

Case Report

Generalized pigmentation with nutritional deficiency

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ABSTRACT

Vitamin B₁₂ deficiency is one of the most underdiagnosed causes of hyperpigmentation. It is known to cause Addisonian pigmentation. We describe a case where a patient presented with hyperpigmentation on the aesthetically significant areas of the body for which he presented to the clinic. Diagnosis was confirmed on histopathology and serum vitamin B₁₂ levels. The hyperpigmentation reversed significantly on treatment.

Keywords: Vitamin B₁₂ deficiency, Generalized hyperpigmentation, Addisonian

INTRODUCTION

Generalized hyperpigmentation is a largely overlooked phenomenon in dermatology. The causes can range from systemic diseases including endocrinological and hematological dyscrasias, infections to hereditary pigmentary disorders and a few acquired ones. Given its wide range of etiologies some with drastic consequences, it is imperative to thoroughly investigate a patient presenting with generalized hyperpigmentation.

Vitamin B₁₂ deficiency is thought to be uncommon in the eastern parts of India including Bengal and the eastern states as compared to the northern and southern parts of India. The importance of cutaneous features in relation to vitamin B₁₂ deficiency is not well described in literature.¹ Megaloblastic pancytopenia due to cobalamin and folate deficiency occurs usually in the age group of 10-30 years with female preponderance. The predominant symptoms are fatigue, anorexia and gastritis, low grade fever, shortness of breath, palpitations and mild jaundice. Common physical findings include pallor (85%), glossitis (29%), and mild icterus (25%) and generalized hyperpigmentation (18%).² Although commonly encountered in clinical practice, knuckle hyper pigmentation has been

rarely reported as the presenting manifestation of vitamin B₁₂ deficiency. Hyperpigmentation of the extremities especially over the dorsum of the hands and feet, with accentuation over the inter-phalangeal joints and terminal phalanges associated with pigmentation of oral mucosa is characteristic of vitamin B₁₂ deficiency.³

CASE REPORT

A 32 year old male presented to outpatient department with complaints of black pigmentation over hands, foot, tongue, buccal mucosa since birth. Patient is a pure vegetarian. History of similar lesion in family could not be elicited. No history of abdominal pain, palpitation, loss of consciousness. On examination there was diffuse pigmentation present over trunk and face. Ill-defined pigmentation over bilateral hands as well as pigmentation over hard palate was present. Dermoscopy of the lesions revealed exaggerated pigment network. On investigation hemoglobin was low at 10 mg/dl with anisocytosis, poikilocytosis and macrocytosis (MCV 120 fl). Vitamin B₁₂ levels were found to be 232.62 pg/ml. On histopathology increased pigmentation in the basal layer with melanophages was present in the upper dermis. Based on clinical and histopathological evidence a diagnosis of vitamin B₁₂ deficiency was reached and

patient was started on injection vitcofol intramuscular once weekly six injections 2 cc intramuscularly. Oral multivitamin supplements for six months. On follow up significant reduction in hyperpigmentation was seen at 6 months.



Figure 1: Hyperpigmentation of face.

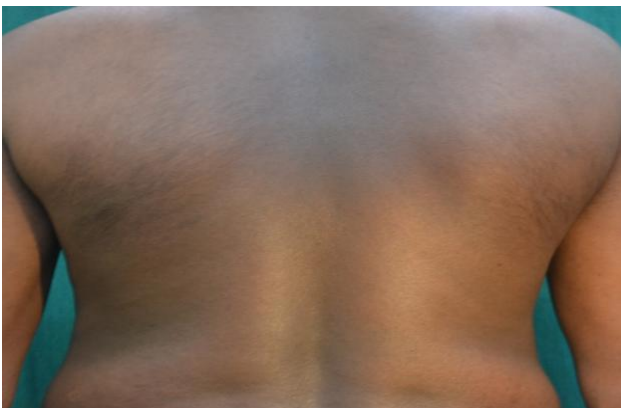


Figure 2: Hyperpigmentation on upper back.



Figure 3: Hyperpigmentation along palmar aspect of hand.



Figure 4: Hyperpigmentation along dorsal aspect of hands.



Figure 5: Dermoscopy increased pigment along the pigmentary network.

