



Evaluation of cutaneous manifestations in patients under treatment with thyroid disease

Tedavi altındaki tiroid hastalarında deri bulgularının değerlendirilmesi

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Abstract

Background and Design: Thyroid diseases often cause various findings in hair, skin and nails. Some of them may be regressed by the treatment of thyroid disease. We aimed to evaluate the cutaneous manifestations in patients with thyroid disease under treatment.

Materials and Methods: This cross-sectional study included 97 consecutive patients with thyroid disease under treatment and 50 healthy controls. Thyroid disease was classified as autoimmune and non-autoimmune. All skin findings and dermatological diseases were recorded.

Results: Of the patient group, 56 (57.7%) had autoimmune, 41 (43.3%) had non-autoimmune thyroid disease. Eighty-four (86.4%) patients were under thyroid hormone therapy and 13 (23.6%) patients were under anti-thyroid therapy. 73.2% of the autoimmune group, 71.4% of non-autoimmune group and 52% of the control group had at least one cutaneous manifestation ($p=0.05$). Xerosis ($p=0.026$), pruritus ($p=0.00$), facial erythema ($p=0.036$), flushing ($p=0.004$), dry hair ($p=0.008$), brittle nails ($p=0.02$), dry nails ($p=0.013$) and longitudinal streaking on nails ($p=0.02$) were more frequent in the autoimmune group than in the non-autoimmune and control group. Alopecia ($p=0.00$) was more frequent in the non-autoimmune group. Furthermore diffuse hyperhidrosis ($p=0.016$), thinning of nails ($p=0.059$) and rosacea disease ($p=0.03$) were more common in the patient group than in the control group. At least one cutaneous manifestation, xerosis and various nail findings were more common in patients under thyroid hormone therapy than in patients under anti-thyroid therapy, but there was no statistically significant difference.

Conclusion: These findings have shown that various cutaneous manifestations can also be seen in patients with thyroid disease under treatment. We believe that further studies comparing thyroid patients who received and did not receive treatment are necessary to clarify the effect of thyroid disease treatment on cutaneous manifestations.

Keywords: Cutaneous manifestations, thyroid diseases, autoimmunity

Öz

Amaç: Tiroid hastalıkları sıklıkla saç, deri ve tırnaklarda çeşitli bulgulara neden olur. Bu bulguların bazıları tiroid hastalığının tedavisi ile gerileyebilir. Bu çalışmada tedavi altındaki tiroid hastalarında deri bulgularını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Bu kesitsel çalışmaya tedavi altındaki 97 tiroid hastası ve 50 sağlıklı kontrol dahil edildi. Tiroid hastalığı otoimmün ve non-otoimmün olarak sınıflandırıldı. Tüm deri bulguları ve dermatolojik hastalıklar kaydedildi.

Bulgular: Hasta grubunun 56'sında (%57,7) otoimmün, 41'inde (%43,3) non-otoimmün tiroid hastalığı mevcuttu. Seksen dört (%86,4) hasta tiroid hormon tedavisi, 13 (%23,6) hasta anti-tiroid tedavi alıyordu. Otoimmün grubun %73,2'sinde, non-otoimmün grubun %71,4'ünde ve kontrol grubunun %52'sinde en az bir deri bulgusu vardı ($p=0,05$). Kseroz ($p=0,026$), kaşıntı ($p=0,00$), fasyal eritem ($p=0,036$), flushing ($p=0,004$), kuru saç ($p=0,008$), kırılabilir tırnaklar ($p=0,02$), kuru tırnaklar ($p=0,013$) ve tırnaklarda uzunlamasına çizgiler ($p=0,02$) otoimmün grupta non-otoimmün ve kontrol grubuna göre daha sıklıkla görüldü. Alopesi ($p=0,00$) non-otoimmün grupta daha sıklıkla görüldü. Ayrıca, hasta grubunda diffüz hiperhidroz ($p=0,016$), tırnaklarda incelme ($p=0,059$) ve rozase hastalığı ($p=0,03$) kontrol grubundan daha sıklıkla görüldü. Tiroid hormon tedavisi alanlarda, en az bir deri bulgusu, kserozis ve çeşitli tırnak bulguları anti-tiroid tedavi alanlara göre daha sıklıkla görüldü. Ancak istatistiksel olarak anlamlı bir fark yoktu.

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Sonuç: Bu bulgular, tedavi altındaki tiroid hastalarında da çeşitli deri bulgularının görülebileceğini göstermiştir. Tiroid hastalığı tedavisinin kütanöz bulgular üzerindeki etkisini netleştirmek için tedavi altında olan ve olmayan tiroid hastalarını karşılaştıran daha ileri çalışmaların gerekli olduğu düşünülüyor.

