

# Reversible Myelopathy on Magnetic Resonance Imaging Due to Cobalamin Deficiency

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Subacute combined degeneration (SCD) is known as myelopathy due to vitamin B12 deficiency. SCD always involves the posterior and lateral columns of the spinal cord, with the neuropathologic change showing vacuolation of the white matter. We describe 2 patients who presented with ataxic gait, impaired proprioception over limbs, and even mental change due to vitamin B12 deficiency. Magnetic resonance imaging (MRI) of the cervical spine showed increased signal intensity on T2-weighted imaging, and laboratory data showed low serum vitamin B12 level. The 2 patients were treated with vitamin B12 injection intramuscularly. There was clinical improvement after treatment along with normalization of the MRI. [*J Chin Med Assoc* 2008;71(7):368–372]

**Key Words:** magnetic resonance imaging, myelopathy, subacute combined degeneration, vitamin B12 deficiency

## Introduction

Vitamin B12 deficiency causes many neurologic problems such as dementia, myelopathy, and peripheral neuropathy. The myelopathy is known as subacute combined degeneration (SCD); it is rarely demonstrated on imaging study. We report 2 cases of SCD—1 presented with gait disturbance and the other presented with dementia and ataxia. Both patients clearly demonstrated clinical improvement along with normalization of cervical cord lesion on magnetic resonance imaging (MRI) after vitamin B12 injection.

## Case Reports

### Case 1

A 65-year-old man developed numbness over bilateral hands 4 years prior to admission, which progressed to bilateral lower legs 2 years later. Unsteady gait and easy falling developed 2 months prior to admission.

On admission, neurologic examination showed normal cognitive function with fluent speech. Cranial nerve

examination was normal. Muscle strength showed Medical Research Council (MRC) grade 4+ over bilateral upper limbs and MRC grade 5 over bilateral lower limbs. Deep tendon reflexes were generalized increased. The plantar responses were of flexor type bilaterally. Sensory examination showed impaired joint position and vibration sensation with normal pin-prick sensation over distal 4 limbs (below the wrists over upper limbs and below the knees over lower limbs). There was no dysmetria. Gait was wide-based, spastic and ataxic. Romberg's test was positive. Laboratory data showed macrocytic anemia (mean corpuscular volume, 117  $\mu\text{m}^3$ ; hemoglobin, 11.4 g/dL) and low serum vitamin B12 level (<100 pg/mL) (Table 1). Nerve conduction study was normal in the patient's upper limbs. Somatosensory evoked potential (SEP) of the median nerve and tibial nerve stimulation showed no response bilaterally. MRI of the cervical spine showed increased signal intensity over the posterior aspect of the spinal cord from C1 to upper T level on T2-weighted imaging (Figure 1A). Bone marrow biopsy showed a picture of megaloblastic anemia.



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**Table 1.** Laboratory data of the patients

	Case 1	Case 2
<b>Blood</b>		
WBC (/mm <sup>3</sup> )	6,360	6,000
Hb (g/dL)	11.4	10.9
MCV (μm <sup>3</sup> )	117.7	107.9
T4 (μg/dL)		8.95
TSH (μIU/mL)		0.928
RPR	Nonreactive	Nonreactive
Vitamin B12 (pg/mL)	< 100	< 100
<b>CSF</b>		
WBC (/mm <sup>3</sup> )		0
RBC (/mm <sup>3</sup> )		3
Protein (mg/dL)		51
Glucose (mg/dL)		71
IgG index		0.53
Immunoelectrophoresis		(-)

WBC = white blood cell count; Hb = hemoglobin; MCV = mean corpuscular volume; T4 = thyroxine; TSH = thyroid stimulating hormone; RPR = rapid plasma regain; CSF = cerebrospinal fluid; RBC = red blood cell count; IgG = immunoglobulin G.

Vitamin B12, 1 mg/day, was given intramuscularly for 5 days, followed by 1 mg monthly. The patient's symptoms improved after vitamin B12 injection, and serum vitamin B12 level had returned to normal 10 months later. He could walk by himself without aid 3 months later but still had mild wide-based gait. The vibration sensation over his upper limbs showed improvement about 6 months after admission, but the vibration sensation over the lower limbs did not improve until 30 months after admission.

