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Skin appendage abnormalities in hypothyroidism: understanding and management

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Abstract

Introduction and purpose

Thyroid ailments are frequently encountered in medical practice, often intertwined with a variety of conditions that may or may not share common underlying factors. Among the organs profoundly influenced by these disorders is the skin, which manifests a diverse array of clinical presentations. However, the exact changes in the structure of skin appendages have not been well studied. Changes in hair structure or nail findings may be helpful in early diagnosis of thyroid disorders and therefore are important for dermatologist education. Hair loss can be a very uncomfortable and embarrassing ailment. Many diseases, nutritional deficiencies, stress and other factors can affect the hair condition and even induce its falling out. This review seeks to explore the numerous skin disorders arising directly or indirectly from thyroid irregularities, offering an updated understanding of the interplay between thyroid function and skin health.

State of Knowledge

It is well-established in scientific literature that thyroid gland disorders, particularly hypothyroidism, induce metabolic deceleration, influencing the inadequate nourishment of

skin appendages, resulting in skin dryness and fragility. Patients commonly report pallor, cold intolerance, and deteriorating hair and nail quality.

Conclusion

We noticed strong correlation between hair loss and the autoimmune process during the dysfunction of thyroid. Euthyroidism plays an important role in hair cycle and any changes can disturb its proper development. In Hashimoto disease elevated levels of antibodies negatively influence hair cycle by excessively inducing telogen phase. Moreover, the blood vessels of the skin constrict disrupting the blood flow which affects hair follicles.

Keywords: hypothyroidism, skin appendage, hair disorders, nails, Hashimoto disease,

Thyroid gland physiology

The thyroid gland produces and releases hormones into the bloodstream: thyroxine and triiodothyronine which are derivatives of the amino acid tyrosine and calcitonin (a hormone involved in calcium-phosphate metabolism). [1]

Thyroxine (T4) is the main secretory product of the thyroid gland with a daily secretion level of approximately 80 μg. Triiodothyronine (T3) is secreted by the thyroid gland in a much smaller amount, approximately 4-6 μg/day but it exhibits 5 times greater activity compared to T4.

It is mainly produced through the conversion of T4 (prohormone) to T3 by deiodinase. [2]

The production and release of thyroid hormones (TH) are mainly controlled by negative feedback from the hypothalamus-pituitary axis. The pituitary gland stimulated by the hypothalamus via thyrotropin-releasing hormone (TRH) and stimulated by decreased TH levels in the blood increases the secretion of thyroid-stimulating hormone (TSH), which in turn stimulates the thyroid gland to produce TH. Increasing TH levels inhibit the function of the hypothalamus and pituitary gland leading to cessation of TSH secretion, consequently inhibiting the production of thyroid hormones. [3]

Hair growth cycle

When considering hair growth we differentiate following main phases: anagen (consisting of six subphases), catagen, telogen, exogen and ketogen. During anagen the cells of the hair follicle multiply rapidly from 2 to 8 years. The majority of the hair remain in this stage. Catagen marks the moment when the proliferation of the cells ceases, and it serves as a bridge to the next step. Telogen is the resting phase of the hair which lasts typically from 2 to 4 months, sometimes extending to 8 months. Exogen is the period when the hair falls out. Before it does, a new one is formed which starts its anagen phase. Lastly, ketogen is a brief period of time when the hair follicle is empty, and a new hair is either not in anlagen yet or is in its very early stages. [4][5] Each of them can be influenced and disrupted by changes that occur during the onset and progression of many diseases.

