Subacute Combined Degeneration of the Spinal Cord Due to Functional B12 Deficiency

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INTRODUCTION

Vitamin B12 deficiency typically presents with megaloblastic anemia with or without neurological abnormalities. Pernicious anemia is a common cause of vitamin B12 deficiency and is thought to be mediated by antibodies against gastric intrinsic factor (IF). Subacute combined degeneration of the spinal cord (SCDC) is one of the most serious neurological manifestations of vitamin B12 deficiency. Severe cases of SCDC are seen less often than in former years as the availability of the vitamin B12 assay has allowed for early diagnosis in most patients when they present with mild hematological or neurological abnormalities.

As physicians, we rely on laboratory tests to guide our workup especially when the clinical presentation is subtle. It is important to know the limitations of common laboratory tests to avoid misdiagnosis or delay in diagnosis.

We report a case of severe pancytopenia and SCDC that initially presented as megaloblastic anemia eight months prior. The diagnosis of B12 deficiency was not made at the time due to spuriously elevated B12 levels possibly related to laboratory interference of intrinsic factor antibodies with the vitamin B12 assay.

CASE REPORT

A 65-year-old right-handed male with Idiopathic Parkinson's disease (PD) for many years presented to the emergency department with a rapidly progressive gait disorder of three weeks' duration that eventually rendered him bedbound. He complained of paresthesias of both hands and feet which slowly ascended up to the waist and elbows. He had a 50-pound weight loss over 1 year associated with decreased appetite and a burning sensation of the tongue.

Eight months prior, he was evaluated for macrocytic anemia. Vitamin B12 levels were >1200 pg/ml (nl 200-1200) on multiple occasions. A subsequent bone marrow biopsy revealed macrocytosis and led to a diagnosis of myelodysplastic syndrome.

Examination during the current presentation was remarkable for vitiligo, slow cognitive processing, and severe loss of joint position and vibration sense in both upper and lower extremities. Pain and temperature modalities were spared. Both ankle reflexes as well as the left knee jerk were absent. Toes were down-going bilaterally. He was unable to ambulate due to severe sensory ataxia. He also had masked facies, rigidity, and bradykinesia, consistent with the diagnosis of PD.

RESULTS

WBC 1.37, Hgb 7.8, Hct 22.8, Plt 52, MCV 104, RDW 30. Peripheral smear: macrocytosis with hypersegmented neutrophils. Vitamin B12 >1200 pg/ml (nl 200-1200).

MRI scan of the spine revealed increased T2 signal involving the posterior columns from the cervical to lumbar segments without any enlargement, edema, or abnormal contrast enhancement.

Subsequently, methylmalonic acid and homocysteine levels were checked which were elevated at 23.53 (nl 0-0.4 µmol/L) and 54.3 (nl 4-12 µmol/L) respectively.

Intrinsic factor antibody was positive. Copper 96 µg/dL (70-140). Folate 15.2 ng/ml (>3.0). B6 2.1 nmol/L (20-125), B1 59 nmol/L (70-180) zinc 77 ug/dL (60-120). Treponema pallidum IgG, Lyme antibody, HIV, and parietal cell antibody tests were negative. Upper endoscopy showed atrophy of the antral mucosa.

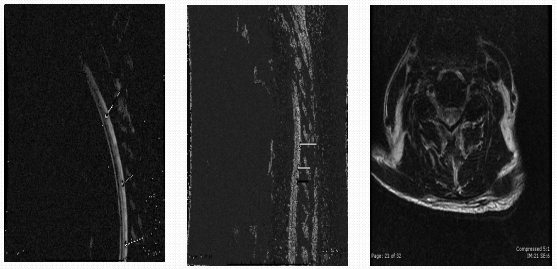

Fig. A&B: T2 FAT-SAT shows T2 hyperintensity in the dorsal aspect of the spinal cord.
Fig. C: Axial T2 of cervical spine showing T2 hyperintensity confined to the posterior columns.

The diagnosis of functional B12 deficiency was made. He was treated with intramuscular injection of cyanocobalamin 1000 µg daily for a week and then weekly thereafter along with oral B6 and B1 supplementation. His symptoms improved over 6 weeks at which point he was able to ambulate with a cane. Pancytopenia improved promptly and at 1 month, WBC was 5.64, Hgb 12.6, MCV 98 and Plt 202. Methymalonic acid and homocysteine levels also normalized at 1 month. His appetite improved and he gained 25 pounds of over 4 months. Currently he does not require assistance to ambulate.

DISCUSSION

A diagnosis of B12 deficiency is made when the serum B12 level is low or low-normal with a concomitant elevation in serum methymalonic acid and homocysteine.

The standard practice guidelines indicate testing methylmalonic acid and homocysteine levels only if the B12 level is low or low-normal, and do not recommend routine testing of methylmalonic acid and homocysteine levels along with the serum B12 levels in order to minimize cost.

In our patient the serum B12 was elevated on multiple occasions above the upper limit of the laboratory range which would normally indicate an adequate B12 reserve. Based on this clinical reasoning, methylmalonic acid and homocysteine levels were not checked.

It has been observed that falsely normal B12 levels can be generated by automated analyzers when the serum of patients with pernicious anemia is tested. Since most assays are based on competitive binding of serum vitamin B12 with reagent intrinsic factor, the falsely normal B12 results have been attributed to the possibility of intrinsic factor–blocking antibodies interfering with the assay. We speculate that the falsely elevated B12 level in our patient was caused by this proposed phenomenon.

There may be insufficient awareness in the neurological community of the possibility of spuriously high vitamin B12 levels in patients with pernicious anemia and intrinsic factor-blocking antibody. Since pernicious anemia is a common cause of vitamin B12 deficiency, we propose that methylmalonic acid and homocysteine levels should be checked in such patients even if vitamin B12 levels are not low.

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