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Case Report

Manifestation of pernicious anaemia as hyperpigmentation of palms and soles

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ABSTRACT

Vitamin B_{12} deficiency produces various manifestations involving CNS, heart, skin, blood and female reproductive systems. It is seen most commonly in the older individuals, malabsorptive states (>60% of all cases) and vegetarians. Pernicious anaemia may be confused to Addison's disease as both may present with similar clinical features. Hereby we report a case of pernicious anaemia presenting with dermatological manifestation in the form of deep pigmentation of both palms of and both soles respectively, cortisol levels normal so Addition's disease ruled out.

Keywords: Pancytopenia, Biguanides, Pernicious anaemia, Methionine

INTRODUCTION

Vitamin B_{12} is a water soluble vitamin existing in 5 forms, they are cyanocobalamin (vitamin B_{12}), hydroxocobalamin (vitamin B_{12a}), aquacobalamin (vitamin B_{12b}), nitritocobalamin (vitamin B_{12c}), 59-deoxyadenosylcobalamin (coenzyme B_{12}), and methylcobalamin (methyl B_{12}). Presentation of B_{12} deficiency usually varies from asymptomatic to affecting multiple organ systems. Early symptoms of B_{12} deficiency include fatigue, indigestion, anorexia, nausea, and menstrual disturbances. Macrocytic anaemia and pancytopenia are common in peripheral smear examination and orthostatic hypotension, paraesthesias and abnormal gait are usual manifestations neurologically.[1,2] Rarely dermatological manifestations such as skin hyper pigmentation, stomatitis hair and nail changes can occur in B_{12} deficiency. Early recognition and treatment of these findings may prevent potentially irreversible complications such as sub-acute combined degeneration (SCD) which often affects peripheral nerves with absent deep tendon reflexes and the spinal cord with plantar extensor reflex suggesting corticospinal tract involvement.

CASE REPORT

48 year old male patient came with complaints of black pigmentation of both palms and soles since 1year. He was a diabetic on metformin 1gm/day for the last 4 years. There was no history of pain abdomen, fever, and cough, diarrhoea. His extremities showed diffuse hyper pigmentation of the palms and soles bilaterally (Figure 1, 2). His vitals were pulse 80/mt, blood pressure 120/70 mm of hg, respiratory rate 18/mt, temperature normal. On general examination there was anemia and on systemic examination his heart, lungs and CNS were normal. Hemogram showed Hb 9.1gm%, T.wbc-6700/cu.m.m, D.C: polymorphs 58%, lymphocytes 35%, esinophils 7%, ESR 12mm/1hr, MCV- 74cm and MCHC- 35%. Peripheral smear examination revealed macrocytic, hypochromic anaemia, blood sugar 130 mg%, urea

30mg%, creatinine 1mg%. Stool was negative for ova, cysts and occult blood. USG abdomen and upper GI endoscopy were normal. CT abdomen showed mild splenomegaly and no evidence of mass lesions. B_{12} levels were 37 pg/ml (N 200 – 650 pg/ml), total iron binding capacity 459µg/ml, serum ferritin <1.50 ng/ml, serum cortisol 236nmol/L, intrinsic factor Ig G 22.7 u/ml, T_3- 0.89, T4- 5.94, TSH-2.01(normal).

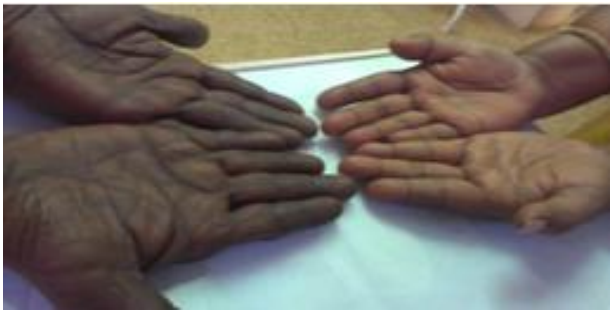

Figure 1: Hyperpigmentation of palms.

Figure 2: Hyperpigmentation of soles.