Anahtar Kelimeler: Kütanöz bulgular, tiroid hastalıkları, otoimmünite

Introduction

Thyroid hormones (TH) play an important role in maintaining normal functions of the skin, so the first signs of TH imbalance are often seen in the skin. TH affects proteoglycan synthesis in the skin by stimulating fibroblasts. They also play a regulatory role in epidermal differentiation through their effects on keratinocytes. Furthermore, TH are very important in hair formation and sebum production^{1,3}. Thyroid diseases often cause changes in hair, skin and nails. Therefore, dermatologists should be familiar with dermatological findings associated with thyroid diseases⁴. Some of these findings may regress with the treatment of thyroid disease; but some findings especially related with autoimmunity may not regress⁵.

To best of our knowledge, there is only one study evaluating cutaneous manifestations in patients with thyroid disease under treatment in the literature⁶. In this study, we aimed to evaluate the cutaneous manifestations in patients with thyroid disease under treatment.

Materials and Methods

Ninety-seven consecutive patients with thyroid disease and 50 healthy controls aged over 18 years were included in this cross-sectional study. Patients were referred by endocrinology department of our hospital. Thyroid patients with untreated, under treatment for less than 1 year and newly diagnosed were excluded. Other exclusion criteria were pregnancy, lactation and having any other systemic diseases and medications. Ethical approval was received from the Eskişehir Osmangazi University, Non-interventional Clinical Research Ethics Committee (approval number: 43, date: 23.07.2019). Informed consent was obtained from all participants.

Graves' disease and Hashimoto's thyroiditis are autoimmune, whereas other diseases such as nodular and diffuse goiter are non-autoimmune thyroid diseases³. Patients with thyroid disease were classified as autoimmune and non-autoimmune by an endocrinologist. Dermatological examination of all patients and controls were performed by the same dermatologist. All cutaneous manifestations and dermatological diseases were recorded.

Statistical Analysis

IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) software was used for the data analyses. Continuous data was presented as mean \pm standard deviation and median. Categorical data was presented in percentage (%). Pearson's chi-square and Pearson's exact chi-square was used to analyze the cross-tables. $P < 0.05$ value was accepted to be statistically significant.

Results

The study included 97 patients with thyroid disease [82 (84.5%) female, 15 (15.5%) male] and 50 healthy controls [38 (76.0%) female,

12 (24.0%) male]. Mean age of patient group was 52.23 ± 12.52 years and mean age of control group was 54.40 ± 14.83 years. The groups were similar in terms of age and gender ($p > 0.05$). Mean disease duration was 7.84 ± 2.14 years in patient group. Of 97 patients with thyroid disease, 56 (57.7%) were autoimmune, 41 (43.3%) were non-autoimmune. Eighty-four (86.4%) were on thyroid hormone therapy and 13 (23.6%) were on anti-thyroid therapy. Mean treatment duration was 6.29 ± 1.98 years. At least one cutaneous manifestation was present in 73.2% of autoimmune group, 71.4% of non-autoimmune group and 52% of control group ($p = 0.05$). Xerosis ($p = 0.026$), pruritus ($p = 0.00$), facial erythema ($p = 0.036$), flushing ($p = 0.004$), dry hair ($p = 0.008$), brittle nails ($p = 0.02$), dry nails ($p = 0.013$), longitudinal streaking on nails ($p = 0.02$) were more frequent in the autoimmune group than the non-autoimmune and control groups. Alopecia ($p = 0.00$) was more frequent in non-autoimmune group (Table 1). In addition, in the patient group, diffuse hyperhidrosis ($p = 0.016$), nail thinning ($p = 0.059$) and rosacea ($p = 0.03$) were more frequent than the control group. When patient group were evaluated according to treatment; at least one cutaneous manifestation, xerosis, facial erythema and various nail findings were more common in thyroid hormone therapy group, whereas pruritus, diffuse hyperhidrosis and alopecia were more common in anti-thyroid therapy group but there was no statistically significant difference (Table 2).

