MRI in Vitamin B_{12} Deficiency Myelopathy

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ABSTRACT: ***Background:*** Little is known about vitamin B_{12} deficiency myelopathy's magnetic resonance imaging (MRI) manifestations and their relationship to the onset, evolution, and resolution of neurologic signs and symptoms. ***Methods:*** We present a case and review eleven additional reported cases of subacute combined degeneration of the spinal cord detected by MRI. ***Results:*** Our patient had increased T2-weighted signal and gadolinium contrast enhancement of the posterior columns in the cervical and thoracic regions and enhancement of the lateral columns in the high cervical region. This is a case with imaging evidence for lateral column lesions. Two prior reports have shown posterior column enhancement. T1-weighted images may show decreased signal in the posterior columns and sometimes demonstrate reversible spinal cord swelling. MRI abnormalities typically improve after vitamin replacement therapy. However, clinical signs may persist despite resolution of imaging abnormalities, and these abnormalities do not always resolve completely. In addition, symptoms may precede the imaging abnormality. ***Conclusions:*** Vitamin B_{12} deficiency may produce an increased T2-weighted signal, decreased T1-weighted signal, and contrast enhancement of the posterior and lateral columns of the spinal cord, mainly of the cervical and upper thoracic segments. Because the symptoms may precede any imaging abnormality, it is clear that spinal cord MRI may not be a highly sensitive, early test for subacute combined degeneration.

RÉSUMÉ: RMN dans la myélopathie due à une déficience en vitamine B_{12}. ***Introduction:*** On connaît peu de choses sur les manifestations de la déficience en vitamine B_{12} à l'imagerie par résonance magnétique (RMN) et sur leur relation avec le début, l'évolution et la résolution des signes et des symptômes neurologiques. ***Méthodes:*** Nous présentons un cas de dégénérescence combinée subaiguë de la moelle détecté par RMN et nous revoyons onze autres cas rapportés dans la littérature. ***Résultats:*** Notre patient avait une augmentation du signal T2 à l'examen en séquence pondérée en T2 et une densification par le gadolinium au niveau de la corne latérale de la moelle à la région cervicale haute. Ceci constitue un cas avec observation à la RMN de lésions de la corne latérale. Chez deux autres cas, on rapportait un rehaussement de la corne postérieure de la moelle. Les images pondérées en T1 peuvent montrer un signal diminué dans les cornes postérieures et parfois un gonflement réversible de la moelle épinière. Il est typique de voir les anomalies de la RMN s'améliorer suite au traitement de remplacement vitaminique. Cependant, les signes cliniques peuvent persister en dépit de la résolution des anomalies observées à l'imagerie et ces anomalies ne disparaissent pas toujours complètement. De plus, les symptômes peuvent précéder les anomalies observées à l'imagerie. ***Conclusions:*** La déficience en vitamine B_{12} peut produire une augmentation du signal pondéré en T2, une diminution du signal pondéré en T1 et un rehaussement du contraste des cornes postérieures et latérales de la moelle, surtout au niveau des segments cervicaux et thoracique supérieurs. Comme les symptômes peuvent précéder les anomalies observées à l'imagerie, il est clair que la RMN de la moelle n'est probablement pas un test hautement sensible pour détecter précocement la dégénérescence combinée subaiguë.

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Patients with subacute combined degeneration may show spinal cord signal abnormalities on MRI.[1-12]

Case Report

A 30-year-old African-American woman presented to another hospital with inability to walk, numbness of her trunk and extremities, and urinary and bowel incontinence.

Eighteen months earlier, she had noticed bilateral hand and foot numbness and tingling, which was followed by progressive leg weakness. Eventually she had become wheelchair bound. She was alert, oriented, and depressed. She could move the upper extremities against some resistance, but she was unable to raise the lower extremities off the bed. Only with great assistance could she stand. Sensation was decreased below the T10 level and was absent in the legs. Tendon reflexes were brisk in the upper extremities and absent in the lower extremities.

