CASE REPORT

A case of subacute combined spinal cord degeneration and suspected leukoencephalopathy associated with vitamin B_{12} deficiency showing improved imaging findings after vitamin B_{12} administration

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Abstract : We report a case of subacute combined spinal cord degeneration (SCD) caused by vegetarianism and autoimmune gastritis, which is rarely reported in Japan, and which showed improvement in symptoms and imaging findings after vitamin B_{12} administration. As delayed treatment can lead to irreversible damage, we suggest that patients with characteristic abnormal signals in the posterior cervical cord should be examined while considering the possibility that SCD may occur even in the absence of a history of gastrectomy or heavy drinking. We also describe the patient's reversible abnormal signals in the cerebral white matter on magnetic resonance imaging, indicative of an early sign of leukoencephalopathy associated with vitamin B_{12} deficiency. J. Med. Invest. 69 : 299-301, August, 2022

Keywords **:** *subacute combined spinal cord degeneration, vitamin B_{12}, autoimmune gastritis, vegetarianism, leukoencephalopathy*

INTRODUCTION

Subacute combined spinal cord degeneration (SCD) is a neurodegenerative disease caused by vitamin B_{12} deficiency. It typically occurs after total gastrectomy, but may also be caused by autoimmune gastritis (AIG), small intestinal diseases, vegetarianism, and chronic alcoholism. We report a case of SCD, which was suspected of being caused by vitamin B_{12} deficiency associated with autoimmune gastritis and vegetarianism, and wherein the imaging findings were improved following vitamin B_{12} administration. We also report the patient's imaging findings suggesting reversible leukoencephalopathy due to vitamin B_{12} deficiency, which is less frequently reported than SCD.

CASE REPORT

A 55-year-old woman with a history of bladder cancer, appendicitis, and cesarean section was admitted because of fever and difficulty in moving. She experienced numbness in her fingers and toes for the preceding 2 weeks, and developed fever and weakness in her lower limbs 3 days before admission. She was alert and well-oriented, evident cognitive dysfunction was not observed. The physical and neurological examinations revealed a body temperature of 38.2°C, gait disturbance, muscle weakness, numbness in the limbs, and disorder of skilled movements. On the manual muscle test (MMT), muscle strength was 4/4 both in the upper and lower limbs. Babinski reflex, increased deep tendon reflex, cranial nerves disorder was absent. She did not smoke or drink, and had been on a vegetarian diet. Specifically, she had avoided animal products such as meat, fish, and eggs for approximately 6 years.

A blood test showed macrocytic anemia (hemoglobin, 8.6 g/dL ; normal range 12.0-15.0 g/dL, mean corpuscular volume, 105.1 fL ; normal range 79.0-100 fL) and low serum vitamin B_{12} levels (<50 pg/mL ; normal range 180-914 pg/mL).

A urine test revealed urinary tract infection (>100 white blood cells per high-power field) and abdominal computed tomography (CT) revealed renal enlargement and peri-renal fat stranding ; thus, her fever was suspected of being caused by acute pyelonephritis. After antibiotic treatment, the patient was completely cured.

Fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) of brain magnetic resonance imaging (MRI) demonstrated slight hyperintensity in the splenium of the corpus callosum and subcortical white matter in the frontal lobe (Fig1). These areas did not show low apparent diffusion coefficient (ADC) values and gadolinium enhancement on contrast-enhanced MRI. T2-weighted image (T2WI) and short tau inversion recovery (STIR) of cervical MRI demonstrated the cervical cord swelling and hyperintensity of posterior columns, so called "inverted V sign," extending from the level of the C2 to the C6 vertebrae (Fig 2). This abnormal intensity area did not exhibit gadolinium enhancement on contrast-enhanced MRI, similar to white matter lesions in the brain. The patient was diagnosed with SCD and the initial stage of leukoencephalopathy associated with vitamin B_{12} deficiency was suspected.

Concurrently with vitamin B_{12} administration, the cause of vitamin B_{12} deficiency was investigated. Additional tests revealed that she was positive for the anti-intrinsic factor antibody and negative for the anti-Helicobacter pylori antibody with endoscopic gastric atrophy. These findings suggested AIG ; herefore, the vegetarian diet along with AIG was suspected of having resulted in vitamin B_{12} deficiency.

