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Evaluation of Clinical and Laboratory Characteristics of Cases Diagnosed with Hashimoto's Thyroiditis

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Abstract

Objective: Hashimoto's thyroiditis is the most common cause of acquired hypothyroidism and goiter in children and adolescents. The clinical picture can range from euthyroid to overt hypothyroidism or hyperthyroidism. In our study, it was aimed to evaluate the clinical and laboratory data of cases diagnosed with Hashimoto's thyroiditis.

Methods: The data of 113 Hashimoto's thyroiditis cases who visited the Pediatric Endocrinology outpatient clinic of Health Sciences University Okmeydanı Training and Research Hospital between January 2015 and December 2018 were retrospectively reviewed.

Results: Of the 113 cases included in the study, 87 (77%) were girls. The mean age at diagnosis was 12.1 ± 3 years, 70.8% of them were pubertal, 13 of the cases were obese at the time of admission, and 69.9% had a family history of thyroid disease. The 60.2% of the cases were diagnosed with no complaints coincidentally during the examinations performed in primary health care institutions for screening purposes only because they had a family history of thyroid disease. When the presence of additional disease was evaluated, it was observed that 67.2% of them did not have any additional disease and 5.3% had an additional autoimmune disease. At the time of admission, 3 (2.7%) patients were found to have hyperthyroidism, 42 (37.2%) patients were euthyroid, 44 (38.9%) patients had subclinical hypothyroidism, and 24 (21.2%) patients had overt hypothyroidism. While 13.3% were positive for thyroid peroxidase antibody and 10.6% of cases were positive for thyroglobulin antibody, both were positive in 76.1% of cases. Thyroid ultrasonography revealed heterogeneity and pseudonodular structures in the parenchyma of 84.9% of the cases, and heterogeneity and solid nodules in the parenchyma of 10.7%.

Conclusion: Hashimoto's thyroiditis is a common disease in adolescence, especially in girls. In childhood, taking a detailed history at every doctor's visit, careful evaluation in physical examination and growth and development monitoring, and early recognition of thyroid dysfunctions are important in terms of preventing their negative effects on growth and development.

Keywords: Hashimoto thyroiditis, goiter, childhood

Introduction

Hashimoto's thyroiditis (HT) is one of the most common thyroid diseases in childhood. The prevalence of HT in childhood is the highest in the period between childhood and the middle of adolescence and is 2/1 higher in females.[1-3] It is thought that HT develops as a result of the interaction of genetic, endogenous, and environmental factors.[4]

Patients with HT often consult a physician with complaints such as goiter, weakness, dry skin, and constipation.[5-7] Hashimoto's thyroiditis constitutes 40% of goiters in adolescence.[2,8] Patients may have euthyroidism, subclinical hypothyroidism, overt hypothyroidism, and rarely hyperthyroidism at the time of admission.[9]

Our study was aimed to evaluate the clinical and laboratory data of cases aged 1-18 years who visited the Pediatric Endocrinology outpatient clinic of Istanbul Health Sciences University Okmeydanı Training and Research Hospital between February 2015 and December 2018 were diagnosed with HT by a pediatric endocrinology specialist.

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Methods

The study was carried out between January 2015 and December 2018 on patients, aged 1-18, who visited the Pediatric Endocrinology outpatient clinic of the Health Sciences University Okmeydanı Training and Research Hospital diagnosed with HT by a pediatric endocrinology specialist. It was performed with a total of 113 cases, 87 of which were females. From the policlinic follow-up files of the cases, the gender, date of birth, age, height and weight measurements, pubertal examination according to Tanner's staging, information about the presence of thyroid disease in the first- and second-degree relatives, complaint, and the presence of any additional disease at the time of admission retrospectively were recorded. Body mass index (BMI) standard deviation scores (SDSs) were calculated from the details of the height and weight recorded in the data form. Body mass index and the SDSs were evaluated according to the growth percentiles and accordingly, those with BMI ≥95 (SDS ≥+2 SDS) percentiles were considered as obese, those between BMI 85≤ and <95 (SDS +1≤ and <2 SDS) percentiles were considered as overweight, BMI 5≤ and <85 (SDS: −2≤ and <+1 SDS) percentile were considered as normal weight, and BMI <5 (SDS <−2 SDS) percentile were

