



HYPERPIGMENTATION IN HYPERTHYROIDISM

General Medicine

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ABSTRACT

Hyperpigmentation is a commonly encountered sign in clinical practice, which is associated with multiple disorders, however its association with the grave's disease have rarely been reported, here we present a case of 30-year-old women who presented with hyperpigmentation mainly on the flexor surface of the forearm along with other features of grave's disease which was later confirmed by evaluating the biochemical parameters.

KEYWORDS

Adrenocorticotrophic Hormone, Grave's Disease, Hemosiderin Deposition, Hyperpigmentation, Thyroid-stimulating Hormone

INTRODUCTION

Endocrinopathies have been associated with hyperpigmentation as seen in Addison's disease and haemochromatosis but have rarely been reported with thyroid dysfunctions. Telangiectasia, eczematous dermatitis, localized myxedema, and alopecia are more common manifestations that are associated with hyperthyroidism. [1-3]

Though the exact mechanism of hyperpigmentation in hyperthyroidism is not clearly understood, but there are various postulates which helps us in understanding the possible mechanism. In one of the studies it was speculated that skin pigmentation in hyperpigmentation can be attributed to presence of TSH receptor on the surface of epidermal melanocytes. [4] K. Banba et al postulated that increased capillary fragility leads to hemosiderin deposit which was confirmed by the iron stain of the area could be the possible cause of the hyperpigmentation. [5] few other researchers have suggested that accelerated degeneration of the cortisol leads to increased release of pituitary ACTH which further leads to increase activity of the melanotropin leading to hyperpigmentation. [6-9]

CASE REPORT

A 30-year-old female patient presented to out hospital with the complaints easy fatiguability, weight loss despite increased of appetite, menstrual irregularities, skin pigmentation as shown in the figure 1, on further examination was found to have fine tremors, neck swelling was present. On general physical examination patient had PR of 120 bpm and BP – 118/80 mm Hg. ECG of the patient also showed sinus tachycardia. There were no significant findings appreciated in an examination of central nervous system, cardiovascular system, respiratory system and gastrointestinal system. Further relevant investigation was performed to establish the diagnosis, which revealed that the patient had elevated level of free t3, free t4 and low TSH, patient was advised for anti-thyroid receptor antibody which turned out to be positive. Rest all biochemical parameters were within normal limits. On the basis of history, examination and laboratory parameter a diagnosis of primary hyperthyroidism was made and patient was initiated on carbimazole and betablockers. On follow up visits there were reduction in the all the symptoms and hyperpigmentation.

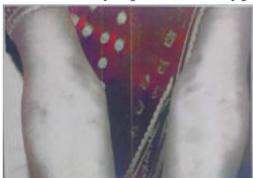


Figure 1: Hyperpigmented lesion on flexor surface of arms

DISCUSSION

Hyperthyroidism presents with various dermatological manifestations among which hyperpigmentation of the skin in less appreciated and reported features. This pigmentation can be the result of direct or indirect action of the thyroid hormone. Direct effect include binding of the all three isoforms of the thyroid hormones to the specific receptor present on the skin and tissues. [10-13] These receptors have been found on in epidermal keratinocytes, skin fibroblasts, hair arrector pili muscle cells, other smooth muscle cells, sebaceous gland cells, vascular endothelial cells, Schwann cells, and a number of cell types that make up the hair follicle. These epidermal keratinocytes and dermal fibroblasts are stimulated by T3 hormone. [14-16] Along with that few genes have also been identified which tend to respond to thyroid hormone. Few researches have shown a promising result in establishing a link between skin and hypothalamic-pituitary-thyroid hormone axis. [17-19]

Indirect effect of thyroid hormone is thought to be due to autoimmunity. Skin biopsy of thyrotoxic patient in one of the reports showed thickened epidermis. [20] the possible explanation to this is majority of the thyrotoxicosis results from grave's disease, which could lead to deposition of the glycosaminoglycan as result of autoimmunity.

Hyperpigmentation in hyperthyroidism is rarely reported clinical feature with very few mentions in the literature Song et.al describes on such case which was encountered by them. [21] Through this case report we would like to draw attentions of the physicians to consider hyperthyroidism as one of the differential diagnoses of the hyperpigmentation.

