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IMPORTANCE OF EVALUATING VITAMIN B12 STATUS IN DEPRESSION AND ANXIETY DISORDERS

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Abstract

Vitamin B12 deficiency is common in Indian population and it can manifest in the form of various systemic abnormalities. Psychiatric manifestations are often the presenting complaints in many cases. Here, we highlight the importance of identifying and treating vitamin B12 deficiency in the patients presenting with psychiatric manifestations.

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INTRODUCTION

Vitamin B12 is a water soluble vitamin commonly present in animal protein. It is important for DNA synthesis, synthesis of neurotransmitters, formation of myelin sheath and erythropoiesis [1].

Daily requirement of vitamin B12 is approximately 1 to 2 mcg [2]. Vitamin B12 deficiency commonly occurs due to insufficient dietary intake or poor absorption from gastrointestinal tract. Dietary deficiency is usually seen in vegans, alcoholics and elderly people[3], whereas malabsorption may occurs in patients suffering from hypochlorhydria, decreased output of gastric intrinsic factor or disorders of small intestines[4]. Further the requirements of vitamin B12 are increased in case of pregnant and breast feeding women, patients with autoimmune disorders, or persons with HIV infection which puts them at high risk for development of its deficiency[1].

Deficiency of vitamin B 12 affects various systems including nervous system, hematological system and gastrointestinal system. Neurological manifestations are paresthesias, peripheral neuropathy, sub-acute combined degeneration of the cord. Hematological manifestation includes macrocyticanemia, pancytopenia [leukopenia, thrombocytopenia][3].

Apart the neurological and haematological disturbances vitamin B12 deficiency also can manifest in the form of various psychiatric manifestations. These include irritability, personality changes, depression, dementia and rarely, psychosis[3]. Neuropsychiatric manifestations are further important because they develop usually many years before the appetence of haematological manifestation like macrocytic anaemia[1]. Here we have reported two cases of vitamin B12 deficiency which presented to our hospital with primarily psychiatric manifestations.

CASE PRESENTATION:

Case 1: An 18-year-old college going boy from a rural background presented with three months history of reduced concentration in studies, low mood, anhedonia, easy fatigability, crying spells and pessimistic attitude towards future. He was well built, strict vegetarian, non-smoker, non-alcoholic with unremarkable past history or drug history. On general physical examination he had reduced pain and temperature sensation in all extremities distally, bilaterally absent ankle jerks and prominent bilateral knuckle hyperpigmentation [Figure. 1]. Mental status examination revealed marked cognitive slowing, reduced sustained attention, reduced psychomotor activity, and predominant

depressive cognition. The investigation revealed severe vitamin B12 deficiency with a level of 50pg/mL [Normal range 180-914pg/mL]; also there was an increase in serum homocysteine with value of 23.4mcmol/L [normal range 6.6-14.8mcmol/L]. Serum folate level was 5.8ng/ml. Haemoglobin was 12.5g%, MCV was 90.8fL, MCH was 30.2pg/mL and MCHC was 34.3g/dL. Serum electrolytes and thyroid function tests were normal. A diagnosis of moderate depressive episode and vitamin B12 deficiency was made. Patient was administered parenteral Methyl-cobalamin 1000µg per day along with oral multivitamin supplements and low dose of antidepressant. Significant improvement in depressive symptoms occurred over one week such that Hamilton Depression Rating Scale[5]scores dropped from 17 to 4.

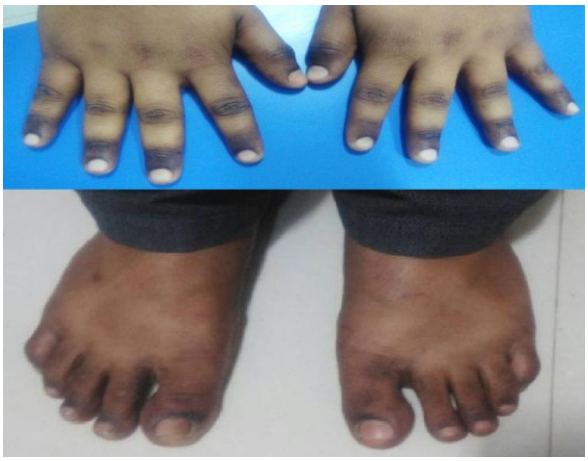

Figure: 1 Case: 1 Prominent knuckle hyperpigmentation

Case 2: A 16-years-old boy was brought to the emergency department with 4 hours history of severe anxiety symptoms characterized by fearfulness, restlessness, palpitation, sweating, difficulty in breathing, choking sensation, giddiness and fear of impending doom. There was history of similar episodes over past 2 years, which were less severe and subsided without any medical intervention. Patient was non-smoker, non-alcoholic with unremarkable history and non-vegetarian diet. On examination patient had mild tremors, tachycardia, sweating, mildly dilated pupils and bilaterally increased reflexes suggestive of severe anxiety. Patient also had prominent bilateral knuckle hyperpigmentation [Figure 2].

