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Case Report

Subacute combined degeneration of the cervical and dorsal spinal cord in a 40-year-old male patient: A case report

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ABSTRACT

Subacute combined degeneration of the spinal cord is a neurologic complication of vitamin B12 deficiency. It presents as a potentially reversible demyelination of the posterior and lateral columns of the cervical and dorsal spinal cord. We present the case of a 40-year-old male with progressive sensory and motor deficit from the lower extremities ascending to the mid-thoracic region. A combination of laboratory tests and magnetic resonance imaging confirmed the diagnosis of subacute degeneration of the spinal cord due to vitamin B12 deficiency.

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Introduction

Vitamin B12 deficiency can cause subacute combined degeneration of the spinal cord, a neurologic complication that presents as demyelination of the posterior and lateral columns of the cervical and dorsal spinal cord. The pathophysiology of this complication is still uncertain and why there is a predilection of the posterior and lateral columns is not yet known [1]. We present a case of patient with progressive sensory and motor deficit and vitamin B12 deficiency, probably caused by a triad of gastric-bypass surgery,

alcohol addiction, and the presence of antiparietal cell antibodies. Magnetic resonance imaging (MRI) imaging showed pathologic imaging findings that confirmed the diagnosis of subacute degeneration of the spinal cord.

Case summary

A 40-year-old male presented in the emergency department with subacute, progressive sensory, and motor deficit from the lower extremities toward the mid-thoracic region with onset after an endovenous laser ablation therapy (EVLT) of

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Fig. 1 – (a) Sagittal T2WI of the cervicodorsal spine showing longitudinally extensive hyperintense signal changes (white arrows) of the posterior part of the spinal cord. (b) Sagittal T2WI of the cervicodorsal spine showing longitudinally extensive hyperintense signal changes (white arrows) of the posterior part of the spinal cord.

varicose veins in the right leg. One week after EVLT, the patient started to experience numbness in the right leg. This was disregarded as a normal finding in the postoperative period. A week after the onset of symptoms, the sensory deficit spread to the left leg, ascended to the thoracoabdominal region to the level of T6. Furthermore, 7 weeks after the initial symptoms, the patient experienced impaired balance, weakness in both legs and erectile dysfunction. His clinical history included EVLT, Roux-en-Y gastric bypass surgery and prior shoulder surgery. His social history was pertinent for heavy alcohol abuse, though he had been in recovery for the past 5 years. Days before he presented to the emergency department, he began taking meloxicam in order to soothe painful muscle cramps. Clinical investigation revealed hyperreflexia, sensory ataxia and deep sensory loss from T6. Furthermore, there was inability to identify crude touch, a loss of vibrational sense and proprioception of the upper limbs. Laboratory tests showed a macrocytic anemia (hemoglobin levels of 11 g/dL [normal values: 14.0–18.0 g/dL]) and a low vitamin B12 (or cobalamin) count (<150 mg/dL). Other test results were normal. On electromyographic examination, there was a symmetric sensory polyneuropathy. Additional blood tests demonstrated antiparietal cell antibodies.

MRI of the brain was performed and showed multiple non-confluent T2/FLAIR hyperintense lesions in the frontoparietal white matter with no other significant abnormalities. MRI of the spine demonstrated a longitudinally extensive spinal cord lesion with T2 hyperintense signal in the dorsal columns of the medulla and the medulla oblongata, extending from the area postrema to the lower thoracic levels (Figs. 1a and

b and 2). The medullary cone was not affected. On axial images, a bilateral T2 hyperintense signal within the posterior funiculus was visible, compatible with an “inverted V-sign” (Fig. 3). There was no cord expansion or atrophy. The T1-weighted images showed no abnormalities. Contrast was not administered in this MRI study. These imaging findings are compatible with subacute combined degeneration of the spinal cord in the setting of severe vitamin B12 deficiency.

Following the diagnosis, the patient was transferred to the rehabilitation unit for 1 month. He was treated with daily subcutaneous injections of cyanocobalamin until clinical improvement, then switched to monthly intramuscular injections of cyanocobalamin. After treatment with cyanocobalamin, the patient showed clinical improvement and he could leave the rehabilitation unit. Five months later, a follow-up MRI of the spine was performed. This MRI showed regression of the longitudinally extensive spinal cord lesions mentioned above (Fig. 4), with a residual limited hyperintense signal change in the cervical spinal cord.

Discussion

Vitamin B12 or cobalamin is contained in foods of animal origin. The average daily Western diet contains around 5–30 μg of vitamin B12, of which approximately only 1–5 μg is absorbed [2]. The gastrointestinal uptake depends on the intrinsic factor and the “cobalamin receptor.” In the gastrointestinal tract, the vitamin B12 molecule is bound to the intrinsic factor (IF), which



Fig. 2 – Sagittal T2WI of the lower dorsal and lumbar spine showing longitudinally extensive hyperintense signal changes (white arrows) in the posterior lower dorsal spinal cord, continuous with the alterations in the cervicodorsal spine. The conus appears normal.

