

Cytological Diagnosis of Hashimoto's Thyroiditis Revealing the Increased Frequency than Expected: A Retrospective Study of 750 Thyroid Aspirates

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ABSTRACT

Background: Hashimoto's thyroiditis (HT), an autoimmune disease is the commonest cause of hypothyroidism in iodine sufficient areas of the world. Fine needle aspiration cytology (FNAC) is the gold standard for the diagnosis of this condition.

Aims: To assess the frequency of HT in total number of thyroid aspirates on the basis of cytomorphology and correlate it with clinical history, radiological findings, thyroid hormone status and antithyroid antibody titres wherever available.

Material and methods: At a tertiary level teaching hospital in north India we retrospectively analysed 750 thyroid aspirates and found 58 HT in these on cytomorphology. Clinical findings, thyroid function and thyroid peroxidase (TPO) antibody profile were correlated with cytomorphological features. We further subdivided it in different age and sex groups to assess the frequency in all these groups.

Results: Fine needle aspiration smears were satisfactory for evaluation in all cases with HT. frequency of HT was more than expected, 58 (7.73%) out of total 750 aspirates. Most patients with HT were women 50 (86.21%) and in 2nd to 3rd decades. Diffuse goitre was the commonest 41 (70.69%) presentation. Hypothyroidism was the commonest 35 (60.34%) feature. Anti TPO antibodies were elevated in 10/12 (83.33%) patients.

INTRODUCTION

In 1912, Haskar Hashimoto was first to describe a chronic disorder of thyroid gland and called it as *struma lymphomatosa*, which bears his name Hashimoto's thyroiditis (HT) later.¹ HT may usually be considered a synonym of chronic lymphocytic thyroiditis or autoimmune thyroiditis.² It has a prevalence rate of 1 – 4% and incidence of 3 – 6/10,000 population per year, the second most common lesion of thyroid diagnosed by cytology, next to endemic goitre.^{3,4} This is an autoimmune disorder affecting women more commonly than men. Diffuse thyroid enlargement is the usual presenting feature, but asymmetry may occur with localized nodular enlargement.⁴ It may be associated with hypothyroidism, euthyroidism or occasionally transient hyperthyroidism but ultimately hypothyroidism develops gradually.³

Fine needle aspiration cytology (FNAC) is highly sensitive in diagnosing HT, with a diagnostic accuracy rate of 92%.⁴ The diagnosis of HT on FNAC smears is made by finding the oxyphilic transformation of epithelial cells (Hurthle cells), infiltration of follicles by lymphocytes and plasma cells, presence of moderate number of it in background with scanty or absence of colloid.⁵

To diagnose HT FNAC is considered superior as well as more cost-effective than antibody screening.⁵⁻⁷ However, there are certain pitfalls of FNAC in diagnosing HT, it may be missed in smears showing abundant colloid or cytologic evidence of

Classical HT was seen in 40 (69%) and florid lymphocytic thyroiditis pattern in 18 (31%) patients.

Conclusion: Hashimoto's thyroiditis is more frequent than expected, especially in women of younger age groups.

Keywords: Fine needle aspiration cytology, Hashimoto's thyroiditis, Thyroid.

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hyperplasia.³ Lymphocytic infiltration of the gland in Grave's disease, marked Hurthle cell change with sparse inflammatory cells mimicking Hurthle cell neoplasm and lymphoma in older patients may result in an overlap of cytological appearances with HT.⁵

We observed that there was more frequent diagnosis of HT on cytology than expected by earlier data. This prompted us to undertake this study to assess if there was any rise in frequency of HT in this region by adhering the strict cytomorphological criteria for diagnosis and correlating it with clinical history, radiological findings, thyroid hormone status and antithyroid antibodies profile wherever available.

MATERIAL AND METHODS

Patients with thyroid swellings were referred to department of pathology for FNAC during May 2008 – April 2016. A proper written consent was obtained from each patient. Aspiration/non-aspiration technique was used. FNA was done with standard technique using aseptic precautions, 10cc/20cc disposable syringe and 23 gauge needle. Two to four rapid passes were given. Air-dried smears were stained with May-Grunwald-Giemsa stain and wet ethanol fixed smears were stained with Papanicolaou stain and hematoxyline & eosine stains. Cases in

which, smears were unsatisfactory, a repeat aspiration was done. The diagnosis of HT on FNAC was based on finding lymphocytic infiltrates in clusters of follicular epithelial cells, Hurthle cell changes, anisonucleosis, increased number of lymphocytes in the background with or without lymphoid follicles, multinucleated giant cells and scanty or absence of colloid.^{1,5} Hurthle cells are large cells forming small syncytial aggregates, having well defined abundant finely granular eosinophilic cytoplasm, nuclei larger than normal and much more variable in size.^{5,9}

Data was collected age, gender, diffuse/nodular enlargement of thyroid, radiological findings, thyroid function, antithyroid antibodies, family history of HT and other autoimmune diseases and analyzed in correlation with cytomorphological findings.

