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Hashimito's thyroiditis - a cytomorphological study with serological correlation

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Abstract

Background: Hashimoto's thyroiditis (HT) is the second most common thyroid lesion diagnosed on FNAC and is one of the most common causes of hypothyroidism in iodine sufficient areas. HT is characterised by Hurthle cell change and increased number of mature and transformed immature lymphocytes impinging on follicular cells. Diagnosis of HT is based on clinical, cytomorphological and serologic parameters. FNAC of thyroid provides a safe and accurate method for diagnosis of HT. The present study was designed to analyse the cytomorphological features of HT and correlate it with serological parameters.

Methods: This is a prospective study done in the Department of Pathology, Kempegowda Institute of Medical Sciences. 39 cases diagnosed as HT on FNAC from Jan 2013 to July 2014 formed the study material.

Results: A total of 39 cases were studied. The age ranged from 17-70 years. 38 cases were females. Serologic study showed 25(64%) patients to be hypothyroid and 6(15%) patients had subclinical hypothyroidism. AMA titre was available in 28 cases of which 26 had elevated titres. In the present study, majority of the patients had grade 2 (43%) and grade 3 (49%) thyroiditis.

Conclusion: FNAC is a simple, cost effective and specific diagnostic tool in HT. Cytologic grading helps in assessing the severity of the disease and can predict thyroid functional status.

Keywords: Hashimoto's thyroiditis, cytological grading, AMA

Introduction

Hashimoto's thyroiditis (HT) was first described by Hakaru Hashimoto in 1912[1].It is the second most common thyroid lesion diagnosed on FNAC after goitre.[2]. It is common in women and has prevalence rate of 1-4% and incidence of 30-60/1 lakh population per year[2].

HT is a leading cause of hypothyroidism in areas of the world where iodine levels are sufficient. Iodine supplementation in iodine deficient areas increases the prevalence of lymphocytic infiltration of the thyroid by three-fold. Also the prevalence of thyroid autoantibody positivity in such areas rises to over 40% within 5 years of initiating supplementation[3].

HT is a classic form of autoimmune thyroiditis beginning with activation of CD4+ T cells which initiate the recruitment

of auto-reactive B cells that secrete a variety of thyroid antibodies, important ones being antithyroglobulin antibody, antimicrosomal antibody (AMA) and TSH blocking antibody. Of these, AMA levels correlate best with degree of lymphocyte infiltration.[4]
HT is characterised by Hurthle cell change and increased number of mature and transformed immature lymphocytes impinging on follicular cells[5,6].
Diagnosis of HT is based on clinical, cytomorphological and serologic parameters. FNAC of thyroid provides a safe and accurate method for diagnosis of HT. Although cytomorphologic criteria for HT are well established, many cases go undiagnosed due to scant material yield on FNAC. The importance of a combined cytomorphologic and serologic approach in the evaluation has been emphasised. The utility of FNA in the diagnosis of seronegative HT is also highlighted and the technique remains the gold standard in its diagnosis[3].
In the present study, cytomorphological analysis of HT was done and correlated with clinical findings and serologic parameters.

Materials and methods

This is a prospective study done in the Department of Pathology, Kempegowda Institute of Medical Sciences. 39 cases diagnosed as HT on FNAC from Jan 2013 to July 2014 formed the study material. Relevant clinical details like age, sex, clinical presentation and nature of thyroid enlargement were noted. FNAC was performed in the supine position with neck extended using a 23-gauge needle attached to a 10 ml syringe. Air dried and ethanol fixed smears were made and stained with May-Grunwald-Giemsa, Hematoxylin and eosin and Papanicolaou method.
A detailed examination of the cytologic smears was done and features like cellularity, amount and nature of colloid, Hurthle cell change, anisonucleosis of follicular cells, spectrum of reactive lymphoid cells and other inflammatory cells like eosinophils, macrophages, giant cells and epithelioid cells were noted.
Cytologic grading of thyroiditis was done according to the Bhatia et al grading. (Table 1)
Thyroid function tests were done using COBAS E analyser. AMA titres were detected by chemiluminiscence assay. Values > 40 IU/ml were considered positive.

Table 1: Grading of thyroiditis- Bhatia et al[4].

Grades	Morphologic Features
0	No lymphoid follicles
I	Few lymphoid cells infiltrating the follicles Increased number of lymphocytes in background
II	Moderate lymphocytic infiltration with Hurthle cell change/ giant cells/ anisonucleosis
III	Florid lymphocytic infiltrate with germinal center formation, very few follicular cells left

Results

In the present study, patients' age ranged from 17-70 years. 38 of the 39 cases were females. 32(82%) patients presented with diffuse thyromegaly. Clinical diagnosis of thyroiditis was given in 12 (30.7%) cases.
Serologic study showed 25(64%) patients to be hypothyroid and 6(15%) had subclinical hypothyroidism, while the rest (21%) were euthyroid. AMA titre was available in 28 cases of which 26 patients had elevated titres.
The cytomorphological features are summarised in table 2.

