A clinical Pandora: Unusual manifestations of Vitamin B12 deficiency

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ABSTRACT

A middle-aged male presented with gradually progressive fatigue and dementia. He was anemic, jaundiced, had cardiomegaly, a multinodular goiter, diffuse muscle wasting, Lhermitte’s sign, and features of neuropathy. Patient was found to be Vitamin B12 deficient as a part of anemia evaluation with associated subclinical hyperthyroidism. Anti-thyroid peroxidase antibody was positive. Pernicious anemia as a part of polyglandular syndrome could not be proven as Schilling's, and other tests were not available. Magnetic resonance imaging of the spinal cord was done to evaluate the muscle wasting which showed myelopathic changes. B12 correction was started which reversed jaundice and anemia. Echocardiogram showed dilated cardiomyopathy probably due to chronic anemia and subclinical hyperthyroidism. The patient was symptomatically better at discharge. On follow-up, the patient had markedly improved symptomatically as well as biochemically. The fact remains that a simple problem might be compounded by a multitude of findings while a major diagnosis and its management would solve a majority of problems faced by the patient.

Key words: Clinical features of B12 deficiency, hyperhomocysteinemia, megaloblastic anemia, Vitamin B12 deficiency

INTRODUCTION

In the Medicine Department, the symptoms which we encountered in our patient are unusual presentations of Vitamin B12 deficiency. They have been mentioned in a few case reports. Muscle wasting has been noted as a part of neuropathy especially noticed in children of vegetarian mothers.[1] Jaundice has also been rarely reported. One case report gave evidence of a polyglandular syndrome including B12 deficiency-induced hemolysis as a part of pernicious anemia.[2] Early recognition of clinical signs, as well as rare symptoms, enables a prompt diagnosis and instigation of appropriate treatment. Furthermore, to be remembered is to rule out concomitant illnesses which may be affecting the patient and complicating the case scenario at the same time. Hence, the importance of our case report.

CASE REPORT

A 50-year-old male, professional lawyer and an avid tennis player presented with a history of rapidly
worsening fatigue since 1 week. He also complained of extreme lethargy at his workplace with lapses in recall as noted since a month or so. He had a similar illness around 10 years back for which he had been evaluated but details were not available. He was also incidentally found to have jaundice and a dilated cardiomyopathy at the time. Coronary angiogram done to rule out ischemic heart disease was normal. The patient symptomatically recovered after the first event and henceforth did not continue any medications.

There was no other significant medical or social history. Family history was not suggestive of hereditary anemias. Patient’s dietary history indicated that he consumed a mixed diet but was mainly vegetarian.

On examination, the patient was pale and moderately icteric and had a multinodular goiter. Jugular venous pressure was normal, but blood pressure was elevated. The liver was just palpable with no splenomegaly. Neurological examination revealed diffuse muscle wasting, particularly in the proximal groups. Deep tendon reflexes were sluggish. Plantars were flexor. There were no other neurological deficits. Other than cardiomegaly cardiac examination was normal. The rest of his physical examination was unremarkable.

Investigations revealed severe anemia with a hemoglobin value of 5.6 g/dl. Mean corpuscular volume was 94.3 femtoliter. The diagnosis was confirmed with a low Vitamin B12 value of 28 pg/ml. Bone marrow examination was also supportive with normal cellularity, erythroid hyperplasia, and megaloblasts. Folate level was normal with elevated homocysteine. Liver function tests showed indirect hyperbilirubinemia with a total bilirubin of 7.2 mg/dL and a direct bilirubin of 3.8 mg/dL with no other abnormality. Coombs test was negative. Goiter was multinodular colloid of Bethesda Stage 2 on Fine needle aspiration cytology and biochemically there was subclinical hyperthyroidism with positive anti-thyroid peroxidase antibodies. Other endocrine evaluation done to investigate for a polyglandular syndrome was normal. Anti-nuclear antibodies were negative. Pernicious anemia could not be evaluated as schilling test and other autoantibody related tests were not available at our center. Ultrasound abdomen showed gall bladder stones indicating chronic hemolysis. Magnetic resonance imaging (MRI) brain indicated age-related atrophy and periventricular leukoaraiosis. MRI spine showed diffuse posterior disc protrusion at C4, C5 levels with anterior sac indentation and spinal narrowing at C5, C6 levels. Nerve conduction studies revealed absent compound motor action potential of left femoral nerve, decreased sensory action potentials of left tibial, right peroneal, bilateral femoral and axillary nerves. Echocardiogram showed left ventricular dysfunction with global hypokinesia.