The patient was treated with 500 - 1000μg/day of mecobalamin intramuscularly for two weeks with a combination of 1000μg/day of cyanocobalamin intravenously for the first 10

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days, and got to walk by herself. After discharge, intramuscular injection three times a week is continuing by her family doctor, which dosage is adjusted according to symptoms. Approximately 7 months later, on follow-up MRI, cervical cord swelling and high signal intensity in the white matter of the brain and cervical spine disappeared (Fig1, 2). However, slight numbness in the limbs was still remained. It was probably going to be a lasting symptom. The patient continued vitamin B_{12} supplementation at her family doctor.

DISCUSSION

SCD typically occurs after gastrectomy (1) ; however, the current case was unique as there was no history of gastrectomy. The SCD in this case was considered to have been caused by a combination of AIG-associated malabsorption and inadequate food intake due to vegetarianism. An additional unique aspect was that the brain MRI scan demonstrated reversible abnormal signal intensity, indicative of "leukoencephalopathy associated with vitamin B_{12} deficiency."

Orally ingested vitamin B_{12} needs the intrinsic factor, produced by the parietal cells of the gastric mucosa, to be absorbed into the body (2). AIG is an autoimmune disease that causes mucosal atrophy in the gastric fundic gland region due to anti-parietal cell and anti-intrinsic antibodies, resulting in malabsorption of vitamin B_{12} (1). The prevalence of autoimmune gastritis in asymptomatic individuals undergoing medical checkups is 0.49% in Japan ; this disease is not very rare (3). However, there are relatively few reported cases of SCD caused by AIG. We suggest some reasons for this discrepancy as follows : 1) AIG is often masked by atrophic gastritis associated with *H. pylori* infection, especially in Japan, and is easily missed by inexperienced endoscopists (3) ; 2) vitamin B_{12} has an intrinsic factor-independent absorption pathway (4), and 3) it takes quite a few years before vitamin B_{12} deficiency develops after the onset of malabsorption, as shown after gastrectomy (5, 6). In the present case, SCD was considered to have been caused not only by AIG, but a combination of AIG and an unbalanced diet.

The imaging findings of SCD are characterized by a mildly enlarged spinal cord and continuous hyperintensity on T2WI in the craniocaudal direction, especially the posterior and lateral columns in the lower cervical to upper thoracic spinal cord (7, 8, 9). If appropriate treatment is given in the early stages of the disease, the spinal cord swelling and abnormal signals on MRI will disappear, but if treatment is delayed, the condition may

