Generalised Hyperpigmentation in Vitamin B12 Deficiency

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Abstract

In developing countries like India, nutritional deficiencies are prevalent and hyperpigmentation due to protein energy malnutrition, zinc deficiency and pellagra are common. Indian women, especially vegetarian are prone to vitamin B12 deficiency. Vitamin B12 deficiency can present as anaemia, neurological defect, gastrointestinal symptoms or dementia. Hyperpigmentation as the first presentation of Vitamin B12 deficiency is rare. Our patient, a 45 year-old Hindu vegetarian female presented to us with generalized hyperpigmentation. Examination revealed associated anaemia and peripheral neuropathy. Laboratory investigation confirmed vitamin B12 deficiency. Clinical features along with hyperpigmentation improved with vitamin B12 supplementation. We report this case to highlight this rare manifestation of vitamin B12 deficiency. A high index of clinical suspicion is warranted to diagnose the case. Since India is a country with a large number of potential vitamin B12 deficiency cases, the physicians need to be aware of all the varied manifestations of this vitamin deficiency. In case of hyperpigmentation, nutritional aspect must be ruled out as it is reversible. Early replacement therapy may also help to prevent morbidities like dementia and neuropathy.

Introduction

Vitamin B12 deficiency (VBD) is now recognised as a common public health problem of India.¹ This can present as anaemia, neurological defect, gastrointestinal symptoms or dementia. Hyperpigmentation as the first presentation of VBD is only rarely reported. We here present a case of VBD presenting with slow onset generalised hyperpigmentation. As far as we could search, this is probably the first report of this manifestation from Eastern India.

Case Report

A 45 year-old Hindu vegetarian female presented to us with generalised hyperpigmentation for last two years. The hyperpigmentation was insidious in onset and slowly progressive. At first, she noticed hyperpigmentation of the sun exposed parts and scars. But later, it became generalised to involve whole of the skin surface, including palms and soles (Figures 1 and 2). Hyperpigmentation was associated with progressive generalised weakness and lassitude. On examination, we found severe pallor and oral ulcers. There was no organomegaly. The ankle jerks were absent and vibration sense was impaired up to ankles in both lower limbs. She had no history of abdominal surgery, any other autoimmune diseases like vitiligo, or no history of any drug intake.

Laboratory studies revealed haemoglobin 3.9 gm%, total leucocyte count 2300/µL (neutrophil 28%; lymphocyte 68%; eosinophil 2%; monocyte 2%) and platelet count of 94000/cmm. Red cell indices revealed MCV 118 µL, MCH 33.3 pg and MCHC 30.8 g/dL. ESR was 75 mm / hour and there was slightly increased rouleaux formation with a normochromic macrocytic blood picture in peripheral smear. Red cell distribution width was 29.5%. Reticulocyte count was 2.7% with production index of 0.351. Fasting sugar, urea and creatinine values were 78 mg%, 16 mg% and 0.9 mg% respectively. Blood electrolytes and liver function tests were also normal.
Blood vitamin B12 level was 81.3 pg/ml (normal: 239-931 pg/ml by electrochemiluminescence COBAS e411) and folate level was 19 ng/ml (normal: 3-17 ng/ml). Upper gastrointestinal endoscopy did not reveal any atrophy of stomach mucosa. Anti-parietal cell antibody was negative. Thyroid function test was normal. Serum ferritin level was 452.1 ng/ml. Stool examination did not reveal any worm infestation and ultrasonography did not reveal any pancreatic pathology. Urine porphyrin levels were negative.

Bone marrow aspiration and biopsy study revealed megaloblastic cells with maturation defect (Figure 3).

Considering the severe pallor, two units of packed red blood cell transfusion was given. Intramuscular hydroxycobalamin (cyanocobalamin being not available) was started. The subsequent haematological pictures improved significantly (Table 1).

The patient did not need any more blood transfusions. However, in the initial period of vitamin replacement, she developed hypokalaemia (serum K⁺ = 2.6 mEq/L) which was corrected by oral supplementation. She is being currently maintained on regular monthly vitamin B12 injections. Her neurological problems of lower limbs resolved and hyperpigmentation improved after three months of treatment (Figure 4).

Table 1: Showing improvement of haematological pictures after initiation of therapy

<table>
<thead>
<tr>
<th></th>
<th>Before therapy</th>
<th>7 days</th>
<th>21 days</th>
<th>2 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g%)</td>
<td>3.9</td>
<td>4.4</td>
<td>8</td>
<td>8.6</td>
</tr>
<tr>
<td>Reticulocyte count (%)</td>
<td>2.7</td>
<td>7.4</td>
<td>9.2</td>
<td>6</td>
</tr>
<tr>
<td>Total leucocyte count (/cmm)</td>
<td>2300</td>
<td>2520</td>
<td>5400</td>
<td>5200</td>
</tr>
<tr>
<td>Platelet count (/cmm)</td>
<td>94000</td>
<td>100000</td>
<td>130000</td>
<td>145000</td>
</tr>
</tbody>
</table>
Discussion

Hyperpigmentation is caused by increase of melanin, an increase in melanocytes, or the deposition of another substance that adds colour to the skin. This may be caused by primary dermatological disorders like melanoma or systemic diseases like haemochromatosis. Protein energy malnutrition, zinc deficiency and pellagra are known to cause hyperpigmentation. VBD is a rare cause of hyperpigmentation. Thus, in developing countries like India, hyperpigmented patients must be investigated for nutritional deficiencies. The cause for hyperpigmentation in VBD is thought to be an increase in melanin synthesis with increased melanosomes in basal layer of skin. Few cases of hyperpigmentation in VBD have been reported from India.

Indian women are prone to VBD; along with iron and folate deficiencies. This reflects the generally poor nutritional status of Indian women. Other than nutritional deficiency VBD may be caused by various other causes like, tropical sprue and/or autoimmune diseases. Often, the use of diluted cow’s milk during weaning of infants may be a predisposing factor in causing VBD and thus, paediatricians also need to be aware of this entity. VBD remains undiagnosed in many cases.

VBD is associated with various muco-cutaneous disorders like hyperpigmentation, vitiligo, hair changes, glossitis and angular stomatitis. Typically, hyperpigmentation of dorsum of hands and feet with oral mucosa is found. One case reported from Varanasi, India showed this type of hyperpigmentation as the initial manifestation of VBD in a strictly vegetarian male. One case reported from Tamil Nadu, India had non-pigmented polymorphic maculopapular eruptions in upper trunk. Sometimes, there may be associated hyperpigmented nails and/or grey hair. Associated pallor, macrocytosis and anti-parietal cell antibodies, if present, can give clue to the underlying cause of hyperpigmentation. All the pigmentary changes are usually quickly reversible with adequate vitamin B12 supplementation. Our patient also showed improvement of pigmentation with vitamin B12 supplementation.

We report this case to highlight this rare manifestation of VBD. Since India is a country with a large number of potential VBD cases, the physicians need to be aware of all the varied manifestations of this vitamin deficiency. Besides pallor and glossitis, atypical signs like hyperpigmentation may also be the initial manifestation of VBD and a high index of clinical suspicion is warranted. In any case of non-resolving hyperpigmentation, the nutritional aspect must be ruled out before investigating for the rare aetiologies. Early replacement therapy may help to prevent morbidities like dementia and neuropathy.

References