Table 2: The cytomorphological features.

Cytomorphologic Findings	Percentage of Cases
Cell yield	low-7.6%, moderate-53.8%, high-38.6%
Hurthle cells	92.7%
Plasma cells	64.1%
Centroblasts	76.9%
Immunoblasts	74.3%
Anisonucleosis	97.4%
Eosinophils	20.1%
Macrophages	61.5%
Giant cells	41%
Epithelioid cells	33%
Colloid	82%

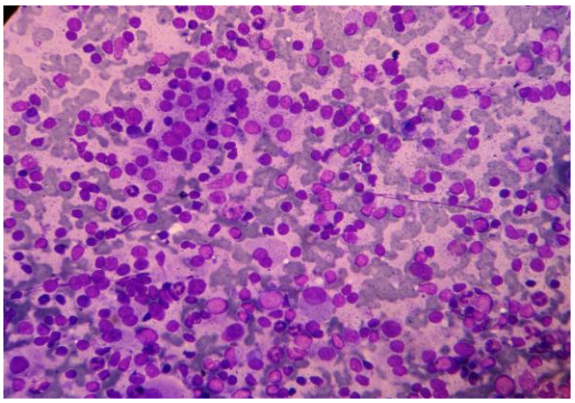

Figure 1: Polymorphous lymphoid population (MGG, 40x).

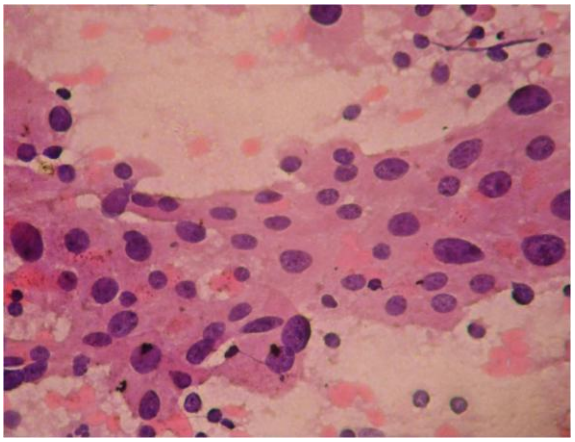

Figure 2: Hurthle cells (H&E, 100x).

Table 3: Cytological grading of thyroiditis.

Grade	Percentage
I	8%
II	43%
III	49%

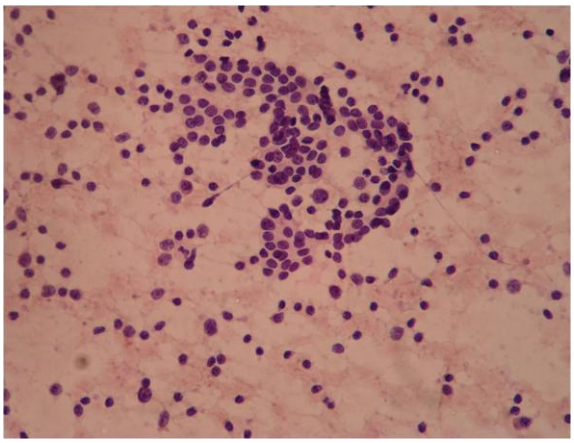

Figure 3: Grade I thyroiditis (PAP, 100x).

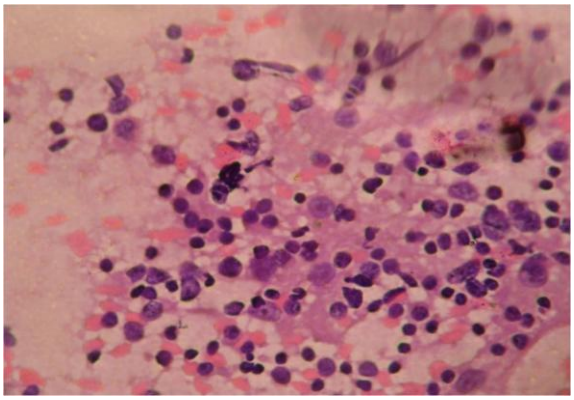

Figure 4: Grade II thyroiditis (H&E, 400x).