considered as underweight.[10] Free thyroxine (fT4), thyroid-stimulating hormone (TSH), thyroglobulin antibody (AntiTg), thyroid peroxidase antibody (AntiTPO) as laboratory data, and thyroid ultrasonography (USG) as imaging data were recorded. Clinically, the cases were classified as euthyroid (fT4 normal [N], TSH N), subclinical hypothyroidism (fT4 N, TSH increased), overt hypothyroidism (fT4 low, TSH increased), and hyperthyroidism (fT4 increased, TSH suppressed) according to thyroid hormone levels. The diagnosis of HT was made with the presence of AntiTPO and/or AntiTg positivity and accompanying radiological findings (findings such as parenchymal heterogeneity, hypoechoic areas, fibrotic bands, and pseudonodules). In laboratory values, the lower and upper limits of the measurement methods of biochemistry laboratory of our hospital were taken as reference, and fT4 0.8-2.3 µg/dL and TSH 0.5-5.7 mIU/L ranges were accepted as normal. Biopsy Fine-needle aspiration biopsy (FNAB) was planned for cases with a nodule diameter greater than 1 cm or between 0.5 cm and 1 cm with a radiologically suspicious appearance or an increase in nodule size. Pathological material was evaluated according to the Bethesda thyroid cytopathology reporting system.[11]

Serum fT4, TSH, AntiTg, and AntiTPO were studied in the dix800 Beckman Coulter device with chemiluminescence. Ultrasound evaluations were made with the Toshiba Aplio 500 device. Thyroid dimensions were evaluated as normal or large according to the data of the Atlas of Ultrasound Measurements.[12]

The data were analyzed with the SPSS-22.0 statistical package program. Numerical data were given as mean, standard deviation, minimum and maximum values, and categorical data were given as numbers and percentages. Mann Whitney-U and Chi-square tests were used in the statistical evaluation of the data. Statistically, $P < .05$ was considered significant. Our study received ethics committee approval from our hospital's local ethic committee. (19.03.2019/1182).

Results

Of the 113 cases included in the study, 87 (77%) were female, 26 (23%) were male, and the female/male ratio was 3:3. The mean age at diagnosis of the cases was 12.1 ± 3 years (2.5-17.08), and 70.8% of the cases were pubertal. There was no statistically significant difference between male and female cases in terms of age at diagnosis and puberty. The mean BMI of the cases was 20.6 ± 4.5, and the BMI SDS was 0 ± 1.4. According to BMI SDS, 5 (4.4%) of the cases were underweight, 73 (64.6%) were in normal weight, 22 (19.5%) were overweight, and 13 (11.5%) were found to be obese. There was no statistically significant difference between female and male in terms of BMI assessment (Table 1). In addition, when the BMI of the subjects was compared with the thyroid functions, no significant correlation was found ($P = .709$).

There was a family history of thyroid disease (in first- and second-degree relatives) in 69.9% of the cases. When the complaints of the cases were evaluated, it was found that 68 (60.2%) cases had no complaints and were diagnosed coincidentally during the examinations performed in primary health care institutions for screening purposes only because they had a family history of thyroid disease. Other complaints, in order of frequency, were 11.5% neck swelling (goiter), 8.8% weight gain, 4.4% dry skin, and 3.4% weight loss.

The most common comorbidities accompanying HT were Down syndrome (2.7%), anorexia (1.8%), alopecia (1.8%), congenital heart disease (1.8%), celiac disease (0.9%), and vitiligo (0.9%), and 5.3% of the accompanying diseases were other autoimmune diseases (Table 1).

Among the thyroid antibodies, 15 (13.3%) were positive only for AntiTPO , 12 (10.6%) were positive only for AntiTg, and 86

Table 1. General Characteristics of Patients diagnosed with Hashimoto's Thyroiditis

	n	%	Mean ± SDS
Age of Diagnosis (years)	–	–	12.1 ± 3.,0
Female			12.1 ± 3.1
Male			12.2 ± 2.7
Gender			
Female	87	77	–
Male	26	23	–
Puberty status			
Prepubertal	33	29.2	–
Pubertal	80	70.8	–
BMI SDS	**–**	**–**	**0 ± 1.4**
Underweight	5	4,4	–
Normal weight	73	64.6	–
Overweight	22	19.5	–
Obese	13	11.5	–
Thyroid disease in the family			
Yes	79	69.9	–
No	34	30.1	–
Admission complaint			
None/random	68	60.2	–
Swelling in the neck	13	11.5	–
Getting fat	10	8.8	–
Dry skin	5	4.4	–
Losing weight	4	3.4	–
Other*	25	11.7	–
Additional illness			
Yes	37	32.8	–
Down syndrome	3	2.7	–
Anorexia	2	1.8	–
Alopecia	2	1.8	–
Congenital heart disease	2	1.8	–
Celiac disease	1	0.9	–
Vitiligo	1	0.9	–
Other**	26	22.9	–
No	76	67.2	–

SDS, standard deviation score; BMI, body mass index; *Other: fatigue (n = 4), menstrual irregularity (n = 3), constipation (n = 2), somnolence (n = 2), follow-up with the diagnosis of celiac disease (n = 1), loss of appetite (n = 1), case with thyroid nodule (n = 1), growth arrest (n = 2), hirsutism (n = 1), dizziness (n = 1), radiotherapy; **Other: Attention deficiency and hyperactivity syndrome (n = 1), Willms tumor (n = 1), Hodgkin lymphoma (n = 1), early puberty (n = 1), juvenile idiopathic arthritis (n = 1), Familial Mediterranean Fever (n = 1), immune thrombocytopenic purpura (n = 1), Addison's disease (n = 1), epilepsy (n = 1), urticaria (n = 1) =1), asthma (n = 1), premature pubarche (n = 1), some cases had more than one disease.