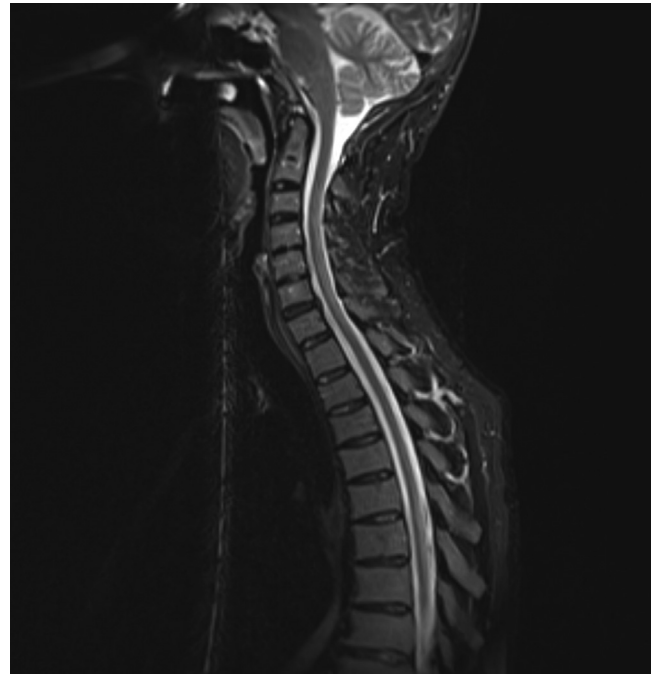


Fig. 4 – Sagittal T2WI of the cervicodorsal spine showing almost complete regression of hyperintense signal changes of the posterior part of the spinal cord as seen in Fig. 1a, with a residual limited hyperintense signal change in the cervical spinal cord.

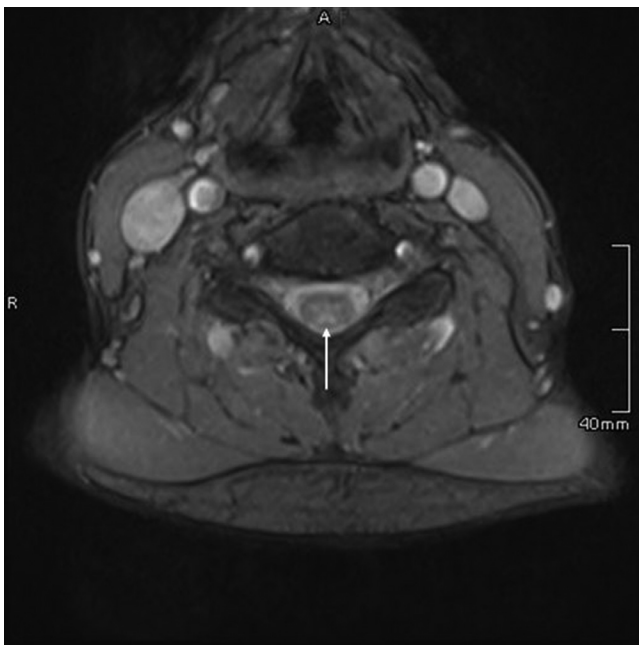


Fig. 3 – Axial T2WI of the cervical spinal cord with a bilateral T2 hyperintense signal within the posterior funiculus, demonstrating the ‘inverted V-sign’ sign (white arrow).

is synthesized by the gastric parietal cells. The B12-IF complex then binds to the mucosa of the terminal ileum where the cubam receptor is integrated and is then absorbed into the body [1]. Deficiency of vitamin B12 has potentially multiple causes: malabsorption (gastrectomy, gastric bypass, autoimmune, metformin use, proton-pump-inhibitor [PPI] use, etc.), dietary deficiency (vegan or vegetarian diet) or (recreational) nitrous oxide (N_2O) use [1]. Autoimmune-induced vitamin B12 deficiency is caused by an autoimmune gastritis, where gastric parietal cells are destroyed by antiparietal cell antibodies and this leads to a lack of IF to bind vitamin B12. Another cause of malabsorption induced vitamin B12 deficiency is the use of PPIs. PPIs block the gastric proton pump, thus inhibiting the secretion of gastric acid. The presence of gastric acid is required to separate vitamin B12 from the food protein. The failure to separate the vitamin and the protein is induced by the reduced amount of gastric acid, which can lead to malabsorption of vitamin B12 [3]. N_2O inactivates vitamin B12 by oxidizing the active Co^+ form of vitamin B12 to Co^{2+} and Co^{3+} forms. These have no biologic activity and cannot be used as cofactors in vitamin B12 pathways [4].