Vitamin B12 replacement was initiated. Thiamine was also replaced in view of the dilated cardiomyopathy (estimation was not available in our set up). Other supportive therapy was given. On follow-up, the patient is symptomatically better at the end of 4 months. Jaundice has reversed, and anemia has improved. Lhermitte’s sign, muscle wasting and clinical features of neuropathy has decreased significantly.

**DISCUSSION**

Vitamin B12 deficiency is a fairly common disorder dealt with in the outpatient department usually presenting as a megaloblastic anemia in vegans particularly in a country like India. It was the myriad of clinical symptoms, i.e., anemia, jaundice, muscle wasting and cardiomyopathy in our patient which made evaluation necessary.

Anemia, as well as other symptoms, has been described in B12 deficiency. Neurological manifestations are those that are next commonly reported. [3]

The various clinical manifestations can be explained on the basis that Vitamin B12 functions as an important cofactor in various biochemical reactions. It is involved in DNA synthesis, which promotes normal maturation of blood cells. It also contributes to the myelination of the central nervous system as well as maintenance of its function.

Intramedullary destruction or hemolysis of fragile and abnormal red blood cell precursors is the result of ineffective erythropoiesis secondary to defective DNA and cell maturation due to the deficiency. This leads to the unconjugated bilirubinemia which is observed. [4]

Pernicious anemia is the most common cause of cobalamin deficiency worldwide. However, among elderly population, food-cobalamin malabsorption which is caused by gradual atrophy of gastric mucosa and hypochlorhydria is responsible for the majority of cases. [5] The syndrome is characterized by the inability to release cobalamin from food for absorption due to reduced gastric acid secretion, but unbound cobalamin can be absorbed normally.

The diagnosis of Vitamin B12 deficiency can be done with an initial Vitamin B12 assay. Extremely low level (<100 pg/ml) is usually associated with clinical deficiency. The disease is confirmed when both methylmalonic acid (MMA) and homocysteine levels are elevated. [6] In the present case, Vitamin B12 was low along with an elevated homocysteine. Both MMA and
homocysteine levels can be used to document adequate therapy as well since both levels will decrease with Vitamin B12 supplementation. Folate deficiency can also cause serum homocysteine to be elevated but not MMA. Folate was found to be normal in our case.\[7\]

Hyperhomocysteinemia plays a role in the development of cardiovascular disease (CVD). Homocysteine and the incidence of myocardial infarction are positively correlated, even after adjustment for other CVD risk factors. Elevated plasma homocysteine may also be a valuable predictive factor for hypertension because circulating homocysteine is related to increased arterial stiffness in prehypertensive patients. As cardiac evaluation was normal, the dilated cardiomyopathy was probably a result of the chronic anemia and subclinical hyperthyroidism which the patient was suffering from.\[8\]

The neurological symptoms described by the patient including the Lhermitte’s sign has been described as part of the posterior column involvement in subacute combined degeneration of the spinal cord\[9,10\] Peripheral neuropathy is also typically seen in Vitamin B12 deficiency.\[11\]

Appropriate treatment initiation on time will help in the rapid recovery of patients with B12 deficiency anemia and its complications.\[12\] Our patient was almost completely normal clinically and biochemically at the end of the 4 months follow-up.

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**Conflicts of interest**

There are no conflicts of interest.

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