

Addison's disease presenting only with hyperpigmentation - A rare case report

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ABSTRACT

Addison's disease or chronic adrenocortical insufficiency, can remain unrecognized for a long time. It usually presents with non-specific symptoms, which are often ignored or misdiagnosed as a sign of other more common diseases. In this case report we focused on subtle findings of diffuse hyperpigmentation. We present a study on 2 skin biopsies from a 38-year-old woman in whom hyperpigmentation lesions were first found on the face and after two months, in the oral cavity. Addison's disease usually presents with non-specific symptoms and this can be a rare case because it presents with hyperpigmentation as its only sign and has no other clinical symptoms. There are a few diagnosed cases of this disease with hyperpigmentation only.

Key words: Addison's Disease; Hyperpigmentation; Biopsy

INTRODUCTION

Addison's disease is a result of primary adrenal insufficiency due to bilateral destruction or damage to the adrenal cortex (NNR). The most common cause of primary adrenal insufficiency is autoimmune adrenalitis (80%) cases (Addison's disease) [1,2].

Less than 10% of cases are caused by a systemic fungal infection such as Histoplasmosis, Cryptococcosis, Blastomycosis, Coccidioidomycosis and by metastatic processes (metastases from breast, bronchial and renal carcinoma) as well as leukemic infiltration [3]. Patients with autoimmune adrenal disease are more likely to have poly glandular autoimmune syndromes [4,5].

The symptoms of adrenal insufficiency usually develop gradually and include chronic fatigue, muscle weakness, loss of appetite, nausea, vomiting and diarrhea. In

about 50% of cases, blood pressure is low causing dizziness or fainting. Skin changes such as areas of hyperpigmentation, can be seen more on the exposed part of the body. Furthermore pigmentation of armpits, mamilla, genitals and palmar creases can be observed.

We present a case of a female who came to our office with hyperpigmentation lesions over her face and had no other clinical signs of Addison's disease.

CASE REPORT

A 38 year old female patient presented with hyperpigmentation of skin since last year. The pigmentation first started during her pregnancy. These lesions were located more on the exposed parts such as the face and back of the hands. The oral cavity was also involved after childbirth. There was a history of hyperthyroidism and she was treated

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with levothyroxine. On dermatological examination she had bluish-black hyperpigmentation of the face, more on the malar area and the back of the hands (Figs. 1 and 2). Tongue and gingiva also showed patchy hyperpigmentation (Fig. 3). The patient was initially diagnosed based on clinical suspicions, upon which two biopsies were taken from the patient's skin. Eventually the diagnosis was confirmed by laboratory test results. Microscopy from the skin lesion revealed a mildly acanthotic epidermis with hyperpigmentation of the basal layer, superficial dermis showed mild perivascular lymphocytic infiltration with scattered pigment incontinence. Melanocytic proliferation was not seen. At first (ACTH) was >1250 pg/ml (normal up to 46) due to the loss of the cortisol-hypothalamic-pituitary feedback. Plasma cortisol level was 27.8 ng/ml (normal 54-287 ng/ml), RBC index was within normal limits. Peripheral smear and B12 levels were not evaluated. Tuberculosis and other infections were ruled out clinically. The patient was referred to an endocrinologist and was treated with hydrocortisone 20 mg in the morning and 5 mg in the evening and fludrocortisone 0.1 mg daily at evening and was advised to take more fruits. The patient started feeling better within weeks with significant improvement in pigmentation and decreased level of ACTH.

DISCUSSION

Hyperpigmentation is defined as an increased deposition of melanin in the skin. When exposed to UV, keratinocytes secrete alpha-melanocyte-stimulating hormone (α -MSH), which stimulates melanocortin 1 receptor (MC1R) to synthesize melanin in melanocytes. Subsequently, activated MC1R elevates intracellular cyclic adenosine monophosphate (cAMP) production and induces tyrosinase expression via cAMP/PKA signaling pathway [6,7]. The inherited form of Addison's disease is mostly characterized by cutaneous and mucosal hyperpigmentation related to ACTH induced melanogenesis. Quite often the first clue is abnormal laboratory tests like hypernatremia, hyperkalemia, hypoglycemia, eosinophilia, neutropenia and hypercalcemia [8].

Elevation of ACTH with low cortisol is diagnostic of a primary adrenal problem. Measurement of cortisol in the ACTH stimulation test may be performed in equivocal cases where baseline lab evaluation cannot confirm the diagnosis [9-11]. (ACTH) hormone and melanocyte



Figure 1: Hyperpigmentation on malar area.



Figure 2: Hyperpigmentation on the back of the hands.



Figure 3: Patchy pigmentation of the tongue.

stimulating hormone are elevated due to loss of the cortisol-hypothalamic-pituitary feedback relationship resulting in characteristic hyperpigmentation which is seen in more than 90% of patients. Pigmentary changes are one of the differentiating features between primary and secondary adrenal insufficiency. This can be a rare

case because it only presents with hyperpigmentation and has no other clinical symptoms.

CONCLUSION

Addison's disease can remain unrecognized for a long time until acute adrenal insufficiency is precipitated by an acute stress. Addison's disease usually presents with non-specific symptoms and this can be a rare case because it presents with hyperpigmentation as its only sign and has no other clinical symptoms. There are a few diagnosed cases of this disease with hyperpigmentation only. This sign is most often ignored or misinterpreted with other more common diseases. This is the major reason that this disease is underdiagnosed.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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