CASE REPORT

Skin pigmentation in a patient with vitamin B12 deficiency presented with sub-acute combined degeneration of spinal cord

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Abstract

Vitamin B12 deficiency results in multisystem manifestations. A 30-years-old man presented with progressive weakness of lower limbs along with numbness. Patient had pale colour and noticed progressive pigmentation over dorsal and palmar aspects of both the hands and the feet. Neurological examination revealed absent ankle jerks, sensory impairment until T5 level, loss of joint position sensation and positive Romberg's sign. Workup showed macrocytic anaemia and hyper-segmented neutrophils. There was no evidence of hypo-cortisolism. Magnetic Resonance Imaging of brain and spine was normal; however, Electromyography/Nerve conduction studies were suggestive of demyelinating neuropathy. His clinical and lab findings were suspicious of B12 deficiency, which was found to be very low. Hyperpigmentation is rare in B12 deficiency as presenting symptoms and diagnosis may be overlooked. Therefore, vitamin B12 levels should be checked as any delay in diagnosis and treatment will result in progression of Subacute Combined Degeneration of the spinal cord to the extent that it becomes irreversible.

Keywords: Skin pigmentation, vitamin B12 deficiency, sub-acute combined degeneration of spinal cord.

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Introduction

Vitamin B12 deficiency results in haematological, neurological and rarely dermatological manifestations.[1] Sub-acute Combined Degeneration (SCD) of the spinal cord is one of the neurological consequences of vitamin B12 deficiency in addition to peripheral neuropathy, dementia, neuropsychiatric abnormalities and rarely optic atrophy.[2] SCD is characterized by degeneration of posterior and lateral columns of the spinal cord and presents with paraesthesia in the fingers, toes or both.[1] Hyperpigmentation is a common skin finding in vitamin B12 deficiency but it is a rare initial presentation and its presence with SCD has only been reported in few cases in the literature.[1]

We report a case of SCD of the spinal cord with skin hyperpigmentation after receiving an informed written consent.

Case Report

A 30 years old man with no comorbidities, presented to the Shalamar Hospital Lahore on Nov 14, 2018, with weakness of both lower limbs for the past 2 months. He was in his usual state of health before presenting to the hospital with complaints of weakness which was sudden in onset, non-episodic, symmetrical and slow in progression. Initially, patient faced difficulty in climbing the stairs but over the past 3 weeks he has been unable to walk without support and had difficulty in writing as well. There were no aggravating or relieving factors. He also had numbness and tingling which started in the feet symmetrically and gradually progressed to involve both legs. There were no preceding respiratory or gastrointestinal symptoms. He did not have fever, headache, vertigo, vomiting, fits, speech or swallowing difficulty, voice changes, diplopia and urinary or faecal incontinence. He also noticed progressive pigmentation involving both palmar and dorsal aspects of the hands including knuckles, creases and feet over the past 2 months. He denied any history of vomiting, abdominal pain, weight loss, diabetes, hypertension, ischaemic heart disease, thyroid disease, tuberculosis, use of drugs or travelling. He is a married, non-smoker, non-alcoholic accountant. His dietary habits were satisfactory.

On examination, he weighed 70 kg and was 5'-7" in height. He had no hyperthyroid/hypothyroid features. He was pale but had no jaundice or lymphadenopathy. His pulse rate was 80/min, BP 130/88 mmHg with no postural drop and he was afebrile. Patient had pigmentation over the interphalangeal joints especially, over the distal phalanges, palmar creases of both hands and feet (Figure), however there was no pigmentation over the buccal mucosa or any other site. He did not have hepatosplenomegaly.

