

Reversible Hyperpigmentation: A Diagnostic Dilemma



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ABSTRACT

Vitamin B12 deficiency presents as megaloblastic anemia with neurological, skin and other clinical manifestations. We present here an interesting case of anemia presenting with generalized weakness and nonspecific symptoms in a female who is a vegetarian. There was acral hyperpigmentation without any other clinical features. Investigations revealed megaloblastic anemia with low vitamin B12 and normal RBC folate levels. The patient improved after blood transfusion and intramuscular vitamin B12 injections and the skin lesions faded away suggesting vitamin B12 deficiency to be the cause of hyperpigmentation, which is an uncommon manifestation. The importance lies in the fact that this cause of reversible hyperpigmentation should be thought of by clinicians to start prompt treatment.

Key words: Anemia; Vitamin B12 deficiency; Acral hyperpigmentation

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INTRODUCTION

Anemia is defined as quantitative or qualitative diminution of hemoglobin or RBC or both depending on the age and sex of the individual. It presents with nonspecific clinical features posing challenges in diagnosis and delay in treatment leading to complications. In vitamin B12 deficiency anemia, prompt treatment with blood transfusion and parenteral vitamin B12 is very effective. The vegetarian diet in history is a very important clue. The case discussed here presented with anemia with hyperpigmentation in the distal parts of upper and lower limbs which disappeared after correction of anemia and vitamin B12 replacement. Clinicians should give importance to skin manifestations of internal disease, so this case is a classic example of a rare and reversible skin manifestation of vitamin B12 deficiency.

CASE PRESENTATION

A 53years old vegetarian, non-diabetic, non-hypertensive, female, housewife, residing in South 24 Parganas presented with generalized weakness for the last 5 months associated with blackish pigmentation of distal part of upper and lower limbs for 3 months. She was lethargic with breathlessness on mild exertion and she also noticed blackish discoloration of the distal part of hands and feet without any itching. She had no history of fever, vomiting, pain abdomen, loose motions, joint pain or swelling. There was no history suggestive of blood loss from any site, nor was there any history of addiction. She had attained menopause 10 years earlier. There was no history of visual impairment or tingling or numbness of the extremities or any abdominal surgery, tuberculosis or loss of consciousness or any history of chemotherapy.

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On examination she was alert, conscious and cooperative with tachypnea. There was severe pallor with blackish discoloration of the distal part of the hands and feet (Figure 1 and 2). Both the palmar and dorsal aspects were affected with accentuated hyperpigmentation over knuckles, creases and terminal phalanges. First and second heart sounds were audible with tachycardia and there was bilateral vesicular breath sounds. A diagnosis of megaloblastic anemia was made with the differential diagnosis of Vitamin B12 or Folic Acid deficiency anemia.

On investigation Hemoglobin was 4.1gm/dl with Mean Corpuscular volume of 115.2fl, Mean Corpuscular Hemoglobin was 41.4 pg and MCHC was 36.0gm/dl. Leucocyte and platelet counts were within normal limits. Fasting plasma glucose, Glycosylated hemoglobin, urea, creatinine, sodium, potassium, thyroid profile were normal. Serum vitamin B12 level was 50 pg/ml (200-911) which was markedly reduced along with normal RBC folate and serum cortisol levels. A diagnosis of megaloblastic anemia due to Vitamin B12 deficiency was made. There was no abnormality detected on chest X ray, Ultrasound whole abdomen, ECG and Echocardiography. Anti-parietal cell antibody and anti-intrinsic factor antibody was negative and the patient did not give consent for endoscopy or bone marrow study.



Figure 1: Hyperpigmentation of hand (dorsum) and foot



Figure 2: Hyperpigmentation of hand (palm) and foot

Transfusion of 4 units of packed red cells was done at the rate of 1 unit per day. Injection Methylcobalamin was started (Hydroxocobalamin was not available) at the dose of 1000 microgram intramuscularly (after proper skin test) once every 3 days for 6 doses. The patient started improving after transfusion; she felt better and was no longer breathless. The skin lesions started to fade rapidly proving that acral hyperpigmentation was due to vitamin B12 deficiency (Figure 3 and 4). The patient was discharged after the 6th injection and was advised to follow up in Hematology OPD. Her hemoglobin was 9.5 gm/dl and MCV was 89.3fl.

DISCUSSION

Vitamin B12 is very important for formation of RBC, DNA production, cellular metabolism and functions of the nervous system. Deficiency affects skin, gastrointestinal



Figure 3: Resolving hyperpigmentation of hand (dorsum) after vitamin B12 injection



Figure 4: Resolving hyperpigmentation of foot after Vitamin B12 injection

tract, nervous system and hematopoietic system. Vitamin B12 deficiency causing hyperpigmentation was initially reported by Cook in 1944 and later on by Baker et al., 1963.¹ Vegetarian diet, achlorhydria, pernicious anemia, bacterial overgrowth and impaired absorption leads to vitamin B12 deficiency. Neurological manifestations are loss of vibration and proprioception, dementia, psychosis. The hyperpigmentation may also occur in Addison's disease, but abdominal pain, postural hypotension, paucity of axillary and pubic hairs, hyponatremia, hypoglycemia and cortisol levels are the differentiating features from Vitamin B12 deficiency. The exact mechanism of hyperpigmentation is unknown, but it is suggested that increased synthesis of melanin due to increased activity of tyrosinase leads to improper transfer of melanin from melanocytes to adjoining keratinocytes.² Treatment is done by 6 intramuscular injections of vitamin B12 1000 mcg at 3-7 days interval. In case oral therapy is the only option, 1000-2000 mcg daily dose is required, but compliance must be monitored.³ Skin manifestations of vitamin B12 deficiency are hyperpigmentation, vitiligo, angular glossitis and scanty hypopigmented hairs which reverses after vitamin B12 treatment.^{4,5} Similar case has been reported by Pahadiya HR et al.⁶ Deficiency of vitamin B12 may cause bleeding and platelet qualitative defect which is alarming, but was not present in the case discussed here.⁷

CONCLUSION WITH LEARNING POINTS

The importance of the case lies in the fact that the hyperpigmentation caused by vitamin B12 deficiency is easily treatable by vitamin B12 supplementation, avoiding unnecessary delay in diagnosis and treatment. Moreover

clinicians should also remember vitamin B12 deficiency as a cause of reversible acral hyperpigmentation. It is a classic example of skin manifestation of treatable internal disease and will help in early diagnosis and treatment to prevent further complications. Strong suspicion is necessary even in the absence of other symptoms.⁸

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