Serum Vitamin B12 level was 63pg/ml suggestive of severe deficiency. An associated increase in serum homocysteine levels was noted with value of 20.7mcmol/L. Haemoglobin was 16.5g%, MCV was 88.1fL, MCH was 32.2pg/mL and MCHC was 36.5g/dL. Serum electrolytes and thyroid functions were normal.

Patient was diagnosed as having anxiety disorder [panic attacks] and vitamin B12 deficiency. He was treated primarily with parenteral Methyl-cobalamin at a dose of 1000 µg per day along with oral multivitamin

supplements and antianxiety medicine. Benzodiazepines were used only to control acute panic symptoms in emergency department. After one week treatment there were minimal anxiety symptoms and Hamilton Anxiety Rating Scale[6] scores had dropped from 28 to 7.

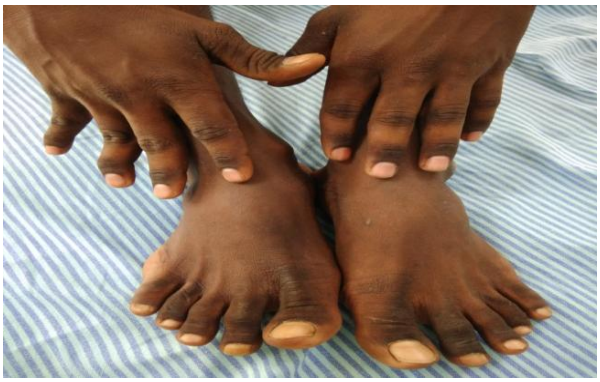

Figure 2: Case 2: Bilateral knuckle hyperpigmentation

DISCUSSION:

Vitamin B12 along with folate is required for the methylation of homocysteine to methionine and in the formation of S-adenosylmethionine. The later is involved in various methylation reactions involving proteins, phospholipids, DNA, and neurotransmitter metabolism[7]. Deficiency of vitamin B12 may lead to disruption of this pathway and manifest as neuropsychiatric disorders. The psychiatric manifestation includes slow cerebration, confusion, memory changes, delirium, depression, acute psychosis etc[8]. Here we have presented two cases which primarily presented with psychiatric manifestations in the form of anxiety and depressive disorder. On careful examination we noted signs and symptoms suggestive of possible vitamin B12 deficiency in them which led us to evaluate it in detail.

In both these cases on physical examination prominent knuckle hyper-pigmentation was noted. We searched for all possible causes of such hyper-pigmentation in both patients and obtained very low levels of serum vitamin B12 which helped us to confirm its deficiency. Hyperpigmentation due to vitamin B12 deficiency characteristically affects the dorsal aspects of the hands and feet especially involving inter-phalangeal joints and terminal phalanges along with pigmentation of oral mucosa[9]. However, similar hyper-pigmentation is also seen in conditions like Addison's disease, thyroid disease, hemochromatosis and rarely homocystinuria[10]. These conditions must be ruled out before attributing hyper-pigmentation due to vitamin B12 deficiency.

Further in both the cases we found increased levels of serum homocysteine. Vitamin B12 deficiency is often associated with elevation of plasma homocysteine level. The neurotoxic effects of homocysteine may also play a role in the neurologic and psychiatric disturbances

that are associated with vitamin B12 deficiency[7]. However elevation in homocysteine levels are also seen in folate deficiency, B6 deficiency, in patients with renal failure and hypothyroidism[11]. These conditions should be ruled out while evaluating for vitamin B12 deficiency.

We treated both patients with parenteral vitamin B12 therapy besides the usual pharmacotherapy for anxiety-depressive disorders with low dose of SSRI. In both cases we observed a very drastic clinical improvement within a week which cannot be expected with SSRI treatment alone. Our observation is supported by anearlier study in which depressive symptoms responded rapidly to vitamin B12 supplementation along with antidepressants[12]. Further research has shown that in the absence of vitamin B12 supplementation recovery with only anti-depressants or anti-anxiety medications may be delayed or even in-complete[13].

Although cobalamin deficiency is routinely treated with parenteral cobalamin particularly in hospitalized patients, oral treatment is also found to be equally effective[2]. Treatment schedules for intramuscular administration vary widely but usually consist of initial loading doses followed by monthly maintenance injections. One regimen consists of daily injections of 1,000µg for one to two weeks, then a maintenance dose of 1,000µg every one to three months. The initial oral replacement dosage consists of a single daily dose of 1,000 to 2,000µg followed by 1000µg per day in maintenance phase for several weeks to months [3].

CONCLUSION

Vitamin B12 deficiency should be ruled out in all the cases presenting with neuropsychiatric manifestations. Identifying and treating vitamin B12 deficiency in such cases may have significant impact on overall recovery.

Conflict of Interest Statement-

There is no conflict of interest.

Informed consent was taken from both the patients.

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