Hemoglobin was 7.9 g/dL, hematocrit 22.8%, and WBC 1 100/µL. The mean corpuscular volume was 123 fL (nl 80-100 fL). Vitamin B_{12} level was 60 pg/mL (nl 200-1610 pg/mL) and folic acid was 12.5 ng/mL (nl 3.0-17 ng/mL). The intrinsic factor blocking antibody was positive, the anti-parietal cell antibody was negative, and the Schilling test was consistent with pernicious anemia. Nerve conduction studies and electromyography showed mild peripheral neuropathy, manifest by

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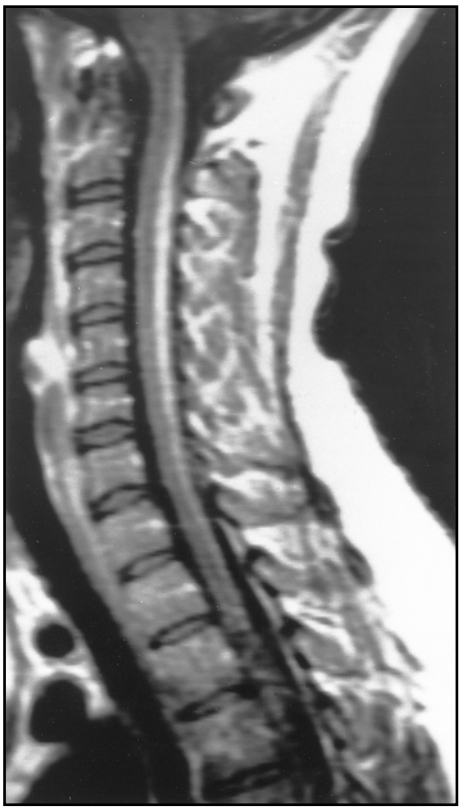

Figure 1A: *Sagittal T1-weighted image demonstrates marked gadolinium enhancement of the posterior aspect of the cord in the cervical and upper thoracic region.*

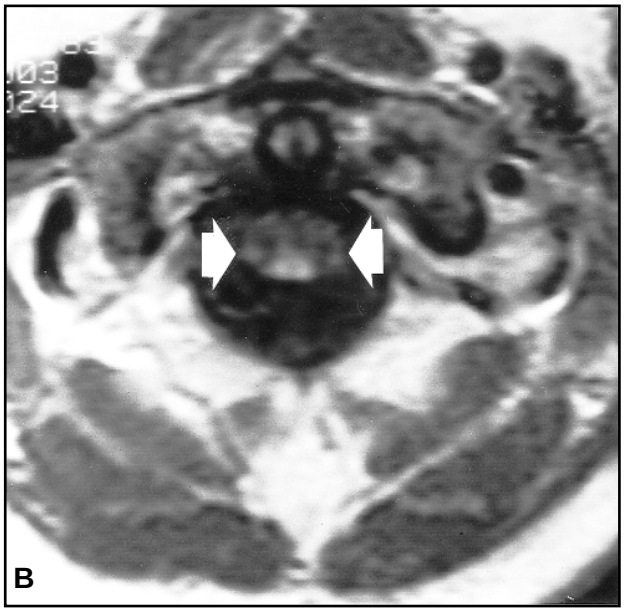

Figure 1B: *Axial image though the upper cervical cord demonstrates marked gadolinium enhancement of the posterior columns and subtle enhancement of the lateral columns, more prominent on the right (arrows).*

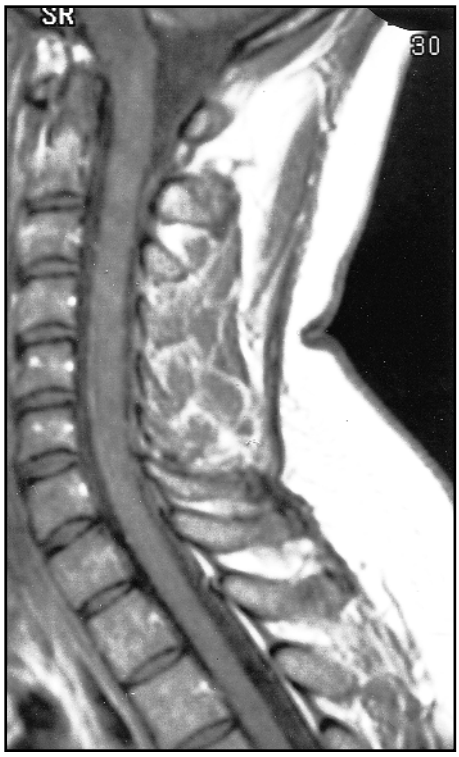

Figure 2: *Sagittal T1-weighted image following treatment demonstrates no residual gadolinium enhancement.*

absent sural sensory responses and distal lower extremity fibrillations. On MRI the brain was normal; however, the spinal cord had increased T2-weighted signal in the posterior columns of the cervical and thoracic regions, mostly at the C3-C8 level. (Figure 1A) In the cervical and upper thoracic spinal cord, the posterior columns showed gadolinium contrast enhancement, marked at the C3-C8 level. At the high cervical region the lateral columns also showed mild enhancement (Figure 1B).