Follow-up MRI of the cervical spine 3 months after the first cervical MRI study showed less high-signal intensity than on the first scan (Figure 1B). The third MRI of the cervical spine, performed 14 months after the first MRI study, showed no abnormal signal intensity over the cervical cord at all (Figure 1C).

### Case 2

A 74-year-old woman had progressive mental deterioration, urinary incontinence, and unsteady gait of about 3 weeks' duration. She was admitted in a bedridden state due to severe unsteadiness. She had a past history of hyperthyroidism under medication treatment. She did not drink or smoke.

Neurologic examination showed impaired cognitive function, and the Mini Mental State Examination score was only 7/30. Cranial nerve examination showed no abnormality. Motor examination showed MRC grade 4 over the 4 limbs. There was generalized hyporeflexia over all 4 limbs, and bilateral plantar responses were

of flexor type. Sensory examination showed impaired vibration and joint position over the patient's bilateral hands and feet. Severe truncal ataxia with easy falling was noted. Laboratory data showed macrocytic anemia (mean corpuscular volume, 107.9 μm<sup>3</sup>; hemoglobin, 10.9 g/dL) and low vitamin B12 level (< 100 pg/mL) (Table 1). Thyroid function test was normal at admission. Brain MRI showed mild brain atrophy without other abnormalities. MRI of the C-spine revealed increased intensity over the posterior aspect of the spinal cord from C1 to C6 on T2-weighted imaging (Figure 2A). Nerve conduction study of the patient's 4 limbs was normal. SEP from median nerve stimulation showed reduced amplitude of cortical responses (N2, P2) from left-side stimulation. SEP from tibial nerve stimulation showed no response. Electroencephalogram study showed generalized background slowing and intermittent polymorphic slow waves over bilateral frontocentral regions. Cerebrospinal fluid study was normal (Table 1).

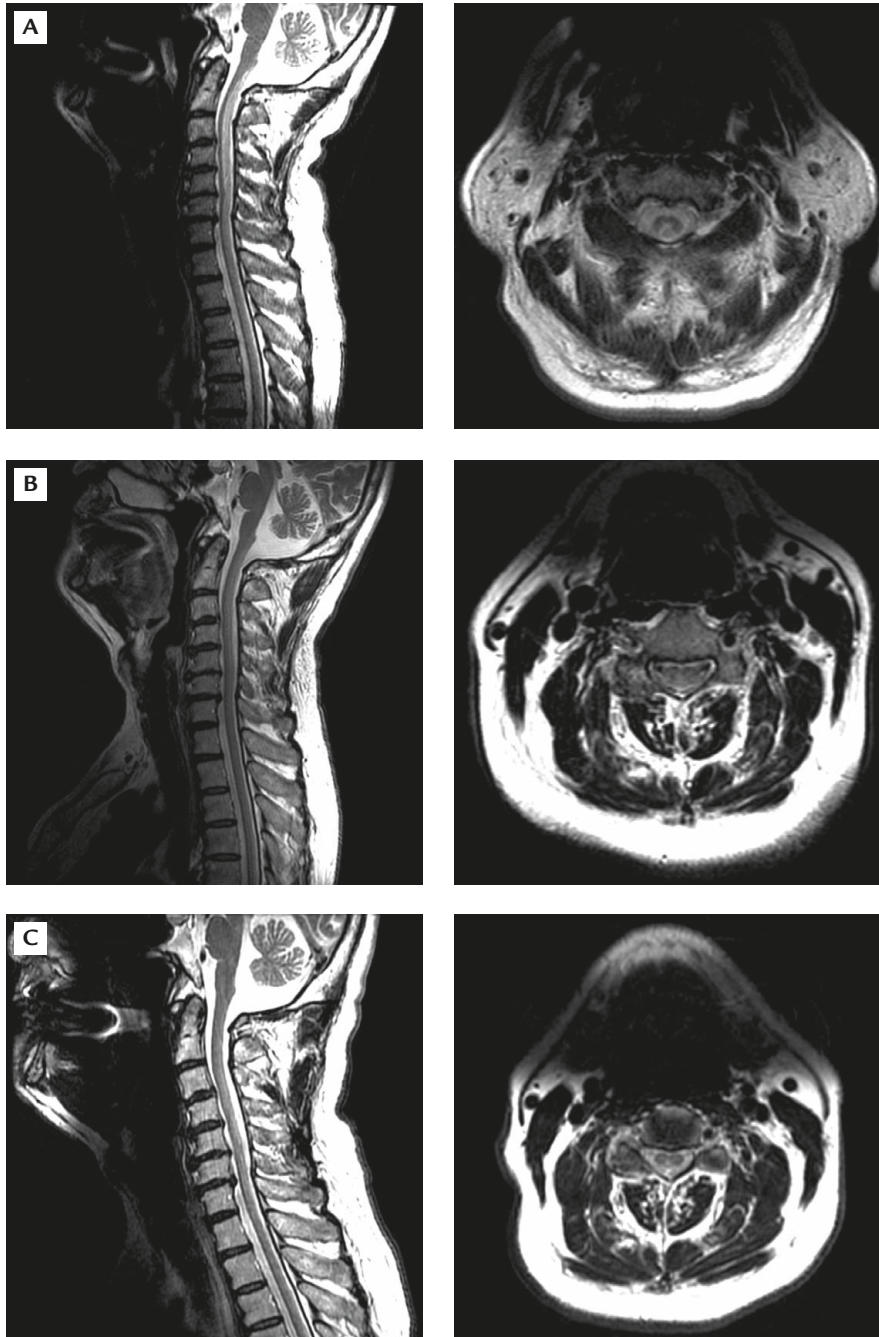
Vitamin B12, 1 mg/day, was given intramuscularly for 5 days, followed by 1 mg per month later. Her symptoms improved after treatment and serum vitamin B12 level had returned to 236 pg/mL 3 months later. She could walk with an aid 3 months after treatment, and her mental state had also improved as noted by her family.