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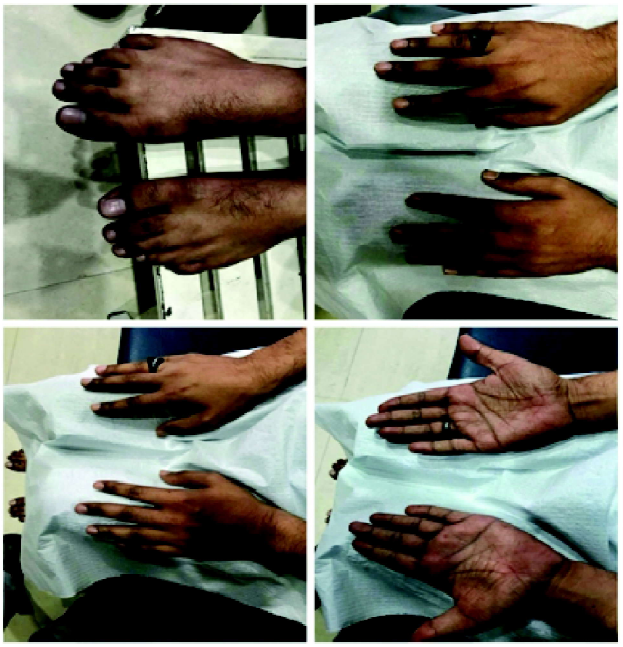

Figure: Marked hyper pigmentation over interphalangeal joints and peri ungal areas of both hands and feet & also over palms before treatment.

Table: Lab investigations before treatment.

INVESTIGATIONS	VALUES
Haemoglobin	11.7g/dL (14-18)
RBC count	$3.20x10^6$ /μL (4-6)
Platelet count	$243x10^3$ /μL (150-450)
MCV	95.3fL (77-93)
ALT	21U/L (5-40)
AST	19U/L (5-40)
Urea	15mg/dL (10-50)
Creatinine	0.7mg/dL (0.5-1.3)
BSR	88mg/dL
TSH	0.90 μIU/ml (0.30-4.2)
HBsAg/ Anti HCV	Negative
Plasma ACTH	9.44 pg/ml (upto 46)
Plasma Cortisol	0.19μg/dL (3.7-19.4)
Short Synacthen test	
Plasma ACTH (basal)	28.67pg/ml (upto 46)
Plasma cortisol (basal)	14.73μg/dL (3.7-19.4)
Inj Synacthen 250ug given IM	
Plasma Cortisol (30 mins after inj)	17.71μg/dL
Plasma Cortisol (60 mins after inj)	19.39μg/dL
Serum Vitamin B12 levels	12.50pg/ml (239-930)

RBC: Red Blood Cell, MCV: Mean Corpuscular Volume, AST: Aspartate Aminotransferases, ALT: Alanine Aminotransferases, BSR: Blood Sugar Random, TSH: Thyroid Stimulating Hormone , HBsAg: Hepatitis B surface Antigen , Anti HCV: Anti Hepatitis C virus , ACTH: Adrenocorticotropic Hormone.

Neurological examination of lower limbs showed normal tone, power 4+/5 in proximal muscles but normal distally. Knee jerks were present bilaterally but ankle jerks were absent on both sides. He had sensory impairment to pin prick in both the lower limbs up to the T5 level and impaired joint position sensation at both distal interphalangeal joints. He had gait ataxia and Romberg's sign was positive. His upper limbs, cranial nerves, higher functions were neurologically normal and had no cerebellar signs.

His baseline investigations revealed haemoglobin to be 11.7 g/dL and mean corpuscular volume to be 95.3fL. His renal and liver function tests, serum electrolytes, thyroid profile, blood glucose level and viral serology were normal (Table). Blood picture depicted low red blood cells count with mixed normocytic normochromic and macrocytic red cells. Some neutrophils showed hypersegmentation. White blood cells and platelets were adequate on smear. Magnetic Resonance Imaging of brain and whole spine with contrast and cerebrospinal fluid analysis were normal. Meanwhile, for skin pigmentation, serum cortisol and Adrenocorticotropic hormone (ACTH) levels were done followed by short synacthen test to rule out Addison's disease. Patient's short synacthen test was consistent with good ACTH stimulation and hence, intact hypothalamic pituitary adrenal axis. His electromyography (EMG)/nerve conduction study (NCS) was suggestive of sensory polyneuropathy of demyelinating variety. His clinical and lab findings were suspicious of vitamin B12 deficiency associated with SCD and skin pigmentation. Hence, we proceeded with the serum vitamin B12 level that was found to be very low; 12.50pg/ml (239-930 pg/ml).

