

Complete Resolution of Myelopathy In A Patient With Vitamin B12 Deficiency: A Case Report

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Abstract

Vitamin B₁₂ deficiency is a common systemic disorder that may affect the nervous system. The cervical and dorsal spinal cord is often affected first and posterolateral columns are the predilection sites. Subacute combined degeneration is a term that specifically denotes the B₁₂ deficiency as the etiologic cause of the spinal cord involvement. If remained untreated, it leads to irreversible neurological deficits. Thus, early diagnosis and treatment are of utmost importance. We present a 70-year-old woman with pernicious anemia who showed clinical and radiological features of myelopathy and severe low serum levels of vitamin B₁₂. With early diagnosis and immediate treatment with vitamin B₁₂ supplementation, all the signs/symptoms have improved and complete resolution of magnetic resonance abnormalities occurred in 3 months after the initial therapy. We review the literature and discuss the importance of early diagnosis and treatment of this preventable nutritional disorder.

INTRODUCTION

Vitamin B₁₂ (B₁₂-cobalamin) deficiency is a systemic disease that affects many organs including the entire nervous system. Even though the spinal cord (SC) is often affected first and exclusively, brain, optic nerves, and peripheral nerves may also be affected. The term “subacute combined degeneration (SCD)” has been used conventionally for the spinal cord involvement of B₁₂ deficiency.

B₁₂ deficiency may result mainly from; a) insufficient dietary intake, b) intestinal diseases that may render the transfer of B₁₂, c) nitrous oxide poisoning, and d) genetic defect of methylmalonyl coenzyme-A mutase (1). The literature shows a total of 29 cases with B₁₂ deficiency leading to myelopathy documented by magnetic resonance imaging (MRI) abnormalities (2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24) and 15 out of 29 cases have been shown to be completely resolved with cobalamin treatment (3,4,6,7,10-12,15,16,19,20,22,25). Furthermore, it has been stated that all neurological symptoms and signs may improve, mostly during the first 3 to 6 months of therapy, and then, at a slower tempo, during the ensuing year or even longer (26).

In this paper we report a further case with considerable improvement of clinical signs/symptoms and complete resolution of radiological abnormalities following cobalamin

treatment.

CASE

In October 2001 a 70-year-old woman was brought to our neurology clinic with complaints of walking inability, sleeplessness and frequent urination. As a lonely living woman without significant health problems, in March 2001 she experienced difficulty in handling utensils because of tingling sensorial feelings. She noticed weakness in her hands. Subsequently, gait imbalance and decreased strength of the lower limbs, especially on the right side has begun. She had “trouble in “controlling her legs”, and stumbled frequently. In the following 7 months the clinical picture progressed steadily until the patient was bedridden.

On presentation, she was oriented to person and place but not to time. Standardized mini mental test score (MMSE) was 17 (out of 30) (27).

Neurological examination disclosed normal findings of cranial nerves. She could not walk even with assistance and the motor strength of the upper limbs were 4/5 and the lower limbs were 2/5. Bilateral limb, and truncal ataxia was noted. Deep tendon reflexes were 2+ in the lower extremities and reduced in the upper extremities. The plantar response was extensor on the left side. Joint position sense was impaired in all extremities. There was loss of vibration sense in the lower extremities and paresthesia on the palmar site of both

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hands. The patient had urine retention, constipation and decreased sweating due to autonomic dysfunction.

Hemoglobin level was 10.3 g/dL; mean corpuscular volume 106 fL; white blood cell count 9.6×10^3 /uL; and platelet count 576×10^3 /uL. Serum iron level and iron binding capacity were 24 μ g/dL (normal range, 49-151 μ g/dL) and 213 μ g/dL (normal range, 250-459 μ g/dL), respectively. Bone marrow was megaloblastic. Serum vitamin B₁₂ level was 10 pg/mL (normal range, 200-950 pg/mL) and folic acid level greater than 20 ng/mL (normal range, 3-17 ng/mL). Free T₃, T₄, and TSH levels were normal. Antiparietal cell, and antiintrinsic factor antibody screening tests were negative. The routine cerebrospinal fluid (CSF) analysis revealed normal findings. Syphilis and Lyme serologic tests and tuberculosis polymerase chain reaction (PCR) in serum and CSF were negative. Biopsy of the gastric mucosa disclosed a massive atrophic gastritis with *Helicobacter* infection.

Electromyography (EMG) showed inexcitability of the sural nerves, and needle EMG of the lower extremities exhibited insufficient activity. Nerve conduction studies showed evidence of a demyelinating polyneuropathy.

Magnetic resonance imaging (MRI) of the cervical and dorsal spine disclosed abnormally increased signal intensity on T₂-weighted sections in the posterior and lateral columns and no enhancement was seen after intravenous administration of gadolinium (Figures-1a and-b).