Pathogenesis of hypothyroidism

Hypothyroidism is a condition caused by a deficiency of thyroid hormones or their inadequate function. The incidence of this condition increases with age, affecting 5% of the population over 60 years old, mainly women. There are different types: primary, secondary, congenital, and acquired. Primary hypothyroidism results from damage to the thyroid gland, which can be caused by thyroid surgery (e.g., thyroidectomy) or inflammation (Hashimoto's disease, subacute thyroiditis, postpartum thyroiditis), or radiation therapy with iodine. Secondary hypothyroidism is caused by deficiency of TSH, usually steming from damage to the pituitary gland or dysfunction of the hypothalamus. Congenital hypothyroidism (cretinism) is usually primary and occurs with a frequency of 1 in 4000 live births. It is caused by suppression or dysfunction of the thyroid gland but it can also occur due to inherited defects of enzymes involved in hormone synthesis. Another cause may be iodine deficiency during pregnancy. Acquired hypothyroidism mainly affects women aged 30–60 years. Among primary acquired hypothyroidism, the most common cause is chronic autoimmune thyroiditis – Hashimoto's disease. [6]

Autoimmune thyroiditis is indicated in the literature as the most common cause of hypothyroidism and affects women 10-20 times more frequently, with the risk increasing with age. It involves impaired immune system function, leading to excessive production of antibodies against thyroid antigens. Additionally, there is progressive destruction of thyroid follicular cells. Both genetic and environmental factors contribute to the etiopathogenesis of Hashimoto's disease, including viral or bacterial infections, stress, smoking, external

irradiation, or treatment with radioactive iodine, selenium deficiency, and excess iodine. Characteristic is the coexistence of other autoimmune diseases alongside Hashimoto's disease, including type 1 diabetes, pernicious anemia, celiac disease, vitiligo, psoriasis, systemic lupus erythematosus and others. [7]

Hashimoto's disease consists of 4 phases. In the beginning no symptoms can be observed. HT, antithyroid peroxidase antibodies (anti-TPO) and antithyroglobulin antibodies (anti-Tg) concentration is normal. The second phase initiates the changes in the antibodies activity in the blood. They become elevated while the HT and TSH concentration is usually normal and the patient remains asymptomatic. However, during this time period hashitoxicosis may occur. The parenchyma cells of thyroid are damaged which leads to HT being released. During the third phase TSH levels are elevated. The patient may start to present symptoms or remain asymptomatic. Finally, the fourth phase presents itself as typical symptoms are observed with different intensity, specific to each case.

Additionally, many physicians may conduct evaluations of a complete blood count and a metabolic profile.

It is estimated that about half of the affected individuals are unaware that they suffer from thyroid gland-related disorders. According to studies conducted on 421 men with thyroid problems, over 37% suffer from diffuse alopecia, the underlying cause of which can mostly be attributed to telogen effluvium, 18% from alopecia areata and the whopping 38% from androgenic alopecia. [8]

Diagnosis and treatment

Initial serum tests will typically include TSH, with FT4 and T3 added if TSH levels are abnormal or if central hypothyroidism is suspected. Moreover, measurement of thyroid peroxidase antibodies is often conducted. Given the higher occurrence of other autoimmune disorders in patients with Hashimoto's thyroiditis, many physicians also conduct evaluations of a complete blood count and a metabolic profile. Upon diagnosis, treatment typically involves administering levothyroxine. [9] A common starting dosage is 1.7 μg/kg, with dose adjustments made within 4 to 6 weeks. [10] The desired TSH level typically falls between 0.5 and 2.5 μU/mL. Levothyroxine treatment does not directly address autoimmune-mediated aspects of the disease, such as pretibial myxedema. [10] In a review conducted by Namrożу et al., it was demonstrated that achieving euthyroidism is potentially attainable through the rationalization of selenium supplementation in patients with subclinical hypothyroidism. The study found that in one-third of patients with subclinical hypothyroidism who received

selenium supplementation without any other treatment, TSH levels decreased to within the normal range. Additionally, TPO antibody levels decreased in both patients who responded to selenium supplementation and the remaining participants in the study group. [11]

