HASHIMOTO'S THYROIDITIS, PRESENTING PATTERNS IN SULAIMANI

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ABSTRACT

Background

Hashimoto's thyroiditis (HT) is a common chronic autoimmune thyroid disease, affecting mostly young and middle-aged females. It causes painless, firm, diffusely enlarged thyroid gland. The clinical presentations and thyroid status are variable. The anti-thyroid autoantibodies and fine-needle aspiration (FNA) cytology with lymphocytic infiltration with Hurthle's cells are pathognomonic.

Objectives

To assess the pattern of Hashimoto's thyroiditis in Sulaimani city, investigating the patients' characteristics, clinical presentations, thyroid status and diagnosis and if these are mosaic, i.e. a mess or proper and organized like Messi.

Patients and Methods

A cross-sectional, descriptive study was carried out in Sulaimani Teaching Hospital, Iraq, from October 2014, to October 2015. The study enrolled eighty patients with Hashimoto's thyroiditis.

Results

The mean age of the patients was 36.7 years. There was only one male patient. Only a quarter of patients had weight gain, but more than that (30%) had weight loss. The firmly diffuse enlarged gland was found in 64 (80%) patients. Over one-third of patients (36.25%) had high ESR. The majority (92.5%) had high anti-thyroid peroxidase antibodies. Variable thyroid status was detected, slightly over half of them were hypothyroid, 30 (37.5%) patients had euthyroid status, and 7 (8.75%) were in hyperthyroid status. Ultrasound scan revealed; hypo-echogenicity (87.5%), enlarged thyroid gland (82.5%), increased vascularity (52.5%) and psuedonodules in (85%) of the patients. Seventy-six patients (95%) had lymphocytic infiltration, and 58 (72.5%) had Hürthle cells.

Conclusion

Hashimoto's thyroiditis has variable clinical presentations and thyroid status, but it causes: hypothyroidism, it is an autoimmune disease, mainly affect women (sex distribution), of middle age, with enlarged thyroid gland, with characteristics ultrasound scan findings, with raised serum antibodies and characteristic lymphocytic cell Infiltration, therefore, has messi.

Keywords: *Hashimoto's thyroiditis, Autoimmune thyroiditis; Autoimmune thyroiditis with the anti-TPO antibody.*

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INTRODUCTION

Hashimoto's thyroiditis (HT) is an autoimmune thyroid disease,[1-3], that affects nearly 5% of the population [2,4] and was first described in 1912 by Hakaru Hashimoto [2]. It is now considered not only the most common autoimmune disease, endocrine disorder but also the most common endocrine disorder and cause of hypothyroidism in the USA [3-6] Worldwide, iodine deficiency in the diet is the most common cause of hypothyroidism [4,5].

Women are at least 8 times more likely than men to have HT [1, 3, 7]. Hashimoto's thyroiditis (HT) occurs mainly during the 5th decade of life [3, 4, 7], and caused by anti-thyroperoxidase (TPO) and anti-thyroglobulin (TG) antibodies, that leads to decrease in thyroid function by the destruction of thyroid tissue [7, 8].

The characteristic histologic features include, atrophic follicles replaced by diffuse lymphocytic infiltration with well-developed germinal centers, and fibrosis [7-12].

The diagnosis of Hashimoto thyroiditis is achieved by a combination of clinical features of goiter, hypothyroidism, the appearance of serum antibodies against thyroid antigens, thyroid ultrasound scan, and the characteristic FNA findings [3, 7].

The prevalence of thyroid nodules on ultrasonography or autopsy is as high as 50%, and that of HT appears to be >10% in patients with thyroid nodules [3, 4, 12, 13].

FNA is carried out when a patient has a thyroid nodule; most of them are true benign tumors [3]. In HT, cytology shows a polymorphic population of lymphoid cells (small mature lymphocytes, larger activated lymphocytes, and occasional plasma cells) accompanied by Hürthle cells (thyrocytes that increase in their size, hyperchromatic nucleus, cytoplasm stained by pink with eosin because it's filled with mitochondria) [7]. Lymphocytes are often associated with thyroid cells; this characteristic feature distinguishes HT from thyroid neoplasms [7, 11, 12].

The aim of this study is to assess the pattern of Hashimoto's thyroiditis in Sulaimani city. Investigating the patients' characteristics, clinical presentations, and diagnosis and if these are mosaic and chaos or proper and organized like Messi.

