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Pathology

Cytomorphological Study of Hashimoto's Thyroiditis and its Correlation with Thyroid Autoantibody

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Abstract **Original Research Article**

Background: Hashimoto's thyroiditis (HT) is the most common type of thyroiditis and is the 2nd most common cause of goiter in iodine deficient areas. The thyroid function may be normal or altered at time of presentation. Anti-Thyroid Peroxidase antibody (Anti TPO) is considered as diagnostic hallmark of HT. On FNAC, Two main cytomorphologic patterns of HT i.e, Classic Hashimoto's thyroiditis (CHT) and Florid lymphocytic thyroiditis (FLT) are seen This study aims to correlate the cytomorphological variants of Hashimoto's thyroiditis with thyroid autoantibody. ***Materials and methods:*** This cross sectional study is done for a period of two years starting from August 20018 in the Department of Pathology, Regional Institute of Medical Sciences (RIMS), Imphal. Sixty-five cases of HT diagnosed during the study period are included. The cytological findings, clinical features, serum levels of T_3, T_4, TSH and Antimicrosomal autoantibody (AMA) titre were the study variables. Statistical analysis: All the data were entered in a database programme and analysed statistically. ***Results and observations:*** Hashimoto's thyroiditis (HT) constituted 16.5% of the total thyroid aspirates (394) during the study period. The main cytomorphologic variants found are 39 cases of classic Hashimoto's thyroiditis (CHT) (60%) & 26 cases of florid lymphocytic thyroiditis (FLT) (40% The mean age is 33.05 years in HT, 36.1± 13.2 years in CHT and 29.5±10.8 years in FLT. Maximum cases presented in euthyroid state (41.5%), hypothyroid (38.6%), subclinical hypothyroid (10.8%) and 9.2% in hyperthyroid state. Anti -TPO antibodies positive in 87.2% of CHT and in 65.4% of FLT and is statistically significant with p value of 0.001. ***Conclusion:*** Recognition of cytomorphologic variants of HT is important as they have different clinical presentations and biochemical parameters.

Keywords: Hashimoto's thyroiditis, Classic Hashimoto's thyroiditis, Florid lymphocytic thyroiditis, Anti-Thyroid Peroxidase antibody.

INTRODUCTION

Hashimoto's thyroiditis (HT), an organ specific autoimmune disease, is the most common type of thyroiditis. Important geographical differences exist in age related prevalence and incidence of HT [1]. It is the most common cause of goiter in iodine sufficient areas and 2nd most common in iodine deficient areas [1,2]. Clinically, patients of HT present with varied manifestation and are usually asymtomatic. It is more common in females and peak age of presentation is 45-65 years. The thyroid function may be normal or altered at time of presentation [1,3]. Later on, most patients develop hypothyroidism. In few cases, transient thyrotoxicosis may also be seen. FNAC is cheap, safe, highly accurate and is considered as gold standard for its diagnosis [4-6].

A cytological diagnosis of HT is made on the presence of Hurtle cells and a variable number of lymphoid cells intermingling with the thyroid epithelial cells. Two main cytomorphologic patterns of HT can be seen on cytology smears, classic HT and florid lymphocytic thyroiditis (FLT) [4-6]. Variable cytological features like fire flares/ colloid suds are present in cases of thyrotoxic Hashimoto's thyroiditis. Multinucleated giant cells are seen in 30% and epithelioid cells in 10% of cases [4-7].

Various thyroid autoantibodies mainly anti-thyroglobulin antibody and anti-thyroid peroxidase antibody (Anti TPO) are elevated in most cases of HT [1,4,8]. They are produced by auto reactive B-cells against the thyroid antigens. They are elevated in most cases of HT and various studies have shown a wide range of significant titre, 65 to 98%. Out of the three auto

antibodies, anti-TPO is the most significant and is considered as diagnostic hallmark of HT [1,2.4].

Thus, FNAC of thyroid gland, estimation of antibody titre, evaluation of thyroid function test helps in confirming a diagnosis of HT. Cytology alone is diagnostic in 91.3% of cases when thyroid auto antibody titre is undetectable or negative and ultrasonographic findings are only suggestive [4,6]. Common sources of error are inadequate sampling and misinterpretation of cytological features of HT [4]. lack of information about the prevalence, mode of clinical presentation, cytomorphlogic pattern and serologic correlation of Hashimoto's thyroiditis in our state has led us to undertake the present study.

