

# CHALLENGES OF CUTANEOUS CARE IN HYPERTHYROIDISM: A CASE REPORT

## ABSTRACT

Cutaneous manifestations of thyroid disease are one of the first notable signs of thyroid hormone dysregulation. Skin changes in hyperthyroidism vary from individual to individual. In dark skinned Africans it may be challenging to detect these dermatoses and care for the patients with these dermatoses if they arise. Making the actual cutaneous diagnosis in hyperthyroidism may be impaired by co-morbidities, drug-drug interactions, hypersensitive reactions, unusual presentation of common diseases, immunosuppression that may result to opportunistic infections and similar presentations of dermatoses. There may be dermatoses that may co-exist with other dermatoses within the same site. The peculiarity of our case report is that we present three females with hyperthyroidism that cut across different age groups with different cutaneous lesions. This case report aims to present the challenges of making accurate skin diagnosis and challenges that arise in actually caring for them. Counselling the patient on the appropriate care and prognosis of these skin lesions would help in improvement of quality of life and unwanted expectations

**Key Words:** Care, Challenges, Cutaneous, Hyperthyroidism, Skin

## INTRODUCTION

Thyroid hormone is considered one of the key regulatory hormones for skin homeostasis. Cutaneous manifestations of thyroid disease are one of the first notable signs of thyroid hormone dysregulation. Multiple skin diseases are associated with thyroid hormone dysregulation.<sup>1</sup> The effect of thyroid hormones on the skin includes converting beta carotene to vitamin A and thermoregulation.<sup>2</sup> Thyroid hormone is also involved in foetal epidermal differentiation, barrier formation, hair growth, wound healing, keratinocyte proliferation and keratin gene expression.<sup>2,3</sup> Skin changes in hyperthyroidism vary from individual to individual.<sup>4</sup> In dark skinned Africans it may be challenging to detect these dermatoses and care for the patients with these dermatoses if they arise.<sup>5</sup> Making the actual cutaneous diagnosis in hyperthyroidism may be impaired by co-morbidities, drug-drug interactions, hypersensitive reactions, unusual presentation of common diseases, immunosuppression that may result to opportunistic infections and similar presentations of dermatoses. There may be dermatoses that may co-exist with other dermatoses. This case report aims to present the challenges of making accurate skin diagnosis in hyperthyroid patient and a literature review on the subject.

## CASE REPORT

## Case 1

A 71 year female who visited the dermatology outpatient clinic with complaints of skin rash of 4 weeks duration located on her forearms and back which were said to be pruritic and with discharge of fine scales. She had also noticed hyperpigmented pruritic patch at her posterior right thigh a week later. She had also intense pruritus of her scalp with discharge of fine scales. She had also a history of diffuse hyperpigmentation of her entire skin which she noticed 22 years ago prior to current complaints. About the same time she was diagnosed as hyperthyroid secondary to toxic multinodular goitre following complaints of neck swelling and intense pruritus for she was placed on carbimazole. She had also noticed non pruritic hypopigmented dot- sized skin discoloration on her lower limbs extending to her thigh and her upper arms which she noticed increases in number each year as she got older. On examination she had tooth pick in her hairs (which she says she uses it to scratch her scalp) hypopigmented patches on her back, forearms and lower limbs. Her hands were sweaty and moist. Skin diagnoses made on different hospital visits were cholinergic urticaria, probable scabies, idiopathic guttate hypomelanosis (IGH) and pityriasis versicolor, seborrhoeic dermatitis, lichenoid dermatitis for the most recent complaints. She was treated with 5% permethrin cream, tabs loratadine 10 mg nocte for 10 days, 2% ketoconazole (shampoo and topical ointments) and carbimazole was continued. She was counselled on her skin conditions and probable risk factors. She was relieved of the pruritus and continues follow up visits in the endocrinology and dermatology clinics.



