Cutaneous Hyperpigmentation As A Primary Presenting Feature In Megaloblastic Anemia Due To Vitamin B 12 Deficiency-----

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ABSTRACT

Megaloblastic anemia occurs due to vitamin B12 and folate deficiency. The clinical manifestations ranges from symptoms of anemia, skin changes, changes in mucous membrane, mild icterus, and various neurological manifestations involving brain, spinal cord and peripheral nerves. Skin manifestations are rarely seen. We present a case of megaloblastic anemia who presented to us only with cutaneous hyperpigmentation as a primary complaint.

Key words: megaloblastic anemia, vitamin B12, folate, icterus, brain, spinal cord, hyperpigmentation.

INTRODUCTION

Vitamin B_{12} deficiency is considered to be rare and presents with different combinations of neurological manifestations, hematological changes, discoloration of skin, hair and nails, weakness, syncope and diarrhea. Common cause of vitamin B_{12} deficiency is malabsorption, usually due to pernicious anemia or gastric resection and rarely inadequate intake.[1] Inadequate intake almost exclusively occurs in strict vegetarians. Hyperpigmentation of skin has been reported only rarely as the presenting manifestation of vitamin B_{12} deficiency.[2]

CASE REPORT

A 38 year old male, lacto-vegeterian presented to us with a chief complaint of increasing blackish discolouration of the hands,feet and face since 2 months. The discolouration started on the feet and gradually involved the hands and face. There were no history of any chronic illness or past abdominal surgery. On asking leading questions he admitted of having a significant decrease in appetite over these 2 months. General physical examination revealed pallor and hyperpigmentation of dorsum of hands, palms & feet. (Fig 1,2). BP 126/78 mm of Hg. Systemic examination including CNS examination was normal.

On investigations Hb-6.2 grams, TLC-4100/mm3, DLC-polymorphs 53%, lymphocytes 42%, eosinophils 4%, monocytes 1%, absolute platelet count was 1,35000/mm3. Peripheral smear showed dimorphic blood picture with predominance of macrocytes. MCV was 108 fl, MCH 37.6 Pg & MCHC was 36%. Bone marrow showed erythroid hyperplasia with macronormoblastic erythropoiesis and a few large atypical megakaryocytes, M:E = 1:1 Serum Vitamin B 12 level was 168 pg/ml (normal range 300 to 900 pg/ml). serum iron and serum ferritin was advised but patient was not willing for the tests.

Anti parietal cell antibody assay was negative. A skin biopsy was advised but the patient denied to consent for the same. A dermatologist opinion was sought. Differential diagnosis of such hyperpigmentation like Addisons diseases, Peutz – Jegher's syndrome, Scleroderma, Pellagra & Chronkhite – Canada syndrome were ruled out.

Table No 1

Differential Diagnosis Considered By The Dermatologist.

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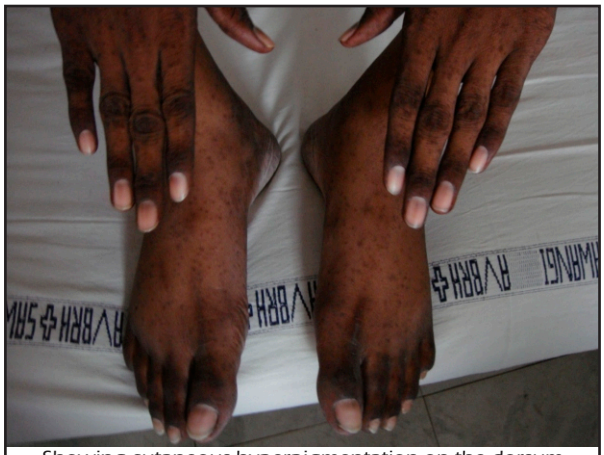
Table No 1