PATIENTS AND METHODS

Design: A cross-sectional descriptive study which enrolled 80 patients in Sulaimani teaching hospital from October 2014 to October 2015.

The data were collected prospectively regarding biographic aspects of the patients, subjective clinical presentation as local neck symptoms (neck pain, neck swelling, difficulty in swallowing, shortness of breath, and change in voice) and systemic features of hypothyroidism. Data also were collected regarding objective presentations: vital signs, thyroid gland enlargement; diffuse or nodular. Thyroid status (clinical features of hypo and hyperthyroidism).

Investigations including CBC and ESR, thyroid function test: free T3, free T4, TSH, and Anti-TPO antibodies.

Ultrasound-scan of the neck and its detailed findings including the: size if enlarged or not, presence of nodule or nodules or psuedonodules, vascularity and its use as a guide for FNA

FNA cytology recording cellularity, presence of lymphocytic infiltration, besides Hürthle cells and existence of any malignant cell,

Socio-demographic characteristics, clinical features, US findings, and investigations of the patients were shown in tabular form (frequency distribution table). Chi-square tests were used to compare the categorical data between different groups of patients in respect to different variables as patient characteristics, presenting features, US finding, laboratory findings, and FNA cytology. Analysis of variance (ANOVA) test was used for the test significant association of laboratory findings, among different age groups –value <0.05 is regarded as bio statistically significant.

Approval of the ethical committee of Sulaimani College of Medicine is obtained.

RESULTS

The study includes 80 patients of HT in Sulaimani Teaching Hospital, Sulaimani Governorate. Seventy-nine patients, (98.75%) of the total sample, were female with only one male patient (1.25%). The age ranged between 18-66 years, with a mean age of 36.9 years.

The patients' characteristics, clinic laboratory variables are shown in Table 1.

Ultrasound of the neck of the patients shows a valuable finding in this study, Table 2.

FNA cytology was performed for the patients and the cellular characteristics of HT , Table 3.

Variable laboratory findings were detected according to age groups:

Ultrasound scan findings were highly suggestive of the diagnosis of HT, Table 5.

There was a statistically significant relationship between the increased vascularity and thyroid status of the patients, Table 5.

There was a statistically significant relationship between the texture of thyroid on USS and the FNA cytology as shown in table 6.

Anti-TPO antibodies increased in most of our patients which is 74 (92.5%) and there was a statistically significant relationship between the elevated anti-TPO antibody and the duration of the diseases, Table 7.

There was no statistically significant relationship between thyroid status and the level of anti-TPO antibody, Table 8.

FNA cytology study revealed the presence of lymphocytic infiltrations (LI) in 76 cases (95%) and LI with Hürthle cells in 58 patients (72.5%) which were statistically highly significant as shown in Table 9.

Table 1. The frequency & percentage of the variables in this study.

Variables		Frequency	Percentages (%)
Complain			
Symptoms(presentation)	*Neck swelling	28	35
	Shortness of Breath	9	11.25
	Neck pain/discomfort	5	6.25
	Total general symptoms	42	52.5
	Symptoms of Hypothyroid	38	47.5
Duration of the condition(months)	1 - 6	41	51.25
	7 - 12	17	21.25
	13 - 24	9	11.25
	25 - 72	13	16.25
Weight change	No change	35	43.75
	Loss	24	30
	Gain	21	26.25
Change in voice	Hoarseness	35	43.75
Goiter(on examination)	Diffuse	64	80
Lab. Findings			
	WBC >11000cells/cm3	10	12.5
	ESR elevated (> 20 mm/h	29	36.25
Thyroid status*	Hypothyroid	43	53.75
(Thyroid Function tests)	Euthyroid	30	37.5
	Hyperthyroid	7	8.75
Auto-Antibody	Elevated Anti-TPO antibody	74	92.25

***The thyroid status was variable in our study, while hypothyroid; was found in slightly more than half of the patients: 43(53.75), but the anti-TPO antibody was raised in all except 6 cases.**

Table 2. The ultrasound findings in this study.

