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Hashimoto thyroiditis in children and adolescents: evaluation of clinical and laboratory findings

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Summary

Aim: The objective of this study was retrospective analysis of clinical and laboratory findings of children and adolescents with Hashimoto thyroiditis.

Material and Method: We evaluated 78 patients with HT who were between 4-17 years of age. Physical examination and family history of the patients, thyroid functions, auto-antibody titers and USG scans were evaluated retrospectively.

Results: Two (2.6%) patients presented with hyperthyroidism, while 10 (11.7%), 17 (21.8%) and 49 (62.8%) patients presented with hypothyroidism, subclinical hypothyroidism and euthyroidism, respectively. The major symptoms included nervousness, sweating, weight gain and loss of appetite. Sixty-three (80.8%) patients had goiter and 52 (66.7%) patients had positive anti-thyroid peroxidase antibody at the time of diagnosis. Among the 19 patients who were euthyroid initially, 2 patients became hyperthyroid, 1 became hypothyroid and 1 became subclinically hypothyroid during follow-up. Familial history of thyroid disease was found in 31 (39%) patients.

Conclusions: Clinical and laboratory findings may vary at the time of diagnosis and during follow-up in children and adolescents with HT. Periodic monitoring of the patients is very important. *(Turk Arch Ped 2011; 46: 309-13)*

Key words: Adolescent, child, Hashimoto, thyroiditis

Introduction

Hashimoto thyroiditis (HT) which is also known as chronic lymphocytic thyroiditis or autoimmune thyroiditis was defined for the first time in 1912 by Hakaru Hashimoto as a result of examination of thyroid tissues obtained by autopsy (1,2). In areas where endemic iodide deficiency is not prevalent, it is the most frequent cause of hypothyroidism (2,3). It is observed more frequently in girls and in individuals with genetic tendency (4,5). The diagnosis of Hashimoto thyroiditis is made by determining increased thyroid antibodies in serum and/or findings of fine-needle aspiration biopsy (6). Most patients present with goiter without complaints and pictures of euthyroidism, hypothyroidism or hyperthyroidism can be observed at presentation (2,6,7).

The objective of this study was retrospective analysis of clinical and laboratory findings of children and adolescents with Hashimoto thyroiditis.

Material and Method

78 patients (67 female and 11 male) between 4 and 17 years of age who were diagnosed as HT in our Pediatric Endocrinology Clinic between 2003 and 2009 with a mean follow up period of 14.5±5.7 (mean ±standard deviation) were included in this study. The diagnosis of Hashimoto thyroiditis was made by demonstrating anti-thyroid antibodies in sera of the patients with goiter and/or abnormal thyroid function tests.

Age, gender, complaints at presentation, family history, clinic and laboratory properties and physical examination and laboratory findings at follow-up visits were examined retrospectively in all subjects. The patients whose thyroid function tests and anti-thyroid peroxidase (anti-TPO) antibody levels were examined were divided into groups as euthyroid (normal T4 and TSH levels), hypothyroid (low T4, high TSH), subclinical hypothyroid (normal T4, high TSH) and hyperthyroid (high T4, suppressed TSH) according to thyroid

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function tests at the time of diagnosis and during follow-up. Thyroid function tests and anti-thyroid antibodies were studied using ECLIA (Electrochemiluminescence immunoassay) method with Beckman Coulter Dx1800 device and with the kit compatible with the device (Beckman Coulter Access kit, USA). Ultrasonographic examination of the thyroid was performed by the same specialist radiologist using the device with the trademark Esaote MPX796FD2. On thyroid ultrasonography, the volume of the thyroid was calculated with the Formula of width x length x deepness x 0.523 and the values above the 97th percentile according to age were considered as goiter (8,9).

SPSS-15,0 package program was used for statistical analysis. Mean, standard deviation and percentages were calculated as descriptive statistics. For statistical comparison Kruskal Wallis was used to compare multiple groups, Mann-Whitney U and Qui-square tests were used to compare paired groups. A p value <0.05 was considered to be significant.

Results

67 (85.9%) of the subjects included in the study were female and 11 (14.1%) were male. 3 of the male subjects (27.3%) were in the puberty at the time of diagnosis. The frequencies of complaints of the subjects at the first presentation are shown in Table 1. The most common complaints at presentation included nervousness, excessive sweating, weight gain and loss of appetite.