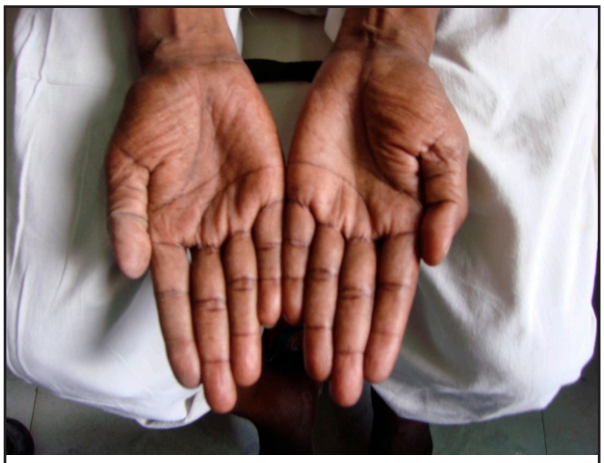
Differential diagnosis considered by the Dermatologist.	Classical signs & symptoms not Present in this case thus, the following possibilities were ruled out.
Addison's disease	No history of weight loss, vomitings, fatigue, and salt craving. Blood pressure normal (126/78 mmh of Hg)
Peutz-Jegher's syndrome	No history of bleeding PR, malena and no evidence of oral melanosis.
Scleroderma	There was no cutaneous sclerosis and features suggestive of CREST syndrome / systemic sclerosis.
Pellagra No	Non alcoholic, pigmentation was not characteristically present over the sun exposed areas (no casal necklace). history of diarrhoea, vomiting, memory loss
Chronkhite Canada syndrome	No history of bleeding PR melana, recurrent abdominal pains, recurrent watery diarrhoea and weight loss. N evidence of alopecia, onycholysis, cataract.

A diagnosis of megaloblastic anemia was made and the patient was given 1 unit of blood transfusion and was started on Vitamin B12 injection 1000 micrograms intramuscularly daily for 7 days. He was discharged on request and was adviced to take Vit. B12 injections weekly for next 2 months, tablet folic acid 5 mg for 2 months and was called for follow up after 1 month.

At the time of discharge his haemoglobin was 9.6 gram%. Pigmentation was slightly decreased though unremarkable. Follow up is awaited after 1 month.



Showing cutaneous hyperpigmentation on the dorsum of hands and feet especially over the interphalangeal joints.



Showing hyperpigmentation of the palms and palmar creases.

DISCUSSION

The megaloblastic anemias are a group of disorders characterized by the presence of distinctive morphologic appearances of the developing red cells in the bone marrow. The cause is usually deficiency of either cobalamin (vitamin B_{12}) or folate, but megaloblastic anemia may arise because of genetic or acquired abnormalities affecting the metabolism of these vitamins or because of defects in DNA synthesis

not related to cobalamin or folate . The marrow is usually cellular, and the anemia is based on ineffective erythropoiesis.

Vitamin B12 deficiency causes a range of disorders and affects all age groups. The main systems affected in vitamin B12 deficiency are the hematologic, gastrointestinal, and nervous systems.[3]

The mucocutaneous manifestations of vitamin B12 deficiency are less commonly encountered. Dr Bramwell Cook, in 1944 first observed that hyperpigmentation of the skin was associated with a macrocytic anemia and interestingly both conditions responded to crude liver extract therapy.[4]

The various skin lesions of vitamin B12 deficiency are: skin hyperpigmentation, vitiligo, hair changes, and recurrent angular stomatitis. Hyperpigmentation especially occurs over the dorsum of the hands and feet, with accentuation over the interphalangeal joints and terminal phalanges associated with pigmentation of oral mucosa which is characteristic of vitamin B12 deficiency.5 These signs can be observed in many other diseases with or without vitamin B12 deficiency. A study reported 21 patients with vitamin B12 deficiency who had hyper-pigmentation of the skin.[4]

