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Skin findings in autoimmune and nonautoimmune thyroid disease with respect to thyroid functional status and healthy controls

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1. Introduction
Thyroid hormone has an integral role in sustaining normal epidermal functions including oxygen consumption, protein synthesis, mitosis, differentiation, and determination of layer thickness (1,2). Given that the skin is often the first organ where a wide range of clinical manifestations of thyroid hormone imbalance arises, thyroid disease can often first be diagnosed by recognizing cutaneous manifestations related to thyroid hormone imbalance (2).

Hence, cutaneous manifestations of thyroid diseases are of vital importance to dermatologists as they not only signal the need of investigating and thus diagnosing an underlying thyroid disorder but also they improve in most cases with the treatment of thyroid disease (2,3).

1. Introduction

Autoimmune thyroid diseases are also of special importance given that they are associated with other organ-specific or systemic autoimmune disorders (4–6).

The present study was designed to evaluate skin manifestations associated with autoimmune and nonautoimmune thyroid disease with respect to thyroid functional status and healthy controls.

2. Materials and methods

2.1. Study population
A total of 300 consecutive patients with either autoimmune (n = 173) or nonautoimmune (n = 127) thyroid disease and 100 healthy control subjects were included in this cross-sectional study. Data on patient demographics, thyroid function tests, and skin findings were recorded for patient and control groups.

Results: Compared to control subjects, patients had higher proportions in populations with alopecia (P < 0.001), nail thinning (P = 0.02), brittle nails (P = 0.001), pruritus (P < 0.001), diffuse hyperhidrosis (P = 0.01), flushing (P = 0.001), and xerosis (P < 0.001). Onycholysis (P = 0.02), yellow skin (P = 0.04), periorbital edema (P = 0.03), psoriasis (P = 0.001), and palmoplantar hyperkeratosis (P = 0.007) were significantly more common in patients with autoimmune than nonautoimmune thyroid disease. A significantly higher percentage of patients with autoimmune rather than nonautoimmune thyroid disease had overall skin findings (P = 0.03) among the hyperthyroid patients.

Conclusions: Our findings indicate that the presence of skin findings in a majority of thyroid patients significantly differs for certain cutaneous manifestations with respect to controls, autoimmune etiology, and thyroid functional status.

Key words: Skin findings, thyroid disease, autoimmune, thyroid status

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Our study group included 300 patients (274 females, 26 males) with thyroid disease, including 173 (58%) patients with autoimmune thyroid disease and 127 (42.0%) with nonautoimmune thyroid disease, and 100 control subjects (90 females, 10 males). Patient and control groups were homogeneous in terms of sex distribution, while patients with nonautoimmune thyroid disease (mean (SD) age: 44.0 ± 10.0 years) were older than patients with autoimmune thyroid disease (42.0 ± 14.0 years) and control subjects (40.0 ± 13.0 years) (P < 0.001 for each) (Table 1).

3.2. Skin findings with respect to autoimmunity
Skin findings were positive in 243 of 300 thyroid disease patients (81.0%) and in 57 of 100 (57.0%) control subjects. The most frequently observed skin findings were xerosis in 135 patients (45.0%), alopecia in 97 (32.3%), pruritus in 82 (27.3%), brittle nails in 66 (22.0%), nail thinning in 39 (13.0%), flushing in 43 (14.3%), and hair dryness in 27 patients (9.0%) (Table 1).

Among the population with at least one skin finding (243 patients and 57 control subjects), 45.0% were patients with autoimmune thyroid disease, 36.0% were patients with nonautoimmune thyroid disease, and only 19.0% were control subjects (P < 0.001). Specifically, patients rather than control subjects had higher proportions in populations with alopecia (54.2%, 36.4%, and 9.3%, respectively, P < 0.001), nail thinning (61.7%, 21.3%, and 17.0%, respectively, P = 0.02), brittle nails (60.8%, 28.4%, and 10.8%, respectively, P = 0.001), pruritus (52.4%, 45.2%, and 2.4%, respectively, P < 0.001), diffuse hyperhidrosis (58.1%, 34.9%, and 7.0%, respectively, P = 0.01), flushing (54.5%, 43.2%, and 2.3%, respectively, P = 0.001), and xerosis (43.7%, 45.7%, and 10.6%, respectively, P < 0.001) along with a higher likelihood of autoimmune than nonautoimmune thyroid patients to have these skin findings except for xerosis (Table 1).