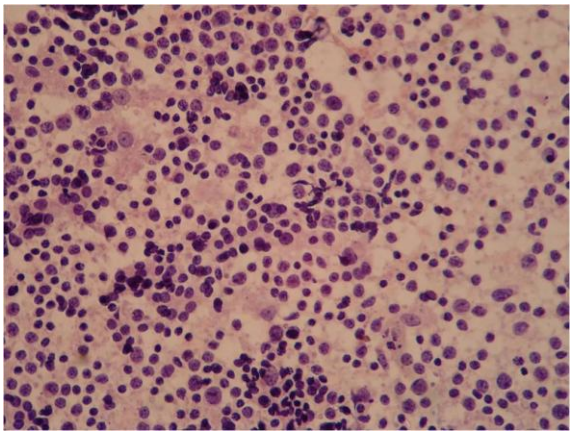

Figure 5: Grade III thyroiditis (PAP, 100x).

The association between hypothyroidism and cytologic grade of thyroiditis was studied (table 4).

Table 4: Cytologic grade of cases showing serologic hypothyroidism (n=25)

Grade	No. of cases
I	1
II	9
III	15

The association of AMA titres with cytologic grading was studied. Of the AMA positive cases, 8(31%) of these cases were found to have grade II thyroiditis while 16(62%) of them showed grade III thyroiditis on cytology.

Table 5: Association of cytologic grade with AMA titres (n=28).

AMA status	Grade		
	I	II	III
Positive(n=26)	2	8	16
Negative(n=2)	-	2	-

Discussion

HT is an autoimmune disease characterised by destruction of thyroid follicles. It is important to diagnose HT as patients subsequently become hypothyroid and require lifelong thyroxine supplementation. Also there is an increased risk of extranodal marginal B cell lymphoma and thyroid carcinoma in these patients which emphasises the need for long term follow up.[6,7]

The present study was designed to analyse the cytomorphological features of HT and correlate it with serological parameters.

Female predominance has been observed in our study with most of the patients being < 50 years of age (87%). The classic age group described in HT is 30-50 years.[4] Diffuse thyromegaly was the most common presentation(82%) which is in concordance with reports in literature.[8] Jayaram et al[9] reported nodular presentation in 33% of patients with HT whereas Friedman[10] et al found nodular presentation in 80% of their patients. Nodules represent early stage of the disease when the clinical and hormonal changes are not established[4].

Hormonal assay showed 64% of patients to be hypothyroid.15% of them were found to have subclinical hypothyroidism which is higher when compared to a study by Bagchi et al[11] who reported an incidence of 8.17%. 26 of 28 (92.8%) patients had increased AMA levels which is similar to published reports by Jayaram et al[5].

The cytological diagnosis of HT was based on evidence of inflammatory destruction of follicular epithelial cells by the lymphocytes in association with varying degrees of Hurthle cell change. The findings observed are compared with previous studies (Table 6).

Majority of the patients had grade 2 (43%) and grade 3 (49%) thyroiditis. This is similar to the studies by Jayaram et al[5] and Singh et al.[1] (Table 7).

Table 6

Cytologic features	Jayaram et al. %	Singh et al. %	Present Study %
Hurthle cells	56	72.7	92.7
Anisonucleosis	44	45	97
Plasma cells	40	55	64.5
Epithelioid cells	16	56	33
Macrophages	-	58	61
Giant cells	39	38	41

Table 7

Authors	No. of patients	Age in years	Females	Grade
Jayaram et al	51	40-50	40	Grade I-13.5% Grade II- 62.2% Grade III- 24.3%
Bhatia et al	76	6 -60	70	Grade I-38.7% Grade II-44% Grade III - 17.3%
Singh et al	150	9-65	140	Grade I- 18% Grade II-26% Grade III- 56%
Present study	39	17-70	38	Grade I-8% Grade II-43% Grade III-49%

Biochemically hypothyroid cases showed high association with grade II and grade III thyroiditis which is in concordance with a study by Uma et al.[12] Similarly, the AMA positive cases also showed higher cytologic grade.

In a study by Guarda and Baskin,[13] only 67.9%(36/53)patients had positive antibodies in their serum. They reported that morphologically the antibody positive cases are indistinguishable from antibody negative cases. In our study, the 2 AMA negative cases did not vary in cytology from the AMA positive cases. Negative serology in HT causes a considerable diagnostic dilemma. However, it is well documented now that localised intra thyroid immune destruction occurs much earlier than the serologic evidence. Antibody titres may change with time ,but cytomorphologic features persist during the course of HT[4].

Conclusion

FNAC is a simple, cost effective and specific diagnostic tool in HT. Cytologic grading helps in assessing the severity of the disease and can predict thyroid functional status. Though serology is a useful adjunct in the diagnosis of HT, in antibody negative cases or biochemically euthyroid cases, FNAC remains the gold standard for diagnosis. In a proper clinical setting, diagnosis of HT may be considered on cytological evidence alone even if antibody titres are negative.

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