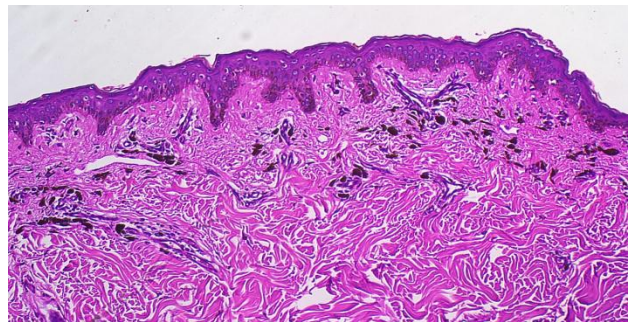


Figure 6: Histopathology-increased pigmentation along basal layer with melanophages.



Figure 7: Post treatment of face.



Figure 8: Post treatment resolution of pigmentation of hands.



Figure 9: Post treatment of trunk.

DISCUSSION

In patients with vitamin B₁₂ deficiency, hyperpigmentation of the extremities- especially over the dorsum of the hands and feet, with accentuation over the interphalangeal joints and terminal phalanges- associated with pigmentation of oral mucosa.

Prevalence of B₁₂ deficiency varies from 3 to 5% in the general population and 5 to 20% among people older than 65 years.⁴

Aaron et al reported a series of 63 patients with vitamin B₁₂ deficiency; 26 out of 63 (41%) patients had skin and mucosal changes.⁵ (31%) most common, skin hyperpigmentation (19%), hair changes (9%), angular stomatitis (8%), and vitiligo (3%). It is suggested that deficiency of vitamin B₁₂ causes decrease in intracellular reduction potential that leads to oxidation of the reduced glutathione and decrease in Glutathione (GSH)/GSSG ratio. The epidermal melanocytes are then stimulated to produce melanin as the tyrosinase inhibiting effect of GSH has been diminished.⁶

Vitamin B₁₂ deficiency was first described by Cook and later by Baker et al.⁷ A serum B₁₂ above 300 pg/ml is interpreted as normal. Patients with B₁₂ levels between 200 and 300 pg/ml are considered borderline, and further enzymatic testing may be helpful in diagnosis. Patients with B₁₂ levels below 200 pg/ml are considered deficient.⁸ The main source of vitamin B₁₂ (cobalamin) in humans is the consumption of meat, poultry and dairy products. The Recommended Dietary Allowances varies with age.⁷ Vitamin B₁₂ is concentrated in animal tissues, hence, vitamin B₁₂ is found only in foods of animal origin. Foods that are high in vitamin B₁₂ (µg/100 g) include: liver (26–58), beef and lamb (1–3), chicken (trace-1), eggs (1–2.5) and dairy foods (0.3–2.4).⁹ A few reports have suggested that vitamin B₁₂ deficiency may in fact be commoner than is generally thought.¹⁰

Under-diagnosis of this condition may reflect a firmly held notion among doctors that the disease is rare.¹⁰

The most frequent cause of the deficiency is pernicious anemia.¹¹

So, the predominant mechanism of hyper pigmentation in vitamin B₁₂ is hypothesised as deficiency of vitamin B₁₂ decreases the level of reduced glutathione, which activate tyrosinase and thus leads to transfer to melanosomes. Defect in the melanin transfer between melanocytes and keratinocytes, resulting in pigmentary incontinence.¹²

Treatment of vitamin B₁₂ deficiency involves repletion with B₁₂. However, depending on the etiology of the deficiency, the duration and route of treatment vary. In patients who are deficient due to a strict vegan diet, an oral supplement of B₁₂ is adequate for repletion.

In patients with a deficiency in intrinsic factor, either due to pernicious anemia or gastric bypass surgery, a parenteral dose of B₁₂ is recommended, as oral B₁₂ will not be fully absorbed due to the lack of intrinsic factor. A dose of 1000 mcg of B₁₂ via the intramuscular route is recommended once a month. In newly diagnosed patients, 1000 mcg of B₁₂ is given intramuscularly once a week for four weeks to replenish stores before switching to once-monthly dosing. Studies have shown that at doses high enough to fully saturate intestinal B₁₂ receptors, oral B₁₂ is also effective, despite a lack of intrinsic factor.⁸

CONCLUSION

In our case we try to stress on the importance of investigating underlying causes in a patient presenting with hyperpigmentation. Also the significance of elucidating a dietary history in establishing a nutritional deficiency as a key culprit cannot be stressed enough. Our patient responded with oral and injectable vitamin B₁₂ ruling out the need of doing schilling test to find out castle intrinsic factor deficiency. This portrays that something as simple and cost effective as a trial of dietary

supplementation in a country like India where majority of vegetarians recedes can go a long way therapeutically while cementing without undergoing costly investigations.

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Ethical approval: Not required

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