Onycholysis (80.0% vs. 20.0%, P = 0.02), yellow skin (64.7% vs. 35.3%, P = 0.04), periordial edema (75.0% vs. 25.0%, P = 0.03), and psoriasis (91.7% vs. 8.3%, P = 0.001) were significantly more common in patients with autoimmune than nonautoimmune thyroid disease, while they were not observed in any of the control subjects. All palmoplantar keratoses cases were observed in patients with autoimmune thyroid disease (P = 0.007) (Table 1).

3.3. Skin findings with respect to thyroid status
A total of 56 (18.7%) patients had hyperthyroidism, 158 (52.7%) patients had hypothyroidism, and 86 (28.7%) patients had euthyroidism. Skin findings were observed in 54 (96.4%), 135 (85.4%), and 77 (89.5%) patients with hyperthyroid, hypothyroid, and euthyroid status, respectively (Table 2).

A significantly higher percentage of patients with autoimmune than nonautoimmune thyroid disease had overall skin findings (70.3% vs. 29.7%, P = 0.03), alopecia (84.6% vs. 15.4%, P = 0.01), and brittle nails (88.9% vs. 11.1%, P = 0.02) among hyperthyroid patients and had nail thinning (90.9% vs. 9.1%, P = 0.01) and periordial
edema (100.0% vs. 0.0%, P = 0.04) among hypothyroid patients. A significantly lower percentage of patients with autoimmune than nonautoimmune thyroid disease had xerosis (20.9% vs. 79.1%, P = 0.006) in the case of euthyroid status (Table 2).

4. Discussion
Our findings in a cohort of patients with thyroid disease and healthy control subjects revealed positive skin findings in 81.0% of thyroid disease patients and in 57.0% of control subjects. The presence of autoimmune thyroid disease was associated with a higher likelihood of skin findings including alopecia, nail thinning, brittle nails, diffuse hyperhidrosis, and flushing as compared with nonautoimmune thyroid disease and normal thyroid functions. There was a significantly higher percentage of patients with autoimmune than nonautoimmune thyroid disease among patients with onycholysis, yellow skin,
Table 2. Skin findings in patients with autoimmune or nonautoimmune thyroid disease with respect to thyroid status.

<table>
<thead>
<tr>
<th>Skin findings (+) n (%)</th>
<th>Hyperthyroid status (n = 56)</th>
<th>Hypothyroid status (n = 158)</th>
<th>Euthyroid status (n = 86)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Autoimmune</td>
<td>Nonautoimmune</td>
<td>P-value</td>
</tr>
<tr>
<td>Overall</td>
<td>38 (70.3)</td>
<td>16 (29.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>Alopecia</td>
<td>22 (84.6)</td>
<td>4 (15.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hair dryness</td>
<td>5 (100)</td>
<td>-</td>
<td>0.16</td>
</tr>
<tr>
<td>Nail thinning</td>
<td>8 (80)</td>
<td>2 (20)</td>
<td>0.31</td>
</tr>
<tr>
<td>Onycholysis</td>
<td>2 (100)</td>
<td>-</td>
<td>0.45</td>
</tr>
<tr>
<td>Pitting</td>
<td>-</td>
<td>2 (100)</td>
<td>0.09</td>
</tr>
<tr>
<td>Brittle nails</td>
<td>16 (88.9)</td>
<td>2 (11.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Xerosis</td>
<td>12 (57.1)</td>
<td>9 (42.9)</td>
<td>0.18</td>
</tr>
<tr>
<td>Pruritus</td>
<td>10 (66.7)</td>
<td>5 (33.3)</td>
<td>0.90</td>
</tr>
<tr>
<td>Diffuse hyperhidrosis</td>
<td>15 (75)</td>
<td>5 (25)</td>
<td>0.39</td>
</tr>
<tr>
<td>Palmoplantar hyperhidrosis</td>
<td>2 (66.7)</td>
<td>1 (33.3)</td>
<td>0.96</td>
</tr>
<tr>
<td>Facial erythema</td>
<td>2 (66.7)</td>
<td>1 (33.3)</td>
<td>0.96</td>
</tr>
<tr>
<td>Flushing</td>
<td>8 (66.7)</td>
<td>4 (33.3)</td>
<td>0.92</td>
</tr>
<tr>
<td>Yellow skin</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Carotenemia</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Periorbital edema</td>
<td>1 (100)</td>
<td>-</td>
<td>0.99</td>
</tr>
<tr>
<td>Diffuse edema</td>
<td>-</td>
<td>1 (100)</td>
<td>0.32</td>
</tr>
<tr>
<td>Palmoplantar hyperkeratosis</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moist skin</td>
<td>6 (66.7)</td>
<td>3 (33.3)</td>
<td>0.99</td>
</tr>
<tr>
<td>Vitiligo</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Alopecia areata</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>1 (100)</td>
<td>-</td>
<td>0.99</td>
</tr>
<tr>
<td>Urticaria</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Acne rosacea</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Contact dermatitis</td>
<td>3 (100)</td>
<td>-</td>
<td>0.99</td>
</tr>
<tr>
<td>Acanthosis nigricans</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Localized hyperpigmentation</td>
<td>-</td>
<td>2 (100)</td>
<td>0.09</td>
</tr>
</tbody>
</table>
peri orbital edema, psoriasis, and palmoplantar keratosis in the overall study population; among hyperthyroid patients with overall skin findings, alopecia, and brittle nails; and among hypothyroid patients with nail thinning and peri orbital edema.