Concomitant diseases of hypothyroidism

The autoimmune aetiology of most cases of primary hypothyroidism predisposes patients with hypothyroidism to a higher likelihood of experiencing other related disorders, such as type 1 diabetes, adrenal insufficiency, premature menopause, inflammatory bowel diseases, rheumatic diseases, gluten enteropathy, multiple sclerosis, or vitiligo. Another indication may be a significant family history, as the propensity for thyroid disorders, including autoimmune hypothyroidism, often runs in families. [12] [13] Maternal hypothyroidism affects a child's development from the earliest stages of fetal life. It influences various processes related to the nervous system, cardiovascular system, and musculoskeletal system. [14]

Clinical signs

The symptoms of hypothyroidism are diverse and depend on the degree of thyroid hormone deficiency, age, and duration of the disease. Typical symptoms of hypothyroidism include dryness, roughness, and pallor of the skin, dryness and hair loss, nail brittleness [15] , cold intolerance, tendency to oedema, weight gain, bradycardia, increased diastolic blood pressure, constipation or change of defecation frequency, drowsiness, apathy, lethargy, concentration disorders, worsening exercise tolerance, hoarseness, hearing impairment, shortness of breath, and heavy menstrual bleeding. Due to such rich and nonspecific symptomatology it is often difficult to establish a proper diagnosis quickly and patients are mistakenly treated as having depression, mental disorders, senile dementia or symptomatically treated for anaemia, oedema, shortness of breath, constipation or infertility. Advanced hypothyroidism can lead to generalized oedema, effusions into body cavities, and even to myxedema coma. Myxedema coma is a life-threatening condition directly endangering the patient's life. It occurs particularly in older individuals in the case of untreated or improperly treated hypothyroidism, most often in the presence of additional predisposing factors such as infection, surgery, trauma, hypothermia, gastrointestinal bleeding or destabilization of heart failure. In overt hypothyroidism, the clinical picture is characteristic - the patient is apathetic, swollen, and appears tired. The thyroid gland in hypothyroidism is usually of normal size, often it may be decreased but also enlarged with visible goiter, non-painful on palpation. [16]

Impact on skin

The skin feels cold and pale due to the constriction of blood vessels and decreased blood flow, with a yellowish tint, showing signs of excessively keratinized epidermis, especially on the elbows and knees. The skin becomes dry, rough, and excessively flaky. The causes of these skin features can be attributed to reduced heat production, inhibition of sebaceous and sweat gland function and disturbances in carotene metabolism. Hypothyroidism may manifest as Gull's disease – myxoedema – caused by the accumulation of mucopolysaccharides that bind water (due to increased breakdown) in the subcutaneous tissue and other tissues. This results in the appearance of edema in the eyelids, face, and subsequently the entire body. The edema takes on a diffuse form without deformation upon pressure.

Myxoedema is caused by the deposition of fibronectin and hydrophilic glycosaminoglycans in the subcutaneous tissue where synthesis is inhibited by triiodothyronine. [17] Myxedema may manifest in areas such as the pretibial, preradial, or scalp regions. [18] [19] Apart from the manifestation of hypothyroidism as Gull's disease, Raynaud's phenomenon is also fairly common. Occasionally, it can be the first and sole symptom of the condition. [20] This symptom is typically triggered by exposure to cold temperatures, stress, or vibrations. It leads to episodic color changes in the fingers or toes, starting with pallor, followed by cyanosis and/or redness, usually accompanied by pain. [21]

The skin tone of individuals with Hashimoto's thyroiditis may take on a characteristic yellowish hue due to the lack of hepatic metabolism of carotene, which consequently accumulates in the stratum corneum of the epidermis. Subsequently, carotene is excreted through sweat and reabsorbed by the skin, predominantly depositing in areas rich in sebaceous glands. [17]

Cutis marmorata is also considered as a symptom of hypothyroidism, characterized by the appearance of reddish-blue streaks in a reticular pattern on the skin (resembling a network or marble) due to a decrease in ambient temperature. [22]

The challenge lies in the fact that numerous of these symptoms lack specificity, and many individuals without a diagnosed thyroid disorder may experience them. The identification of primary hypothyroidism relies on an elevated TSH level alongside either normal or decreased FT4 and T3 levels. These standards primarily pertain to patients in outpatient settings, as individuals with systemic illnesses admitted to hospitals may present abnormal thyroid function tests without actually suffering from hypothyroidism, a phenomenon referred to as euthyroid sick syndrome. [23][24]