(76.1%) patients were positive for both. When the clinical status was evaluated at admission, it was found that hyperthyroidism was present in 3 (2.7%) cases, euthyroidism in 42 (37.2%) cases, subclinical hypothyroidism in 44 (38.9%) cases, and overt hypothyroidism in 24 (21.2%) cases. The incidence of hypothyroidism and hyperthyroidism was found to be significantly higher in females than in males ($P = .024$) (Table 2).

According to the results of thyroid USG, 5 (4.4%) of the cases had normal parenchyma, 96 (84.9%) had heterogeneity and pseudonodular parenchyma specific for HT, and 12 (10.7%) had heterogeneity and solid parenchyma (Table 2). Fine-needle aspiration biopsy (FNAB) in cases with nodules was planned for cases with a nodule diameter greater than 1 cm or between 0.5 and 1 cm with a suspicious radiological appearance or with an increase in nodule size. The material was evaluated according to the Bethesda thyroid cytopathology reporting system.[11] Biopsy was performed in 1 case with nodules and its pathology was reported as benign.

Table 2. Laboratory Findings of Cases Diagnosed with Hashimoto's Thyroiditis

	n	%
Thyroid antibodies		
Anti-TPO positivity	15	13.3
Anti-Tg positivity	12	10.6
Ani-TPO vs anti-TG positivity together	86	76.1
Clinical status on admission		
Euthyroid	42	37.2
Female	34	40.5
Male	8	30.8
Subclinical hypothyroidism	44	38.9
Female	28	33.2
Male	16	61.5
Overt hypothyroidism	24	21.2
Female	22	26.2
Male	2	7.7
Hyperthyroidism	3	2.7
Female	3	3.4
Male	0	0
Thyroid USG		
Normal	5	4.4
Heterogeneous parenchyma	96	84.9
Heterogeneous parenchyma and nodule	12	10.7

Anti-TPO, thyroid peroxidase antibody; AntiTg, thyroglobulin antibody; USG, ultrasonography.

Discussion

Hashimoto's thyroiditis is the most common cause of goiter, acquired thyroid disease, and hypothyroidism in children and adolescents in iodine-supplemented regions of the world. In our study, the mean age of the cases at presentation was 12.16 ± 3.04 years (2.58-17.08), consistent with the literature data,[6,7,9,13,14] and the peak age of HT was in early to mid-adolescence. In our study, the ratio of female to male (F/M) was 3:3 in cases with a diagnosis of HT, and 70.8% of the cases were pubertal. The higher rate of female gender and pubertal cases was in parallel with the studies in the literature.[6,9,13-17]

In acquired hypothyroidism, growth retardation and increase in body weight are generally expected findings in children.[18] It was found that 22 (19.5%) of the cases included in our study were overweight and 13 (11.5%) were obese. When the patients' BMI and thyroid functions were compared, no significant relationship was found. In some studies, no significant difference was found between the BMIs of patients with normal thyroid functions and those with hypothyroidism, and it was said that the relationship between body weight and clinical status of HT was weak.[13,19] There are also studies that found a positive correlation between TSH increase and body weight increase.[20,21]

Asymptomatic goiter is the most common reason for HT to consult a physician in childhood and adolescence.[22] It has been shown that immunoglobin accumulation and increased TSH level are among the causes of thyroid enlargement in HT.[23,24] In our study, 68 (60.2%) of the cases were diagnosed with no complaints coincidentally during the examinations performed in primary health care institutions for screening purposes only because they had a family history of thyroid disease and 13 (11.5%) was found to be present with swelling in the neck (goiter). There are studies in the literature indicating the presence of asymptomatic goiter between 40% and 90%.[6,13-15,17,25,26] In our study, apart from the incidental finding, the most common reason for the presenting complaint was swelling in the neck, which was parallel to the literature. De Vries et al[13] found no clinical symptoms and signs in 1/3 of the cases at the time of the first admission, and the rate was 30% in Satan et al's study.[15] In our study, this rate was higher with 60.2%, which was attributed to the routine screening program performed in primary health care institutions at the time of the study. When other symptoms of hypothyroidism other than goiter are evaluated at the time of admission, similar to the literature[6,7,13,15,16] weight gain, dry skin, weight loss, weakness, constipation, menstrual irregularity, sleepiness, being followed up with the diagnosis of celiac, anorexia, thyroid nodule, growth arrest, hirsutism, dizziness, and detection in the controls after radiotherapy were found.

