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Revisiting femoral cartilage thickness in cases with Hashimoto's thyroiditis in thyroidology: a single institute experience

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SUMMARY

OBJECTIVE: Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis or autoimmune thyroiditis, is a considerable part of the spectrum of chronic autoimmune thyroid gland disorders which is pathologically associated with various degrees of lymphocytic infiltration. The purpose of the present study was to evaluate whether cartilage thickness is affected in patients with Hashimoto's thyroiditis or not in thyroidology.

METHODS: A total of 61 individuals had been evaluated in this case-control study, including 32 euthyroid Hashimoto's thyroiditis patients and 29 healthy subjects comparable in age, sex, and body mass index. The patients with a history of knee trauma or knee surgery, an additional systemic disease such as diabetes mellitus, or an inflammatory disease like rheumatoid arthritis, systemic lupus erythematosus, and scleroderma had not been included in the study. The thickness of the femoral articular cartilage was measured using B-mode ultrasonography, and the right lateral condyle, right intercondylar area, right medial condyle, left medial condyle, left intercondylar area, and left lateral condyle were also measured.

RESULTS: No statistically significant difference between patients with Hashimoto's thyroiditis diagnosis and healthy controls in terms of age, age groups, gender, and body mass index ($p>0.05$).

CONCLUSION: As a consequence, no obvious connection between autoimmune markers and cartilage thickness in patients with Hashimoto's thyroiditis was recognized. Although the diverse manifestation of Hashimoto's thyroiditis could be observed, it seems to be no liaison between thyroid autoimmunity and cartilage thickness.

KEYWORDS: Thyroid gland. Thyroiditis. Cartilage. Cytology. Pathology.

INTRODUCTION

Hashimoto's thyroiditis (HThy) is an autoimmune thyroid disorder, which is also known as chronic lymphocytic thyroiditis or struma lymphomatosa, and characterized by lymphoplasmacytic infiltration and lymphoid follicle formation with well-developed germinal centers. Although patients may have euthyroidism, hypothyroidism, and rarely hyperthyroidism, "hashitoxicosis" may accompany them but hypothyroidism is usually observed. The articular cartilage surrounding the joint surface is a worthy issue for the normal function of the joint. The proper formation, development, and maintenance of the cartilage tissue are important in preventing the development of osteoarthritis, which is a degenerative disorder leading to pain and disability. Similarly, thyroid hormones play a crucial role in cartilage homeostasis. To this end, sonographic evaluation of articular cartilage has been performed in patients with hypothyroidism[3] and autoimmune diseases such as systemic lupus erythematosus and scleroderma[1-6].

However, sonographic evaluation of cartilage thickness in patients with HThy has not yet been reported in the literature. Herein, this study aimed to evaluate the femoral cartilage thickness (FCT) in cases with HThy with ultrasonography.

METHODS

The present study enrolled 32 euthyroid HThy and 29 healthy subjects comparable in age, sex, and body mass index (BMI). Patients with a history of knee trauma or knee surgery, an additional systemic disease such as diabetes mellitus, or an inflammatory disease like rheumatoid arthritis, systemic lupus erythematosus, and scleroderma had not been

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included in the study. All the subjects included in the present study signed the informed consent. The present study was approved by the Research and Ethics Committee of Clinical Studies linked to Giresun University, under the 90139838-000-E.28156/2019 approval number. The studied cases had laid down in the supine position, both knees in maximum flexion were examined, and the thickness of their femoral articular cartilage was measured using B-mode sonography (3–13 MHz MyLabSix; Esaote Biomedica, Italy). To this end, the probe was placed in the axial plane on the upper edge of the patella and the right lateral condyle, right intercondylar area, right medial condyle with the left medial condyle, left intercondylar area, and left lateral condyle were measured meticulously (Figure 1). Afterward, cartilage thickness was interpreted as the distance between the thin hyperechoic line at the synovial space/cartilage interface and the sharp hyperechoic line at the cartilage–bone interface[7].

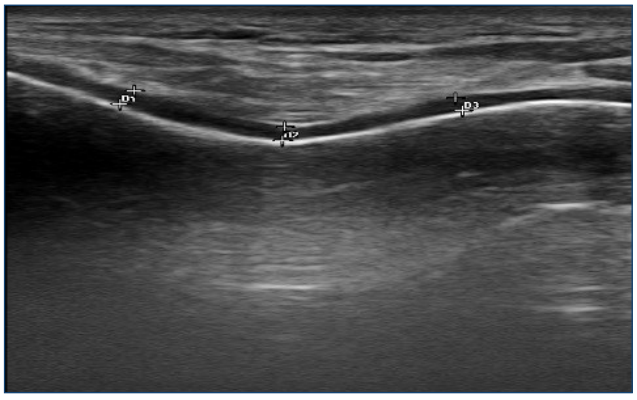

Figure 1. Sonographic image, exhibiting the right femoral distal cartilage measurements (D1 right lateral condyle, D2 right intercondylar area, and D3 right medial condyle).