US Findings		Frequency	Percentages (%)
US Enlargement	Yes	66	83.54
	No	13	16.46
US Texture	Decrease echo	70	87.50
	Homogenous	1	1.25
	Hyper echo	1	1.25
	Normal echo	8	10.00
US vascularity	Normal	21	26.25
	Decrease	17	21.25
	Increase	42	52.50
US Nodularity	Multiple (Psuedonodules)	68	85.00
	Single	12	15.00

Table 3. FNA cytology findings in 80 patients.

FNAB Findings	Frequency	Percentages (%)
Cellularity (mixed)	78	97.50
Lymphatic infiltration	76	95.00
Hurthle 's cells	58	72.50
Malignant cells	1	1.25

Table 4. The relation between the Laboratory findings & age groups.

Lab Findings Mean ± SD	Age group			P-value
	18 - 30 Years	31 - 44 Years	45 - 66 Years	
Hb%	12.83 ± 1.05	12.32 ± 1.36	11.95 ± 1.70	0.10
WBC	7.84 ± 1.96	8.19 ± 2.26	6.84 ± 1.54	0.09
ESR	15.54 ± 9.41	23.31 ± 17.80	32.06 ± 31.26	0.02 *
FT3	4.58 ± 1.84	5.40 ± 3.66	4.23 ± 1.80	0.30
FT4	12.83 ± 7.32	14.57 ± 15.51	16.77 ± 11.19	0.59

***p-value < 0.05 and is statistically significant.**

Table 5. The relation between ultrasound findings & thyroid status of the patients.

US Findings/ Thyroid status		Thyroid status			P-value
		Hypothyroid	Euthyroid	Hyperthyroid	
US Enlargement	Yes	35	25	6	0.99
	No	7	5	1	
US Texture	Decrease echo	38	25	7	0.71
	Homogenous	0	1	0	
	Hyperecho	1	0	0	
	Normal echo	4	4	0	
US Vascularity	No	10	9	2	0.03 *
	Decrease	5	8	4	
	Increase	28	13	1	
US Nodularity	Absent	30	18	4	0.54
	Single	4	7	1	
	Multiple	9	5	2	

*** p-value <0.05 and is significant**

Table 6. The relation between U/S findings & FNA cytology.

US findings		Cellularity		P-value
		Present	Absent	
US Enlargement	Yes	65	1	0.2
	No	12	1	
US Texture	Decrease echo	70	0	< 0.001
	Homogenous	1	0	
	Hyperecho	0	1	
	Normal echo	7	1	
US vascularity	No	20	1	0.64
	Decrease	17	0	
	Increase	41	1	
US Nodularity	Absent	51	1	0.34
	Single	11	1	
	Multiple	16	0	

Table 7. The relation between duration of illness and anti-TPO antibody.

Duration of illness(months)	Elevated(high) Anti-TPO Ab Frequency (No.) Percentage (%)	P-value
1-6	36 45	< 0.001
7-12	16 20	
13-24	9 11.25	
25-72	13 16.25	

Table 8. The relation between thyroid status and anti-TPO antibodies.

Thyroid Status	Anti-TPO antibodies		P-value
	Normal	High	
Hypothyroid	3 (7%)	40(93%)	
Euthyroid	1 (3.3%)	29(96.7%)	0.07
Hyperthyroid	2 (28.6%)	5(71.4%)	

Table 9. The relation between FNA cytology findings and the level of anti-TPO antibodies.

FNA cytology findings	Frequency	Percentage (%)	P-value
Cellularity	73	91.25	<0.001
Presence of LI with Hurthle's cells	57	71.25	
Malignant cells	1	1.25	

DISCUSSION

Gender: In this study HT was more common in women, this fact resembles to other studies [4, 5, 14-17].

Age: the mean age was in the 4th decade of life and this goes with other studies [2, 3, 7].

Local neck symptoms: Over half of the patients presented with local neck symptoms and the rest with symptoms of hypothyroidism. Similar to other studies [3.6, 11, 17].

Bodyweight in this study: was variable and only a quarter of them had weight gain. This is against the classical gain in the body weight of a patient with hypothyroidism [3, 14,17].

Goiter in this study: Thyroid glands were firm and diffusely enlarged in the majority of the patients (80%), this goes with other studies [3, 7,18].

Lab. Findings: Minority of the patients had elevated WBC (12.5%), an elevated neutrophil counts in HT predicts ongoing inflammation, also, a decrease in lymphocyte s is considered to be an indicator of poor prognosis. A neutrophil-lymphocyte ratio had been used as an important parameter in the diagnosis of HT [19].

