Acral hyperpigmentation due to vitamin B12 deficiency

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A 46-year-old female patient presented with generalised weakness, weight loss and progressive darkening of the skin on both hands and feet over the previous year. There was no history of fever, altered bowel habits, sensation of tingling or numbness, memory loss, seizure, diabetes mellitus, tuberculosis, abdominal surgery or intake of any regular medication. The patient was a non-smoker, did not drink alcohol and followed a vegetarian diet. The physical examination revealed pallor and hyperpigmentation over palmar and dorsal aspect of hands and feet, with accentuation over terminal phalanges, knuckles, and creases (Figure 1, 2). Other mucocutaneous and systemic examination was non-contributory. Laboratory analysis showed reduced haemoglobin (7.3 gm/dl; reference range 12.1 to 15.1 gm/dl), and vitamin B12 level (69 pg/ml; normal 180-900 pg/ml). Serum cortisol, electrolytes, folic acid, iron, fasting blood sugar, liver, renal and thyroid profile were within normal limits. The upper gastrointestinal endoscopy was unremarkable. Based on the clinical and laboratory findings, a diagnosis of vitamin B12 deficiency was established. The patient was then treated with oral cyanocobalamin 1mg daily for initial two weeks and then weekly. A significant improvement was seen in the first month of treatment.

Vitamin B12 (cobalamin) is a water-soluble vitamin that serves many essential functions in our body including red blood cell formation, cell metabolism, nerve function and the production of DNA. Deficiency of vitamin B12 results in various muco-cutaneous, hematologic, gastrointestinal and neuropsychiatric manifestations. Hyperpigmentation due to vitamin B12 deficiency was first documented by Cook in 1944 and later by Baker et al in 1963[1]. Deficiency of vitamin B12 is biochemically established when serum cobalamin levels reduce to less than 200 pg/mL. Values of between 200-300 pg/mL indicate borderline low vitamin B12 deficiency. Inadequate intake and low consumption of animal-source foods, achlorhydria, pernicious anaemia (low intrinsic factor), bacterial overgrowth in the gut and impaired absorption due to Crohn's disease, Whipple disease, Zollinger-Ellison syndrome, and celiac disease usually leads to this deficiency disorder[2]. The common presenting features seen with vitamin B12 deficiency are the manifestations of anaemia resulting in easy fatigability, weight loss and anorexia. Neurological involvement leads to loss of vibration and proprioception sense, spasticity, paraplegia, and urinary incontinence. It may cause apathy, somnolence irritability, memory loss, dementia, and on some occasions psychosis. The characteristic muco-cutaneous features of vitamin B12 deficiency includes atrophic glossitis, angular cheilitis, brittle hair, premature depigmentation of hair

Figure 1 Addisonian hyperpigmentation over dorsa of the hands and feet, with accentuation over the interphalangeal joints, terminal phalanges

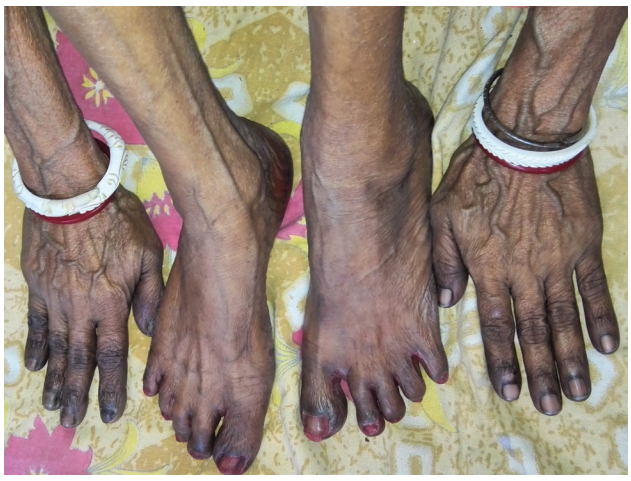

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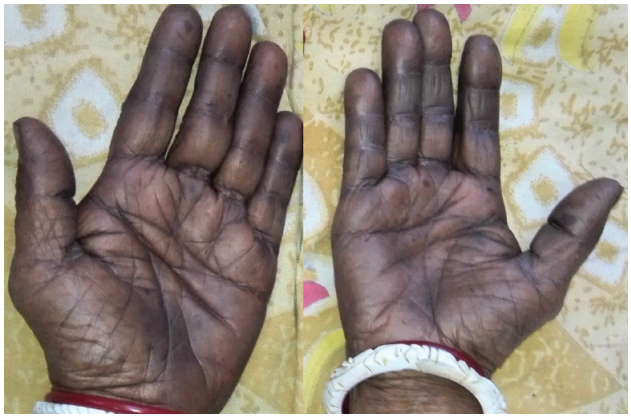
Figure 2 Hyperpigmentation over palms with accentuation over palmer creases



(canities) and cutaneous hyperpigmentation[3] Characteristic Addisonian hyperpigmentation of the extremities, especially over dorsa of the hands and feet with accentuation over the interphalangeal joints, terminal phalanges, palmar creases, combined with pigmentation of the oral mucosa are characteristics of vitamin B12 deficiency[4]. However, absence of decreased pubic and axillary hair in women, postural hypotension and abdominal pain helps distinguish these symptoms from pigmentation seen in Addison's disease. Acral hyperpigmentation is also observed in hypothyroidism, hyperthyroidism, systemic sclerosis, Cushing's syndrome and as an adverse effect of drugs such as busulphan, cyclophosphamide and doxorubicin.

The exact pathophysiologic mechanism associated with hyperpigmentation in vitamin B12 deficiency is poorly understood. It is proposed that it may be due to increased melanin synthesis due to increased tyrosinase activity and defective melanin transfer from melanocytes to adjacent keratinocytes.[5]

Treatment of vitamin B12 deficiency depends on the underlying causes. Blocked or reduced oral bioavailability such as in patients with pernicious anaemia, and impaired absorption in cases of ileal resection requires parenteral administration of vitamin B12. Otherwise, oral supplementation of 1 mg to 2 mg cyanocobalamin daily at treatment initiation and gradually tapered to weekly and then monthly is recommended.[4, 5]

The purpose of documenting this case is to familiarise physicians with the various mucocutaneous features of vitamin B12 deficiency. Though a rare presentation, acral hyperpigmentation serves as an important clue in diagnosing an underlying vitamin B12 deficiency, even in the absence of other symptoms. Strong clinical suspicion and prompt treatment is necessary to prevent the occurrence of haematological and neurological complications of this deficiency disorder.

References:

1 Baker SJ, Ignatius M, Johnson S, et al. Hyperpigmentation of skin. a sign of vitamin-B12 deficiency. *Br Med J* 1963;1:1713-15.
2 Oh R, Brown D. Vitamin B12 deficiency. *Am Fam Physician* 2003;67:979-86.
3 Graells J, Ojeda RM, Muniesa C, et al. Glossitis with linear lesions: an early sign of vitamin B12 deficiency. *J Am Acad Dermatol* 2009;60:498-500.
4 Jithendriya M, Kumaran S, P IB. Addisonian Pigmentation and Vitamin B12 Deficiency: A Case Series and Review of the Literature. *Cutis* 2013;92:94-9.
5 Mori K, Ando I, Kukita A. Generalized hyperpigmentation of the skin due to vitamin B12 deficiency. *J Dermatol* 2001;28:282-5.