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Clinical Images

A Quarterly Column

Subacute Combined Degeneration of the Spinal Cord

Richard Marshall, MD, James Michael Milburn, MD

Department of Radiology, Ochsner Clinic Foundation, New Orleans, LA

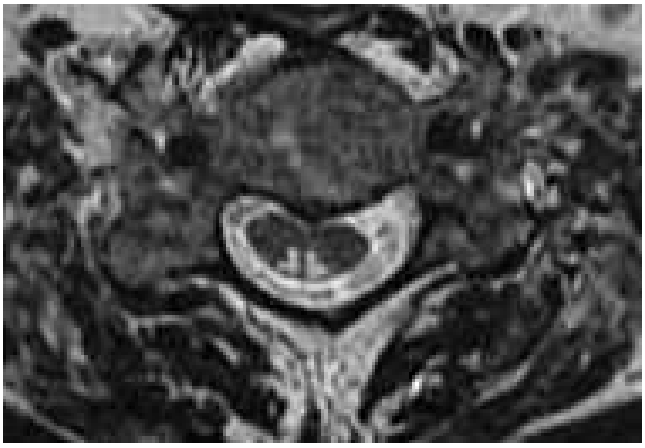

Figure 1. T2 axial fast-recovery fast spin echo demonstrating an inverted V in the posterior columns of the spinal cord.

INTRODUCTION

Subacute combined degeneration (SCD) of the spinal cord is a treatable and potentially reversible myelopathy that primarily affects the dorsal and lateral columns. Its causes directly and indirectly involve vitamin B12 deficiency, and symptoms range from mild paresthesias to paraplegia and incontinence.

HISTORY

A 73-year-old male with a history of Parkinson disease, type 2 diabetes, transient ischemic attack, and treated hypothyroidism presented to the emergency room for a single episode of presyncope when rising from his bed. Upon further questioning, he described multiple episodes of weakness and paresthesias in his hands for 3 weeks. Physical examination revealed a loss of sensation on his torso and decreased sensation to vibration in his lower extremities bilaterally. Magnetic resonance imaging (MRI) was ordered to evaluate the brain and cervical spinal cord. Serum B12 analysis confirmed the diagnosis of

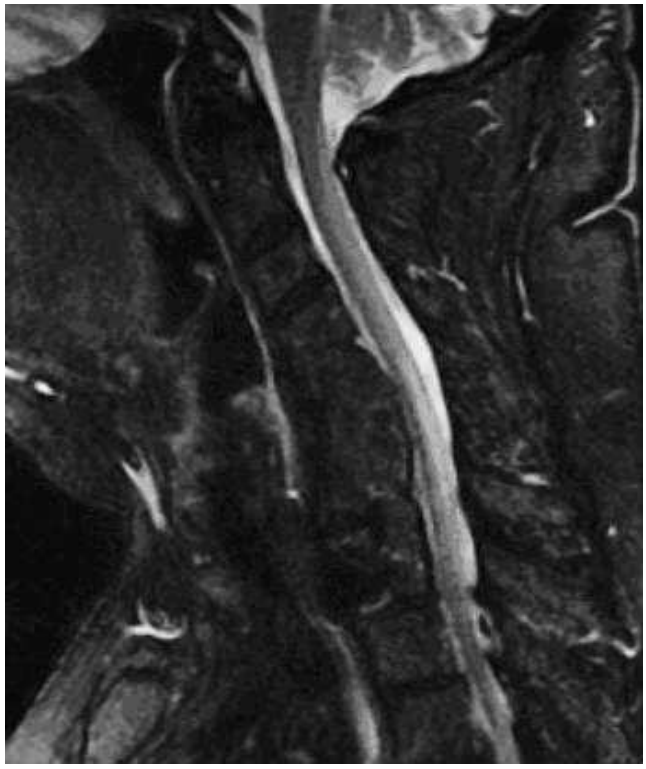

Figure 2. T2 sagittal fast-recovery fast spin-echo of the midline showing an increased fluid signal in the posterior columns of the spinal cord spanning more than 2 vertebral body heights in length.

B12 deficiency with levels <60 pg/mL (normal 210-950 pg/mL).