Statistical analysis

The research data were uploaded to the computer environment and evaluated using SPSS (Statistical Package for Social Sciences) for Windows 22.0 (SPSS Inc., Chicago, IL). Descriptive statistics were presented as mean±standard deviation (minimum–maximum), frequency distribution, and percentage, and a Pearson chi-square test was used to evaluate categorical variables. The conformity of the variables to the normal distribution had been examined using visual (histogram and probability graphs) and analytical methods (Shapiro-Wilk test). The Mann-Whitney U test was used to determine the statistical significance between two independent groups for the variables found to be non-normally distributed, and the Student's t-test was used to determine the variables with normal distribution. The relationship between the variables was evaluated with the Spearman correlation test and the significance level was accepted as $p<0.05$.

RESULTS

A total of 61 subjects had been involved in the present prospective study. Of these, 32 cases had HThy, while the remaining 29 were healthy controls. The distribution of age, gender, and BMI between the HThy and control groups showed no statistically significant difference between patients with HThy and healthy controls in terms of age, age groups, gender, and BMI ($p>0.05$) (Table 1). The distribution of FCT between the HThy and control groups is presented in Table 2. No significant difference between the cases with HThy and the control in terms of both the right and left medial, lateral, and intercondylar FCTs has been detected ($p>0.05$) (Table 2). In addition, Table 3 reveals the relationship between age and FCT within the HThy and control without a significant correlation between

Table 1. Distribution of age, gender, and BMI between Hashimoto's thyroiditis and control.

	Hashimoto's thyroiditis (n=32)	Control (n=29)	p-value
Age, year, mean±SD (min–max)	33.5±11.2 (18–60)	32.6±6.8 (19–40)	0.960[a]
Age groups (years), n (%)			
<25	11 (34.4)	6 (20.7)	
25–35	9 (28.1)	1 (37.9)	0.466[b]
>35	12 (37.5)	12 (41.4)	
Gender, n (%)			
Male	7 (21.9)	5 (17.2)	0.649[b]
Female	25 (78.1)	24 (82.8)	
BMI, kg/m²	21.73±1.70 (19.54–26.14)	21.18±1.12 (19.42–23.20)	0.315[a]

n: number of individuals; %: column percentage; SD: standard deviation; [a]Mann-Whitney U test; [b]Pearson chi-square test.

Table 2. Distribution of femoral cartilage thicknesses between Hashimoto's thyroiditis and control.

		Hashimoto's thyroiditis (n=32)	Control (n=29)	p-value
		mean±SD (min–max)	mean±SD (min–max)	
Femoral cartilage thickness, mm				
Right	Medial	2.13±0.44 (1.3–3.1)	2.18±0.34 (1.5–2.7)	0.597[a]
	Lateral	2.11±0.38 (1.5–3.1)	2.02±0.37 (1.5–2.7)	0.341[b]
	Intercondylar	2.49±0.80 (0.8–4.0)	2.50±0.50 (1.6–3.5)	0.946[a]
Left	Medial	2.15±0.57 (1.1–4.2)	2.18±0.49 (1.0–3.2)	0.832[a]
	Lateral	2.02±0.51 (1.1–3.1)	2.07±0.46 (1.4–3.0)	0.701[b]
	Intercondylar	2.49±0.78 (0.9–4.5)	2.39±0.51 (1.5–3.2)	0.811[b]

n: number of persons; SD: standard deviation; [a]Student's t-test; [b]Mann-Whitney U test.

Table 3. The relationship between age and femoral cartilage thickness in Hashimoto's thyroiditis and control.

		Hashimoto's thyroiditis (n=32)		Control (n=29)	
		r	p-value	r	p-value
Femoral cartilage thickness, (mm)					
Right	Medial	0.221	0.225	-0.088	0.648
	Lateral	0.087	0.637	-0.340	0.072
	Intercondylar	0.323	0.071	-0.239	0.211
Left	Medial	-0.001	0.998	0.232	0.226
	Lateral	0.106	0.563	-0.171	0.376
	Intercondylar	0.172	0.346	-0.126	0.513

n: number of cases; r: Spearman correlation coefficient.

the ages of the cases with HThy and the healthy controls in the control and all the FCTs ($p>0.05$).

