Nail hyperpigmentation in ACTH-secreting pituitary adenoma (Cushing’s disease) and its resolution after successful trans-sphenoidal excision

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DESCRIPTION

Hyperpigmentation is a known physical examination finding in conditions where adrenocorticotropic hormone (ACTH) is excessive. This is because ACTH shares the same affinity with α-melanocyte-stimulating hormone (MSH) for the melanocortin-1 receptor (MC1R). MC1R is considered the most important melanocortin receptor that regulates melanogenic activity. This shared affinity of ACTH and MSH for MC1R is because these two peptides share the common four-amino acid sequence, His-Phen-Arg-Trp, which is necessary for melanotropic activity.

In Cushing’s disease, the excessive ACTH is from a functioning pituitary adenoma, and this leads to various manifestations of hypercortisolism or Cushing’s syndrome.

A 37-year-old Filipino woman reported a 3-year duration of amenorrhea and 5-month duration of progressive weight gain, facial roundedness, acne, leg weakness, easy bruising and blurring of vision. On physical examination, she was hypertensive at 155/99 mm Hg, had central obesity, moon facies, facial plethora, buffalo hump, violet abdominal striae, ecchymoses and bipedal oedema. Generalised skin hyperpigmentation was difficult to ascertain because of the normal brown skin colour of Filipinos. Her fingernails and periungual tissues were particularly hyperpigmented, as shown in figure 1.

Performance of the 1 mg overnight dexamethasone suppression test showed non-suppression of 8-hour serum cortisol at 551 nmol/L (normal suppression: <50 nmol/L). Plasma adrenocorticotropic hormone (ACTH) was elevated at 82.67 pg/mL (normal <40 pg/mL). MRI of the head showed a 46×41×70 mm lobulated, heterogeneously enhancing sellar-suprasellar mass with cystic and necrotic components. These investigations led to a diagnosis of ACTH-secreting pituitary macroadenoma (Cushing’s disease).

After successful trans-sphenoidal excision of the pituitary mass, plasma ACTH level significantly decreased to 1.96 pg/mL. Histopathological evaluation confirmed pituitary adenoma. However, immunostaining for ACTH and Ki-67 was not done. There was subsequent 8 kg weight loss and improvements in blood pressure, vision, facial plethora, acne, lower extremity motor strength and bipedal oedema. Six months postsurgery, plasma ACTH was 18 pg/mL and 8-hour serum cortisol was 499 pmol/L in the absence of any exogenous hormones.

Patient’s perspective

I am happy that my appearance has changed after my surgery. I have now lost weight. I now feel more beautiful as my skin appears lighter and my pimples have lessened. My doctor has pointed out that my nails and surrounding parts have darkened as well. We are happy that the colour has normalised already. I have allowed my case to be written so that others will learn from my experience.

Learning points

- Adrenocorticotropic hormone (ACTH), together with α-melanocyte-stimulating hormone, stimulates the melanocortin-1 receptor, which controls melanogenesis. Excessive ACTH then leads to hyperpigmentation.
- Hyperpigmentation can affect the nails of patients with ACTH-secreting pituitary adenoma. After successful treatment, the nail that grows out does not appear hyperpigmented anymore.
- We can inform our patients that the bothersome changes in their appearance, nail hyperpigmentation in particular, can change with successful treatment.
glucocorticoid. Hence, she did not require glucocorticoid replacement. Likewise, free thyroxine was 18 nmol/L, and thyroid-stimulating hormone was 0.05 μIU/mL, not necessitating thyroid hormone replacement.

The photograph taken 4 months postsurgery (see figure 1) showed a colour gradient with the distal part of the nail to be hyperpigmented while the proximal part already appeared normal. By 6 months postsurgery, the entire nail is not hyperpigmented anymore. Likewise, the periungual tissues were now less pigmented. This clearly demonstrates that with successful treatment, there is resolution of nail hyperpigmentation as the nail subsequently grows out and that there is lightening of the periungual tissues.

We can thus inform our patients that these physical changes which are bothersome for them do change if the condition is successfully treated.

Acknowledgements We thank Ms Cheenee Calantoc of the Research Grants Administration Office of the University of the Philippines Manila for her assistance in the review of the literature.

Contributors MASS was the attending endocrinologist and RGB was the endocrine fellow who took care of the patient. Both were involved in the conceptualisation of the report, collection of data and photograph, and writing of the article.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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