

Reversible Myelopathy in a 34-Year-Old Man With Vitamin B₁₂ Deficiency

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Vitamin B₁₂ deficiency is common, with most patients lacking classic features of advanced severe deficiency. Early diagnosis and treatment prevent severe anemia and irreversible damage to the nervous system. We describe a 34-year-old man with pernicious anemia who presented with clinical and radiologic features of early myelopathy and borderline low serum levels of vitamin B₁₂. Prompt diagnosis based on the measurement of serum methylmalonic acid and treatment with cyanocobalamin injections led to

rapid resolution of clinical manifestations and magnetic resonance imaging abnormalities. We review the literature of magnetic resonance imaging in vitamin B₁₂ deficiency myelopathy and discuss the issues relating to diagnosis and early treatment of this potentially reversible condition.

Mayo Clin Proc. 2002;77:291-294

MMA = methylmalonic acid; MRI = magnetic resonance imaging; SCD = subacute combined degeneration

Vitamin B₁₂ deficiency causes a wide range of neurologic disorders, including myelopathy, neuropathy, neuropsychiatric disturbances, and less often, optic neuropathy.¹ A survey of the literature revealed 28 cases of vitamin B₁₂ deficiency myelopathy with documented magnetic resonance imaging (MRI) abnormalities.²⁻²⁴ Some of these cases included a description of the temporal relationship of the MRI findings to the neurologic symptoms and changes in response to therapy. Most reported cases respond well to cobalamin treatment if it is instituted early, although residual neurologic and radiologic abnormalities can occur if therapy is delayed. We report complete resolution of clinical and MRI abnormalities in a patient with vitamin B₁₂ deficiency myelopathy following cyanocobalamin supplementation and discuss the approach to diagnosis and early recognition of this treatable and reversible condition.

REPORT OF A CASE

A 34-year-old man developed subacute progressive paresthesias (tingling) of both hands. Four weeks later he noticed Lhermitte phenomenon, which he described as an electrical tingling sensation that extended from his neck down the spine and into both upper and lower extremities, triggered by neck flexion. He complained of pain, swelling, and tenderness of the tongue for 3 months before the onset of neurologic symptoms. On presentation, he was alert, with normal findings on examination of mental status,

cranial nerves, gait, tone, and coordination. Strength was normal except for mild weakness of the left triceps muscle. Deep tendon reflexes were hyperactive with flexor plantar responses. Sensory testing revealed mild stocking-and-glove distribution loss of light touch and pain sensation with preservation of proprioception and vibration. His brother had pernicious anemia and was receiving monthly cyanocobalamin injections but had no neurologic complaints. His mother had diabetes mellitus and hypothyroidism. He had no prior exposure to nitrous oxide and had a normal diet.

Laboratory studies demonstrated a normal complete blood cell count, a serum vitamin B₁₂ level of 203 ng/L (reference range, 250-700 ng/L), and a folic acid level of 15.4 µg/L (reference value, >2.8 µg/L). His serum methylmalonic acid (MMA) level was 38 µmol/L (reference value, <0.4 µmol/L). The serologic test result for intrinsic factor antibodies was positive. The results of cerebrospinal fluid analysis, including cells, glucose, protein, index, and oligoclonal banding, were normal. Syphilis and Lyme serologic test results were negative.

Brain MRI, including T1, T2, fluid-attenuated inversion recovery, and gadolinium-enhanced T1-weighted images, was normal. Spine MRI revealed increased T2-weighted signal in the posterior columns of the cervical cord at the C1 through C5 level (Figure 1, left). Enhancement on T1-weighted images with gadolinium was normal. Thoracic and lumbar cord MRI was normal.

Therapy with 2000 µg of cyanocobalamin administered subcutaneously was commenced at a frequency of every 2 weeks for 3 months and then monthly thereafter. Within 1 month of the initiation of therapy, the patient's symptoms of hand paresthesias and Lhermitte phenomenon resolved completely, and the neurologic examination revealed nor-

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Figure 1. Left, Sagittal T2-weighted image demonstrates high signal abnormality in the posterior aspect of the cervical cord extending from C1 through C5. Right, Sagittal T2-weighted image reveals resolution of signal abnormality in cervical cord after therapy.

mal triceps power and normal light touch and pain sensation in the hands and feet. A subsequent MRI 10 weeks after therapy was started revealed resolution of the signal abnormality in the cervical cord (Figure 1, right). Subsequent measurements of serum vitamin B₁₂ and serum MMA were 366 ng/L and 0.18 μ mol/L, respectively.

DISCUSSION

This patient had pernicious anemia with resultant vitamin B₁₂ deficiency myelopathy. Despite an obvious cervical cord signal abnormality on T2-weighted MRI, replacement of vitamin B₁₂ early in his illness resulted in complete resolution of symptoms, signs, and MRI abnormalities.

