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Original Research Article

An Observational Study Elucidating and Reiterating the Tell-tale Cutaneous Markers of Hypothyroidism

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Abstract: Thyroid disorders, particularly hypothyroidism are invariably associated with cutaneous abnormalities. Skin manifestations of hypothyroidism range from as subtle as dry coarse hair and mild xerosis to overt features as acquired ichthyosis or myxedema. Dermatologists very frequently come across skin ailments due to underlying endocrinological diseases especially hypothyroidism, in their routine practice. While overt skin changes like ichthyosis and alopecia are evaluated for underlying hypothyroidism, the less conspicuous and rather more common clues like dry skin, coarse hair are often missed. The aim of the study is to evaluate and record the skin changes observed in hypothyroid cases and correlate them with serum thyroid hormone levels. A total of 80 patients clinically suspected to be hypothyroid according to the observed cutaneous changes, were enrolled in the study conducted over 1 year duration in dermatology out-patient department in G.G.S Medical College & hospital. Diagnosis was confirmed by serum thyroid function tests. All skin, hair and nail findings in confirmed cases were recorded and all cases were evaluated for other associated autoimmune disorders. Out of 80 enrolled cases, 70 were confirmed to be hypothyroid. The most common cutaneous change was coarse, dry brittle hair seen in 96% cases, followed by xerosis in 90% cases. Other changes in order of their frequency were telogen effluvium, myxedema and puffiness of hands, feet and face, ichthyosis and generalised loss of body hair and madrosis. Our study highlights the importance of keen observation and high index of suspicion on part of dermatologist to relate even subtle cutaneous findings to a more sinister but reversible cause of thyroid dysfunction.
Keywords: Xerosis, Ichthyosis, coarse hair, Hypothyroidism.

INTRODUCTION

Skin and its appendages serve as a mirror of overall health and wellbeing, such that even subtle cutaneous abnormalities may act as valuable indicators of various systemic disorders. Endocrinological abnormalities, particularly thyroid disorders are among the commonly encountered systemic diseases with prominent cutaneous manifestations presenting to the dermatologist. Many a times good clinical observation and examination on part of dermatologist is helpful for early diagnosis and accurate treatment of thyroid dysfunction.

Skin manifestations of thyroid dysfunction are quite distinct and can be classified into 3 categories depending on their etiology:

1. Due to direct action of thyroid hormone on skin tissue
2. Due to direct thyroid hormone action on non-skin tissues
3. Autoimmune skin disease associated with thyroid dysfunction of autoimmune etiology

Thyroid hormone receptors (TRs) have been detected in epidermal keratinocytes, skin fibroblasts, sebaceous gland cells, vascular endothelial cells, Schwann cells and in various cell types in hair follicle [1-3]. Also, a number of thyroid hormone responsive genes have been identified in skin tissues like the keratin genes, the “hairless” (hr) gene and ZAKI-4 gene [4-8]. Various in vitro studies have shown thyroid hormone to stimulate the growth of both epidermal keratinocytes and dermal fibroblasts, [9-11] only negative thyroid hormone response elements have been identified for these thyroid response genes [4]. This implies that hypothyroidism more often presents with cutaneous manifestations due to direct effect on thyroid response genes, while in thyrotoxicosis most cutaneous findings result from autoimmunity.

Majority of hypothyroid cases have coarse dry skin, decreased swating, dry and dull, brittle hair and nails. Skin changes observed in cases of hypothyroidism have been enumerated in table I. Also, autoimmune thyroid disorders are associated with increased risk of other autoimmune skin diseases, most commonly alopecia areata and vitiligo.

This study was conducted to determine the effect of hypothyroidism on hair and skin and to emphasize upon the role of dermatologist in early diagnosis and hence, prompt management of thyroid dysfunction.

MATERIAL AND METHODS

This study was a prospective and observational study conducted in dermatology department of Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab. A total of 60 clinically suspected cases of thyroid dysfunction, presenting to dermatology out-patient department with hair and skin abnormalities, during a period of 1 year from June 2013 to May 2014, were enrolled in the study.