As the patient has macrocytosis and hypochromic anaemia, evidence of intrinsic factor antibodies, low levels of B_{12} (37pg/ml), no evidence of tuberculosis in the form of ileal mass lesions on CT abdomen, no gastric atrophy on upper GI Endoscopy, he was diagnosed to have pernicious anaemia and given 1000µg parenteral B12 daily for 2weeks followed by once in a week for further 4 months. The hyper pigmentation of hands and feet had resolved with no recurrence in 4 months as shown in (Figures 3, 4). His B_{12} levels were >2000pg/ml in 4 months after treatment, continued on B_{12} injections.

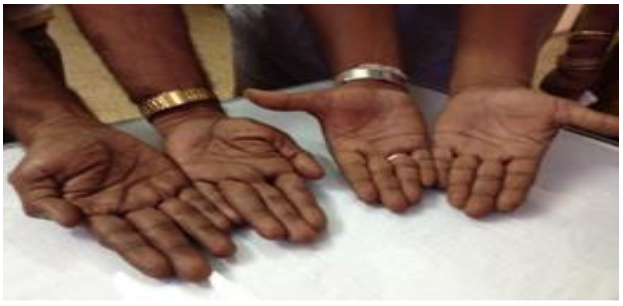

Figure 3: Disappearance of hyperpigmentation of palms after B_{12} therapy.

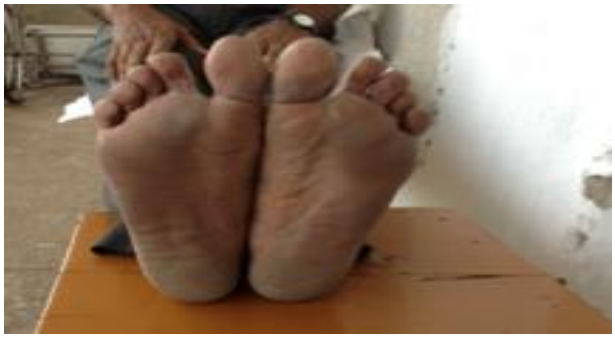

Figure 4: Disappearance of hyperpigmentation of soles after B_{12} therapy.

DISCUSSION

Incidence of cobalamine deficiency is around 20% all over the world.[2] The vitamin B_{12} is abundant in products like cheese, other milk products, non-vegetarian diet like eggs, mutton, fish, and shellfish. Vitamin B_{12} deficiency was very significant in high-risk populations like older individuals, malabsorptive states like in gastric and ileal resection or autoimmune gastric mucosal disease or gastric atrophy, coeliac disease, Crohn's disease, ileitis, pancreatic insufficiency, vegetarians and long-term use of proton pump inhibitors, histamine (H_2) receptor antagonists or biguanides.[3-5]

In pernicious anaemia, the gastric parietal cells are targeted by the autoimmune process. Hence, the production of intrinsic factor is affected leading to defective absorption of vitamin B_{12}. Moreover vitamin B_{12} deficiency affects blood, CNS, and digestive systems and it has been considered as a cause of orthostatic hypotension.[6] Myocardial infarction, stroke and retinal haemorrhages, mood disorders, dementia, psychosis, depression also can occur in B_{12} deficiency.

Thomas Addison described pernicious anaemia and Addison's disease. Both diseases share clinical features such as asthenia, gastrointestinal symptoms, hyper pigmentation, and hypotension. Hence B_{12} estimation should always be done to rule out B_{12} deficiency in these patients.

In 1944 by Dr. Bramwell Cook described dermatological manifestations include skin hyper pigmentation, hyper pigmentation of surgical scars, vitiligo, recurrent angular stomatitis, and hair changes.[7] In a study of 63 patients by Aaron et al glossitis (31%) was the most common mucocutaneous presentation, followed by skin hyper pigmentation (19%), hair changes (9%), angular stomatitis (8%), and vitiligo (3%).[8] The hyper pigmentation is observed characteristically in the oral mucosa and over the knuckles of hands and dorsum of feet, with accentuation over the interphalangeal joints and terminal phalanges in majority of patients. Increased melanin synthesis due to excessive secretion of melanin stimulating hormone (MSH) has been suggested as the

cause for hyper pigmentation. B_{12} deficiency causes decreased glutathione which stimulates tyrosinase leading to transfer to melanosomes. Melanin transfer between melanocytes and keratinocytes when affected produces pigmentary changes.[9]