SCD of SC was diagnosed and treatment with cobalamin was started. A daily dose of 1000 μ g cobalamin was administered intramuscularly for ten days and thereafter this dose was repeated weekly for a month and then monthly. Clinical improvement was noted within 2 weeks of initiation of the treatment; paresthesias in hands resolved substantially and the muscle strength of the lower limbs increased (3/5). At the end of the third week after treatment, the mental state returned to normal (MMSE score was 27/30). After 1 month, limb and truncal ataxia resolved substantially. The result of bone marrow biopsy showed normal profile of the cells. Furthermore, joint position sense in all extremities, vibration sense in the lower extremities, and autonomic dysfunction noted as improved considerably at the end of the second month of the therapy.

Figure 1

Figure-1a: Sagittal T2-weighted image of the dorsal spine demonstrates high signal abnormality in the posterior aspect extending from T1 to T7.



Figure 2

Figure-1b: Axial T2-weighted scan at C5 demonstrates high signal in the posterior and lateral aspects of the cord.



In the third month of the follow up, the patient was able to stand up and walk unassisted and her strength was also normal in all limbs. MRI showed improvement of the abnormalities detected in the posterior and lateral columns of cervical and dorsal spinal cord (Figures-2a and-b).

Figure 3

Figure-2a: Three months after replacement therapy with cobalamin, sagittal T2-weighted image of the dorsal spine reveals resolution of signal abnormality after.

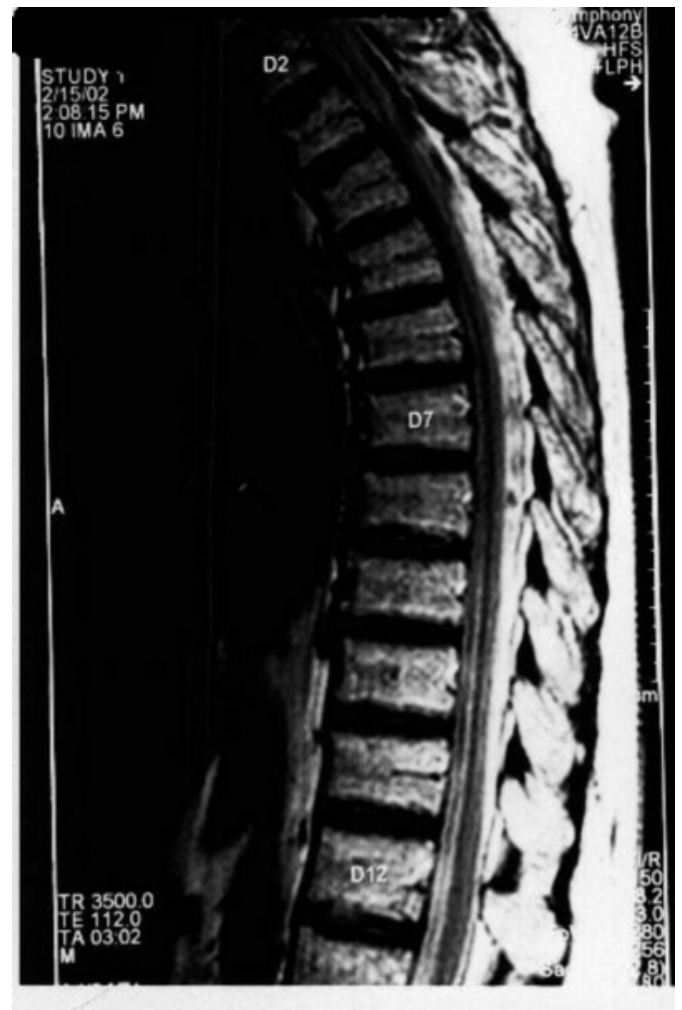
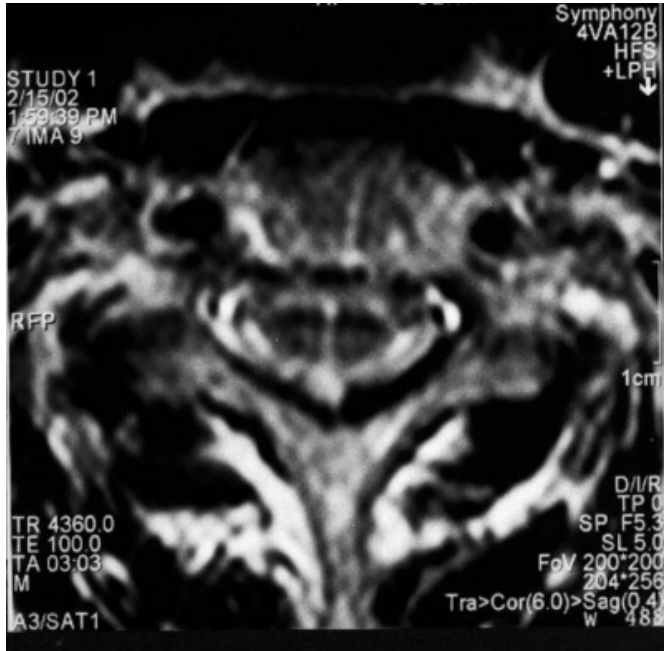


Figure 4

Figure-2b: Axial T2-weighted section of cervical cord at the same level shown in figure-1b, shows the hyperintense lesions of the posterolateral columns disappeared after treatment.