Discussion

TH play important roles in maintaining normal skin functions. The effect of TH in cutaneous biology including epidermis, dermis and hair has been shown². Cutaneous manifestations usually occur after the development of thyroid disease; but they may be the first sign of thyroid disease. They can be divided into two main categories; 1. Direct effect of TH on skin tissues 2. Skin diseases caused by autoimmune etiology^{2,7}. Some of these findings may regress with the treatment of thyroid disease^{1,8}. Previous studies have evaluated skin findings in thyroid patients before treatment. In these studies, at least one cutaneous manifestation was found in 81% and 56.8% of patients with thyroid disease^{5,8}. In our study, skin findings before treatment were not evaluated and 72.1% of patients with thyroid disease on treatment had at least one cutaneous manifestation.

Thyroid diseases may cause various symptoms in hair, skin and nails⁴. Different cutaneous manifestations may be seen in hypothyroidism and hyperthyroidism^{1,4}. In our study, there was no thyroid hormone levels of participants but they were categorized by thyroid hormone therapy and anti-thyroid therapy groups. At least one cutaneous manifestation, xerosis, facial erythema and various nail findings were more common in thyroid hormone therapy group, whereas pruritus, diffuse hyperhidrosis and alopecia was more common in anti-thyroid therapy group but there was no statistically significant difference. This results may be related to the fact that the number of participants in the groups were not similar. The skin is characteristically cold, xerotic and pale in hypothyroidism^{1,4,9,10}. The cause of cold skin is peripheral vasoconstriction. Xerosis is

Table 1. Cutaneous manifestations in autoimmune, non-autoimmune and control groups

	Autoimmune group (n=41), n (%)	Non-autoimmune group (n=56), n (%)	Control group (n=50), n (%)	p*
At least one cutaneous manifestation	30 (73.2)	40 (71.4)	26 (52.0)	0.05
Xerosis	18 (43.9)	23 (41.1)	10 (20.0)	0.026
Pruritus	17 (41.5)	18 (32.1)	2 (4.0)	0.00
Moist skin	0	0	0	-
Yellow skin	0	0	0	-
Diffuse hyperhidrosis	4 (9.8)	6 (10.7)	0 (0)	0.062
Palmoplantar hyperhidrosis	1 (2.4)	1 (1.8)	0 (0)	0.747
Palmoplantar hyperkeratosis	0	0	0	-
Facial erythema	9 (22.0)	9 (16.1)	2 (4.0)	0.036
Flushing	7 (17.1)	3 (5.4)	0 (0)	0.004
Periorbital edema	2 (4.9)	2 (3.6)	0 (0)	0.458
Pretibial myxedema	0	0	0	-
Diffuse edema	1 (2.4)	0 (0)	0 (0)	0.282
Xanthelasma	0 (0)	1 (1.8)	0 (0)	1.00
Local hyperpigmentation	1 (2.4)	0 (0)	1 (2.0)	0.53
Diffuse hyperpigmentation	0	0	0	-
Melasma	2 (4.9)	7 (12.5)	2 (4.0)	0.21
Acanthosis nigricans	0	0	0	-
Keratosis pilaris	2 (4.9)	1 (1.8)	0 (0)	0.27
Eyebrow loss	2 (4.9)	4 (7.1)	0 (0)	0.17
Alopecia	29 (70.7)	40 (71.4)	18 (36.0)	0.00
Dandruff	7 (17.1)	8 (14.3)	7 (14.0)	0.90
Hair graying	38 (92.7)	51 (91.1)	48 (96.0)	0.652
Hair dryness	6 (14.6)	9 (16.1)	0 (0)	0.013
Alopecia areata	0 (0)	1 (1.8)	0 (0)	1.00
Seborrheic dermatitis	2 (4.9)	3 (5.4)	0 (0)	0.26
Shiny nails	0 (0)	1 (1.8)	0 (0)	1.00
Soft nails	3 (7.3)	2 (3.6)	0 (0)	0.15
Fine nails	5 (12.2)	6 (10.7)	1 (2.0)	0.13
Brittle nails	9 (22.0)	11 (19.6)	2 (4.0)	0.02
Dry nails	3 (7.3)	6 (10.7)	0 (0)	0.63
Rough nails	0 (0)	1 (1.8)	0 (0)	1.00
Onycholysis	0 (0)	2 (3.6)	0 (0)	0.33
Distal separation	0 (0)	2 (3.6)	0 (0)	0.33
Hyperkeratotic nails	1 (2.4)	1 (1.8)	0 (0)	0.74
Transverse streaking on nails	1 (2.4)	0 (0)	0 (0)	0.28
Longitudinal streaking on nails	6 (14.6)	5 (8.9)	0 (0)	0.02
Clubbing	0	0	0	-
Vitiligo	0 (0)	0 (0)	1 (2.0)	0.624
Psoriasis	1 (2.4)	4 (7.1)	0 (0)	0.10
Urticaria	1 (2.4)	2 (3.6)	0 (0)	0.63
Rosacea	7 (17.1)	12 (21.4)	3 (6.0)	0.077
Acne	2 (4.9)	1 (1.8)	1 (2.0)	0.67
Contact dermatitis	4 (9.8)	2 (3.6)	2 (4.0)	0.43