Table 1: Age and sex distribution of 58 patients with Hashimotos thyroiditis

Age groups (years)	Male	Female	Total
10 - 20	4	17	21
21 - 30	0	18	18
31 - 40	1	8	9
41 - 50	1	5	6
51 - 60	1	2	3
61 - 70	1	0	1

Table 2: Clinical and laboratory findings in patients with Hashimotos thyroiditis

Frequency	7.73%
Female : Male	6.25 : 1
Nodular presentation	13.70%
Most common age group	2 nd – 3 rd decades
Thyroid function	Available in 51 patients (87.93%)
Hypothyroid	22 (37.93%)
Euthyroid	35 (60.34%)
Hyperthyroid	1 (1.72%)
Antithyroid antibodies	Available in 12 patients (20.69%)
Elevated anti TPO antibodies	10 (83.33%)

Table 3: Frequency of cytomorphological features in patients with Hashimotos thyroiditis

Cytomorphological features	Number of patients
Increased background lymphoid cells	58
Lymphocytic infiltration of follicles	45
Hurthle cell changes	42
Anisokaryosis	52
Giant cells	7
Presence of colloid	4
Plasma cells	4
Histiocytes	3
Eosinophils	2

RESULTS

We included 750 thyroid aspirates, 603 (80.40%) were females and 147 (19.60%) were males with F:M ratio 4.10:1. All the patients aspirated, had a history of goitre.

Out of these 750 thyroid aspirates 58 (7.73%) were diagnosed as HT, 50 (86.21%) females and 8 (13.78%) males with F:M ratio 6.25:1 (Table-2), their age ranged from 10 to 60 years (mean age female, 35 years and males 38 years) with majority in 2nd to 3rd decades of life (Table-1).

On examination at the time of FNAC 41 (70.69%) had diffuse goitre, 16 (27.59%) had uneven enlargement of thyroid and 1 (1.72%) had solitary nodule. Thyroid hormone evaluation was done in 51 (87.93%) patients, which revealed 22 (37.93%) hypothyroid, 35 (60.34%) euthyroid or had subclinical disease and 1 (1.72%) hyperthyroid. The serum TPO antibody titre were determined in 12 (20.69%) patients, values were elevated in 10 (83.33%) and normal in 2 (16.67%). Ultrasonography (USG) was done in 40 patients showed diffusely enlarged thyroid with heterogenous echotexture in 25 (62.50%) and micronodules in 12 (30%), dominant nodule in 2 (5%) and echogenic septation in 10 (25%).

FNAC was performed from multiple sites. (Table-3) shows the frequency of cytomorphological features. Increased background lymphoid cells on smear was observed in all 58 cases (Fig-1), lymphocytic infiltration of follicular epithelial cells in 45 (Fig-2), Hurthle cell changes in 42 (Fig-3), plasma cells 4, histiocytes 3 (Fig-4) and colloid was present in only 4 cases.

DISCUSSION

Hashimoto's thyroiditis is an autoimmune chronic inflammatory disease of the thyroid gland.⁹ It involves lymphocytic infiltration of thyroid gland which is reactive to thyroid antigens. Activated B – lymphocytes secrete autoantibodies and cytotoxic T-lymphocytes are largely responsible for destruction of thyroid follicles. Gradually in course of disease the thyroid parenchyma is totally destroyed and replaced by fibrosis. During active phase of destruction there are transient clinical manifestations of thyrotoxicosis due to rapid release of hormones, but ultimately as the gland parenchyma is being replaced by inactive cells and fibrosis the subclinical and overt hypothyroidism ensues.