MATERIALS AND METHODS

This cross sectional study is done for a period of two years starting from August 2018 in the Department of Pathology, Regional Institute of Medical Sciences (RIMS), Imphal. Approval from the Institutional Ethical Committee (IEC), RIMS, was taken before starting the study. Sixty-five patients diagnosed as Hashimoto's thyroiditis on FNAC are included in the study. The cases were cytomorphologically classified into classic Hashimoto's thyroiditis (CHT) and florid lymphocytic thyroiditis (FLT). Smears showing few lymphocytes in the background were not included in the study [4-6]. The clinical features including signs of hypothyroidism and hyperthyroidism, serum levels of T_3, T_4, TSH and Anti- TPO titre were the other study variables.

Fine needle aspiration was done using a 24 gauge needle and aspirated material was stained with Giemsa stain and examined under light microscopy. In all cases, estimation of serum levels of T_3, T_4, TSH and antimicrosomal autoantibody. The estimation was carried out by immunoenzymetric assay using AccuBind^{TM} ELISA MicroWells kits. Sensivity was 0.04 ng/ml for T3, 0.4µg/dl for T4, 0.O78 µIU/ml for TSH) and 1.5 IU/ml for antimicrosomal antibody (AMA). All the data were entered in a database programme. Chi square test and Fisher's exact test were used for determination of differences in proportion.

RESULTS

Hashimoto's thyroiditis (HT) constituted 16.5% of the total thyroid aspirates (394) during the study period. The main cytomorphologic variants found in the study were 39 cases of classic Hashimoto's thyroiditis (CHT) (60%) & 26 cases of florid lymphocytic thyroiditis (FLT) (40%). The male to female ratio was found to be 1:64.

The age of the patients ranged from 11 years to sixty five years. The mean age was found to be 33.05 years in Hashimoto's thyroiditis. The mean age of presentation in CHT was 36.1$\pm$ 13.2 years and 29.5$\pm$10.8 years in FLT. CHT presented at a relatively older age as compared to FLT. This was found to be statistically significant (p=0.039, t=2.1). The most common presenting complaint was a painless thyroid swelling. Others were discomfort in the throat, off and on pain, pain with fever etc. The majority of the patients presented with a firm, diffuse thyroid swelling (81.53%) and with nodular swelling in 18.46%.

The main cytomorphologic features seen in HT and its variants are shown in the following table:

Table 1: Table showing cytological features in different types of HT

Cytologic features	CHT	FLT
Lymphocytes	39 (100%)	26 (100%)
Follicular cells	39 (100%)	26 (100%)
Hurthle cells	39 (100%)	0
Plasma cells	35 (89.7%)	20 (76.9%)
Giant cells	21 (53.8%)	7 (26.9%)
Epithelioid cells	16 (41.0%)	10 (38.5%)
Granuloma	8 (20.5%)	2 (7.7%)
Fire flares	2 (5.1%)	1 (3.8%)
Colloid	23	3

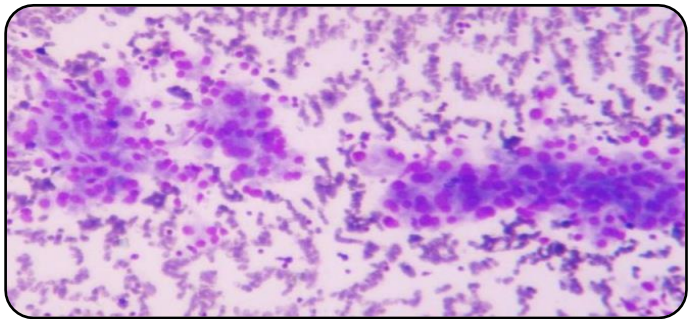

Fig. 1: Aspiration smear of classic Hashimoto's thyroiditis showing Hurthle cells, follicular cells, plasma cell, lymphocytes (Giemsa x100)