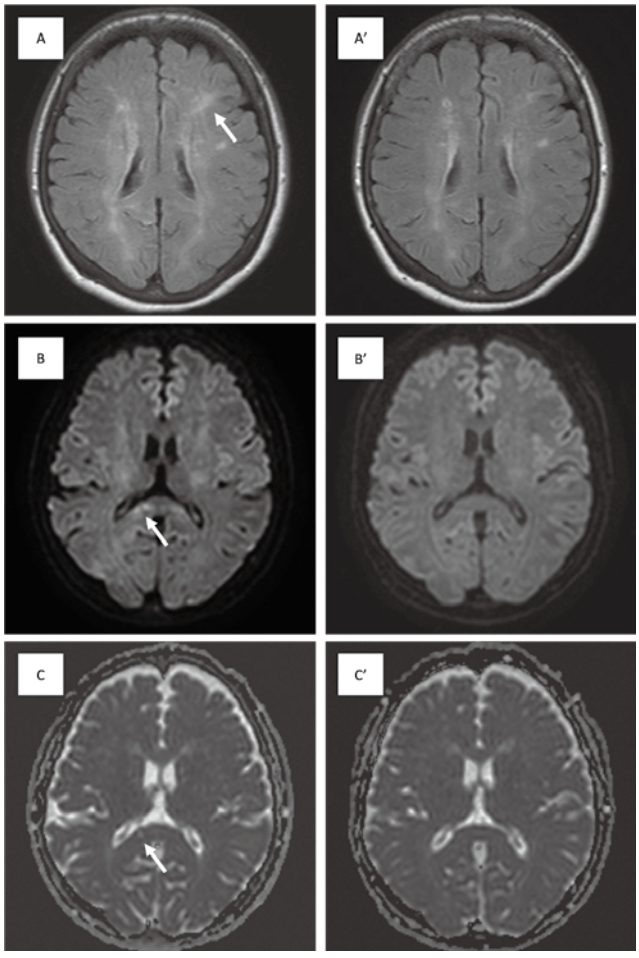

Fig 1. brain MRI – FLAIR (A – before, A' – after), DWI (B – before, B' – after), ADC map (C – before, C' – after)
Slight hyperintensity changes in the splenium of the corpus callosum and subcortical white matter in the frontal lobe were detected before treatment (A, B). These areas did not show low intensity in ADC maps (C). Seven months after treatment initiation, these abnormal signals almost disappeared (A', B', C').

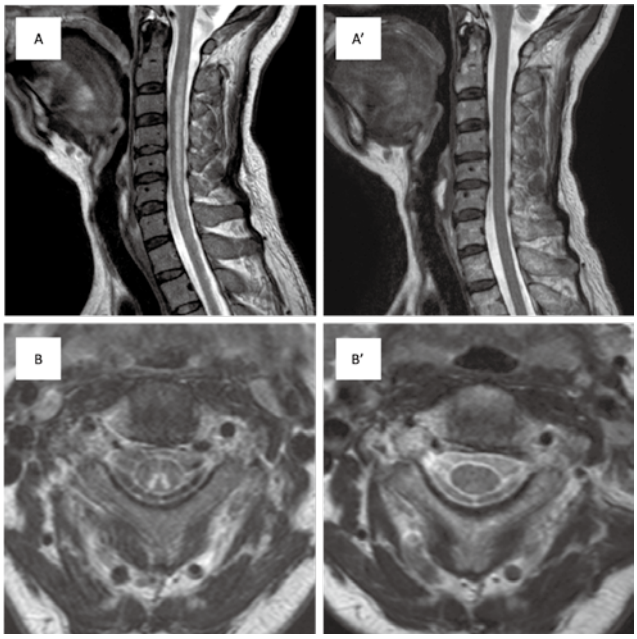

Fig 2. cervical MRI – T2WI (A, B – before, A', B' – after)
The first MRI revealed cervical cord swelling and hyperintensity of the posterior column, the so-called "inverted V sign," extending from the level of the C2 to the C6 vertebrae (A, B). Seven months after treatment initiation, these abnormal findings disappeared (A', B').

not improve (2). Moreover, gadolinium-enhancement or non-enhancement is not constant (2, 7). In the present case, cervical MRI scan demonstrated typical signal changes, so called the "inverted V" shape on T2WI and STIR which disappeared on repeated MRI. This treatment was initiated within 2-3 weeks of awareness of symptoms and the patient showed almost full recovery. However, permanent damage has been reported ; therefore, diagnosis and treatment should begin as soon as possible.

Reports of vitamin B_{12} deficiency-associated leukoencephalopathy are quite rare, and we could not find any reports regarding its association with AIG and vegetarianism. Based on a review of the PubMed database from 1983 to 2021 using the keywords "vitamin B_{12}," "cobalamin," and "leukoencephalopathy," 20 references were found, of which less than 10 were reports of leukoencephalopathy associated with vitamin B_{12} deficiency, similar to this case. MRI findings of leukoencephalopathy associated with vitamin B_{12} deficiency reportedly includes multiple focal or confluent T2WI/FLAIR-high signal intensities in the periventricular white matter, with some reports showing abnormal signals in the cerebellum (2, 10, 11). There are few reports describing DWI, with some reports indicating that it was completely or partially reversible (12, 13), whereas others showed a high signal but no description of responsiveness to treatment (14). Moreover, we could not find any reports describing ADC map. In the present case, it was difficult to make a definitive diagnosis of leukoencephalopathy associated with vitamin B_{12} deficiency because the distribution of the signals was limited and their intensity was faint compared to those of previously reported images. However, the signal abnormality was improved on repeated MRI, therefore, it was considered that it might have been the initial stage of leukoencephalopathy.