Having been given the diagnosis of pernicious anemia with subacute combined degeneration of the spinal cord, the patient received 7 daily intramuscular vitamin B_{12} (1000 µg) injections. Thereafter she continued to receive the same dose once weekly. Hypothyroidism was treated with oral levothyroxin (100 mcg/day).

After 20 days of vitamin B_{12} therapy, the patient was transferred to The National Rehabilitation Hospital. Mental status, language, and cranial nerve examinations were normal, including Humphrey and Goldmann visual field testing. Motor, sensory, and cerebellar examinations were normal in the upper extremities. Although, unable to walk or stand, she could move the right leg against gravity and the left leg against some resistance. Tendon reflexes were absent; a Babinski sign was present on the right. In the lower extremities, vibration sense and proprioception were absent, and sensation to light touch and to pinprick were decreased.

After 42 days of vitamin B_{12} therapy the spinal cord MRI was normal (Figure 2). There was improvement in mood. Standing and walking were possible with much assistance. Patellar reflexes were present but ankle reflexes were absent. Light touch and pin-prick sensation were decreased, moderately up the hips and minimally to midthoracic level. Hypersensitivity of the feet to light and noxious stimuli interferred with plantar reflex evaluation.

DISCUSSION

Subacute combined degeneration of the spinal cord was documented by the clinical features (paresthesias, loss of vibration

and position sense, and paraparesis with Babinski sign), the evidence of vitamin B_{12} deficiency, the presence of posterior and lateral column lesions on MRI, and the improvement with vitamin B_{12} replacement. This is the first report with imaging documentation of lateral column lesions and the third case reported with gadolinium enhancement of the posterior columns.

There are twelve prior single case studies reporting MRI spinal cord signal abnormalities associated with vitamin B_{12} deficiency.[1-12] All patients were treated with intramuscular vitamin B_{12}. In 1992, Tracey and Schiffman first reported a 36-year-old woman with Lhermitte's symptom for one year, bilateral hand and foot numbness for 2 months, and a C5 sensory level.[1] The posterior columns at the C3-C6 levels showed increased T2-weighted signal on the MRI scan. A repeat scan was normal after 4 months of therapy. Timms et al. next reported a 69-year-old man with unsteady gait and burning dysesthesias of his hands and feet.[2] After 2 weeks of symptoms, cervical MRI was normal. However, after 3 more months of symptom progression, repeat MRI showed increased T2-weighted signal in the posterior columns at the cervical and thoracic levels. The MRI showed no lateral column involvement. The MRI was improved after 5 and again after 10 months of vitamin therapy. Murata et al. reported a 66-year-old man with 3 months of marked sensory ataxia associated with a high T2-weighted MRI signal at the T9-T11 level in the posterior columns; the abnormality was absent on a repeat scan performed after 10 weeks of vitamin replacement. There is no explicit statement indicating whether the cervical region was scanned.[3] Tajima et al. also described a B_{12} deficient patient with high signal in the posterior columns of the cervical region on T2-weighted images.[4] Wolansky et al. presented a 10-year-old child with 2 weeks of sensory ataxia.[5] There was increased T2-weighted signal and decreased T1-weighted signal in the posterior columns at all spinal cord levels. With gadolinium injection there was symmetric contrast enhancement of the posterior columns. This was the first report of contrast enhancement in this disease. There was no repeat spinal cord MRI scan. In 1996 Duprez et al. observed a 65-year-old woman with gradual onset of a spastic tetraparesis, a T8 sensory level, loss of vibration and position sense, and bladder dysfunction.[6] There was increased T2-weighted signal in the posterior columns at the C2-C7 levels and low vertebral bone marrow signal on both T1- and T2-weighted images. On MRI, 10 weeks after vitamin replacement, there was incomplete improvement of the spinal cord lesions.