In a past study conducted with Turkish patients with thyroid disease (n = 220), skin findings were reported to be detected in 56.8% of patients with chronic urticaria (6.8%), vitiligo (6.8%), diffuse alopecia (6%), acne vulgaris (5%), and acne rosacea (3.6%) as the most common findings (7).

In our study population 81.0% of patients had skin findings with xerosis (45.0%), alopecia (32.3%), pruritus (27.3%), brittle nails (22.0%), nail thinning (13.0%), flushing (14.3%), and hair dryness (9.0%) as the most commonly observed ones. When compared to controls, the likelihood of alopecia, nail thinning, brittle nails, diffuse hyperhidrosis, flushing, and xerosis was higher in thyroid patients. Hence, our findings support the likelihood of thyroid diseases to manifest with a wide range of changes in the hair, skin, and nails depending on the thyroid status and are in agreement with the positivity of skin findings such as diffuse alopecia, xerosis, hyperhidrosis, soft and friable nails, onycholysis, and pruritus reported in past studies (3,5,7–11).

Xerosis is one of the characteristic cutaneous symptoms in adults with hypothyroidism that has been considered to occur as a result of peripheral cutaneous vasoconstriction, hypohydrosis, and decline in epidermal steroid biosynthesis and sebaceous gland secretion (2). Moreover, a potential role for topical thyroid hormone has also been suggested in the management of xerosis, even in patients with euthyroidism (12). Hence, identification of xerosis as the most common skin finding in our cohort of patients seems consistent with the fact that 52.7% of overall patients were hypothyroid and 28.7% were euthyroid.

None of our patients had thyroid acropachy, pretibial myxedema, xhantoma, generalized myxedema, bullous pemphigoid, or lupus erythematosus, along with identification of vitiligo, alopecia areata, urticaria, acne rosacea, acanthosis nigricans, and localized hyperpigmentation in less than 1% of our patients.

Among the skin manifestations observed more commonly in patient than in control groups in our cohort, diffuse alopecia, nail thinning, and brittle nails are more commonly associated with hypothyroidism (1,2), while diffuse hyperhidrosis and flushing are among the typical skin findings in hyperthyroid patients, attributed to increased cutaneous blood flow and peripheral vasodilation (13).

Diffuse alopecia and thyroid diseases have been suggested to be associated in 60% of cases, mainly of autoimmune origin (9–11). In a past study from Turkey diffuse alopecia was noted in 6% of overall patients with thyroid disease, being higher in both autoimmune hyperthyroidism and hypothyroidism patients when compared to healthy controls (7). In our study population, alopecia was the second most common skin finding in overall patients, while among hyperthyroid patients with alopecia, autoimmune rather than nonautoimmune origin was more likely. This seems interesting given that alopecia areata rather than diffuse alopecia was in fact associated particularly with a history of atopy and autoimmune disease (14–16).