REFERENCES

1. Taketomo Y, Noso S, Babaya N, et al. Common phenotype and different non-HLA genes in Graves' disease and alopecia areata. *Hum Immunol* 2017; 78:185-9.
2. Shih SR, Lin MS, Li HY, et al. Observing pretibial myxedema in patients with Graves' disease using digital infrared thermal imaging and high-resolution ultrasonography: for better records, early detection, and further investigation. *Eur J Endocrinol* 2011; 164:605-11.
3. Lause M, Kamboj A, Fernandez Faith E. Dermatologic manifestations of endocrine disorders. *Transl Pediatr* 2017; 6:300-12.
4. Slominski A, Wortsman J, Kohn L, et al. Expression of hypothalamic pituitary-thyroid axis related genes in the human skin. *J Invest Dermatol* 2002; 119:1449-55.
5. Banba K, Tanaka N, Fujioka A, et al. Hyperpigmentation caused by hyperthyroidism: differences from the pigmentation of Addison's disease. *Clin Exp Dermatol* 1999; 24:196-8.
6. Slominski A, Tobin DJ, Shibahara S, et al. Melanin pigmentation in mammalian skin and its hormonal regulation. *Physiol Rev* 2004; 84:1155-228.
7. Leonhardt JM, Heymann WR. Thyroid disease and the skin. *Dermatol Clin* 2002; 20:473-81.
8. Yamamoto H, Yamane T, Iguchi K, et al. Melanin production through novel processing of proopiomelanocortin in the extracellular compartment of the auricular skin of C57BL/6 mice after UV-irradiation. *Sci Rep* 2015; 5:14579.

9. Diven DG, Gwinup G, Newton RC. The thyroid. *Dermatol Clin* 1989; 7:547–58.
10. Ahsan MK, Urano Y, Kato S, Oura H, Arase S. Immunohistochemical localization of thyroid hormone nuclear receptors in human hair follicles and in vitro effect of L-triiodothyronine on cultured cells of hair follicles and skin. *Journal of Medical Investigation* 1998; 44:179-84.
11. Torma H, Rollman O, Vahlquist A. Detection of mRNA transcripts for retinoic acid, vitamin D3 and thyroid hormone (c-erb-A) nuclear receptors in human skin using reverse transcription and polymerase chain reaction. *Acta Derm Venereol* 1993; 73:102-7.
12. Billoni N, Buan B, Gautier B, Gaillard O, Mahe YF, Bernhard BA. Thyroid hormone receptor beta-1 is expressed in the human hair follicle. *British Journal of Dermatology* 2000; 142:645-52.
13. Torma H, Karlsson T, Michaelsson G, Rollman O, Vahlquist A. Decreased mRNA levels of retinoic acid receptor-alpha, retinoid X receptor-alpha and thyroid hormone receptor-alpha in lesional psoriatic skin. *Acta Derm Venereol* 2000; 80:4-9
14. Safer JD, Fraser LM, Ray S, Holick MF. Topical triiodothyronine stimulates epidermal proliferation, dermal thickening and hair growth in mice and rats. *Thyroid* 2001; 11:717-24.
15. Safer JD, Crawford TM, Fraser LM, Hoa M, Ray S, Chen TC, et al. Thyroid hormone action on skin: Diverging effects of topical versus intraperitoneal administration. *Thyroid* 2003; 13:159-65.
16. Holt PJA. In vitro responses of the epidermis to triiodothyronine. *J Invest Derm* 1978; 71:202-4.
17. Slominski A, Wortsman J, Kohn L, Ain KB, Venkataraman GM, Pisarchik A, et al. Expression of hypothalamic-pituitary-thyroid axis related genes in human skin. *J Invest Dermatol* 2002; 119:1449-55.
18. Bodó E, Kany B, Gáspár E, Knüver J, Kromminga A, Ramot Y, et al. Thyroid-stimulating hormone, a novel, locally produced modulator of human epidermal functions, is regulated by thyrotropin-releasing hormone and thyroid hormones. *Endocrinology* 2010; 151:1633-42.
19. Paus R. Exploring the “thyroid-skin connection”: concepts, questions and clinical relevance. *J Invest Dermatol* 2010; 130:93-101.
20. Holt PJA, Marks R. The epidermal response to change in thyroid status. *Journal of Investigative Dermatology* 1977; 68:299-301.
21. Song, Xiaoxiao MD, PhDa; Shen, Yimin MBBSa,b; Zhou, Ying MSc; Lou, Qinhua MBBSb; Han, Li MBBSb; Ho, Jon Kee MSb; Ren, Yuezhong MDa. General hyperpigmentation induced by Grave's disease, *Medicine*: December 2018 - Volume 97 - Issue 49 - p e13279