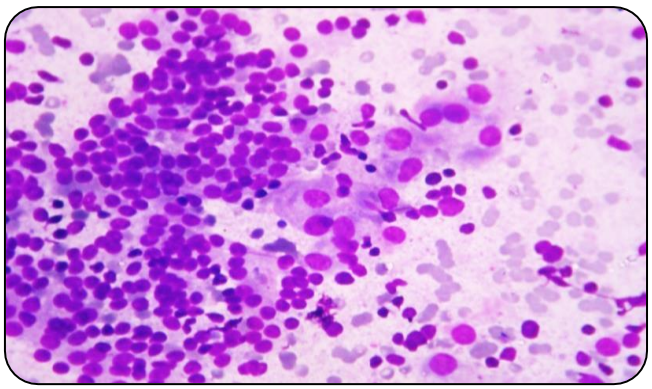

Fig. 2: Aspiration smear showing lymptocytes resembling a reactive lymph node in florid lymphocytic thyroiditis (Giemsax 400)

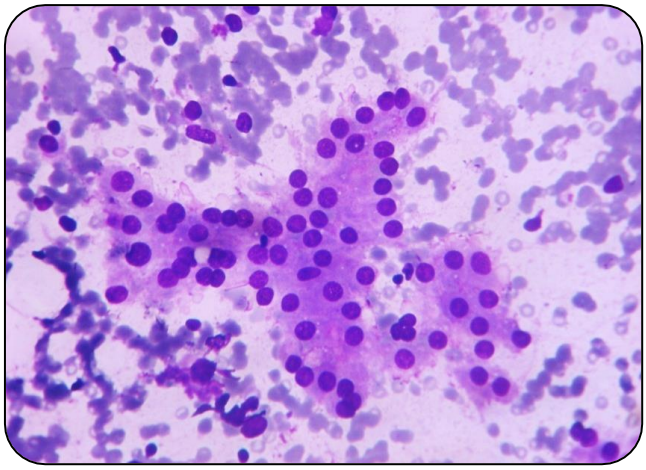

Fig. 3: Aspiration smear showing follicular cells with fire flares (colloid suds) in hashitoxicosis (Giemsa x400)

Thyroid function in Hashimoto's thyroiditis:

we found that maximum number of the patients (27/41.5%) presented in euthyroid state, 25 patients (38.6%) presented in hypothyroid state, 7 (10.8%) in subclinical hypothyroid state and 6 patients (9.2%) in hyperthyroid state. The thyroid function changes seen in variants of HT were analysed and showed the following findings.

Table-2: Thyroid function in variants of Hashimoto's thyroiditis.

Variant of HT	Thyroid function test (TFT)	
	No. of cases with altered TFT	No. of cases with normal TFT
CHT	28 (71.8%)	11(28.2%)
FLT	10 (42.3%)	16 (61.5%)

(x^2 = 5.83, p=0.015)

The thyroid function changes was associated more with CHT than with FLT which is found to be statistically significant (p value =.015). Majority of patients with CHT presented with alterations in thyroid function test (71.8%) and hypothyroidism is the commonest change seen in these patients (51.3%). Latent hypothyroidism and hyperthyroidism is seen in 10% each. Euthyroid state is seen in 28.2% of CHT. In FLT, majority of patients presented in euthyroid state (61.5%). The remaining cases presented in hypothyroid state (19.2%), latent hypothyroid state (11.5%) and hyperthyroid state (7.7%). The thyroid function changes associated with variants of HT have been found to be statistically significant (p value of 0.015).

The serum Anti thyroid peroxidase autoantibody (Anti-TPO Ab) titre was determined in all the cases and shows the following findings.

Table 3: Table showing distribution of Anti-TPO Ab titre in Hashimoto's thyroiditis

Anti TPO Ab	No. of cases	%
Positive	51	78.46%
Negative	14	21.54%
Total no. of cases(n)	65	100%

Table 4: Table showing Anti-TPO Ab titre in variants of HT

Variant of HT	No. of cases	
	Positive titre (>40 IU/ml)	Negative titre (≤40 IU/ml)
CHT	34(52.3%)	5
FLT	17(26.2%)	9

p=0.001(by Fishers Exact Test)

CHT is found to be more commonly associated with positive titre of Anti TPO Ab than FLT. This finding is found to be highly statistically significant with p value of 0.001.