Impact on hair and scalp

In hypothyroidism hair becomes dull, thinner, brittle which may lead to its excessive fallout, including eyebrows. Nails become brittle, thinner, and may split. In addition to changes in hormone secretion within the thyroid-pituitary-hypothalamus axis, hypothyroidism affects the functioning of other hormones, reducing growth hormone secretion and increasing prolactin secretion. [25]

A deficiency in thyroid hormones causes swelling of the subcutaneous tissue, responsible for nourishing the hair, which significantly affects the condition of the shaft. In the course of Hashimoto's disease there is dryness of the hair which can lead to easy breakage caused by a decrease in sebum secretion from the sebaceous glands [26] and there is also a delay in the onset and rate of hair growth. Concurrent acquired hair fragility (trichoclasis) may be caused by side effects of hormonal medications, antibiotics, vitamin deficiencies, and hypothyroidism. As a result of this disorder the hair becomes thin, dry, lacking softness, and prone to shortening and thinning. It is often associated with split ends (trichoptilosis) [27]

During the course of Hashimoto's disease, alopecia, which is increased or sudden hair loss without concurrent objective changes on the skin, may occur. It can occur on a limited area or the entire scalp in a transient or permanent manner. An example of hormonal alopecia is thyroid alopecia, caused by excessive or insufficient secretion of triiodothyronine and thyroxine. The decrease in metabolism in hypothyroidism also affects hair cells. Hair follicles undergo miniaturization, followed by atrophy (the first symptoms appear after about 2-4 months). [27]

Thyroid hormones have a significant impact on the functioning of the hair follicle. Their presence in the vicinity of hair follicles has been confirmed in numerous studies. They have been found in the papilla and in the outer sheath of the hair root. [28] However, in numerous clinical studies a relationship has been demonstrated between the occurrence of baldness and the presence of antibodies directed against the thyroid, namely anti-TPO and anti-Tg. However, no significant correlation has been observed between thyroid hormonal disorders and the frequency of baldness. This suggests that the main factor responsible for the balding process in autoimmune diseases (including Hashimoto's disease) is autoimmune processes (associated with elevated antibody levels), rather than abnormalities in clinical presentation or thyroid hormone levels. [29]

In Hashimoto's disease, hair loss is attributed to the telogen mechanism, which typically involves a sudden transition of a significant number of hairs from the growth phase to the

resting phase. As a result, when the resting phase concludes a greater amount of hair than usual falls out. Additionally, an increased occurrence of patchy hair loss is observed, as confirmed by numerous studies and analyses. [30]

Thyroid hormones not only affect hair on the head but also eyebrows and eyelashes. The loss of the eyelashes is called milphosis and hypothyroidism is its main reason. [31] It causes lesser tensile strength and telogen effluvium which describes the hair follicles entry into the resting phase too early which lead to their excessive falling out. [31] Their insufficient amount in bloodstream may even lead to Queen Anne sign which manifests as loss of the outer third of eyebrows although it’s not its typical cause. [32]

Impact on nails

Hashimoto's disease causes nail fragility (onychoclasis), which means a tendency for the nail plate to crack, making it brittle. The most common form of nail fragility is lamellar onychoschizia - nail plate dystrophy (splitting of the plate), in which the distal part of the nail plate separates horizontally into many irregular layers. Another form is onychorrhexis - longitudinal fragility, where the nail plate becomes brittle with the formation of cracks near the distal edge of the nail. Autoimmune diseases, such as chronic Hashimoto's thyroiditis, affect nail thinning and increased fragility. The result of nail plate fragility is difficulty in performing manual tasks and the need to trim the nails.