DISCUSSION

SCD was first described as a clinical entity by Russell, et al in 1900 (28) and with the isolation of B₁₂, and development of an assay for this vitamin in the late 1940s, it was assumed that the majority of SCD was due to B₁₂ deficiency.

Histopathological studies have shown that the main neuropathologic changes are diffuse and uneven degeneration of the white matter of SC and less frequently of the brain in B₁₂ deficiency (26). Nearly all papers in the literature describing myelopathy secondary to B₁₂ deficiency were case reports and up to date a total of 29 cases with myelopathy documented by MRI have been reported (2-24). Results of such reports indicated that early treatment can lead to complete recovery of radiological abnormalities and clinical signs/symptoms.

Histopathologically, swelling of the myelin sheath has been shown to be the earliest event caused mainly by intramyelinic vacuole formation. This degeneration begins in the posterior columns of the lower cervical and upper thoracic SC and may spread up and down the cord and into the lateral and anterior columns in advanced cases (29). In later stages degenerative processes involve axon cylinders and results eventually in axonal loss. Sum of these histopathological events lead to development of atrophy of the posterior and lateral columns of SC in advanced stages of

the disease. However, the point at which SCD becomes irreversible is not clearly understood.

Review of the literature shows that the characteristic appearance is the high signal intensity on T2-weighted MRI (best visible in axial sections) of posterior and lateral columns of cervical and thoracic cords and in advanced cases of the anterior column (10,21,23). The high signal intensity has been supposed to be due to high water content caused by demyelination (2,5,7). In addition, contrast enhancement was also reported recently and this was explained as the result of disruption of the blood-cord barrier that may occur in advanced stages (9,10,20).

Complete resolution of MRI abnormalities has been described in 15 patients (3,4,6,7,10-12,15,16,19,20,22,25). All had duration of symptoms ranged from 0.5 to 12 months and follow-up MRI 18 days to 36 months after initiation of cobalamin treatment. It seems that the degree of resolution in MRI abnormalities depends on the duration of symptoms. Fifteen patients showing complete disappearance of MRI abnormalities and significant improvement of clinical symptoms after cobalamin treatment had duration of symptoms less than 12 months. On the other hand, the patients with duration of symptoms more than 12 months had partial resolution of MRI abnormalities despite complete clinical improvement (2,6,13). All these findings suggest that the duration of symptoms may predict the presence of irreversible axonal degeneration.

It seems also that the duration of the symptoms is the most important factor in response to treatment (2-24), whereas age, sex, and the degree of anemia are relatively unimportant (26). There is a correlation between resolution in MRI abnormalities and improvement of the clinical picture if therapy begins in the early stages of the disease. As the therapy leads to remyelination of the affected white matter, the signal intensity returns to normal in parallel with clinical improvement. In longstanding cases, due to the axonal loss high signal intensity persists even after the treatment.

Our patient gave a history of symptoms beginning at least 7 months before the MRI. No atrophy and contrast enhancement was noted suggesting the early stage of the disease. Rapid improvement in clinical picture began within 2 weeks of treatment and at the 3rd month of the therapy the patient was free of symptoms and no high signal intensity was noted on T₂-weighted MRI scans. This improvement either in clinical picture and MRI abnormalities brings us to think the treatment was instituted in demyelination stage,

or early stage of the disease. Thus review of the literature and this case expose that complete recovery in terms of radiological and clinical findings may be the result if the treatment is instituted within a few months after the onset of neurological symptoms, at least before the onset of fibrous gliosis.

Since increased T2-signal intensity in the postero-lateral columns of the cervical and thoracal cords may also be encountered in infections, postinfectious myelitis, sarcoidosis, multiple sclerosis, acute transverse myelitis, and other rare conditions (5,21,26), diagnosis of SCD is mainly based on combination of the clinical findings, radiological features and laboratory estimation of B₁₂ level. MRI is also the choice of study for showing demyelination and for assessing response to treatment.

The finding of high serum concentrations of cobalamin metabolites-methylmalonic acid (normal range, 73-271 nmol/L) and homocysteine (normal range, 5.4-16.2 μmol/L) is probably the most reliable indicator of an intracellular cobalamin deficiency and can be used to establish the diagnosis (30). However we think that measurement of such metabolites should be taken into consideration when low-normal serum vit. B₁₂ level is obtained. In our case B₁₂ level was so low that (10 pg/mL), we made the diagnosis of SCD certainly together with the clinical findings. In this respect, we did not need to measure the serum levels of methylmalonic acid and homocysteine.

In conclusion we added one additional case into the list of the patients who had complete resolution of MRI abnormalities of SCD myelopathy. With the help of the literature and the case presented here, we strongly recommend that;

- a. regardless of the patient's age, cobalamin deficiency must be kept in mind in differential diagnosis of an ascending sensory paralysis,
- b. increased signal intensity on T₂-weighted MRI in the posterior and lateral columns of cervical and dorsal spine should alert the physicians for screening B₁₂ deficiency,
- c. MRI should be the choice of follow up studies as a tool for assessing the response to therapy,
- d. and finally, it must be kept in mind that, early diagnosis and treatment are of paramount importance in the prevention of irreversible symptoms in this disorder.

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