Aside from alopecia areata, vitiligo and chronic urticaria have also been considered among the dermatological diseases associated with autoimmune thyroid disorders (15,16). In a past study from Turkey, chronic urticaria, vitiligo, and pruritus were reported to be significantly more common among thyroid patients, while urticaria, vitiligo, and diffuse alopecia were more common among patients with autoimmune thyroid diseases as compared with healthy control subjects (7). However, none of these skin findings were more common in autoimmune than in nonautoimmune disease in our cohort, and they were observed in less than 1% of patients.

Nail changes are frequently encountered in thyroid diseases with thin, striated, and brittle nails in hypothyroidism and yellow nails in hyperthyroidism as well as onycholysis in both conditions (3,5,8,9,17). Accordingly, brittle nails were the most common thyroid disease-related change in nails among our patients, and like diffuse alopecia, among hyperthyroid patients with brittle nails, autoimmune rather than nonautoimmune origin of thyroid disease was more likely.

Being among the typical cutaneous manifestations of autoimmune hypothyroidism and/or hyperthyroidism (2), onycholysis, yellow skin, peri orbital edema, psoriasis, and palmoplantar keratosis were not observed among control subjects, while they were more likely in the case of autoimmune than nonautoimmune origin of thyroid disease in our cohort. Based on the clinical and biochemical overlap between Hashimoto’s thyroiditis and Graves’ hyperthyroidism, the occurrence of the same dermatologic and ophthalmologic manifestations has been considered likely (8,10,18–21). Hence, our findings seem to indicate that special emphasis should be placed on skin manifestations of autoimmune etiologies of hypothyroidism (i.e. Hashimoto’s thyroiditis) and hyperthyroidism (i.e. Graves’ disease) (2,5,22).

Skin findings were observed in 96.4%, 85.4%, and 89.5% of our patients with hyperthyroid, hypothyroid, and euthyroid status, respectively. Notably, there were significantly higher percentages of patients with autoimmune than nonautoimmune thyroid disease among hyperthyroid patients with overall skin findings, alopecia, and brittle nails and among hypothyroid patients with nail thinning and peri orbital edema.
In contrast to our findings no statistical difference was reported between “autoimmune vs. nonautoimmune” hyperthyroidism, hypothyroidism, and euthyroidism in a past study, while vitiligo and diffuse alopecia in patients with autoimmune hyperthyroidism and vitiligo in patients with autoimmune hypothyroidism were reported to be higher as compared with the control group (7).

In this regard, our findings emphasize the higher likelihood of certain cutaneous manifestations among patients with autoimmune thyroid disease as compared not only with controls but also with nonautoimmune thyroid disease even in hyperthyroid and hypothyroid states.

Autoimmune thyroid diseases are frequently associated with other organ-specific or systemic autoimmune disorders (4), while both thyroid autoimmunity and increased TSH were reported to represent independent risk factors for thyroid malignancy (6). Hence, upon the diagnosis of autoimmune thyroid disease, clinicians are suggested to be vigilant for any of the potential associated disorders for which the patient may be at risk throughout the patient’s entire life (5,23).

Hyperthyroid patients had significantly higher likelihoods of overall skin manifestations in the case of autoimmune than nonautoimmune origin of thyroid disease, while hypothyroid and euthyroid patients with autoimmune thyroid disease showed higher prevalences of only certain skin findings. Hence, our findings emphasize the importance of recognizing cutaneous manifestations and thus screening for thyroid autoimmunity and function for early identification of thyroid dysfunction and potential comorbidities when the thyroid disease is to be classified as autoimmune, particularly among hyperthyroid patients.

In conclusion, our findings indicate the presence of skin findings in a majority of thyroid patients, the prevalence of which significantly differs for certain cutaneous manifestations with respect to controls, autoimmune etiology, and thyroid functional status. Early recognition of cutaneous manifestations in thyroid patients, particularly among patients with autoimmune hyperthyroidism, seems to enhance timely screening for thyroid autoimmunity and function and thus early identification of thyroid dysfunction and potential comorbidities.

References


