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Original Research Article

Chronic Lymphocytic Thyroiditis- Cytological Grades, Radiological and Biochemical Evaluation- An Integrated Approach

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Abstract

Introduction: Chronic lymphocytic thyroiditis (CLT) is one of the common autoimmune disorders of thyroid. There is rise in the incidence and diagnosis of CLT due to iodine supplementation of diet and improved diagnostic techniques repectively. Various diagnostic modalities including TFT's, USG, anti-TPO antibody levels & FNAC help in its early diagnosis and thereby facilitate in planning of treatment.

Aims & Objectives: To correlate Cytological findings in Chronic lymphocytic thyroiditis with TFT, USG & with anti-thyroid antibody levels.

Material and methods: Total 313 cases of chronic lymphocytic thyroiditis diagnosed on cytology were included in the study group, of which 165 were prospective & 148 were retrospective. In all cases, FNAC findings were statistically correlated with TFT, USG & anti-TPO using Chi-square test.

Conclusion: CLT can have unusual presentations like euthyroid status, Solitary thyroid nodule & negative ant-TPO antibody levels, for early diagnosis of such cases FNAC plays a key role.

Keywords: Anti-TPO antibody, FNAC, Lymphocytic thyroiditis, Ultrasonography

Introduction

Chronic lymphocytic thyroiditis is one of the common autoimmune disorders of thyroid. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases.[1] Chronic lymphocytic thyroiditis (CLT) is included in non-neoplastic thyroid lesions. Its pathophysiological hallmark is lymphocytic infiltration of thyroid follicles resulting in autoimmune glandular destruction. There is rise in the incidence and diagnosis of CLT due to iodine supplementation of diet and improved diagnostic techniques respectively. [2] Though classically CLT has been described to present as diffuse enlargement

of thyroid associated with hypothyroidism, today, a change in trend has been observed in its clinical presentation.

Recent advances in diagnosis help in early detection of the thyroid lesion and facilitate planning of treatment. Various diagnostic modalities include thyroid function tests, Ultrasonography, Thyroid auto antibodies and Fine needle aspiration cytology (FNAC).

Thyroid functional status is assessed by measuring serum TSH, T4 & T3 levels, but significant changes in their levels are seen late in the disease process. The basic function of thyroid hormone is to increase the basal metabolic rate of body. The symptoms of thyroiditis are predominantly due to destruction of thyroid tissue, leading to decreased thyroid hormone production and ultimately decreased metabolism. [3]

Ultrasonography appears to be ideal screening method for diffuse as well as nodular thyroid diseases. In lymphocytic thyroiditis, echogenecity of thyroid gland is reduced (hypoechoic) as a result of underlying lymphocytic infiltration of the gland. [4]

Thyroid auto antibodies have added new dimensions for diagnosis of autoimmune thyroid diseases, however all above mentioned investigations are unable to give morphological diagnosis of lesion.

FNAC is an excellent, cost effective, simple method for morphological diagnosis of thyroid lesions.[3] Cytological features of CLT though variable; FNAC shows high sensitivity in diagnosing CLT and has diagnostic accuracy of 92%. Bhatia et al have proposed cytological grading of thyroiditis based on various features such as lymphocytic infiltrate, follicular destruction, Hurthle cell metaplasia etc. [5]

Thus in present study, we have attempted to correlate cytological findings with TFT, USG & Thyroid auto-antibodies.

Aims & Objectives

To Correlate Cytological findings in Chronic lymphocytic thyroiditis with TFT, USG & with anti-thyroid antibody levels.

Material & methods

This is a prospective and retrospective study of FNAC of thyroid done in pathology department of a tertiary care hospital.

Total 313 cases of chronic lymphocytic thyroiditis diagnosed on cytology were selected for this study. Of these cases 165 were included in prospective group and 148 were in retrospective group.

Clinical details and investigations including TFT, USG & anti-TPO titers were noted in prescribed case record form wherever available. For statistical analysis, on analyzing TFT, cases were divided into Euthyroid, Hypothyroid & Hyperthyroid functional groups, whereas for ultrasonographic findings cases were divided as those with Diffuse, Multinodular & Solitary thyroid nodular neck swelling.

For FNAC,

1. Informed written consent was taken.
2. Depending upon thyroid gland examination findings FNAC site/sites were chosen i.e for diffuse swelling: both lobes-2 passes each. For Solitary thyroid nodule: 2 passes, 1 from the nodule and 1 from the surrounding thyroid if palpable.

FNAC Procedure:

1. For FNAC-23 gauze needle was used and performed using non-aspiration technique
2. For each FNAC alcohol fixed smears stained with Papinicolou (Pap) stain and air-dried smears stained with MGG stain were used.
3. For colloid fluid aspirate-smears from sediment were prepared.
4. For non-palpable nodules-USG guided FNAC was performed.

Inclusion criteria: All the cases of lymphocytic thyroiditis diagnosed on cytology

Cytomorphological parameters were studied in detail and cases of lymphocytic thyroiditis were graded as per Bhatia et al. grading system. [5]

In all the cases, FNAC findings were statistically correlated with thyroid function tests, anti-thyroid peroxidase antibody (TPO) & USG findings.