*Pearson's chi-square

caused by peripheral vasoconstriction, reduction in epidermal sterol biosynthesis and sebaceous gland secretion and hypohidrosis^{1,2,10}. In previous studies, xerosis was observed in 37-45% of patients with

Table 2. Cutaneous manifestations in anti-thyroid and thyroid hormone groups

	Anti-thyroid group (n=13), n (%)	Thyroid hormone group (n=84), n (%)	p*
At least one cutaneous manifestation	8 (61.5)	62 (73.8)	0.50
Xerosis	2 (15.4)	39 (46.4)	0.06
Pruritus	7 (53.8)	28 (33.3)	0.21
Diffuse hyperhidrosis	2 (15.4)	8 (9.5)	0.61
Palmoplantar hyperhidrosis	0	2 (2.4)	1.00
Facial erythema	1 (7.7)	17 (20.2)	0.45
Flushing	1 (7.7)	9 (10.7)	1.00
Periorbital edema	0	4 (4.8)	0.64
Diffuse edema	0	1 (1.2)	1.00
Xanthelasma	0 (0)	1 (1.2)	1.00
Local hyperpigmentation	0 (0)	1 (1.2)	1.00
Melasma	2 (15.4)	7 (8.3)	0.60
Keratosis pilaris	1 (7.7)	2 (2.4)	0.35
Eyebrow loss	0 (0)	6 (7.1)	0.59
Alopecia	9 (69.2)	4 (30.8)	1.00
Dandruff	1 (7.7)	14 (16.7)	0.47
Hair graying	10 (76.9)	79 (94.0)	0.07
Hair dryness	1 (7.7)	14 (16.7)	0.47
Alopecia areata	0 (0)	1 (1.2)	1.00
Seborrheic dermatitis	0 (0)	5 (6.0)	0.61
Shiny nails	0 (0)	1 (1.2)	1.00
Soft nails	1 (7.7)	4 (4.8)	0.65
Fine nails	0 (0)	11 (13.1)	0.35
Brittle nails	2 (15.4)	18 (21.4)	0.73
Dry nails	1 (7.7)	8 (9.5)	1.00
Rough nails	0 (0)	1 (1.2)	1.00
Onycholysis	0 (0)	2 (2.4)	1.00
Distal separation	0 (0)	2 (2.4)	1.00
Hyperkeratotic nails	1 (7.7)	1 (1.2)	0.25
Transverse streaking on nails	0 (0)	1 (1.2)	1.00
Longitudinal streaking on nails	1 (7.7)	10 (11.9)	1.00
Psoriasis	1 (7.7)	4 (4.8)	0.65
Urticaria	0 (0)	3 (3.6)	1.00
Rosacea	1 (7.7)	18 (21.4)	0.30
Acne	0 (0)	3 (3.6)	1.00
Contact dermatitis	2 (15.4)	4 (4.8)	0.18

*Pearson's chi-square

thyroid disease, respectively^{6,8}. In our study, 42.2% of patients with thyroid disease had xerosis and it was the most common cutaneous manifestation. Pruritus (36.1%) was one of the most common cutaneous manifestation in our study similar to literature⁸. Xerosis is the most common skin finding in hypothyroidism². In our study, xerosis was more common in thyroid hormone therapy group but there was no statistically significant difference in our study.

Skin is warm, soft, moist, smooth and also itchy in patients with hyperthyroidism^{2,4,9,10}. Warmth is caused by increased cutaneous blood flow. The moisture is a reflection of the underlying metabolic situation. In addition, facial erythema, flushing, palmar erythema, palmoplantar and diffuse hyperhidrosis may be seen^{2,9,10}. In our study, facial erythema, flushing and diffuse hyperhidrosis were the common cutaneous manifestations similar to literature⁸.