DISCUSSION

SCD is caused by vitamin B12 deficiency primarily affecting the posterior and lateral columns of the spinal cord and is the result of abnormal axonal myelin in these areas.[1-3] Nerve transmission is reduced, producing clinical symptoms that begin with

paresthesias, loss of vibratory sensation, and proprioception.[1,2,4] The disease can progress to severe weakness, spasticity, clonus, paraplegia, and urinary and fecal incontinence.[2,4] Several etiologies for myelin damage in these areas exist.

Vitamin B12 (cobalamin) deficiency in the form of pernicious anemia is the most common cause of SCD, and SCD is almost always present in B12 deficiency.[1] B12 is a necessary cofactor in the production of myelin in 2 pathways. In 1 route, adenosylcobalamin acts as a cofactor in the conversion of methylmalonyl-CoA to succinyl-CoA, which is a critical step in lipid synthesis.[2,5] Without adenosylcobalamin, methylmalonyl-CoA builds up and causes a decrease in normal myelin formation, leading to incorporation of abnormal fatty acids into neuronal lipids.[2,5] In another pathway, the cause of myelopathy is attributed to abnormal DNA synthesis and the role of B12 as a cofactor in the production of tetrahydrofolate, which hinders oligodendrocyte growth, resulting in ineffective myelin production.[2] Other clinical findings in B12 deficiency include macrocytic anemia (not always present in B12 deficiency), peripheral neuropathy, optic nerve atrophy, and psychiatric syndromes.[2]

Folate deficiency indirectly causes a state of B12 deficiency through its role as an activator of B12. Folate is transformed to methyltetrahydrofolate, a critical donor of methyl groups used in many reactions within the cell.[6] B12 is activated through a reaction in which tetrahydrofolate donates a methyl group to B12, forming methylcobalamin (CoB12).[6] Without this methylation, CoB12 is not produced, effectively making B12 unavailable for use and producing clinical signs of B12 deficiency. A lack of folate causes a buildup of homocysteine, which is normally broken down by derivatives of folate and CoB12 to methionine and is measurable in serum and in urine.[5]

The anesthetic agent nitrous oxide can cause SCD by interacting with and deactivating CoB12.[4] This causes an intracellular B12 deficiency and inhibits the normal production of myelin. Patients who are borderline B12 deficient before exposure to nitrous oxide are prime candidates for SCD.[4] Nitrous oxide anesthesia has been shown to induce hypersegmentation of neutrophils after surgical procedures, and its effects on B12 and cell replication have been used to potentiate the effects of chemotherapy in chronic and acute myeloid leukemia patients.[7] However, nitrous oxide is such a powerful agent in inhibiting the production of white blood cells that its use has led to fatal pneumonias and sepsis in several patients who underwent mastectomies with nitrous oxide followed by methotrexate and other chemotherapy agents.[8]

Methotrexate decreases levels of B12 in red blood cells in patients taking the drug systemically. It also causes SCD when injected intrathecally as chemotherapy.[9,10] Methotrexate functions by inhibiting dihydrofolate reductase and limiting the production of tetrahydrofolate. These actions induce a state similar to folic acid deficiency with a subsequent decrease in B12 methylation, which can ultimately lead to SCD, among other symptoms.

RADIOGRAPHIC APPEARANCE

The appearance of SCD on MRI depends on the extent of damage to the spinal cord and its tracts. Typically, posterior and lateral columns are most affected and appear hyperintense on T2 weighted image.[1] Predominant involvement of the posterior columns appears as an inverted V with the apex of the V at the center of the cord. A modest expansion of the cord may be present.[3] The differential in a case of intramedullary lesion is broad and includes demyelinating diseases (multiple sclerosis), infectious causes (human immunodeficiency virus vacuolar myelopathy and herpes viruses), inflammatory processes (sarcoidosis), ischemia, and neoplasms (astrocytomas and ependymomas).[3] However, several features of SCD make it unique, particularly the hyperintensity of the dorsal and lateral tracts that occurs over the length of several vertebral bodies.[3] Although the location is suggestive of demyelinating disease, this type of presentation is inconsistent with an inflammatory process, which would not be expected to exceed the length of 2 vertebral bodies and should be multifocal.[3] Other processes such as vacuolar myelopathy associated with acquired immunodeficiency syndrome can clearly be distinguished using patient history.[3]

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