**Figure 1: Cutaneous lesions in elderly female with hyperthyroidism**

## Case 2

A 45 year female was seen on request on account of skin rash of 1 year, with a preceding history of generalised pruritus of 5 months duration. Pruritus was worse with perspiration over the anterior neck. She was being managed by endocrinology and cardiology units for congestive heart failure secondary to hyperthyroidism and was on carbimazole, propranolol, toremide, atorvastatin, and clopidogrel. She had also received a short course of systemic antibiotics- ceftriaxone and metronidazole. On examination, she had diffuse loss of fine hair worse on the frontal area, no eyesigns were noted and neck swelling was asymmetrically enlarged, she had generalized hyperpigmented macules and papules with central hypopigmentation with dorsal sparing of the upper limb, hyperpigmented distal nails and onycholysis. There was also bilateral hyperpigmentation extending from the mid shin to the ankle area with few hyperpigmented discrete papulonodular lesions on the lower limbs. A diagnosis of mild non- scarring alopecia,

papular urticaria and Plummer nails with chronic stasis dermatitis was made. Complete blood count showed hyperesinophilia. Skin biopsy was planned for to rule out thyroid dermopathy however patient declined due to financial constraints. Patient was treated with fexofenadine 180mg tablets daily for 1 week, prednisolone 20mg daily for 1 week and 0.05% clobetasol propionate cream daily for 6 weeks. The anti-thyroid drug was sustained and increased appropriately. The pruritus ceased and the hair growth improved.



**Figure 2: Cutaneous lesions in middle aged female with hyperthyroidism**

### Case 3

A 24 year old unemployed lady who was referred by colleague via telephone for complaints of generalized body itching for past three years. Scabicides have been commenced prior to dermatology visit. On examination she had, hyperhidrosis, bilateral ophthalmopathy, diffuse neck swelling, pallor and tachycardia. There was no skin rash seen. A diagnosis of thyrotoxicosis was made. Tabs loratadine 10mg nocte for 10 days, 40 mg propranolol and 20 mg of carbimazole was commenced immediately. She was counselled about the disease condition and referred to the endocrinology unit where thyroid function done confirmed the diagnosis of thyrotoxicosis secondary to Grave's disease. She is being followed up in the endocrinology unit.

### Discussion

We present three different case scenarios of skin complaints in those with hyperthyroidism. They were all females within three different age groups- the young, middle aged and the elderly. Hyperthyroidism in Nigeria has been known to be commonly caused by Grave's disease and is commoner in females.<sup>6</sup> The action of thyroid hormone on skin is mediated by G-coupled thyroid receptors.<sup>3,8</sup> There are different ways in which thyroid diseases result in skin diseases and they include- direct action of thyroid hormone on skin tissues, direct thyroid hormone action on non-skin tissues that lie within the skin structure such as blood vessels and glands and autoimmune skin disease (AISD) associated with thyroid dysfunction of autoimmune aetiology.<sup>7</sup> Other cutaneous manifestations can arise from opportunistic skin infections and infestations from the immunosuppression caused by the thyroid disease and by the drug induced side

effects. Hyperthyroidism has a variable effect on the epidermal diameter.<sup>7</sup> In some cases it causes increase in epidermal keratinocytes and dermal fibroblasts via thyroid receptors.<sup>3,7,8</sup> It may also cause increase in collagen catabolism leading to epidermal thinness.<sup>7</sup> The consequence of the direction of hyperthyroidism causes the skin to be smooth, warm, moist and velvety like an infant's skin.<sup>1,8</sup> In some cases it is described as being smooth and thin but not atrophic.<sup>7</sup> Hyperhidrosis has been noted to be a frequent manifestation of thyroid hormone-related epidermal disease in hyperthyroidism.<sup>1</sup> This manifestation was clearly seen in two of the cases.

The direct effect on non-skin tissues in hyperthyroidism includes action on the sweat glands as a result of increased sympathetic activity from the synergistic action with catecholamines leading to hyperhidrosis.<sup>1,7,8</sup> On the capillaries the excess thyroid hormones cause increased cutaneous blood flow that is responsible for the erythema. There is also peripheral vasodilation that also results in palmar erythema and facial flushing.<sup>1,7,8</sup> Increased pituitary adrenocorticotropic hormone (ACTH) compensating for accelerated cortisol degradation leading to hyperpigmentation is seen in hyperthyroidism.<sup>8</sup> Hyperpigmentation is a known physical examination finding in conditions where adrenocorticotropic hormone (ACTH) is excessive. This is because ACTH shares the same affinity with  $\alpha$ -melanocyte-stimulating hormone (MSH) for the melanocortin-1 receptor (MC1R). MC1R is considered the most important melanocortin receptor that regulates melanogenic activity.<sup>9</sup> ACTH has also been shown to act directly on melanocytes to stimulate melanogenesis--an in vitro study.<sup>10</sup> Hyperpigmentation was reported in the patients in this case report.