Follow-up MRI of the C-spine 3 months later showed decreased signal intensity over the previous lesion site (Figure 2B). Follow-up SEP of medial and tibial nerve stimulation 3 months later showed no improvement. Electroencephalogram study was normal 3 months later.

## Discussion

Our 2 patients had paraesthesia and tingling over their distal limbs, ataxic gait, and impairment of joint position sensation and vibration. Extramedullary compressive lesions, such as tumor, hematoma, ruptured or protruded disc, and intramedullary lesions, such as demyelinating, infectious, inflammatory, ischemic, neoplastic and metabolic disorders, should be considered. If impairment of cognitive function is noted, as in Case 2, other conditions such as normal pressure hydrocephalus, encephalitis, and Creutzfeldt-Jakob disease should be considered. MRI of the C-spine in both patients and brain MRI in Case 2 excluded structural mass lesions. Cerebrospinal fluid study in Case 2 excluded infectious and inflammatory disorders.

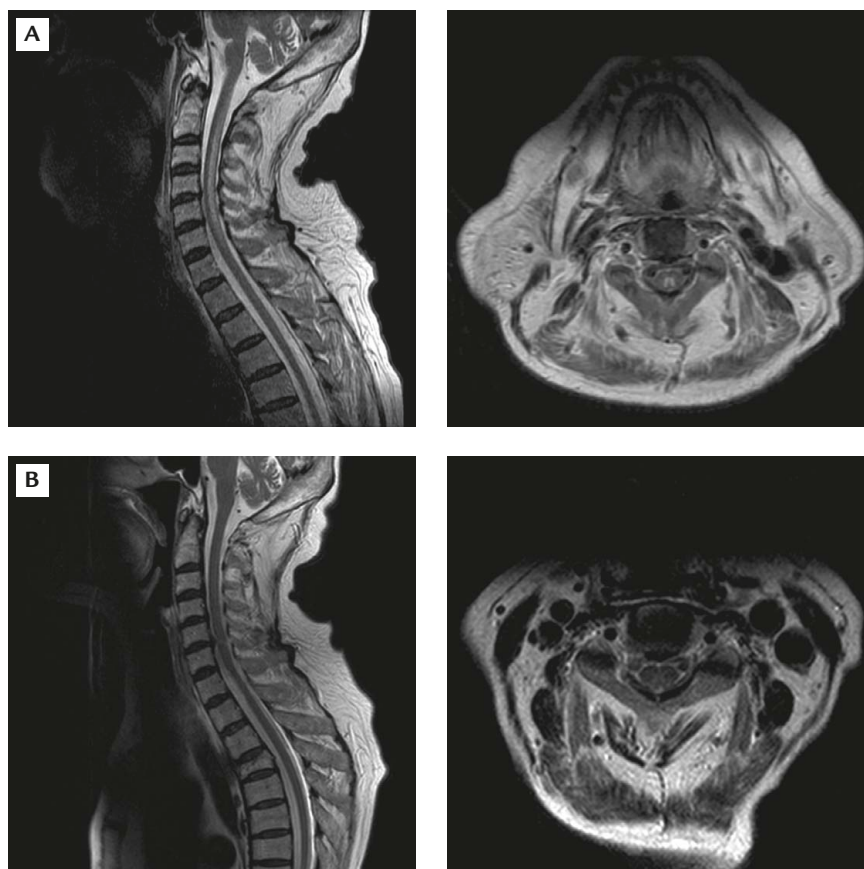
Spinal cord lesion caused by vitamin B12 deficiency is known as SCD. It always involves the posterior and



