specimens. The most common cytomorphological finding was Grade II thyroiditis, which was observed in 40 (80%) of the cases. Grade I was found in 8 (16%) cases, while Grade III was seen in 2 (4%) cases.

Table 1 presents the breakdown of age, sex, and cytological grades of lymphocytic thyroiditis. In 17 (34%) of cases, the TSH level was within the normal range. However, in 15 (30%) of cases, it was found to be increased, while in 18 (36%) of cases, it was found to be decreased.

There were 35 cases where Anti TPO tested positive. The correlation between thyroid hormone status, TPO antibody, and cytological grades of lymphocytic thyroiditis is illustrated in Table 2.

Table 1: Distribution of grade of lymphocytic thyroiditis with age and sex (n=50)

Age group	Grade 1		Grade 2		Grade 3	
	Male	female	Male	female	Male	female
<20	-	2	1	2	-	-
21-40	-	3	-	24	-	-
41-60	1	2	2	9	1	1
>60	-	-	1	1	-	-
Total	1	7	4	36	1	1

Table 2: Relation of cytological grade of lymphocytic thyroiditis, thyroid peroxidase, and thyroid-stimulating hormone status (n=35)

Status of anti-TPO and TSH	Grade 1	Grade 2	Grade 3	Total
Anti-TPO increased; TSH increased	2	8	0	10
Anti-TPO increased; TSH normal	2	7	0	9
Anti-TPO increased; TSH decreased	2	11	1	14
Anti-TPO normal; TSH increased	0	2	0	2

TSH: Thyroid-stimulating hormone, TPO: Thyroid peroxidase

Discussion

Hakaru Hashimoto is credited with describing chronic lymphocytic thyroiditis. Hashimoto's thyroiditis is often referred to as chronic lymphocytic thyroiditis or autoimmune thyroiditis, which can include atrophic and non-goitrous thyroiditis. [11] There has been a significant rise in thyroid disorders worldwide in recent times. Thyroid disorders stand out from other endocrine disorders due to the noticeable enlargement of the gland and the straightforward diagnostic approach.

This allows for early initiation of treatment. It is worth noting that the disease tends to occur more frequently in women aged 45 to 65. There is a notable disparity in disease prevalence between females and males, with females being 10 to 20 times more likely to be affected. [5] India is currently in a transitional phase, moving from a state of iodine deficiency to becoming iodine sufficient. It is worth noting that a significant majority, around 91%, of individuals have access to iodised salt. In areas with iodine deficiency, giving iodine supplementation can triple the prevalence of lymphocytic infiltration of the thyroid. After taking supplements, the rate of anti-TPO positivity increases to approximately 40% within a span of 5 years. [12] In our study, we found that 24% of patients with thyroid swelling who underwent FNA had lymphocytic thyroiditis. In hospital-based studies conducted in India, the prevalence ranged from 7.6% to 15.3%. [13,14] According to a countrywide screening, it was found that 7.5% of goitrous healthy young girls between the ages of 10-18 have this condition. [3] There could be a higher prevalence in our study for a couple of reasons. It could be because of an immunogenic predisposition in this population or because of iodisation in a known endemic region. The majority of the patients were women. There is a disparity in this case, which can be attributed to the influence of female sex steroid hormones and the presence of certain sex and immune related genes on the X chromosome. A significant portion of the patients fell within the age range of 21 to 40 years. It is worth noting that this finding aligns with previous studies conducted in India, which differ from western studies that typically diagnose it in the 4th–6th decade. Young

patients often experience a higher occurrence of the disease due to a lack of iodine in non-coastal regions. This issue continues to persist, even with the national iodine deficiency disease control program in place. On the other hand, in older individuals, the disease can appear in regions where iodine levels are adequate. Some authors have linked the increased occurrence of Hashimoto's thyroiditis, especially in coastal regions, to an excessive consumption of iodine or in populations with adequate iodine levels. [9,10]

Furthermore, a small percentage of patients (8%) experienced pain in the neck as a related symptom. Hashimoto's thyroiditis is typically a painless condition, with only a few rare cases of painful presentation being reported. [15] Two cases in our study exhibited cervical lymphadenopathy. Both patients exhibited reactive hyperplasia in their lymph node cytology. It is quite common to find benign hyperplastic neck lymph nodes in cases of chronic autoimmune thyroiditis. [16] A diffusely enlarged gland with hypoechoic echotexture was observed in 56% of patients during ultrasonography. In the remaining patients, the gland showed diffuse enlargement with a varied texture, or multiple nodules were detected. Studies from India have reported normal to hypoechogenicity. [17,18] When examining the thyroid using ultrasound, one may observe certain characteristics that indicate Hashimoto's thyroiditis. These include a widespread enlargement of the thyroid gland, reduced brightness on the ultrasound image, uneven texture, increased blood flow, and the existence of small nodules with a dark center and bright outer edge. [19] Thyroid enlargement with diffuse hypoechogenicity suggests the possibility of autoimmune thyroid disease. The low echogenicity is a result of changes in the structure of the thyroid, caused by the disruption of follicles and the presence of diffuse lymphocytic infiltration.20 The correlation between cytology grades and ultrasound findings in this study was found to be poor. In this study, the presence of Anti TPO was found to be positive in 94.5% of cases. These findings align with similar studies conducted in India. [16,17,20]

The clinical presentation of HT can range from a generalised enlargement of the thyroid gland to the presence of nodular disease. Although cytological grading can offer insight into the autoimmune activity in the thyroid gland, it may not accurately indicate the gland's functional status. For example, individuals with early-stage HT might show signs of nodular disease and have normal TSH levels, even though their antithyroid antibodies are elevated. [5,6] Our study revealed a significant correlation between cytology and antibody levels. On the other hand, other studies have acknowledged the discrepancy between cytological and antibody findings. [8,9,11] The majority of patients in our study were classified as cytology Grade II, with Grade I being the second most common classification. There have been varying results observed on cytological grading in different studies. Other studies have also found similar results, as reported by Kumar et al. [14] and Iha et al. [11]

In this study, the researchers found that 34% of the patients had either normal thyroid hormone levels or were experiencing hyperthyroidism. It was found that 15 (30%) patients in this study had hypothyroidism. While hypothyroidism is commonly seen in cases of lymphocytic thyroiditis, various studies have shown that the cytomorphological features do not consistently indicate the hormonal status. In the early stages of the disease, patients may show indications, symptoms, and laboratory results that resemble hyperthyroidism or fall within the normal range. The destruction of the thyroid gland cells can occur intermittently. The current understanding of the clinical significance of euthyroid patients with cytological evidence of lymphocytic thyroiditis remains uncertain. There is limited information available regarding the transition from a normal thyroid function to a hypothyroid state in adults with Hashimoto's thyroiditis. There is a suggestion that children with HT may progress from a euthyroid to a hypothyroid state. [21]

A common drawback of both the current study and previous ones is the limited sample size. Further research may be necessary to fully understand the connection between cytological grades and biochemical parameters. In addition, conducting longitudinal studies could offer valuable insights into how HT progresses and how hypothyroidism develops over time.

Conclusion

Cytological grading into mild, moderate, and severe grades of thyroiditis correlates poorly with clinical, biochemical, and ultrasonographic findings. Serological evidence of autoimmunity by the presence of TPO antibody is strong in our patients and correlates well with cytology. Serology a noninvasive method is not inferior to cytomorphology in making a diagnosis of lymphocytic thyroiditis in our population.

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