The incidence of Hashimoto's thyroiditis seems to be increasing in the recent times. In a study conducted by Marwaha RK et al, among 764 goitrous girls 10 to 18 years age from different states of India, 5.6% of them have diagnosed to have HT on the basis of FNAC.¹⁰ A study conducted by Benvenga et al, concluded that HT has become 10 times more common than it was until the early 1990.¹¹ Another study by Zois et al, among school children has shown a three times increase in the incidence of autoimmune thyroiditis compared to a similar survey done 7 years earlier.¹² In the present study we included 750 successful thyroid aspirates out of which 58 were diagnosed as ht on cytology, which is quite higher than the earlier documented prevalence of 1-4%.³ Marwaha RK et al, conducted their study on girls of 10 to 18 years and found 5.6% HT among them, in recent study 73 goitrous thyroid were aspirated in this age group and ht was found in 14 (19.18%). Iodine induced thyroiditis has been well documented in animals,¹³ whereas in humans the prevalence of autoimmune thyroiditis is correlated with high iodine intake.¹⁴ Many studies reported increase in prevalence of elevated serum antithyroid antibodies titre and lymphocytic infiltration on cytology and histopathology after introduction of iodine prophylaxis.¹⁵⁻²⁰ Across the world, with advent of iodization, autoimmune thyroid disease has become the most common cause of hypothyroidism.²¹

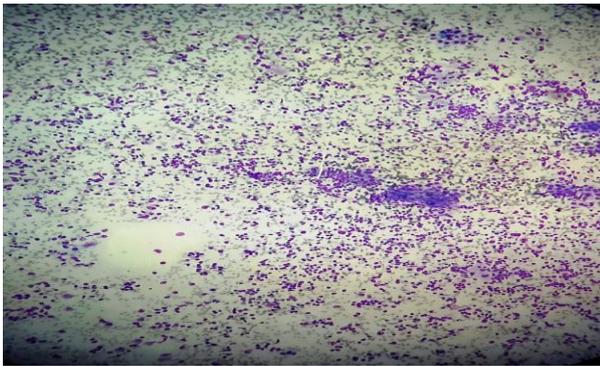


Fig 1: Hurthle cells with increased background lymphocytes (May-Grunwald-Giemsa stain, x100)

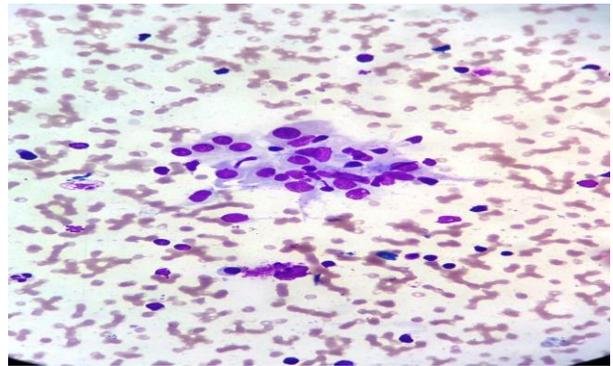


Fig 2: Lymphocytic infiltration in follicular epithelial cells (May-Grunwald-Giemsa stain, x400)

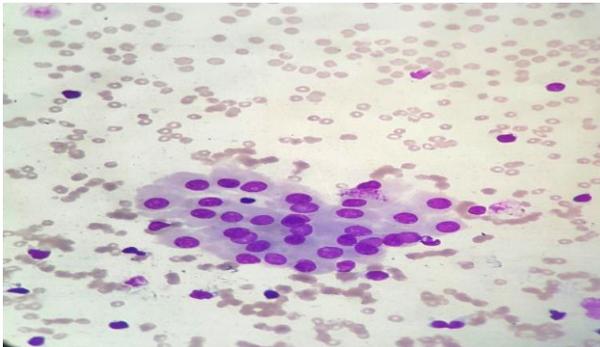


Fig 3: Hurthle cell changes of follicular epithelial cells (May-Grunwald-Giemsa stain, x400)

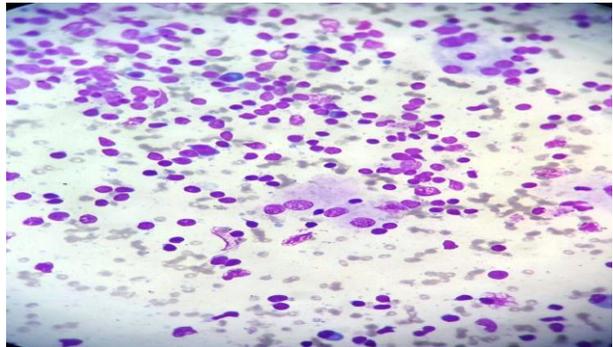


Fig 4: Plasma cells and histiocytes in the background (May-Grunwald-Giemsa stain, x400)