DISCUSSION

Hashimoto's thyroiditis is now recognized as an autoimmune thyroid disorder that is characterized by high titers of circulating antibodies. Microscopically, it involves lymphoplasmacytic infiltration and lymphoid follicle formation with well-developed germinal centers, although it does not histopathologically possess a homogeneous lesion. Of note, several subtypes of HThy, presenting the clinicopathological features, have been reported, which are quite distinct from that of typical HThy. To this end, the most salient subtype is the fibrous variant of HThy with marked fibrous replacement of the thyroid gland parenchyma and typical microscopic changes of HThy in the remaining tissue, which is contrary to Riedel's thyroiditis, in case of not possessing extrathyroidal fibrosis[1].

To the best of our knowledge, this is the first study in the English-language literature in the era of FCT *vs.* HThy. It has been revealed that the FCT of the control was recognized to be similar in the cases with HThy, which is the most common autoimmune disorder that frequently affects females. Its clinical features include local and systemic manifestations. Systemic ones frequently result from loss of function of the thyroid gland. Since thyroid hormones have effects on most organs and tissues, the symptoms and signs of hypothyroidism are also quite diverse. The hypertrophic appearance of the muscles is mentioned due to myxedematous infiltration in the connective tissues, which usually causes pain and cramps in its effects on the musculoskeletal system[8]. Although osteoarthritis has a high prevalence and morbidity rate, no effective treatment has yet been found. To prevent and treat this disease effectively, the molecular mechanism of the cartilage structure should be initially recognized[9]. Since the cartilage structure has a very tight connection with the function of its architecture, the ability to reconstruct the structure was found to be necessary

for regeneration[10]. To this end, many different methods have been investigated in the treatment modalities of osteoarthritis, including disease-modifying drug treatments[11] and marrow stimulation techniques[12], and also cell therapy, tissue engineering, and gene therapy have been the subject of research[13-20]. However, these treatment options are quite demanding, so it is important to predict and prevent the causes that may lead to osteoarthritis.

Hypothyroidism is one of the causes of secondary osteoarthritis in thyroidology. Of note, the thyroid hormones are essential and crucial for endochondral ossification, chondrocyte maturation, and matrix synthesis. In fact, the evaluation of the articular cartilage using sonographic and pre-osteoarthritic evaluation of the knees with ultrasound possesses a prognostic value[2,21-23]. Devrimsel et al.[4] observed thinner femoral cartilage measurements in hypothyroid cases compared to the healthy volunteers. Based on this result, close monitoring of hormone levels in euthyroid patients is propounded as valuable for the prevention of osteoarthritis.

The thickness of the articular cartilage and possible mechanisms that may cause cartilage degradation have been investigated in some autoimmune disorders. The cartilage thickness was reduced in patients with Behcet's disease, and some authors propounded that it might be related to increased levels of IL-1β in the synovial fluid[24]. Serum levels of human cartilage glycoprotein-39 (HC gp-39), an indicator of cartilage damage or degradation, have been found to be increased in early rheumatoid arthritis and systemic scleroderma[25]. Cartilage oligomeric matrix protein (COMP), a structural component of cartilage, was highly found in patients with scleroderma. In addition, medial condyle cartilage thickness attenuates in cases with scleroderma[24]. However, decreased cartilage thickness in cases with scleroderma may also be a result of vascular dysfunction or synovial fibrosis in this disease, and the nutritional status of cartilage plays an important role in maintaining normal cartilage balance. In the present study, investigating whether cartilage destruction may emerge in an autoimmune disorder such as euthyroid HThy, and no significant cartilage thinning was detected in these patients.

Limitations

Some limitations can be detected in our study. Biomarkers that may be associated with cartilage thickness or metabolism in cases with HThy and cartilage volume are the missing parameters in the present study.

CONCLUSION

The outcomes of our preliminary study have revealed that no relation between autoimmune markers and cartilage thickness in the cases with HThy has been recognized. Although the diverse manifestation of HThy could be observed, it seems no relationship exists between thyroid gland autoimmunity and cartilage thickness in thyroidology.

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AUTHORS' CONTRIBUTIONS

NCY Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft. **OD:** Methodology, Project administration, Resources, Validation, Visualization. **FK:** Methodology, Project administration, Resources, Validation, Visualization. **IFS:** Methodology, Project administration, Resources, Validation, Visualization. **DS:** Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **IS:** Investigation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing.

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