Autoimmune destruction of skin and non-skin tissues as a result of autoantibodies such as anti-thyroid peroxidase (TPO) IgE antibodies (Anti TPO) seen in thyroid dermatopathy. Other autoantibodies found in Grave's disease are anti-thyroglobulin antibodies and anti-TSH receptor antibodies.<sup>8</sup> Thyroid dermatopathy seen more in Grave's disease, rarely in Hashimoto thyroiditis or hypothyroidism. Hashimoto thyroiditis can also present as hyperthyroidism (thyrotoxicosis) or hypothyroidism.<sup>8</sup> The term thyroid dermatopathy refers to the unique manifestation of the thick velvety appearance of the skin which can occur on any part of the body but this may not be readily appreciated in dark skinned individuals.<sup>1,7,8</sup> Dependent oedema when present in the lower limbs may also contribute to either the fibroblast stimulation or hyaluronic acid build up and hence be the reason why thyroid dermatopathy tends to occur in the lower limbs.<sup>8</sup> This is the essence of requesting for a skin punch biopsy and histopathology. The presentation is variable clinically from being well circumscribed patch to having nodules, plaques that is non-pitting with a peau d'orange appearance occurring usually on the lower limbs but can occur in any part of the body such as the lips where it is commonly looked for.<sup>8</sup> Other dermatologic diseases that have been associated with Grave's disease autoimmune disorder include anetoderma, dermatitis herpetiformis, mid-dermal elastolysis pemphigus gestationis, pemphigus vulgaris, Sweet's syndrome.<sup>1,4,8</sup> Hyperthyroidism particularly Grave's disease can cause increase in the proteoglycans associated with the dermal papilla leading to hypertrichosis. Acropachy which is

rare is described as digital clubbing with soft tissue swelling plus periosteal new bone formation can be seen in hyperthyroidism. Opportunistic skin infections such as pityriasis versicolor in hyperthyroidism are due to hyperhidrosis that favours *Malassesia furfur* that was observed in the first case. There are also cutaneous skin reactions that can result from anti-thyroid drugs. Carbimazole is noted to cause allergic drug reactions, aplasia cutis and alopecia.<sup>7, 11, 12</sup> Propylthiouracil can also cause allergic drug reactions, urticaria, drug induced lupus and leukocytoclastic vasculitis.<sup>11</sup>

Pruritus in hyperthyroidism is multifactorial. Generalized pruritus as seen in these cases is likely due to the activated kinins such as bradykinins from increased tissue metabolism or there may be reduction in the itch threshold as a result of warmth and vasodilation.<sup>13</sup> It can be due to jaundice occasionally seen in hyperthyroidism, opportunistic fungal infections that thrive in hyperhidrosis or drug induced allergic reactions such as urticaria from anti-thyroid drugs.

Challenges of cutaneous care in hyperthyroidism have arisen because of several factors relating to making accurate diagnosis. Similar clinical presentations can be seen in any of the thyroid imbalance disorders; either hyperthyroidism or hypothyroidism. Examples are thyroid dermopathy, pruritus, nail changes and hair loss. The replacement of thyroid hormone in hypothyroidism can be a cause of iatrogenic hyperthyroidism leading to cutaneous effect such as myxedema or thyroid dermopathy.<sup>3, 14</sup> This can be resolved by doing thyroid function tests of which thyrotropin (thyroid stimulating hormone) is the most important. Subclinical hyperthyroidism can also manifest as hyperthyroidism presenting with subtle cutaneous manifestations.<sup>1</sup> These common skin manifestations certainly have different mechanisms in which they occur in the different conditions. In recent years, hyperthyroidism has been found to manifest with common, unusual, subtle, or simply bizarre cutaneous manifestations that challenge our traditional understanding. Knowing different presentations of hyperthyroidism related skin disease can help point a clinician to the correct diagnosis.<sup>1</sup> The cost of care for skin manifestations as priority has to be set in terms of managing the likely life threatening hyperthyroid manifestations such as heart disease as seen in the middle aged female in this case report. The cosmetic concerns and quality of life that cutaneous disorders pose should be weighed against patient's financial status hence the need for adequate counselling and psychosocial support. In making diagnosis, there are several differential diagnoses that can be possible. The elderly patient presented with hypopigmented macules on different parts of her body. The possible causes were IGH, pityriasis versicolor and vitiligo. It is also important to note that there may be physiological changes that may cause cutaneous changes such as IGH in aging adults and actual pathological changes from vitiligo. These two distinct skin manifestations both have autoimmune mechanisms responsible for them however the triggers and pathogenesis are different.<sup>15</sup> A good history, physical examination and investigations such as Wood light, autoimmune antibodies and skin punch biopsy would aid in making accurate diagnosis; distinguishing similar cutaneous manifestations.