In another study,in a series of 63 patients with vitamin B12 deficiency; 26 out of 63 (41%) patients had skin and mucosal changes. Glossitis (31%) was the most common mucocutaneous manifestation, followed by skin hyperpigmentation (19%), hair changes (9%), angular stomatitis (8%), and vitiligo (3%). The hyperpigmentation noted was an important general examination finding.[5] The hyperpigmentation related to vitamin B12 deficiency is more common in darker-skinned patients. Few other cases of skin hyperpigmentation due to vitamin B12 deficiency have been reported in the literature.[6-10] The mechanism of hyperpigmentation is due to increased melanin synthesis rather than a defect in melanin.[11]

All most all the cutaneous changes are reversible within months after commencement of vitamin B12 therapy. A few reports have suggested that vitamin B_{12} deficiency may in fact be commoner than is generally thought. Under-diagnosis of this condition may reflect a firmly held notion among the treating physicians that the disease is rare.[12] It may be worthwhile to consider the possibility of vitamin B12 deficiency in a patient with unexplained pigmentary changes. Early detection and adequate treatment will also prevent partially irreversible neurological manifestations.

CONCLUSION

A patient presenting with cutaneous hyperpigmentation alone should make us highly suspicious of the possibility of vitamin B12 deficiency. While examining such cases, a meticulous search for other signs of megaloblastic anemia should be done. It is worthwhile to mention here that anemia is not a sole criterion to diagnose the same,rather patients can have advanced clinical disease without clinically detectable anemia and indeed! this is the irony of megaloblastic anemia. We should be more aware that cutaneous hyperpigmentation not responding to conventional therapy could very likely be an indication of vitamin B12 deficiency. These skin manifestations respond quickly to vitamin B12 therapy. Early treatment with vitamin B12 will prevent the serious complications of vitamin B12 deficiency.

REFERENCE

1. Bernard M, Babior H, Franklin B. Megaloblastic anemias. In : Harrison's Principles of Internal Medicine. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. 16th ed. McGraw-Hill: New York; 2005. p. 601-7.
2. Hoffman CF, Palmer DM, Papadopoulos D. Vitamin B12 deficiency: A case report of ongoing cutaneous hyperpigmentation. Cutis 2003;71:127-30.
3. Oh R, Brown DL. Vitamin B12 deficiency. Am Fam Physician. 2003;67(5):979–86.
4. Baker SJ, Ignatius M, Johnson S, Vaish SK. Pigmentation and vitamin B12 deficiency [Correspondence]. Br Med J.

1963;2(5366):1205. 4.

5. Aaron S, Kumar S, Vijayan J, Jacob J, Alexander M, Gnanamuthu C. Clinical and laboratory features and response to treatment in patients presenting with vitamin B12 deficiency–related neurological syndromes. Neurol India. 2005;53(1):55–8.
6. Baker SJ, Ignatius M, Johnson S, Vaish SK. Hyperpigmentation of skin. A sign of vitamin-B12 deficiency. Br Med J. 1963;1(5347):1713–5
7. Lee SH, Lee WS, Whang KC, Lee SJ, Chung JB. Hyperpigmentation in megaloblastic anemia. Int J Dermatol. 1988;27(8):571–5.
8. Noppakun N, Swasdikul D. Reversible hyperpigmentation of skin and nails with white hair due to vitamin B12 deficiency. Arch Dermatol. 1986;122(8):896–9.
9. Lin SH, Sourial NA, Lu KC, Hsueh EJ. Imerslund–Grasbeck syndrome in a Chinese family with distinct skin lesions refractory to vitamin B12. J Clin Pathol. 1994;47(10):956–8.
10. Hoffman CF, Palmer DM, Papadopoulos D. Vitamin B12 deficiency: a case report of ongoing cutaneous hyperpigmentation. Cutis. 2003;71(2):127–30. Erratum in: Cutis 2003;71(4):322.
11. Sabatino D, Kosuri S, Remollino A, Shotter B. Cobalamin deficiency presenting with cutaneous hyperpigmentation: a report of two siblings. Pediatr Hematol Oncol. 1998;15(5):447–50.
12. Mori K, Ando I, Kukita A. Generalized hyperpigmentation of the skin due to vitamin B12 deficiency. J Dermatol. 2001;28(5):282–5.