It is believed that hyperintensity on DWI with restricted water diffusion on ADC maps in SCD is consistent with the co-existence of intramyelin edema (2), and leukoencephalopathy associated with vitamin B_{12} deficiency may be caused by a similar mechanism. In this case, however, the brain MRI scan only revealed a faint hyperintensity on DWI and did not show lower ADC values, suggesting that intramyelin edema had not yet been complete. This might be related to the reversibility of the imaging findings and good response to treatment.

CONCLUSION

We encountered a case of SCD caused by vitamin B_{12} deficiency due to AIG and vegetarianism, which is rarely reported in Japan. Furthermore, brain MRI revealed abnormal signal intensity, which was suspected to be the initial stage of leukoencephalopathy associated with vitamin B_{12} deficiency. If treatment is delayed, irreversible damage may occur. Therefore, when characteristic signal changes in the posterior cervical spinal cord are observed, SCD should be considered even in the absence of a history of gastrectomy or heavy drinking and the causes of vitamin B_{12} deficiency should be investigated. Further, attention should be paid to the presence or absence of a high signal on DWI or lower ADC values which may reflect the condition of intramyelin edema and therapeutic response.

CONFLICT OF INTEREST

None

REFERENCES

1. Ota K, Yamaguchi R, Tsukahara A, Nishida S, Shigekiyo T, Harada S, Kojima Y, Takeuchi T, Arawaka S, Higuchi K : Subacute Combined Degeneration of the Spinal Cord Caused by Autoimmune Gastritis. Intern Med 59 : 2113-2116, 2020
2. Briani C, Torre CD, Citton V, Manara R, Pompanin S, Binotto G, Adami F : Cobalamin Deficiency : Clinical Picture and Radiological Findings. Nutrients 5 : 4521-4539, 2013
3. Notsu T, Adachi K, Mishiro T, Fujihara H, Toda T, Takaki S, Kinoshita Y : Prevalence of Autoimmune Gastritis in Individuals Undergoing Medical Checkups in Japan. Intern Med 58 : 1817-1823, 2019
4. Elia M : Oral or Parenteral Therapy for B_{12} deficiency. Lancet 352 : 7211-7212, 1998
5. Hu Y, Kim HI, Hyung WJ, Song KJ, Lee JH, Kim YM, Noh SH : Vitamin B_{12} Deficiency After Gastrectomy for Gastric Cancer An Analysis of Clinical Patterns and Risk Factors. Ann Surg 258 : 970-975, 2013
6. Tovey F, Godfrey J, Lewin M : A Gastrectomy Population : 25-30 Years On. Postgrad Med J 66 : 450-456, 1990
7. Ravina B, Loevner LA, Bank W : MR Findings in Subacute Combined Degeneration of the Spinal Cord. Am J Roentgenol 174 : 863-865, 2000
8. Naidich MJ, Ho SU : Case 87 : Subacute Combined Degeneration. Radiology 237 : 101-105, 2005
9. Narra R, Mandapalli A, Jukuri N, Guddanti P : "Inverted V sign" in Sub-Acute Combined Degeneration of Cord. J Clin Diagn Res 9 : TJ01, 2015
10. Chatterjee A, Yapundich R, Palmer CA, Marson DC, Mitchell GW : Leukoencephalopathy Associated with Cobalamin Deficiency. Neurology 46 : 832-834, 1996
11. Morita S, Miwa H, Kihira T, Kondo T : Cerebellar Ataxia and Leukoencephalopathy Associated with Cobalamin Deficiency. J Neurol Sci 216 : 183-184, 2003
12. Biotti D, Mader ME, Diot E, Acquaviva C, Guffon N, Tilikete C, Benoist JF, Labauge P, Vighetto A : A Young Woman with Rapid Mental Deterioration and Leukoencephalopathy. Neurology 83 : 182-186, 2014
13. Kori S : Hyperintense Splenium in Vitamin B_{12} Deficiency. Neurol India 53 : 377-378, 2005
14. Pacheco FT, Scoppetta TLPD, Sznirer M, Paes RA, Rocha AJ : Acute Demyelination with Leukoencephalopathy and Cerebellar Involvement in Vitamin B_{12} Deficiency. Arq Neuropsiquiatr 73 : 257, 2015