Clinical Observations

Reversible Facial Hyperpigmentation Associated With Vitamin B12 Deficiency

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Abstract
Vitamin B12 (cobalamin) deficiency is common in developing countries. Its dermatologic manifestations include hair and nail changes and glossitis. Cases of generalized hyperpigmentation associated with vitamin B12 deficiency have rarely been reported. Localized hyperpigmentation is less frequently described, affecting palms, soles, and flexural areas. We report a rare case of reversible melasma-like cutaneous hyperpigmentation associated with pernicious anemia and discuss the possible mechanisms of this association. (Nutr Clin Pract. XXXX; xx: xx-xx)

Keywords
vitamin B12; vitamin B12 deficiency; cobalamin; pernicious anemia; hyperpigmentation

Observation
Pernicious anemia (PA) is caused by lack of intrinsic factor. A common cause is autoimmune disease in which antibodies are produced against intrinsic factor and gastric parietal cells. PA is associated with atrophy of the fundus and body of the stomach, as well as vitamin B12 (cobalamin) malabsorption and deficiency. The most common manifestations of vitamin B12 deficiency are neurological, but there are some physical signs, including hair and nail changes and glossitis. Skin changes such as hyperpigmentation are rarely reported.

daily 1000-mg intramuscular vitamin B12 injections were started for 1 week, followed by monthly 1000-mg intramuscular cobalamin injections, leading to rapid improvement in the hematologic tests and neurologic status. The hyperpigmentation slowly but remarkably ameliorated without any further treatments.

Discussion
The association between vitamin B12 deficiency and hyperpigmentation, although unusual, has been previously described. In most of the reported cases, the hyperpigmentation was generalized, involving sun-exposed areas, flexural areas, oral mucosa, and nails. Cases of localized hyperpigmentation were less frequently described, affecting commonly the palms, soles, and the interphalangeal joints. In our case, the hyperpigmentation affected the face and mucosa. The main differential diagnoses are melasma and postinflammatory hyperpigmentation. In the absence of family history, significant sun exposure, and particularly hormonal factors in this patient with primary ovarian failure, the diagnosis of melasma is deemed improbable.

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Vitamin B12 deficiency is probably an underrecognized etiology of localized hyperpigmentation. The presence of neuropathy, atrophy of gastric mucosa, and glossitis are classical findings in PA. The exact mechanism of hyperpigmentation is unknown, but there are many hypotheses. It has been suggested that vitamin B12 deficiency causes a decrease in the amount of intracellular reduced glutathione, which inhibits tyrosinase. This results in an increase in melanogenesis manifesting clinically as hyperpigmentation. A second hypothesis is through biopterin. Biopterin is necessary for the hydroxylation of phenylalanine (a major substrate in melanin biosynthesis), and elevated levels are found in folate deficiency. This could explain the hyperpigmentation also found in vitamin B12 deficiency. Another mechanism could be related to a defect in melanin transport and incorporation into keratinocytes. Finally, as vitamin B12 is essential for purine and pyrimidine metabolism, its deficiency may lead to a decrease in the ability to synthesize DNA and consequently epidermal changes.

This unusual presentation of melasma-like hyperpigmentation in association with PA should alert the physician to the possibility of nutrition deficiencies in case of pigmentary changes.

Statement of Authorship

L. Tayem, M. Jones, N. Litaiem, and F. Zeglaoui all contributed to the acquisition, analysis, and interpretation of the data; L. Tayem and M. Jones contributed to the first draft of the manuscript; N. Litaiem critically revised the manuscript; and F. Zeglaoui critically revised the manuscript and gave final approval. All authors read and approved the final manuscript and agree to be fully accountable for ensuring the integrity and accuracy of the work.

References