Table 1. Distribution of the patients by clinical findings

Complaint	Number of patients (n)
Nervousness	21 (26.9%)
Excessive sweating	11 (14.1%)
Loss of appetite	7 (8.9%)
Weight gain	7 (8.9%)
Hair loss	6 (7.6%)
Palpitations	4 (5.1%)
Constipation	3 (3.8%)
Hyperactivity	1 (1.2%)
Short stature	1 (1.2%)

The mean thyroid hormone levels and antibody levels of the patients at the time of presentation were found to be as follows: fT4: 0.039 ±0.25 ng/dL, TSH: 0.45±0.55 µIU/mL and anti-TPO: 464.4±585 IU/mL. While antiTPO was found to be positive in 52 subjects (66.7%) at the time of diagnosis, hypertyroidism was found in 2 of the subjects (2.6%), hypothyroidism was found in 10 of the subjects (11.7%), subclinical hypothryoidism was found in 17 of the subjects (21.8%) and euthyroid state was found in 49 of the subjects (62.8%). Gender, age, the presence of goiter and anti-TPO levels of the patients according to thyroid function state are shown in Table 2. When the subjects were compared according to thyroid function, no significant difference was found in terms of anti-TPO levels, age and gender ($p<0.05$), but the rate of euthyroid patients was found to be significanly higher among the subjects who were found to have goiter (p=0,022). Thyroid volumes according to ages for the patients with goiter and without goiter are shown in Figure 1 and Figure 2.

When the subjects were evaluated according to gender and the state of puberty, no difference was found in terms of the frequency of goiter at the time of presentation ($p<0.05$) (Table 3).

While treatment was given to 52 of the subjects (66.7%) just after the diagnosis, 26 subjects (33.3%) were followed up without treatment. 28 patients (51.8%) were given treatment for the aim of suppression, 16 patients (30.8%) were given treatment because of subclinical hypothyroidism, 6 (11.5%) were given treatment because of hypothyroidism and two patients were given treatment because of hyperthyroidism (3.8%).

In 25 of 29 subjects who were followed up more than one year, goiter was found at the beginning. In 15 of these patients (60%), goiter was observed to be disappeared in the follow up. During the follow up of the patients who were not given treatment, treatment was started because hyperthyroidism developed in 2 patients, hypothyroidism developed in one patient and subclinical hypothyroidism developed in another patient. Thyroid states during follow up and after treatment in the subjects who were followed up for more than one year are shown in Table 4.

Table 2. Comparison of gender, age, frequency of goiter and antibody levels of the subjects according to thyroid function

	Hyperthyroidism	Hypothyroidism	Subclinical hypothyroidism	Euthyroidism	p
Number of patients n (%)	2 (2.6%)	10 (12.8%)	17 (21.8%)	49 (62.8%)	0.120
Gender					
Female	20	10	16	39	0.127
Male	0	0	1	10	0.206
Mean age (years)	11.8±0.2	11.1±2.2	12.7±2.0	12.3±3.0	0.311
Goiter (+)	1	7	13	42	0.022
Goiter (-)	1	3	4	7	0.436
Anti-TPO (IU/mL)	212	489±644	573±636	426±570	0.542

Thyroid ultrasonography was performed in all patients. While thyroid USG was found to be normal in 19 patients (26.8%), heterogeneity was found in 46 patients (66.2%) and nodule was found in 5 patients (7%). Fine needle aspiration biopsy was performed in 4 patients because of nodule and appearance compatible with lymphocytic thyroiditis was found in all of them.

Urinary iodide excretion was evaluated in 19 of the patients. Iodide deficiency was found in 13 (68.4%) patients and necessary recommendations were made. In 31 of the subjects (39%), a familial history of HT or idiopathic hypothyroidism was present. Other autoimmune diseases were not found in any of our subjects.

Discussion

Hashimoto thyroiditis is the most commonly observed acquired disease causing hypothyroidism and enlargement of the thyroid gland in children and adolescents (4,7,10-12). Enviromental factors including excessive intake of iodide, various viral infections and drugs are considered to be responsible in the etiology (1,3,7,11). The fact that an association of Hashimoto thyroiditis with some HLA antigen groups has been reported suggests that the disease develops on a background of genetic tendency (2,7,12,13). Damage and atrophy in the thyroid tissue resulting from involvement of the thyroid follicles by lymphocytes and plasma cells constitutes the pathogenesis of the disease (7,13-15).

Hashimoto thyroiditis occurs most commonly between the ages of 12 and 14 years in the childhood and adolescence age group. Although cases in the infancy have been reported, it is rather rare below the age of four (2,3,13,16,17). In our country, the mean age of HT was found to be 12.4±2.97 years in the study performed by Yeşilkaya et al. (13). Our study is compatible with the literature in that the mean age for HT was found to be 12.20±0.31 years and no patients was below the age of four (1,2,13).