In 1997 a flurry of case reports appeared. Larner et al. reported a 38-year-old woman with 3 months of sensory ataxia.[7] The MRI showed slight but definite swelling of the upper cervical cord on T1-weighted images and increased T2-weighted signal of the posterior columns at the C1-C5 levels. Six months after vitamin replacement, spinal cord MRI was normal. Küker et al. reported a 50-year-old woman with 5 months of sensory ataxia.[8] The MRI showed an ill-defined increased T2-weighted signal in the posterior parts of the thoracic spinal cord. T1-weighted images showed multifocal, slightly expansive, contrast enhancing lesions in the posterior columns of the cervical and thoracic spinal cord. After 18 days of vitamin replacement, the lesions had disappeared; this case report was the first to document resolution of contrast enhancing lesions. Ng et al. documented a 19-year-old vegetarian man, with absent reflexes and sensory impairment only in the upper extremities.[9] MRI showed a swollen cervical cord and increased T2-weighted signal of the posterior aspect of the cord from the cervico-medullary junction to the C6-C7 level. He had a complete clinical recovery after 6 months of vitamin replacement. On T2-weighted images, only a faint diffuse increased signal was seen in the posterior columns. Imaiso et al. described a 54-year-old man with sensory ataxia limited to the upper extremities.[10] T2-weighted images showed increased signal in the posterior columns at the C1-T1 levels, especially in the fasciculus cuneatus. Finally, Springer and Key presented a 17-year-old man, who carried the diagnosis of agammaglobulinemia of Bruton and who then had suffered with peripheral paresthesias and sensory ataxia for 6 weeks.[11] He was diagnosed as having vitamin B_{12} deficiency. MRI images showed increased T2-weighted signal of the posterior columns at the C1-C7 levels. The authors did not comment on the post contrast images. No follow-up imaging was reported. None of these 11 cases in the previously published literature had lateral column involvement by MRI criteria.

After careful review, we have excluded one case, a 43-year-old patient with pernicious anemia and Lhermitte's symptom as the only neurologic abnormality.[12] Axial T2 gradient echo images at the C3-C4 level and sagittal T2-weighted images showed a increased spinal cord signal centrally. Because these MRI findings were not in the characteristic distribution of the spinal cord lesions of vitamin B_{12} deficiency and because the neurologic exam was normal, we are not confident that the MRI findings in this case reflect subacute combined degeneration.

Of the spinal cord cases discussed above, four had MRI of the brain. In our patient and in two other cases the brain MRI was normal.[7,11] In the fourth case, T2-weighted brain images showed non-specific small high-signal foci within the cerebral hemispheres.[2] The findings could not be attributed to vitamin deficiency. Haan described five patients with vitamin B_{12} deficiency.[13] In 3 of these patients brain MRI showed increased T2-weighted signal in the periventricular white matter. There is no documentation of improvement of these lesions with treatment; it is unlikely that they were related to vitamin B_{12} deficiency. Chatterjee et al. and Stojsavljevic et al. each reported a patient with leukoencephalopathy, who improved clinically and radiographically after vitamin B12 replacement.[14,15] MRI of the spinal cord was not performed in any of these reported cases of leukoencephalopathy.

Whether in brain or spinal cord, the abnormal signal detected in advanced cases of vitamin B_{12} deficiency, presumably reflects increased water content of the tissue, similar to that seen in multiple sclerosis or spinal cord infarction. It is the location and relative symmetry of the lesions rather than their signal characteristics which allow differentiation of this disease from other intramedullary lesions of the spinal cord.[16]

In summary, spinal cord lesions of vitamin B_{12} deficiency may produce increased signal on T2-weighted images, spinal cord swelling, decreased signal on T1-weighted images, and gadolinium enhancement. Symptoms may precede MRI abnormalities. MRI changes appear primarily in the cervical or cervico-thoracic region, a distribution consistent with the classical pathological descriptions.[17,18] On MRI, involvement of the posterior columns is more commonly seen; similarly on pathological examination posterior column involvement is earlier in onset and

more severe than that of the lateral columns.[17,18] The multifocal involvement of the posterior columns reported in one MRI case also has precedent in pathological studies.[18] Usually, but not always, MRI abnormalities improve after vitamin replacement therapy. However, neurological signs may persist despite resolution of the MRI abnormalities. Thus far there are no convincing cases of combined MRI evidence of leukoencephalopathy and subacute combined degeneration of the spinal cord in the same B_{12} deficient patient.

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