It is also important to note that skin disorders can co-exist. Thyroid dermopathy can co-exist with chronic stasis dermatitis following prolonged pedal oedema which has been known to favour the manifestation of thyroid dermopathy via increased stimulation of dermal fibroblast as suspected in the middle aged female in this case report.<sup>8</sup> Treatment varies based on whether the skin manifestation is a direct result of thyroid hormone action or its extra-thyroidal manifestations.<sup>1</sup> The treatment response of the cutaneous lesions is also important to note. There are certain cutaneous manifestations that may ease with time as the patient responds to anti-thyroid treatment while others may persist throughout the course of illness which may be life-long. These dermatoses are likely to cause the patient to present to the dermatology clinic or may be of extreme concern to the patient and impair the quality of life even while facing acute complications such as having heart failure secondary to hyperthyroidism. Treatment of thyroid dermopathy is often challenging. Control of hyperthyroidism has been shown to have no effect on this cutaneous manifestation.<sup>1,16</sup> Intra-lesional or topical corticosteroids with or without occlusion, complete decompressive physiotherapy, surgical excision, octreotide, an insulin analogue, pentoxifylline, high-dose intravenous immunoglobulin treatment and plasmapheresis have been used with improvement in mild cases.<sup>1,16</sup> Urticaria and angioedema have good response with anti-thyroid treatment while pruritus, alopecia areata and hyperpigmentation have poor response to treatment.<sup>1</sup> It is also important to note that some cutaneous manifestations of hyperthyroidism are not pathognomonic to the disorder such as Plummer's nails that has been described as dirty nails characterised by dirt trapped within the distal onycholysis.<sup>17</sup> There is need to rule other systemic disorders which can equally co-exist with hyperthyroidism that may be responsible for the cutaneous defects such as nutritional deficiencies and other autoimmune skin conditions. Other therapies used for managing complications of hyperthyroidism can also present with cutaneous side effects. Propranolol used in thyroid storm and thyrotoxicosis can present with alopecia, erythema multiforme, lichenoid reactions and Peyronie's disease.<sup>18</sup> Previous self-prescribed therapies used for perceived skin lesions, might distort the original appearance of skin lesions, worsen the skin lesions, resolve the skin lesions or make no difference at all, as it was seen in the young female in this report.<sup>19</sup> This can cause financial constraints or frustrate the hyperthyroid patient resulting in distrust of conventional therapies.<sup>19</sup> There is need for public enlightenment, health education and appropriate referral as it was done in this report. Drugs used in solving a cutaneous manifestation from hyperthyroidism may result in another skin disorder. This is described as a dermatological dilemma and can be a challenge for dermatologists.<sup>20</sup> There is need for appropriate counselling of the patient and patient education of possible side effects of interventions including bizarre or idiosyncratic drug reactions that occur with virtually any drug.<sup>20</sup> Financial constraint is one of the major challenges in cutaneous care in hyperthyroidism particularly in this setting; where all health needs are out of pocket expenditure.<sup>21</sup> Health insurance hardly covers skin care in many countries except for some skin diseases like skin cancers.<sup>22</sup> Cure for these cutaneous lesions may not always be feasible hence appropriate counselling and hope for better therapies in the future.<sup>21, 22</sup>

## CONCLUSION

Hyperthyroidism can present with varying cutaneous lesions, some which are directly related to excess hormones and others which are indirectly related as result of immunosuppression, alteration of immune systems or in the course of treatment. There are several challenges that can affect the management of these cutaneous lesions. Counselling the patient on the appropriate care and prognosis of these lesions would help in improvement of quality of life and unwanted expectations

#### Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

#### Ethical Approval:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

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