Hashimoto thyroiditis is observed more frequently in girls. Female/male ration in the literature has been reported to be 2-9/1 (1,2,7,10,13,15,16,18,19). In this study, female/male ratio was found to be 6/1 which was compatible with the literature.

In Hashimoto thryroiditis, complaints at presentation can vary widely. Complaints including short stature, nervousness, constipation and irregular menstruation occur in relation to hypothyroidism or subclinical hypothyroidism which develop because of insufficient release of thyroid hormones from the thyroid gland (7). In our study, the most common five findings

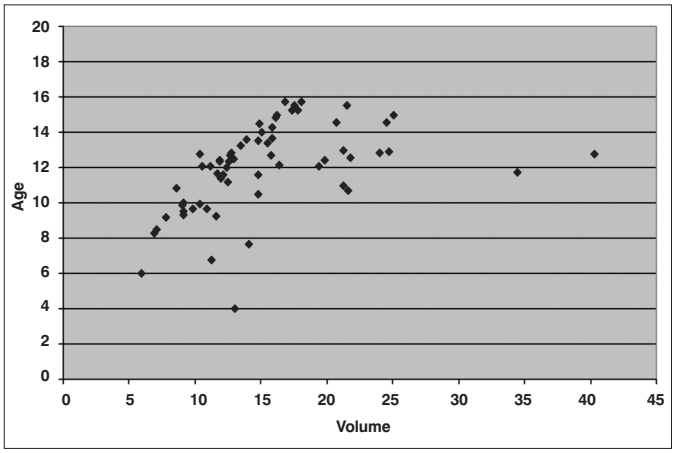

Figure 1: Age-thyroid volume relation in patients without goiter

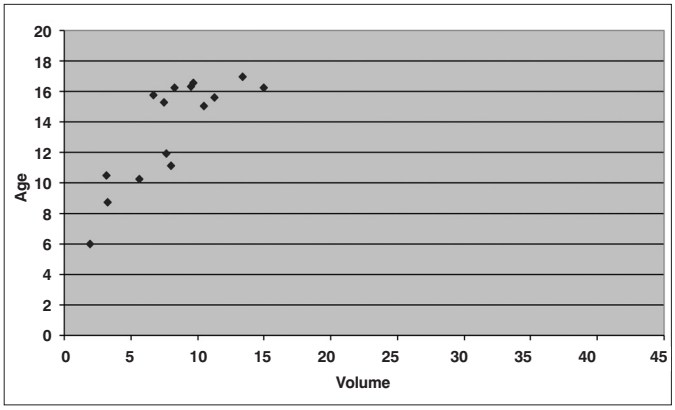

Figure 2: Age-thyroid volume relation in patients with goiter

Table 3. The distribution of the frequency of goiter in the subjects according to age and pubertal state

	Goiter (+) (n)) %	Goiter (-) (n) %	p
Female	14 (20.9%)	53 (79.1%)	0.364
Male	1 (9.1%)	10 (90.9%)	0.271
Puberty	47 (83.9%)	9 (16.1%)	0.264
Prepubertal	16 (72.7%)	6 (27.3%)	0.312

Table 4. Thyroid function states of the subjects with a follow up period of >12 months at presentation and at the end of 12 months

At presentation	At the end of 12 months				Total
	Hypothyroidism	Hyperthyroidism	Subclinical hypothyroidism	Euthroidism	
Hypothyroidism	1	0	0	1	2
Subclinical hypothyroidism	0	0	2	6	8
Euthyroidism	1	2	1	15	19
Total	2	2	3	22	29

reported by our subjects as complaints at presentation were found to be nervousness, excessive sweating, loss of appetite and hair loss.

Although Hashimoto thyroiditis frequently leads to hypothyroidism, hyperthyroid and euthyroid pictures can also be observed in the patients (2,4,7,15,20). Since the patients are mostly diagnosed in the initial phase of thyroiditis, thyroid function tests are normal in most of them at the time of diagnosis (7,12). However, in a study performed by Gopalakrishnan et al. (29), hypothyroidism was reported in 43% of the subjects, subclinical hypothyroidism was reported in 33% of the subjects and euthyroidism was reported in 24% of the subjects at presentation. We believe the fact that the number of subjects with euthyroidism and subclinical hypothyroidism was higher than the subjects with hypothyroidism in our study can be explained by early presentation of our patients. In our study, measurements including age, gender and antibody titer were not found to be related to the clinical state at presentation.

