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Rare Presentation of a Very Common Deficiency (Vitamin B12 Deficiency)

Dr. Bhakti Godbole[1], Dr. Siddhant Kamble[2], Dr. Sanjay Agrawal[3], Dr. Supriya Patil[4], Dr. Bhakti Godbole[5]

[1]Junior Resident, Department of Medicine, Shri Bhausaheb Hire Govt. Medical College and Hospital, Dhule
Corresponding Author Email id: *bhaktigodbole. bg[at]gmail.com*
Mobile: 7507573484

[2]Junior Resident, Department of Medicine, Shri Bhausaheb Hire Govt. Medical College and Hospital, Dhule
Mobile: 9359348499

[3]Professor, Department of Medicine, Shri Bhausaheb Hire Govt. Medical College and Hospital, Dhule

[4]Associate Professor, Department of Medicine, Shri Bhausaheb Hire Govt. Medical College and Hospital, Dhule

[5]Junior Resident, Department of Medicine, Shri Bhausaheb Hire Govt. Medical College and Hospital, Chakkarbardi Road, Dhule, 424001
Mobile: 7507573484

Abstract: ***Vitamin B12 deficiency has multisystem involvement with hematologic, neurologic, psychiatric, gastrointestinal, dermatologic, and cardiovascular manifestations. Skin hyperpigmentation, vitiligo, angular stomatitis, and hair changes are dermatological manifestations. Mucocutaneous manifestations as the only and primary symptom of vitamin B12 deficiency can be often overlooked as these signs are not specific to B12 deficiency and very few cases are reported in literature. Here, we present such a case where hyperpigmentation was the primary and solo symptom of vitamin B12 deficiency. This case underlines the need to rule out vitamin B12 deficiency when clinicians encounter hyperpigmentation as a solo presentation and also emphasizes the significance of early treatment in preventing the irreversible neurological manifestations of vitamin B12 deficiency which can be a late manifestation.***

Keywords: Vitamin B12 deficiency, skin hyperpigmentation, primary symptom

1. Introduction

Vitamin B12 deficiency has multisystem involvement with hematologic, neurologic, psychiatric, gastrointestinal, dermatologic, and cardiovascular manifestations due to its important role in DNA synthesis. Hematological manifestations are frequent - megaloblastic anemia and pancytopenia. Neurological involvement can be disabling like peripheral neuropathy, subacute combined degeneration of the spinal cord, ataxia, optic atrophy, psychosis, depression, and dementia. Under investigation is it being a possible risk factor for atherosclerosis. [1]

Skin hyperpigmentation, vitiligo, angular stomatitis, and hair changes are dermatological manifestations.[2] Mucocutaneous manifestations as the only and primary symptom of vitamin B12 deficiency can be often overlooked as these signs are not specific to B12 deficiency and very few cases are reported in literature.

Here, we present such a case where hyper- pigmentation was the primary and solo symptom of vitamin B12 deficiency. Such cases highlight the importance of evaluation of such symptoms for vitamin deficiency.

2. Case Details

A 52 year old male presented in August 2022 with hyperpigmentation of both hands, tongue and oral mucosa since 2016.
Patient had hyperpigmentation over both hands on dorsal and palmar aspect more over the knuckles associated with hyperpigmentation on tongue and oral mucosa which was generalized and had gradually progressed since 2016, not associated with itching over affected area or photosensitivity

He was pure vegetarian.

He worked in packaging of detergent powder factory in 2016 for a few months, then left work because of hyperpigmentation as he thought that it was some chemical which was causing allergy and hyperpigmentation. His symptoms did not resolve even after leaving the job.

On examination, hyperpigmentation was present on dorsum and palmar aspects of hand, dorsum of feet, oral mucosa, tongue and gums.

No marks of itching or wounds on limbs.

No evidence of glossitis or angular cheilosis.

Neurological examination was also within normal limits.

3. Investigations

CBC - TLC - 7600/mm3
Hb - 12.1gm/dl
HCT - 38 %
MCV - 84 fL
Platelets - 200 X 10^3 /mm3
Peripheral smear - RBCs – normocytic normochromic
Platelets - adequate

S. Creatinine - 0.8 m/dl
BUL - 28 mg/dl
S. Bili - 0.9 mg/dl
SGOT - 45mg/dl

SGPT - 38 mg/dl
S. ALP - 124mg/dl
S. Na^+ - 135mmol/L
S. K^+ - 4.0 mmol/L
S. Cortisol (8.00 AM) - 17.70 µg/dl (8 - 25)
S. Vitamin B12 level - 180.0 pg/ml (220 - 883)

Skin Punch Biopsy: Full thickness skin biopsy composed of epidermis, dermis, and subcutaneous fat. Epidermis is thinned out at places and lined by stratified squamous epithelium showing hyperkeratosis, parakeratosis and acanthosis. Pigment incontinence is evident in basal layer of epidermis. Dermis shows mild periadnexallympocytic infiltrates.