The hairs of scalp and body are usually dry, rough and brittle in hypothyroidism^{1,2,10}. Dry hair is one of the most common cutaneous findings in patients with thyroid disease^{6,8}. In our study, it was also one of the most common cutaneous manifestation. Patients with thyroid disease often have diffuse or partial alopecia^{1,2,4,10}. In previous studies, alopecia was observed in 32.3%-45% of patients with thyroid disease^{6,8}. In our study, 72.1% of patients had alopecia. The high rate may be related with higher mean age of our patient group. The loss of the lateral third of the eyebrows is one of the common cutaneous manifestations in patients with both hyperthyroidism and hypothyroidism^{1,2,9,10}. Six patients (6.2%) had this finding in our study. Localized and generalized hyperpigmentation may be seen in patients with hyperthyroidism^{2,10}. It is thought to be caused by increased pituitary adrenocorticotrophic hormone². In addition, it has been reported that there is a relationship between melasma and thyroid autoimmunity^{11,12}. In a previous study, Dogra et al.¹³ reported that 18.7% of patients with hypothyroid had melasma and 6.2% had periocular pigmentation. Melasma was more common in patients with thyroid disease (9.3%) in our study; but there was not statistically significant difference.

Patients with thyroid disease may have various nail findings. Dry, brittle, dull nails and longitudinal and transverse streakings on nails may be seen in hypothyroidism patients; whereas shiny, soft, friable nails and Plummer's nails (distal onycholysis) in hyperthyroidism patients^{1,2,4,9,10}. In a previous study it was reported that 64% of thyroid disease patients had nail findings and the most common nail findings were longitudinal streaking on nails and distal onycholysis⁶. Takir et al.⁸ reported that the most common nail findings were brittle nail (22.0%) and nail thinning (13.0%) in patients with thyroid disease. In our study, brittle nail (20.6%) and longitudinal streaking on nail (11.3%) were more common in thyroid patients. In addition nail findings were more common in thyroid hormone therapy group than anti-thyroid therapy group but the difference was not significant.

There may be a relationship between thyroid diseases and inflammatory skin diseases. It was reported that psoriasis and rosacea were associated with thyroid diseases in recent studies^{5,14,15}. In our study, rosacea (19.6%) was more frequent in patients with thyroid disease than healthy controls. Five (5.2%) patients had psoriasis; but there was no statistically significant difference.

Thyroid autoimmunity is often associated with various skin diseases such as vitiligo, pemphigus, chronic urticaria, dermatitis herpetiformis, connective tissue diseases and alopecia areata^{2,4,7,10}. These skin findings may be related to thyroid hormone levels or T and/or B-cell

abnormalities². Cutaneous manifestations are more common in autoimmune thyroid diseases⁸. In our study, skin findings were also more common in patients with autoimmune thyroid disease. Previous studies have shown a relationship between chronic urticaria, vitiligo, alopecia areata and rosacea and thyroid autoimmunity^{5,8,15-19}. In our study, chronic urticaria was more common in patients with thyroid disease; but there was no statistically significant difference. There was no another autoimmune skin disease in patients with thyroid disease in our study. Vitiligo and alopecia areata usually occur many years before thyroid dysfunction. Therefore, the presence of high thyroid autoantibodies in these patients may serve as a useful clinical tool to identify patients at risk for thyroid diseases^{2,18,19}.

In summary, alopecia, xerosis, pruritus, diffuse hyperhidrosis, various nail findings and rosacea were more common in patients with thyroid disease in our study. Furthermore, in this study the most common cutaneous manifestations were generally similar to the other studies in not receiving treatment patients with thyroid disease^{5,8}. These results suggested that some cutaneous manifestations may be seen in thyroid disease patients on treatment too.

Study Limitation

Limitations of this study were relatively small sample size, absence of thyroid hormone levels in participants and absence of untreated group.

Conclusion

Various cutaneous manifestations may be seen in patients with thyroid disease on treatment too. We conclude that further studies which comparing thyroid patients on treatment and non-treatment are needed in order to clarify the effect of treatment of thyroid disease on cutaneous manifestations.

Ethics

Ethics Committee Approval: Ethical approval was received from the Eskişehir Osmangazi University, Non-interventional Clinical Research Ethics Committee (approval number: 43, date: 23.07.2019).

Informed Consent: Informed consent was obtained from all participants.

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Authorship Contributions

Concept: E.A., E.Ağ., G.Y. Design: E.A., E.Ağ., G.Y., H.K.E., E.S.A., Z.N.S., M.B., Data Collection or Processing: E.A., E.Ağ., G.Y., H.K.E., E.S.A. Analysis or Interpretation: E.A., E.Ağ., G.Y., H.K.E., M.B., Literature Search: E.A., E.Ağ., G.Y., H.K.E., E.S.A., Writing: E.A., E.Ağ., G.Y., H.K.E., E.S.A., Z.N.S., M.B.

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