Patients were subjected to detailed medical history, physical examination and serum thyroid function test including serum Thyroid Stimulating Hormone (TSH); free Thyroxine hormone (T3, T4) levels along with routine investigations like complete blood count and fasting blood sugar. Out of 60 suspected cases of thyroid dysfunction enrolled, 10 cases were found to be euthyroid and were excluded from study, while remaining cases were diagnosed as hypothyroid based on serum thyroid function test results. The normal range for thyroid function test is serum T3 level 2.5-3.9 pmol/l, T4 level 0.61-1.12 pmol/l and serum TSH 0.35-5.5 mIU/ml. Hypothyroidism is diagnosed with serum TSH > 5.5 and serum T4 < 0.61. Hair and skin abnormalities in these patients were recorded. Direct microscopic examination of hair follicle including Potassium hydroxide examination was done to detect any structural hair shaft abnormality, fungal infection or exclamation mark hair of alopecia areata. Other concomitant autoimmune skin diseases observed during history and examination were also noted.

RESULTS

Most of the patients enrolled in our study were females in adolescence or young adults. Male to female ratio of hypothyroid cases was 1:2 and age ranged from 8 years to 50 years. Among the 50 confirmed cases of hypothyroidism, xerosis was the most common cutaneous finding with dry coarse scaly skin observed in about 45 cases (90%). In 6 cases (12%), severe and extensive xerosis was seen with ichthyotic scaly lesions and generalised loss of hair all over the body, predominantly affecting bilateral arms, legs and abdomen. These cases were found to have very low levels of T4 and high TSH, 0.01 pmol/l and >100 mIU/ml respectively.

Table 1: Skin manifestations of hypothyroidism

DUE TO DIRECT ACTION OF LOW THYROID HORMONE LEVEL ON SKIN TISSUES	INDIRECT EFFECT DUE TO ACTION OF LOW THYROID HORMONE LEVELS ON OTHER TISSUES
Cutaneous changes	**Cutaneous changes**
Dry, coarse, scaly and wrinkled skin	Pallor
Xerosis	Cold intolerance
Ichthyosis	Delayed wound healing
Myxedema (Non-Pitting edema)	Purpura and ecchymosis
Edema and puffiness of face, eyelids, hands	Punctate telangiectasias on arms and fingertips
Carotenemia (Ivory–yellow skin colour)	Drooping of upper eyelids
Palmoplantar keratoderma	Nerve entrapment syndromes
Absence of sweating	Xanthomatosis (secondary to hyperlipidemia)
Hair changes	**ASSOCIATED AUTOIMMUNE DISEASES**
Dry, brittle, coarse scalp hair	Alopecia areata
Alopecia (Telogen Effluvium)	Vitiligo
Loss of pubic, axillary and facial hair)	Lichen planus, Lichen planopilaris
Madarosis (Loss of lateral third of eyebrows)	Chronic urticaria
Premature greying of hair	Dermatitis herpetiformis
Candida folliculitis	Pemphigus
	Bullous pemphigoid
Nail changes	Lupus erythematosus
Dull, thin, brittle and striated nails	Scleroderma
Slow nail growth	Lichen sclerosus et atrophicus
	Acanthosis nigricans with insulin resistance
Oral changes	Granuloma annulare
Large tongue	
Gingival swelling (in congenital hypothyroidism)	

Diffuse loss of scalp hair and telogen effluvium was observed in about 32 cases (64%) while hair were coarse and dry in majority of patients 96% cases. Also, density of body hair was reduced, particularly with sparsity of axillary, pubic and facial hair, accompanied with facial puffiness and myxedema of bilateral hands and feet in 12 cases (24%). In few cases, 4 cases madarosis was seen. Serum TSH levels were markedly elevated in these cases with low T4 levels suggestive of severe hypothyroidism.

3 out of 50 cases showed patchy hair loss over scalp with positive hair pull test and exclamation mark hair on direct microscopic examination suggestive of alopecia areata and 1 case had lichen planopilaris of scalp. Various hair and skin abnormalities observed in hypothyroid cases in our study along with their thyroid function tests are listed in Table 2.

Table 2: Hair and skin abnormalities along with respective thyroid function results observed in our study