DISCUSSION

This study was done to correlate the cytomorphologic patterns of Hashimoto's thyroiditis (HT) with the thyroid function test and serum level of anti thyroid peroxidase autoantibody (Anti-TPO Ab). The main morphologic variants of HT seen in the study were classic Hashimoto's thyroiditis (60%) and florid lymphocytic thyroiditis (40%) which is similar to Ahmad F *et al.,* [9]. In this study, Hashimoto's thyroiditis was typed as CHT & FLT based on Orell SR and Jayaram G [4]. However, some authors used the Bhatia A *et al.,* [7] cytological grading based on lymphocytic infiltration. CHT corresponds to grade I & II and FLT corresponds to grade III of Bhatia A *et al.,* grading system [7]. In this grading system, the FLT type was found to be in higher than other workers like IHA *et al.,* (22.6%), Shetty A *et al.,* (8.6%) [10], Singh N *et al.,* (22,7%) [11]. These findings may indicate that these variants of HT represent the spectrum of the disease.

As seen in other thyroid lesions, the female predominance of HT have been documented in all the studies carried out so far by other workers. (by Kumar N *et al.,* [12], Jayaram G *et al.,* [3], Bhatia A *et al.,* [7]). This may be attributed to female hormone oestrogen as in other thyroid lesions compounded by chance exclusion of male patients in the study. Maximum number of the patients (81.5 %) presented with diffuse thyroid swelling which is similar to that of Bhatia A *et al.,* [7], IHA *et al.,* [8], Shetty A *et al.,* [10], Singh N *et al.,* [11] etc.

The mean age of the patients was found to be 33.05 years which is similar with Bhatia A *et al.,* [7] (34.2 years), Singh N *et al.,* [11] (32.75). The most common age group affected is 2nd- 3rd decade in our study which is similar to most of the studies carried out by other workers.

The thyroid function test and anti-TPO level were compared with other studies as shown in the following table. Hormonal alterations was more common in CHT (71.8%) than in FLT (42.3%), statistically significant, p value of 0.015. Maximum cases in our study presented in euthyroid state which is similar with Ahmed F *et al.,* [9] but in other studies maximum number of cases presented in hypothyroid state. This difference may be due to the patients coming for treatment at a later stage.

The serum anti-TPO Ab titre was elevated in 78.46 % of cases which is similar to that of Singh N *et al.,* [11], Praveen K *et al.,* [13] (78.72 %). Association of positive titre of TPO Ab with CHT (52.3%) more than with FLT (26.2%) was found to be statistically significant (p = 0.001) and similar with Gutteridge and Orell [5]. As CHT represents a late stage of disease, high TPOAb titre was noted more than in FLT.

Table 5: Comparision of thyroid function and anti-TPO in various studies

Authors	Euthyroid (%)	Subclinical Hypothyroid (%)	Hypothyroid (%)	Hyperthyroid (%)	TPO + (%)
Present study	41.5	10.8	38.6	9.2	78.46
IHA *et al.,* [8]	16.20	-	54.80	29.0	83.87
Ahmad F *et al.,* [9]	60.34	-	37.93	1.72	83.33
Shetty A *et al.,* [10]	18.9	39.6	34.6	7	95.2
Thomas T *et al.,* [14]	32.8	-	45.8	21.4	92.3
Singh N *et al.,* [11]	37.3	19.3	38	5.3	79.3

CONCLUSION

The pattern of Hashimoto's thyroiditis seen in our state is similar with the pattern seen in other parts of India and the world as a whole with few differences. Cytology alone is diagnostic in 91.3% of cases when thyroid auto antibody titre is undetectable and is undetectable and ultrasonographic findings are only suggestive. The variants of HT correlated well with the thyroid function test and serum anti TPO Ab titre. Any patient presenting with a painless, diffuse thyroid swelling irrespective of age and sex should be subjected to FNAC to rule out HT and any associated lesion. Further larger studies need to be taken up in this part of

the country for understanding this puzzling disease. This will also help in proper management of the patients and will also reduce unwarranted surgical interventions.

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