Hashimoto's thyroiditis is in the class of autoimmune diseases and can be seen together with many different diseases. Autoimmune thyroid disease can be seen at a rate of 10% in type 1 autoimmune polyglandular syndrome and 70-75% in type 2 autoimmune polyglandular syndrome.[12,27] Hashimoto's thyroiditis also tends to be associated with other autoimmune diseases such as celiac disease, pernicious anemia, vitiligo, alopecia, and ITP.[4,23,27] Among chromosomal diseases, autoimmune thyroid disease is observed with a frequency of 50% in Turner syndrome and 20% in Down syndrome.[28] In our study, 37 (32.8%) of the cases were diagnosed with an additional disease and 6 (5.3%) of them were with autoimmune diseases (alopecia, ITP, Addison's disease, celiac disease, and vitiligo). In similar studies, the rate of accompanying autoimmune disease was found to be 13.9-26%.[7,9,15,26] This difference is due to the fact that concurrent type 1 diabetes mellitus (T1DM) was not diagnosed in the cases included in our study. It was attributed to the fact that the cases diagnosed with T1DM did not apply to us with goiter or other thyroid-related complaints since HT was also under control in the endocrine centers where they were followed.

It has been shown that there is a relationship between some tissue groups such as HLA DR3, DR4, and DR5 in the pathophysiology of HT and in the development of the disease.[1] In our study, the history of thyroid disease in the first- and second-degree relatives of the cases was determined as 69.9%. Positive family history was reported as 52% in De Vries et al's,[13] 37% in Markovic et al's,[26] 21% in Özsu et al's,[9] and 36% Satan's[15] studies. Sengi et al[29] reported that 58% had a history of thyroid disease in their mothers and 26% in their fathers, Yeşilkaya et al[7] reported that 25% had a history of thyroid disease in first-degree relatives and 15.6% in second-degree relatives. The rate of family history of thyroid disease, which we found in our study, is slightly higher than in the literature. This was due to the fact that some of the cases who applied to us did not have any complaints but were examined and diagnosed in the primary health care centers only because they had a family history of thyroid disease, and a history of thyroid disease was due to both first- and second-degree relatives.

Although the clinical picture in HT is variable, it is the most common hypothyroidism in children. In our study, 60.1% of the cases were found to have hypothyroidism (38.9% subclinical hypothyroidism, 21.2% overt hypothyroidism) at the time of diagnosis. De Vries et al[13] reported the rate of hypothyroidism at the time of diagnosis 79%, Demirbilek et al[6] 45%, Yeşilkaya et al[7] 55.6%, Dilek et al[17] 72.6%. In our study, it was found that 26.2% of the females and 7.7% of the males had overt hypothyroidism, and the difference was significant. It was thought that this difference was due to the fact that the autoimmune process started earlier in females and that increased destruction led to a more pronounced hypothyroidism picture.[30] Korkmaz et al[16] found that 20% of females and 10.5% of males had hypothyroidism in their study.

Thyroid antibody positivity is another criterion used in the diagnosis of HT. In our study, 13.3% were positive only for AntiTPO, 10.6% were positive only for AntiTg, and 76.1% patients were positive for both. Dilek et al[17] found 29.4% were positive only for AntiTPO, 16.7% were positive only for AntiTg, and 53.9% of cases were positive for both, similar to our study.

Thyroid USG is an important examination to support the diagnosis of HT and to show whether there are thyroid nodules. On USG, enlargement of the thyroid gland, heterogeneity in the thyroid gland, hypoechoic or pseudonodular appearance are findings compatible with HT.[5,13,23] When the thyroid USG results were evaluated in our study, heterogenity and pseudonodular structures in the parenchyma were found in 84.9% of patients, which is similar to the literature.[6,7,15] When the thyroid dimensions measured on USG were examined, 42.5% of them were found to be larger than normal. Nodules found in children are more likely to be malignant than in adults.[4] In our study, it was found that 10.7% of the cases had heterogeneity and solid nodules in the parenchyma, and biopsy was conducted for 1 of the 12 nodules for which pathology test resulted as a benign nodule. In a study, thyroid nodules were detected in 39 of 300 patients and 2 of them were diagnosed with papillary thyroid carcinoma.[31]

In conclusion, HT is a common thyroid disease, especially in adolescence and girls. Although the clinical picture in the cases is mostly hypothyroidism, it may be variable like euthyroidism or hyperthyroidism. For the early diagnosis and treatment of HT, which has an important role in growth and development, in cases with a goiter family history, it is important to examine thyroid autoantibodies together with thyroid hormones.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Okmeydanı Research and Training Hospital (Date: March 19, 2019 No: 48670771-514.10).

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