The diagnosis of vitamin B12 deficiency is made by measuring vitamin B12 levels in the serum. Studies have shown that serum vitamin B12 levels do not always represent the correct cellular B12 status [5]. Secondly plasma methylmalonic acid (MMA) levels can be measured, MMA-determining plasma homocysteine (HC) may also be helpful but it is less specific than the measurement of MMA levels. Both MMA and HC require vitamin B12 to be converted in respectively Succinyl-CoA and

methionine, vitamin B12 deficiency will lead to an elevation of MMA and/or HC [2]. Hematologic changes are absent in one quarter of patients with neurologic symptoms, which highlights the importance of imaging analysis of patients with normal vitamin B12 levels but clear neurologic symptoms and high clinical suspicion [6].

Vitamin B12 deficiency causes a reversible megaloblastic anemia and a broad range of neurologic symptoms, as vitamin B12 is fundamental for the adequate development and maintenance of myelination in the central nervous system. Lack of vitamin B12 has been associated with demyelination of the posterior and lateral columns of the cervical and dorsal spinal cord. Additionally, demyelination of the white matter in the brain and cranial and peripheral nerves have been described [6]. The underlying pathophysiology of the demyelination is still uncertain. Lack of vitamin B12 causes an overproduction of Tumor Necrosis Factor- α (TNF- α), which in turn leads to a downregulation of epidermal growth factor and interleukin-6, 2 neurotrophic factors [7]. Neuropathologic studies of the subacute combined degeneration of the spinal cord show spongiform changes with focal myelin and axonal destruction in the posterior and lateral columns. Destruction of the anterior columns has been described in a few advanced cases. The reason for the predilection of the posterior and lateral columns is not yet known. This spinal cord degeneration is visible on MRI [8].

The clinical symptoms of subacute combined degeneration are characterized by the predominant involvement of the posterior columns in the cervicodorsal spine, resulting in impairment of proprioception, loss of vibration sense, dysesthesia, and muscle weakness. The initial symptoms are most commonly paresthesia in the hands and/or the feet. Symptoms are mostly symmetric and they tend to progress from distal to proximal [9]. Specific findings during clinical examination are loss of vibratory sense and loss of proprioception, weakness, spasticity, and hyperreflexia [9].

The imaging modality of choice for the diagnosis of subacute combined degeneration of the spinal cord is MRI. Subacute combined degeneration of the spinal cord mostly affects the cervical and higher thoracic spinal cord [10]. Imaging findings include no or mild expansion of the spinal cord and generally symmetrical high-intensity T2-weighted lesions, similar to the T2-weighted signal abnormalities of longitudinal extensive transverse myelitis (LETM). LETM is defined as intramedullary hyperintense T2-weighted signal abnormality that spans 3 or more vertebral segments, mostly affecting the cervical and thoracic cord. LETM has a broad list of differential diagnoses, ranging from multiple sclerosis to spinal cord infarction. LETM is known to have a hyperacute, acute, subacute, or chronic onset [11]. LETM with a subacute onset is seen in subacute degeneration of the spinal cord as mentioned above. The T2-weighted lesions seen in subacute degeneration of the spine are usually confined to the centers of the dorsal and lateral columns, although rare some cases of anterior column destruction have been described. On the axial planes, the bilateral high-intensity T2 signals within the posterior funiculus of the cervical spinal cord resemble the appearance of an inverted letter “V,” thus called the inverted V-sign [10,12–14]. One case series mentioned high-intensity T2 signal resembling a “dumbbell” or “binoculars”

on the axial planes of the thoracic spinal cord [15]. Contrast enhancement of the spinal cord has been sporadically described [10,16].

Brain abnormalities in patients with subacute combined degeneration of the spinal cord are rare. Possible findings include leukoencephalopathy with hyperintense signal changes on T2-weighted images in the centrum semiovale and enhancement of the optic nerve on T1-weighted images, which is compatible with neuropathy [12]. Gupta et al. showed that microstructural changes of the affected cerebral white matter can be detected on diffusion tensor imaging. In their study, patients with subacute combined degeneration of the spine showed significant reductions in the fractional anisotropy and an increase in apparent diffusion coefficient and radial diffusivity values in multiple brain regions [17].

The treatment of subacute combined degeneration depends on the underlying cause. It is important to distinguish B12 deficiency from other causes of myelopathy as it is treatable with oral, intramuscular or subcutaneous vitamin repletion. Early detection and treatment often result in full clinical recovery [10,18]. Most vitamin B12 deficient individuals are treated with intramuscular vitamin B12. Intramuscular vitamin B12 can be administered in two different forms: cyanocobalamin and hydroxocobalamin [2,19].

Our case is interesting because of the extent of the pathological imaging findings and clear regression of the extensive spinal cord lesions after treatment with intramuscular cyanocobalamin. The exact cause of the subacute combined degeneration is probably a combination of three factors: gastric-bypass surgery and alcohol addiction which cause severe vitamin deficiencies and most importantly the presence of antiparietal cell antibodies.

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