**Figure 1.** (A) Increased signal intensity over the posterior aspect of the spinal cord on T2-weighted imaging from C1 to the upper T-spine level. (B) Improvement of the previous abnormal signals in (A). (C) The abnormal signals have almost disappeared after 14 months of vitamin B12 injection therapy.

lateral columns of the spinal cord.<sup>1</sup> Involvement of the anterior column of the spinal cord has also been reported.<sup>2</sup> The main symptoms of SCD are paraesthesia, stiffness, numbness or tingling of the limbs, sensory ataxia, and impaired vibration and joint position sensation. Spastic paraparesis may develop if untreated. Babinski signs may present, and the deep tendon reflexes are variable.

The MRI findings of the spinal cord in SCD are high-signal intensity on T2-weighted imaging within the posterior or lateral columns. Brain lesions of vitamin B12 deficiency over the medulla oblongata, pons, mesencephalon and crus cerebelli have also been reported.<sup>3-6</sup> If patients have the above mentioned common symptoms of SCD and macrocytic anemia, the possibility of SCD should be highly considered.



**Figure 2.** (A) Abnormal increased signal intensity over the posterior aspect of the spinal cord on T2-weighted imaging over the C-spine level. (B) Improvement of the abnormalities over the spinal cord was noted after 3 months of vitamin B12 injection therapy.

However, the hematologic abnormalities of vitamin B12 deficiency (macrocytic anemia) may develop after the neurologic abnormalities. Some SCD patients might have minimal symptoms without hematologic abnormalities initially, such as acroparesthesia and Lhermitte's sign only. At this moment, in the early stage, in addition to blood vitamin B12 and homocystine levels, spinal MRI may be a good diagnostic tool.<sup>7</sup> Once the diagnosis of SCD is suspected, the treatment of vitamin B12 injection should be started as early as possible to avoid irreversible neurologic damage. The clinical symptoms and MRI abnormalities showed improvement in our 2 patients 3 months later, as in previous cases reports.<sup>3,4,6-9</sup>

The neuropathologic changes of SCD show vacuolation of the white matter of the spinal cord, especially affecting the posterior and lateral columns. The vacuolation is conceived as spongiform demyelination, which selectively involves the largest-diameter fibers with the thickest myelin sheaths.<sup>10</sup> A recent study found high tumor necrosis factor- $\alpha$  (myelinolytic agent) level and low levels of epidermal growth factors (neurotropic agent) in the cerebrospinal fluid of cobalamin-deficient

patients. The imbalance in tumor necrosis factor- $\alpha$  and epidermal growth factors can be corrected when the cobalamin deficiency is corrected by cobalamin therapy.<sup>11</sup> However, histopathologic examination of the spinal cord in SCD patients show no inflammatory reaction, and the neurons also do not seem to be affected in SCD. The nature of SCD is neither a degenerative disease nor an inflammatory disease but a demyelinating disease.

SCD seems to be a reversible disease after vitamin B12 therapy. However, complete recovery from the disease was not seen in the previous reports. The timing of diagnosis and duration of illness may play an important role in the treatment response and prognosis of SCD. We should diagnose SCD patients early by having a high index of suspicion and use diagnostic tools such as MRI.

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