In a retrospective study performed in Taiwanese children by Wang et al. (21), 88% of the euthyroid subjects were reported to have remained euthyroid during the follow up. In our study, 22 (75,9%) of 29 subjects who were followed up for more than one year were observed to remain euthyroid in the follow up period and the other euthyroid subjects were observed to be transformed to clinical pictures of hypothyroidism, subclinical hypothyroidism and hyperthyroidism in time. This shows that HT has a dynamic and variable clinical picture also in pediatric subjects and close follow up is important.

In Hashimoto thyroiditis, a picture of hyperthyroidism can occur at the beginning or during the follow up with entering of hormones into the circulation due to tissue damage. These cases can be differentiated from Graves disease by generally lower thyrotropine receptor antibody levels and a good response to symptomatic treatment (22). In our study, 2 subjects were found to have hyperthyroidism in the beginning and 2 euthyroid subjects were found to develop hyperthyroidism during the follow up. We can not make comments on the clinical course of these subjects, because the follow up periods were inadequate. However, the antibody levels and mean ages of these subjects were not significantly different compared to the other subjects. In all subjects with hyperthyroidism, thyrotropine receptor antibodies were found to be negative and a good response was obtained only with beta blocker treatment. These results suggest that HT should be considered in the differential diagnosis in patients with hyperthyroidism.

Enlargement of the thyroid gland is a common finding in Hashimoto thyroiditis (2,15). The most common reason for presentation is goiter without complaints with a frequency of 50-90% (12). Doeker et al.(4) found thyroid enlargement with a rate of 85% in the subjects with HT in the study they performed. In our study, the frequency of goiter without complaints was found to be 80.7% which was compatible with the literature and this suggests that HT should definitely be considered in the differential diagnosis in patients with goiter (3). In our study, the frequency of goiter was not related to antibody level, age or gender and the highest rate of goiter was found in euthyroid subjects. This suggests that lymphocytic involvement of the thyroid gland plays a role in the etiology of goiter rather than hypothyroidism in HT.

High levels of autoantibodies are important in terms of the diagnosis of HT and it has been reported that anti-TPO positivity can be found with a rate up to 90% (1,11,15,20). In our study, anti-TPO positivity was found in 66.6% of the subjects in the beginning. Antibody positivity developed during the follow up in the other subjects. This supports the view that the subjects should definitely be monitored in terms of antibody positivity and autoantibodies may become positive later (15,20). Zak et al.(1) found the anti-TPO level to be higher in the euthyroid group compared to the hypothyroid group, but no relation was found between antibody positivity and the severity of the disease and gender distribution in the literature. Similarly, no relation was found between antibody positivity and the severity of the disease, gender or age distribution in our study.

In Hashimoto thyroiditis, diffuse heterogeneity and hypoechoic appearance are observed typically and micronodulary pattern can also be observed on thyroid ultrasonography (2,7,15,23). Diffuse heterogeneity and hypoechoic appearance and multinodulary goiter can also be observed in other thyroid pathologies including Graves disease or subacute thyroiditis. Rarely, localized nodulary appearance can also be observed (23). In our study, micronodulary appearance, hypoechogenity and nodulary appearance were observed on thyroid USG in 66% of our patients. This shows the significance of USG in the diagnosis of HT.

In patients with Hashimoto thyroiditis, treatment is recommended especially in the presence of goiter and hypothyroidism and it is known that reduction of goiter and regression of the signs occur with L-thyroxine treatment (2,7,18,20). In our study, reduction of goiter was found in a significant portion of the subjects in whom treatment for goiter for the aim of suppression was started and who were followed up for one year.

Hashimoto thyroiditis can be observed in combination with other autoimmune disease including type 1 diabetes mellitus and celiac disease (7,12). Since Hashimoto thyroiditis is among polyglandular autoimmune diseases, the patients should be followed up in terms of pernicious anemia, adrenal insufficiency and diabetes mellitus (2,10). In our subjects, other autoimmune diseases were not found at the time of diagnosis and no additional autoimmune disease developed during the follow up time of one year.

In the literature, positive familial history is reported to be 23-25% (1,16). In our study, familial HT or thyroid disease was found with a rate of 39%. This shows that individuals with a positive family history should be monitored more closely in terms of HT.

Conclusively, age, gender, distribution of findings, USG and laboratory findings of our patients with HT followed up in our clinic were found to be compatible with the literature. The changes found during the follow-up period prove that HT is a dynamic and variable disease and emphasize the significance of clinical follow up in these patients.

Conflict of interest. None declared.

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