The specific spinal cord lesion caused by vitamin B₁₂ deficiency is known as subacute combined degeneration (SCD). Neuropathologic studies of SCD show spongiform changes with foci of myelin and axonal destruction mainly in the posterior and lateral columns, but also involving anterior columns in a few advanced cases.^{1,25} The point at which SCD becomes irreversible is poorly understood. Cases of complete resolution of clinical manifestations and radiologic abnormalities indicate that early treatment can

lead to reversal of pathologic changes. Delay in the diagnosis and/or initiation of therapy may result in permanent irreversible injury to the spinal cord with little or no improvement on treatment. Complete recovery is more likely after early intervention. Paresthesias often resolve within weeks, possibly because of a peripheral nerve involvement or reversible impairment of central sensory conduction. Objective signs of spinal cord dysfunction, including weakness, spasticity, and proprioceptive deficits, may require months to improve.^{26,27} With early recognition, patients may resume a normal lifestyle with limited impairment of gait. Relapses may occur because of noncompliance with long-term supplementation.²⁷

A review of reported cases of MRI use in patients with vitamin B₁₂ deficiency myelopathy revealed variable MRI abnormalities.³⁻²⁴ The most common finding was increased T2-weighted signal in the posterior columns of the cervical and/or thoracic spinal cord. Swelling of the cervical cord on T1-weighted imaging,^{10,21,23} enhancement of posterior columns and lateral columns on postcontrast T1-weighted imaging,^{9,11,20} and increased signal on T2-weighted imaging in the posterior columns with variable involvement of the

lateral and anterior columns^{13,21} have also been described in vitamin B₁₂ deficiency. Atrophy of the thoracic cord has been reported in patients with long-standing symptoms (20 months).²

Complete resolution of MRI abnormalities has been described in 14 patients; all had symptoms of less than 12 months' duration and follow-up MRI scans 18 days to 36 months after initiation of treatment.^{3,4,6,7,10-12,15,16,19,20,22} Improvement in imaging findings was reported in most other patients with follow-up scans.^{5,13,14,17,23} In some cases, only partial resolution of clinical symptoms occurred despite complete disappearance of MRI abnormalities, suggesting the presence of irreversible axonal degeneration. An associated peripheral neuropathy could also account for this observation, but in many cases there was no evidence of diffuse peripheral neuropathy on electrodiagnostic studies.^{4,18,23}

Clinical manifestations of patients described in the literature with MRI evidence of myelopathy varied in severity, type, and distribution. Severity of symptoms and signs ranged from very mild (as in our case) with minimal or no disability to severe with loss of ambulation. Symptoms and signs in increasing order of severity included Lhermitte phenomenon, paresthesias of the hands and feet, loss of sensation (often with a cervical sensory level), sensory ataxia (with mild to absent vibration and proprioception) that resulted in inability to walk in some patients, and upper motor neuron distribution weakness (with spastic tetraparesis in 1 patient).²⁻²⁴ Although from our review of the literature it would appear that less severe clinical manifestations and early institution of therapy correlated with more rapid and complete recovery, some patients have severe and progressive symptoms that improve notably despite severe initial disability.^{2-24,28}

Patients with vitamin B₁₂ deficiency may have overt neurologic disease in the absence of hematologic findings.^{29,30} Pernicious anemia caused by defective intrinsic factor production by parietal cells accounts for most cases of vitamin B₁₂ deficiency. A variety of autoantibodies are detected in serum samples from patients with pernicious anemia, including antibodies to gastric parietal cells and to the intrinsic factor.²⁹ Despite being present in 85% of affected patients, parietal cell antibodies are nonspecific, often being detected in other organ-specific autoimmune diseases and in 3% to 10% of healthy persons. The anti-intrinsic factor antibody test is highly specific for pernicious anemia but relatively insensitive, being positive in approximately half of the patients.³¹

Elevated serum or urinary levels of MMA and homocysteine are sensitive for the diagnosis of vitamin B₁₂ deficiency and usually precede the development of hematologic abnormalities and reductions in the serum vitamin

B₁₂ level.³² Measurement of these metabolites is especially useful in those with low-normal serum vitamin B₁₂ levels (as in this case) in the range of 200 to 350 ng/L.^{29,32}

Timms et al⁵ described a patient who developed unsteady gait and burning dysesthesias of his hands and feet 2 weeks after receiving nitrous oxide during general anesthesia. Initial cervical spine MRI was normal. Subsequent MRI 3 months after disease progression revealed T2-weighted signal abnormality in the posterior columns of the cervical and thoracic cord. Laboratory studies at that time revealed findings consistent with vitamin B₁₂ deficiency. Thus, symptoms may precede the MRI abnormalities, and a normal MRI early in the disease does not exclude the diagnosis.⁵

Differential diagnoses of abnormal MRI signal in the cervical or cervicothoracic cord include infection (eg, *tabes dorsalis*, human immunodeficiency virus, herpes zoster) or postinfectious myelitis (eg, viral or mycoplasma), sarcoidosis, multiple sclerosis, acute transverse myelitis, lymphoma and other neoplasms, paraneoplastic myelopathy, cervical spondylosis with cord compression, toxins (eg, n-hexane, hexanedione, nitrous oxide), radiation myelitis, arterial or venous ischemia, vascular malformations of the dura and spinal cord, and syringomyelia. Many of these diagnoses can be excluded on clinical grounds or with appropriate diagnostic testing.

Although MRI findings in these diseases are nonspecific, the findings of increased T2-signal intensity in the cervical cord, in conjunction with the clinical examination findings and laboratory testing, can help make the diagnosis of vitamin B₁₂ deficiency myelopathy. In addition, MRI can be used in conjunction with clinical and laboratory testing to assess response to treatment.

This case illustrates the importance of considering vitamin B₁₂ deficiency in any patient who presents with myelopathy, even when serum vitamin B₁₂ levels are in the lower range of normal. The importance of early diagnosis and treatment in the prevention of irreversible neurologic injury secondary to SCD is also emphasized. Since most patients with early neurologic symptoms secondary to vitamin B₁₂ deficiency present initially to primary care physicians, it is important that all primary caregivers become familiar with this entity, since delay in diagnosis or treatment can result in permanent neurologic injury and reduced responsiveness to therapy.

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