Hair and Skin abnormalities observed	Number of cases observed	Thyroid Function Test (mean value)
Diffuse loss of scalp hair	64% (32/50)	T4 (0.34 +/- 0.25 pmol/L) TSH (26.79 +/- 8.2 mIU/ml)
Loss of body hair, especially axillary, pubic and facial hair	24% (12/50)	T4 (0.30 +/- 0.28 pmol/L) TSH (18.65 +/- 5.5 mIU/ml)
Dry coarse brittle hair	96% (48/50)	T4 (0.38 +/- 0.30 pmol/L) TSH (12.56 +/- 3.44 mIU/ml)
Madarosis	8% (4/50)	T4 (0.13 +/- 0.1 pmol/L) TSH (59.11 +/- 24 mIU/ml)
Xerosis with dry coarse scaly skin	90% (45/50)	T4 (0.38 +/- 0.20 pmol/L) TSH (12.10 +/- 6.5 mIU/L)
Ichthyosis	12% (6/50)	T4 (0.09 +/- 0.04 pmol/L) TSH (180 +/- 62 mIU/ml)
Myxedema (Non-pitting edema) of bilateral hands and feet	24% (12/50)	T4 (0.05 +/- 0.01 pmol/L) TSH (210 +/- 65 mIU/ml
Facial puffiness	24% (12/50)	T4 (0.12 +/- 0.2 pmol/L) TSH (59.11 +/- 28 mIU/L)
Alopecia areata	6% (3/50)	T4 (0.36 +/- 0.30 pmol/L) TSH (38.09 +/- 14.55 mIU/L)
Lichen planopilaris	2% (1/50)	T4 (0.34 +/- 0.22 pmol/L) TSH (23.67 +/- 10.33 mIU/L)

DISCUSSION

Our study conducted over 1 year duration in the dermatology outpatient department of a tertiary level hospital in Punjab showed significantly high frequency of skin and hair changes in hypothyroid patients.

Direct action of thyroid hormone on skin is mediated through Thyroid hormone receptors (TRs) that have been identified in epidermal keratinocytes, skin fibroblasts, and cells making up hair follicle, sebaceous gland cells, and sweat glands. Even elements of Hypothalamic-Pituitary-Thyroid hormone axis have been identified in human skin [12-14].

Various in vitro tissue culture studies have shown T3 to stimulate proliferation of both epidermal keratinocytes and dermal fibroblasts, [10,11] however in vivo this effect is subdued by inhibiting factors dependent on systemic T3 levels [9]. Hypothyroidism often presents with coarse dry scaly skin, sometimes with ichthyosis due to retention hyperkeratosis as low thyroxine hormone levels result in decreased levels of plasminogen activator, required for normal corneocyte desquamation [15] and elevated transglutaminase levels required for formation of cornified envelope [18]. Also the normal barrier function of stratum corneum is defective due to abnormal development of lamellar granule [16].

Reduced eccrine gland secretion due to atrophy of sweat glands in hypothyroidism, may in addition contribute to xerosis [17, 18]. In cases with severe hypothyroidism, skin is pale cool and myxedematous with puffiness of face and body. These results due to increased accumulation of mucopoly saccharides, particularly hyaluronic acid in the dermis, which being extremely hygroscopic swells to thousand times its dry weight when hydrated [19, 20]. Increased dermal water content also results from extravascular transudation of albumin protein into dermis, due to increased intracapillary hydrostatic pressure. This myxedematous state is further worsened by impaired lymphatic drainage leading to non-pitting edema [21]. Hypothyroidism reduces basal metabolic rate, thereby decreasing core body temperature which is compensated by reflex vasoconstriction of cutaneous

capillaries leading to reduced skin perfusion, accounting for cool pale skin [22-24].

Telogen effluvium, dry brittle sparse hair not responding to conventional treatment and madarosis, often prompts the dermatologist to evaluate for underlying thyroid dysfunction. The direct action of thyroxine hormone on hair growth cycles have been demonstrated by Hale and Ebling , who reported increased hair cycle turn over, reducing the time for hair restoration post epilation by 10%, though net hair length remained unchanged [25]. Also, exogenous application of thyroxine in combination with insulin and growth hormone has shown to increase hair count over a 6 month treatment period in males with androgenetic alopecia [26].

Hypothyroidism is associated with reduced expression of 'hr' gene which is expressed and regulated by TR in brain [7, 8] and addition of exogenous T3 restores its expression [18]. Mutation of this gene is known to be associated with alopecia [27-30]. Alopecia areata is often associated with autoimmune thyroid disease including Hashimoto thyroiditis. Routine screening of patients with autoimmune skin diseases like alopecia areata, vitiligo, urticaria, lichen planopilaris, lichen sclerosus ET atrophicus, bullous diseases like pemphigus and lupus erythematosus, aids in early detection and timely management of associated autoimmune thyroid dysfunction.

Our study highlights the importance of keen observation and high index of suspicion on part of dermatologist to relate cutaneous findings as subtle as coarse brittle hair and reduced body hair to a more sinister but reversible cause of thyroid dysfunction. This study emphasizes that all cases of xerosis with pruritus and patients with dry coarse brittle hair, not responding to conventional treatment must be evaluated for underlying hypothyroidism as these are the earliest and most common cutaneous manifestations of low serum thyroid hormone levels and a dermatologist should recognize these subtle signs for the prompt and proper management of hypothyroidism.

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