Before Treatment

Image 1: Hyperpigmentation on tongue and oral mucosa

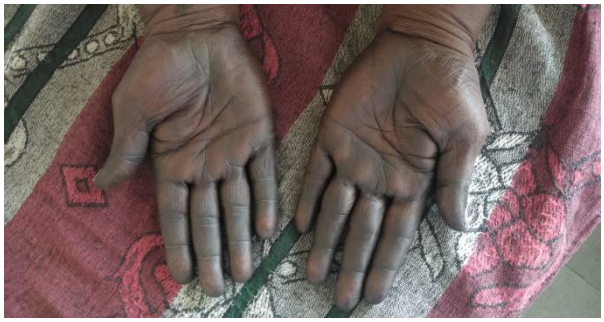

Image 2: Diffuse hyperpigmentation on palms

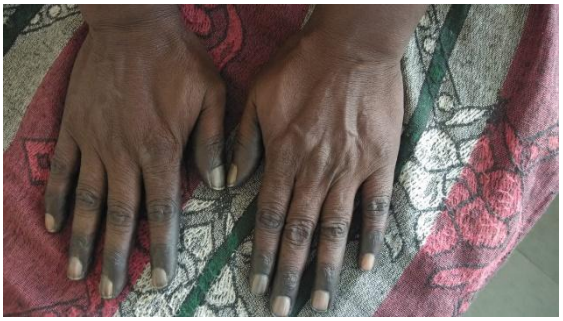

Image 3: Hyperpigmentation on dorsum of hands with prominence over knuckles

After 4 Weeks of Treatment

Image 4: Hyperpigmentation of tongue and oral mucosa resolved

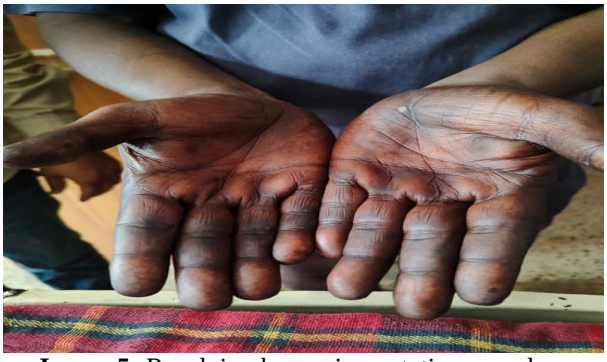

Image 5: Resolving hyperpigmentation on palms

Image 6: Resolving hyperpigmentation over dorsum of hand

4. Discussion

Differentials for our case were Addison's disease, chemical toxin induced and vitamin B 12 deficiency. Addison's was ruled out as with normal electrolytes and serum cortisol level and also he did not have any other features. Chemical toxin induced hyperpigmentation was considered in view of history of chemical exposure in a detergent factory but history was not clear about onset of hyperpigmentation and working in the detergent packaging unit and hyperpigmentation was progressive even after stopping the exposure with involvement of the oral mucosa and tongue was seen where there was no direct exposure.

Serum vitamin B12 concentration of less than 200 pg/ml (148pmol/L) is considered for defining vitamin B12 deficiency. Inadequate dietary intake, pernicious anemia, food - bound cobalamin malabsorption partly due to gastric

atrophy, past surgeries like gastrectomy are the causes of low serum Vitamin B12. [3]

Vitamin B12 sources in diet are foods of animal origin, including fish, meat, poultry, eggs, dairy products and fortified foods. In our case, dietary deficiency was the probable cause as he was a pure vegetarian with low intake of dairy products. The patient was treated with 1000mcg methylcobalamine daily for 5 days followed by 1000 mcg on alternate days for 5 days followed by 1000mcg weekly for 4 weeks, after which there was improvement in hyperpigmentation. During follow up patients must be assessed for any neurological signs or symptoms as it can be a late manifestation which was not seen in our case.

Aaron S et al. found that 41% (26 out of 63) of his patients presented with cutaneous changes as a primary symptom of vitamin B12 deficiency. While 52% of these 26 patients (22% of the total) presented with mucosal changes, glossitis was specifically seen in 31% (19 out of 63), hyperpigmentation of the skin in 19% (12 out of 63), hair changes in 9% (6 out of 63), angular stomatitis in 8% (5 out of 63), and lastly, vitiligo was seen in only 3% (2 out of 63). [4]

Characteristic of mucocutaneous hyperpigmentation in vitamin B12 deficiency is hyperpimentation of the extremities especially over the dorsum of the hands and feet, with prominence over the inter - phalangeal joints and terminal phalanges associated with pigmentation of oral mucosa. [5] As seen in our case the patient had hyperpigmentation on dorsal and palmer aspects of hand with prominence over the knuckles, dorsal aspect of feet and oral mucosa, with this being the sole presentation.

The pathophysiologic cause of increased pigmentation is postulated to be that under conditions of hypocobalaminemia melanocytes exhibit increased intracellular ROS levels, GSH depletion, and acceleration of melanogenesis via tyrosinase activation leading to increased melanin synthesis and the inadequate transfer of the pigment from the melanocytes to the nearby keratinocytes. [6]

As evidenced in a study by James, et al, the skin biopsy in our case suggested irregular epidermal thinning with parakeratosis and increased pigment deposition in basal layer. [7] The defect in melanin transfer between the melanocytes and keratinocytes leads to pigmentary incontinence. [8]

5. Conclusion

This case underlines the need to rule out vitamin B12 deficiency when clinicians encounter hyperpigmentation as a solo presentation and also emphasizes the significance of early treatment in preventing the irreversible neurological manifestations of vitamin B12 deficiency which can be a late manifestation.

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