Methylmalonyl-CoA gets converted to succinyl-CoA in the cell mitochondria and methionine is formed from homocysteine in the cytoplasm by methyl transfer reaction. At the same time conversion of homocysteine to methionine is followed by the conversion of methyltetrahydrofolate to tetrahydrofolate which is a precursor for purine and pyrimidine synthesis. In vitamin B_{12} deficiency interferes with the conversion of methyltetrahydrofolate to tetrahydrofolate which in turn impairs the synthesis of DNA and a megaloblastic maturation pattern of hematopoietic cells.[10] S-adenosylmethionine (SAM) is formed from methionine which methylates neurotransmitters and phospholipids. Vitamin B_{12} deficiency interferes with production of choline and choline-containing phospholipids, oligodendrocyte function, and myelin basic protein methylation.[11] Demyelination is the initial process of neurological damage followed by axonal degeneration that eventually leads to irreversible axonal death. If B_{12} is supplemented early, the neurological damage can get reversed.

In this patient, the gastric mucosa is normal on upper GI endoscopy, no mass lesions or gastrointestinal tuberculosis on CT abdomen, blood picture showed macrocytosis, B_{12} levels low and Ig G intrinsic factor antibodies positive hence the diagnosis of pernicious anaemia (B_{12} deficiency) was considered and treated accordingly. This patient is a vegetarian, who might have also contributed for the deficiency of B_{12} and also he was on metformin for diabetes for the last 4 years but it may be too short a period to produce B_{12} deficiency as the time taken normally for developing this complication was 12 to 15 years. Poor intake of B_{12} with decreased intrinsic factor and metformin usage might be the cause for his B_{12} deficiency.

CONCLUSION

Vitamin B_{12} deficiency should be considered in all hyper pigmentation cases and determine serum B_{12} levels in them as it is a treatable condition. Early diagnosis of B_{12} deficiency and treatment will help in reducing morbidity and hyperpigmentation.

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REFERENCES

1. Stabler SP, Allen RH, Savage DG, Lindenbaum J. Clinical spectrum and diagnosis of cobalamin deficiency. Blood. 1990;76(5):871-81.
2. Andrès E, Loukili NH, Noel E, Kaltenbach G, Abdelgheni MB, Perrin AE, et al. Vitamin B_{12} (cobalamin) deficiency in elderly patients. Canadian Medical Association Journal. 2004;171(3):251-9.
3. Marcuard SP, Albernaz L, Khazanie PG. Omeprazole therapy causes malabsorption of cyanocobalamin (vitamin B_{12}). Annals of internal Medicine. 1994;120(3):211-5.
4. Andrès E, Noel E, Abdelghani MB. Vitamin B12 deficiency associated with chronic acid suppression therapy. Annals of Pharmacotherapy. 2003;37(11, article 1730).
5. Adams JF, Clark JS, Ireland JT. Malabsorption of vitamin B12 and intrinsic factor secretion during biguanide therapy. Diabetologia. 1983;24(1):16-8.
6. Ganjehei L, Massumi A, Razavi M, Wilson JM. Orthostatic hypotension as a manifestation of vitamin B_{12} deficiency. Texas Heart Institute Journal. 2012;39(5):722-3.
7. Ogbuawa O, Trowell J, Williams JT. Hyperpigmentation of pernicious anemia in Blacks. Report of three cases. Archives of Internal Medicine. 1978;138(3):388-9.
8. 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 B_{12} deficiency-related neurological syndromes. Neurology India. 2005;53(1):55-8.
9. Mori K, Ando I, Kukita A. Generalised hyper pigmentation of B12 deficiency. J Dermatol. 2001;28:282-5.
10. Tefferi A, Pruthi RK. The biochemical basis of cobalamin deficiency. Mayo Clinic Proceedings. 1994;69(2):181-6.
11. Cherqaoui R, Husain M, Madduri S, Okolie P, Nunlee-Bland G, Williams J. A reversible cause of skin hyper pigmentation and postural hypotension. Case Reports in Hematology. 2013;2013:680489.

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