Clinical diagnosis of SCD associated with skin pigmentation due to vitamin B12 deficiency was made. Patient was started on intramuscular cyanocobalamin 1000ug daily for 7 days, then weekly for next 4 weeks and thereafter once monthly. To find out the cause of B12 deficiency, we planned for an upper GI endoscopy, which was refused by the patient and an anti-intrinsic factor antibody was done later, which came out negative. Further, serology for H. pylori (IgG) was positive, likely suggestive of H. pylori associated atrophic gastritis and he was then started on H. Pylori eradication therapy. After treatment, pigmentation and neurological symptoms improved within 3 weeks.

Discussion

Vitamin B12 deficiency is a major public health problem affecting millions of people worldwide. Previous national level data regarding prevalence of B12 deficiency in

Pakistan is not available, however a small scale cross sectional study, conducted in 2009 revealed 6.8% of adults to be B12 deficient.[3] Inadequate intake of animal source food, pernicious anaemia, malabsorption and gastric atrophy are the main causes of low serum B12 levels.[4] Normal serum levels range from 160-200pg/ml to 100pg/ml. Values between 100-200pg/ml are regarded as borderline but with cobalamin deficiency, the level is usually <100pg/ml. As in this case, the level is too low i.e. 12.50pg/ml. Serum methylmalonate and homocysteine have been recommended for the early diagnosis.[5]

Vitamin B12 deficiency can present with haematological, gastrointestinal, neuropsychiatric and rarely dermatological abnormalities.[1,2] Haematological abnormalities are common and early manifestation, characterized by anaemia, raised MCV and the presence of macrocytosis and hypersegmented neutrophils on peripheral blood film,[2] as seen in this patient. Pancytopenia due to B12 deficiency is very rare and about <5% in different series.[6]

Neurological manifestations occur late and include myelopathy, neuropathy, dementia, optic atrophy and neuropsychiatric abnormalities including psychosis, personality changes and rarely delirium. SCD is frequently seen with B12 deficiency, although it is a rare cause of myelopathy. Typical signs include spastic paraparesis, extensor plantar response, impaired sense of joint position and vibration and it may have associated peripheral neuropathy,[2] that explains this patient's sensory impairment and absent ankle jerks.

MRI and electrophysiological findings in SCD are diverse in different studies. Axonal neuropathy was predominantly seen on NCS while some showed demyelinating or sensorimotor neuropathy of mainly axonal variety.[2,7] However, this patient had sensory demyelinating polyneuropathy and had normal motor NCS in both upper and lower limbs. MRI spine typically show high signal in dorsal column bilaterally on T2W image, predominantly in upper and mid thoracic regions.[2] Although these lesions are common but are not present in every patient'; MRI may be normal as in this case and in a study conducted by B Hemmer et al.[7]

The dermatological manifestations of B12 deficiency include, skin hyper pigmentation, vitiligo, hair changes and angular stomatitis. Hyperpigmentation predominantly involve dorsum of hands and feet, palms and soles with accentuation over terminal phalanges and interphalangeal joints, along with oral mucosa involvement, simulating pigmentation of Addison's disease.[1,8] Similar pigmentation was seen in our case but there was no oral mucosa involvement or other skin manifestations. Although it is a common skin finding in B12 deficiency but its presence with SCD has been reported in few cases[1,8] as seen in this patient. Its pathophysiology involves low reduced glutathione levels due to B12 deficiency, which increases tyrosinase activity that results in melanocytes stimulation to produce melanin.[8] Skin biopsy was not conducted in this case. Whether hyperpigmentation develops at a certain low level of serum B12, is not known.[1]

With treatment, hyperpigmentation resolves in 6-12 weeks.[1] Neurological response usually starts in first week and is completely evident within 6 months. However, it is often variable and may be incomplete if deficiency is severe and there is a delay in the initiation of treatment.[2]

Though a rare presentation, pigmentation due to B12 deficiency should always be kept in mind especially, when the patient is having neurological signs and symptoms. Such patients should be diagnosed and treated early as delay in diagnosis and treatment will result in SCD symptoms to progress to the extent that they become irreversible.

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