Over 1/3rd of our patients had elevated ESR and this goes with other studies as an elevated ESR as other acute phase reactants, reflects the presence of and intensity of inflammation [20]

Thyroid status: Variable thyroid status was detected in this study and only slightly over half of them were hypothyroid. Approximately one third were euthyroid, while only 7 (8.75%) of them had hyperthyroidism (hashitoxicosis). A study; most of Hashimoto's patients (75%) were euthyroid at the time of diagnosis, while the remaining have subclinical hypothyroidism [3,4]. While another study revealed that the patients with HT had thyrotoxicosis (hashitoxicosis) initially between 3-24months and later become permanent hypothyroidism [21].

Autoantibody: Elevation of serum anti-TPO antibody is the best marker for confirming the diagnosis [3,7,22]. In this study, the majority of the patients (92.5%) had high anti-TPO antibodies titer and this result resembles other studies in which 95% of patients with HT have high anti-TPO antibodies [3, 7, 23].

Antibodies & Duration of the disease: In this study over 1/3rd of patients with short duration of illness had high anti-TPO antibody titer, This is maybe due to silent HT and those patients had this disease for long period without any clinical manifestations and this is similar to other studies [24, 25]. Our finding does not go with a classical time of presentation of anti-TPO antibodies in other studies where anti-TPO antibodies characterize by a later adaptive immune reaction. [26] In 13 cases (16.25%) had high antibodies titer and their durations of illness were over 2 years and this is as in other studies [27]. There is a strong relationship between high anti-TPO antibody and hypothyroid status which

was found in half of our patients and this resembles the result of other studies [28].

USS &HT: In this study ultrasound scan (USS) shows typical features of HT like other studies [19,22] . There is a strong correlation between lymphocytic infiltration and decrease echogenicity of the thyroid gland (hypo-echoic) with peudonodules with ill-defined margins (Giraffe pattern) [29] , which were found in the majority of the patients(85%). These results were similar to other studies [30]. Only 15% of the patients had a single nodule, with high anti-TPO antibodies in their serological investigations; whether those patients had 2 pathological thyroid diseases or both findings are correlating to the HT as one pathology. This is the same difficulty found in other studies [31], for that reason, FNA cytology is highly indicated in these cases.

FNA &HT: Lymphocytic infiltration(LI) is the most common cytological finding and was detected in most of our patients which cause destruction and replacement of thyroid follicular cells as a similar result were detected in other studies [14,32]. Furthermore, Three-quarter of the patients had positive FNA cytology for both (Lymphocytic infiltrations and Hürthle cells). Almost all of them were benign. Only one case was suspicious for malignancy and this is similar to the study [33].

Lymphocytic infiltration & thyroid status: The LI of the gland associated with hypothyroid status in more than half of patients and this result different from other studies where LI associated with hyperthyroidism [3,7]. This hyperthyroid status due to autoimmune reaction and destructive inflammation and release of already stored thyroid hormone and does not relate to thyroid gland hyperfunction [4, 3, 30, 33] .

Hurtle cell Dilemma ?Absence of lymphocytic infiltration with positive Hürthle cells in FNA cytology in one patient (1.25%) made the diagnosis difficult to distinguish whether these Hürthle cells are associated with HT or other cause of Hürthle cell conditions (Hürthle cells adenoma or carcinoma). This is also found in other studies [1,12], our result was suspicion of malignancy and thyroid surgery for proper histo-pathological examination was performed similar to other studies where they performed surgery when in doubt [33, 34],

In conclusion; Hashimoto's Thyroiditis has MESSI.

H= Hypothyroidism.(not all patients)

A= Autoimmune disease

S = Sex (gender); predominantly affects females.

M=Middle aged patient, 4th decade of life, but may affect any age group

E = Enlarged thyroid gland (Goiter) (some has a normal size or even atrophic thyroid gland

S = Serum anti- TPOAntibody is present in the majority of the patients

S = Sonography – very characteristics and highly suggestive (Giraffe skin pattern)

I= Infiltration of lymphocytes, & Hurthle cells are very important & hallmark for FNA cytological diagnosis. Hurthle cells - very suggestive for diagnosis especially if associated with lymphocytic infiltration, but if present alone may raise the suspicion of tumor.

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