Statistical analysis: In all the cases, statistical correlation between various parameters like functional status, USG findings, Anti-TPO antibody titre, and cytological grading was done using chi-square test.

Results

In the present study, the age group of lymphocytic thyroiditis ranged from 8-70 years. Majority of the cases (74.86%) occurred in the age group of 21- 50 years with peak in 4th decade. Female preponderance of 90.45% was noted. Biochemically hypothyroid state was seen in 46.74% followed by euthyroid state in 28.52%. Hyperthyroid hormonal profile was noted in 24.74%. On ultrasonographic evaluation, majority of our patients (64.4%) presented with diffuse enlargement of thyroid and multinodular presentation in 22.3% cases. Whereas 13.3% cases were also noted to present with solitary thyroid nodule. Anti- TPO antibody positivity has been observed in 75.98% of the cases & negative in 24.02% of cases.

Cytological parameters were analysed in all the cases of chronic lymphocytic thyroiditis and grading was done as per Bhatia et al. Grading system. Accordingly, majority of the cases showed grade II Lymphocytic thyroiditis (80.2%), Grade I in 12.77% & grade III in 7.03% of the cases.

Table 1: Correlation of USG with functional status (n=288)

USG	Functional status			Total
	Hypothyroid	Euthyroid	Hyperthyroid	
Diffuse	112	37	36	185
	83.0%	44.6%	51.4%	64.2%
MNG	13	31	20	64
	9.6%	37.3%	28.6%	22.2%
STN	10	15	14	39
	7.4%	18.1%	20%	13.6%
Total	135	83	70	288
	100.0%	100.0%	100.0%	100.0%

Chi-Square test	Value	df	P Value	Association
Pearson Chi-Square	41.130	4	<0.001	Significant

Majority (83.0%) of the cases with hypothyroidism showed diffuse enlargement of thyroid. 18.1% of euthyroid patients presented as solitary thyroid nodule.

Table 2: Correlation of Anti-TPO values with functional status (n=199)

Anti-TPO	Functional status			Total
	Hypothyroid	Euthyroid	Hyperthyroid	
Positive	83	31	36	150
	88.3%	53.4%	76.6%	75.4%
Negative	11	27	11	49
	11.7%	46.6%	23.4%	24.6%
Total	94	58	47	199
	100.0%	100.0%	100.0%	100.0%

Chi-Square test	Value	df	P Value	Association is
Pearson Chi-Square	23.520	2	0.000	Significant

88.3% of hypothyroid cases were found to be anti-TPO positive. Among the euthyroid patients, 53.4% were anti-TPO positive and 46.6% were anti-TPO negative.

Table 3: Correlation of cytological grades with functional status (n=291)

Grades	Functional status			Total
	Hypothyroid	Euthyroid	Hyperthyroid	
I	14	12	12	38
	10.3%	14.5%	16.7%	13.0%
II	110	65	56	231
	80.9%	78.3%	77.8%	79.4%
III	12	6	4	22
	8.8%	7.2%	5.5%	4.6%
Total	136	83	72	291
	100.0%	100.0%	100.0%	100.0%

Chi-Square test	Value	df	P Value	Association is
Pearson Chi-Square	2.340	4	0.671	Not Significant

Majority of patients were hypothyroid and showed grade II thyroiditis (80.9%). Grade II being the most frequent in all three functional groups.

Table 4: Correlation of USG with cytological grades (n=309)

USG	Grades			Total
	I	II	III	
Diffuse	20	167	12	199
	52.6%	67.1%	54.5%	64.4%
MNG	11	52	6	69
	28.9%	20.9%	27.3%	22.3%
STN	7	30	4	41
	18.4%	12.0%	18.2%	13.3%
Total	38	249	22	309
	100.0%	100.0%	100.0%	100.0%

Chi-Square test	Value	df	P Value	Association is
Pearson Chi-Square	7.380	4	0.116	Not Significant

Diffuse enlargement was the most common finding in all the three grades. No significant correlation was found between USG and cytological grades of lymphocytic thyroiditis.

Table 5: Correlation of Anti-TPO levels with cytological grades (n=204)

Anti-TPO	Grades			Total
	I	II	III	
Positive	14	121	20	155
	42.4%	80.7%	95.2%	75.98%
Negative	19	29	1	49
	57.6%	19.3%	4.8%	24.02%
Total	33	150	21	204
	100.0%	100.0%	100.0%	100.0%

Chi-Square test	Value	df	P Value	Association is
Pearson Chi-Square	51.446(a)	4	0.000	Significant

95.2% of grade III and 80.7% of grade II lymphocytic thyroiditis showed positivity of anti-TPO antibodies.