Onycholysis is an additional nail plate irregularity occurring in Hashimoto's disease. This condition involves the detachment of the outer portion of the nail plate from the nail bed, typically starting distally and potentially progressing towards the proximal part. The visibly separated section of the plate often exhibits a whitish hue due to air trapped between the plate and the nail bed. Onycholysis occurs in patients of all races and appears in both hyperthyroidism and hypothyroidism. Onycholysis occurs in patients of all races and appears in both hyperthyroidism and hypothyroidism. [33]

In the course of thyroid disorders, vertical ridging of the nail plate can be observed, running along the longitudinal axis of the finger. This condition manifests as a single, deeper groove or numerous, fine lines. The causes of vertical lines on nails are attributed to genetic predispositions, advanced age, repeated mechanical injuries, iron deficiency, psoriasis, lichen planus, and thyroid diseases. [34]

Another defect is Beau's lines, characterized by uniform depressions in the nails running transversely and parallel. These changes resemble grooves with palpable elevations and are curved towards the distal part of the nail plate. The width of the transverse groove

corresponds to the duration of the disease affecting the nail matrix. When the distal boundary of the groove ends sharply, it indicates a sudden onset of the disease, whereas when the ridging is inclined, it suggests a more chronic course. These lines may be a symptom of autoimmune thyroid diseases, among others. Taguchi described in 2018 a case of a patient with hypothyroidism resulting from Hashimoto's thyroiditis, who reported dry skin, hair loss, and thickened, brittle nails with transverse ridges. After 5 years of taking levothyroxine, the above symptoms subsided. [35]

Koilonychia, also known as spoon nails, is a nail plate shape disorder characterized by thinning with a central concavity and raised lateral edges of the nail. The shape resembles a spoon capable of holding a drop of water. The diagnosis utilizes the so-called bead test, which involves placing a bead on the nail plate to check if the object remains in the depression of the plate. The etiopathogenesis of koilonychia is not fully understood. The causes of isolated spoon-shaped nails (without co-occurrence of other disorders) include disturbances within endocrinological diseases, including thyroid dysfunction. [36]

Skincare

Treating hair loss caused by thyroid dysfunction ought to combine internal modification of autoimmune process and products used externally that contain substances of proven effectiveness and positive influence on hair condition. Extract derived from birch is known to aid in skin conditions, including hair loss which can lead to balding. Applying products that inhibit 5α-reductase may turn out to be more effective. Extracts from green tea, pumpkin seeds, saw palmetto and licorice should be taken into consideration. Moreover, applying them together enhances their effect. It has been proven that alcohol-based solutions containing chilli pepper or rosemary by warming up the skin they stimulate blood flow and make it easier for the extracts to penetrate it. Another example is grape seed oil which supports cell division in hair follicle. [5]

Conclusion

Thyroid function disruption such as Hashimoto disease affects many organs in human body and skin is one of them. Untreated it can lead to very bothersome symptoms which affect both the body and mental health. Lowered levels of thyroid hormones don’t affect the hair cycle as much as it had been assumed. Greater role in hair thinning and eventually hair loss is nowadays attributed to the autoimmune processes happening in the organism. If the condition is managed properly by administered medication hair care, the progression to balding is possible to cease but it isn’t always a guaranteed outcome. Regular hair, skin, and nail care

allows for mitigating the effects of the disease to such an extent that their condition is indistinguishable from that of healthy individuals. While the symptoms of thyroid disorders often present with ambiguity and lack specificity, hypothyroidism should be considered in the list of potential diagnoses when observing potential skin manifestations of thyroid disease, and thyroid function tests should be conducted. Effective treatment hinges on a comprehensive grasp of the underlying pathophysiology, alongside prompt recognition and intervention. Unfortunately, levothyroxine treatment does not directly address autoimmune-mediated aspects of the disease, such as pretibial myxoedema.

Abbreviations: T3-triiodothyronine, T4-thyroxine, TH-thyroid hormones, TRH-thyrotropin releasing hormone, TSH-thyroid-stimulating hormone, anti-Tg- antithyroglobulin antibodies, anti-TPO- antithyroid peroxidase antibodies

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