The diagnosis of HT is important because the patient can become hypothyroid and will need lifelong thyroxine supplementation. The prevalence of hypothyroidism in India is higher (11%) in comparison to UK (2%) and USA (4.6%).²¹ There is also an increased risk of extranodal marginal B-cell lymphoma in patients with HT. The frequency of carcinoma in patients with HT varies between 0.5 and 23.7%.⁴ This emphasises the need for diagnosing HT so that the patients can be on long term follow up. In the present study, out of 52 patients, maximum (n=39) were in 2nd and 3rd decades (Table-1). This is in contrast to the study by Vanderpump et al, in which patients were mainly older women with a mean age at diagnosis being 59 years.²² According to Bhatia et al, majority of patients were in 3rd and 4th decades.¹ This disparity may be due to the occurrence of HT in young patients in iodine sufficient areas such as ours. This is similar and supported by a study conducted by Chandanwale SS et al, in which most affected patient with ht were in 2nd, 3rd and 4th decades.²³ Most patient had diffuse enlargement of thyroid (n=41), uneven enlargement was present in only 16 patient with one had solitary nodule. According to previous reports on HT, nodular presentation was seen in about one third of cases (33%). Transformation from diffuse to nodular goitre may be due to the process of regeneration and retrogression. Maximum number of patients were euthyroid 35 (60.34%) in our study it is understandable due to most patients were of younger age group and early stage of disease at the time of diagnosis. Raised levels of TSH with normal T3 & T4 indicates subclinical hypothyroidism and represents evolutionary phase of the disease. Hypothyroid including subclinical forms were 22 (37.93%) in our study. Transient hyperthyroid state of HT is due to acute aggravation of thyroid autoimmunity induced destruction of thyroid follicles called as Hashitoxicosis,²⁴ found in only one case in our study.

Antithyroid antibody estimation was done only in 12 (20.69%) patients and serum TPO antibody titres were elevated in 10/12 (83.33%) patients. Previous studies reported raised titres in up to 95% of the patients.²⁵ About 20% adult females without any clinical disease have detectable TPO/Tg antibodies, raising suspicion in its diagnostic value. With proper clinical examination and presentation, the diagnosis of HT may be considered on cytology alone even if antibody titres are negative.³

There are two pattern of HT in cytology

1. Classical HT: seen mostly in older patients, usually hypothyroid, cytology smears shows increased background lymphocytes, infiltration of follicular epithelial cells with or without Hurthle cell changes and colloid remains scanty or absent.
2. Florid lymphocytic thyroiditis: seen mostly in young patients, shows mixed population of numerous lymphoid cells as in reactive lymphadenopathy, epithelioid cells may be scanty.^{5,26} In our study classic HT was seen in 40 (69%) patients and florid lymphocytic thyroiditis was seen in 18 (31%) patients, out of which 13 patients were in 2nd decade, 4 patients in 3rd decade and only one in 5th decade of life. This is explainable on the basis of most patients with HT in our study are of 2nd and 3rd decade of age group and occurrence of florid lymphocytic pattern in younger individuals, and close to the study by Chandanwale SS et al.²³

Despite superiority of FNAC in diagnosing HT, have some diagnostic pitfalls. De Quervain's thyroiditis can be a close differential diagnosis on cytomorphology which can be differentiated with mixed inflammatory cell reaction, epithelioid cells, large multinucleated giant cells and degenerating follicular cells on dirty background.

Distinction of autoimmune thyroiditis from lymphoma can be difficult at times specially in adults and elderly. The help can be from age of patient as florid lymphocytic pattern which is closest to

the lymphoma is common in young patients and lymphoma in adults and elderly. Flow cytometry to demonstrate the monoclonality may be needed for confirmation of diagnosis.

Studies suggest frequency of carcinoma in patients with HT between 0.5 – 23.7%.⁴ Lymphoma of thyroid arises in the background of HT. In our study there was no associated malignancy, reason can be explained with the fact that most of our patients were in the younger age group at the time of diagnosis and no significant long term follow-up was available.

CONCLUSION

We report here the increased frequency of HT in different age groups on the basis of cytomorphological study which is gold standard for diagnosing HT, also correlated with clinical history, radiological findings, thyroid hormone status and antithyroid antibody titres wherever available. We also found that HT 6 to 7 times more frequent in females than in males and unexpectedly large number of individuals are of younger age group and mostly females. HT is the most common cause of hypothyroidism in non-endemic areas. Untreated or inadequately treated hypothyroidism in pregnant women can compromise foetal neurocognitive development. So, early diagnosis and treatment will prevent irreversible mental retardation in a large number of newborns.

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