Discussion

Statistical Analysis:

Correlation of USG findings with functional status: (Table 1)

In this study, 83% of cases with hypothyroidism showed diffuse enlargement of thyroid at presentation. This is the classic clinical presentation of chronic lymphocytic thyroiditis. Statistically significant correlation (p value- <0.001) was found between USG findings and thyroid functional status of the study group. Among the euthyroid patients, 37.3% presented as multinodular goitre and 18.1% presented as solitary nodules. Cytological evaluation and correlation with antibody titres are important in these cases in order to prevent unnecessary surgery.

The USG not only helps in diagnosis of lymphocytic thyroiditis but also in selecting the patients with suspicious nodules for work up of malignancy. [6] In the present study no neoplastic lesion was found.

Correlation of Anti-TPO antibody titres with the functional status: (Table 2)

Anti-TPO antibody titres represent the degree of lymphocytic infiltration of the thyroid gland, reflecting the current activity of lymphocytic thyroiditis. [7]

The present study showed overall anti-TPO positivity in 75.98 % of cases (Graph-7). Functional status could be correlated with Anti TPO antibody in 199 cases. Among the TPO positive cases, majority were hypothyroid followed by hyperthyroid and euthyroid cases. It has been observed that the typical patients with lymphocytic thyroiditis have an elevated TSH with normal T3 and T4 levels. However, in early stages of the disease, TSH may be normal and anti-TPO antibodies may be positive. [7] Similarly in our study, 31 cases had normal TSH level (euthyroid) with increased anti-TPO antibodies.

Majority of Anti-TPO negative cases were euthyroid. In such cases, cytology aids in diagnosis of thyroiditis.

Statistical correlation between Anti-TPO positivity and functional status in our study group was found to be significant (p value <0.001). In contrast to our findings,

Singh et al did not report statistically significant correlation. [8]

Correlation of grades of lymphocytic thyroiditis with functional status: (Table 3)

In the present study, grades were equally distributed in all the three functional groups with grade II being the commonest in every functional group. This can be attributed to variable stages of disease presentation. Statistically no significant correlation was observed between grades and functional status (p value-0.67) in the present study. This is comparable to study of Kumar et al, Bhatia et al and Singh et al who carried out correlation of grade of lymphocytic thyroiditis with functional status but found no significant correlation. [9,5,8] This may be due to the fact that grading on FNAC smears is also affected by other factors like dilution by blood, technique of FNAC and the number of aspirations used. One needs to consider that the aspirates are obtained from very tiny portion of thyroid gland and may not at times represent the pathology in entirety.

Correlation of grades of lymphocytic thyroiditis with USG findings: (Table 4)

In present study, diffuse thyroid gland enlargement on USG was the commonest presentation in all three grades. Diffuse enlargement was followed by multinodular enlargement (MNG) and solitary thyroid nodule (STN) which was similar to other authors. [10,11,12,13] However, statistically no significant correlation was found between USG findings (diffuse, MNG, STN) and cytological grades of lymphocytic thyroiditis. Similarly, Bhatia et al found no significant correlation between cytological grades and USG findings. [5]

Correlation of grades of lymphocytic thyroiditis with Anti-TPO antibody titres: (Table 5)

In our study, Anti-TPO antibody titres were also correlated with cytological grades of lymphocytic thyroiditis. In 95.2% of grade III thyroiditis and 80.7% of grade II cases were TPO positive. Grade III thyroiditis shows florid lymphocytic infiltration of the gland with only few follicular cells left. This indicates that a high lymphoid: epithelial ratio correlates strongly with TPO positivity. In this study statistically significant correlation was found between grades of thyroiditis and anti-TPO titres (p value < 0.001). This was comparable with the study done by Singh et al, which showed that a high lymphoid: epithelial ratio strongly correlates with TPO positivity.[8] Relative percentage of Anti-TPO antibody positivity showed rise with rise in cytological grades from I to III.

In 24.02% of cases, Anti-TPO antibody titres were found to be negative and in all these cases FNAC showed cytological features of lymphocytic thyroiditis. Negative results for Anti-TPO antibody were observed in 57.6% of grade I cases, in 19.3% of grade II cases and in 4.8% of grade III cases. This finding of negative antibody titres in cytologically diagnosed cases of lymphocytic thyroiditis could be explained by the fact that localized intrathyroidal immune destruction occurs much earlier than serologic evidence of the disease. [9] The antibody titres might change with time, but cytomorphological features persist during the course of lymphocytic thyroiditis. So, even if anti thyroid antibodies are negative, diagnosis of lymphocytic thyroiditis can still be made on FNAC.

Conclusion

On statistical analysis, significant correlation was seen between

a. USG & functional status
b. Anti-TPO & functional status
c. Anti-TPO & cytological grades,

Whereas no statistical significance was found between

a. Cytological grades with functional status
b. Cytological grades with USG,

So, we conclude,

1. FNAC plays key role in diagnosis of Chronic lymphocytic thyroiditis, especially in cases with unusual presentations like euthyroid status, Solitary thyroid nodule & negative anti-TPO antibody levels.
2. Cytological analysis also helps to differentiate between Hashitoxicosis & Grave's disease in hyperthyroid patients.

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