Original Article

Conventional MRI for diagnosis of subacute combined degeneration (SCD) of the spinal cord due to vitamin B-12 deficiency

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Subacute combined degeneration of the spinal cord (SCD) is often found in vitamin B-12 deficiency and typically shows hyperintensity on T2-weighted images of the lateral and posterior columns. The purpose of the study was to evaluate the use of conventional magnetic resonance examination in diagnosing SCD. Thirty-six patients were clinically confirmed and retrospectively analyzed; conventional spine MRIs were available for all patients and eight of them had contrast enhancement MRIs. 19 out of 36 patients showed abnormal signal intensity on T2 weighted images with a sensitivity of 52.8%, among which 18 in the posterior aspect of the spinal cord and 1 in the anterior horn of the thoracic spinal cord The spinal cord abnormalities were seen at the cervical spine in 12 patients (33.3%) and at the thoracic spine in the other 7 patients (19.4%). Axial T2-weighted images showed symmetric linear T2-hyperintensity as an "inverted V" at the cervical spinal cord in 5 patients, which has been reported as a typical sign of SCD. For patients with thoracic spinal cord abnormalities, the bilateral paired nodular T2-hyperintensity looked like "binoculars" at the thoracic spinal cord. Only one out of the eight patients showed slight enhancement after injection with contrast agent. All the 36 patients reported clinical improvement after appropriate vitamin B-12 treatment. The two follow-up spine MRIs showed a decreased extent of the lesion. Therefore, conventional MRI is useful in the diagnosis and management of SCD caused by vitamin B-12 deficiency.

Key Words: conventional magnetic resonance imaging, subacute combined degeneration of the spinal cord, vitamin B-12, deficiency, nutrition

INTRODUCTION

Vitamin B-12 has a fundamental role in central nervous system function at all ages, its deficiency can present with brain, optic nerve, spinal cord, and peripheral nervous system disorders.[1] Vitamin B-12 deficiency is common in both developed and developing countries. As China is entering an ageing society, there are more old people who cannot get enough vitamin B-12 whether due to gastrointestinal disease or inadequate dietary intake. In western countries, subacute combined degeneration of the spinal cord due to vitamin B-12 deficiency mainly happens among vegans, and especially strict vegetarians. The lack of vitamin B-12 can be clearly seen by examining the serum concentration of vitamin B-12 and methylmalonic acid (MAA).

Subacute combined degeneration (SCD) is characterized by posterior and lateral column damage of the spinal cord, which causes loss of propioception and vibration sense in the feet, legs and hands, paresthesiae in the extremities, and corticospinal signs such as spasticity, hyperreflexia and the Babinski sign. The most consistent MRI finding is a symmetrical abnormally increased T2 signal intensity limited to posterior or posterior and lateral columns in the cervical and thoracic spinal cord, and on axial T2-weighted images "inverted V" sign can be seen. The cervical and upper thoracic cord is most commonly and severely affected.[2]

Studies on SCD had been done retrospectively or prospectively. Some suggested that conventional MRI had low sensitivity in diagnosing SCD when prospectively studied, but their sample size was small which limits their conclusion. We aimed to assess conventional MRI features and clinical characteristics of Asian patients in this study, to assess the value of conventional MRI in diagnosing SCD of spinal cord.

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MATERIALS AND METHODS

Patients

The institutional ethics committee approved the study (45th, 2014). A total thirty-six patients (20 men and 16 women, the median age=50 years, and age range=26 to 76 years) with biochemically proven vitamin B-12 deficiency (<189 pg/mL) and abnormal clinical manifestations were included in the study. Written informed consent was obtained from all subjects after the purpose of the study was explained to them. The duration from onset of paresthesia of the distal limbs varied from half a month to eight years. In this study, 14 patients had a history of gastrointestinal disorders and 5 had psychiatric manifestations, and positive Romberg signs could be seen in 9 patients.

Clinical evaluation

Serum vitamin B-12 level was measured by electrochemiluminescence (COBAS e411) [Roche diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim, Germany] method. Neurological examination was performed by a neurologist independently to define the severity of impairment in these patients with vitamin B-12 deficiency.

Conventional MRI protocol

Conventional MRI data were acquired on a 3T Simens Verio and a 1.5T Simens Avanto MRI scanner, performed on a 12-channel head-neck-spine coil by using T1 fluid attenuated inversion recovery (FLAIR) and T2 fast recovery (FSE) in the sagittal and axial planes. Imaging parameters for T1 FLAIR in sagittal plane were TR=2400 ms, TE=25 ms, TI=1000 ms, NEX=1, slice thickness=3 mm, flip angle=90°, acquisition matrix=384 × 256, FOV= 280 mm, reconstructed matrix=512×512. T2 FS in sagittal plane had the following parameters TR=6000 ms, TE= 100 ms, NEX=2, slice thickness=3 mm, flip angle=90°, acquisition matrix=384×256, FOV=320 mm, reconstructed matrix=512×512. Imaging parameters for T2 FS in axial plane were TR=3500 ms, TE=120 ms, NEX=2, slice thickness=3 mm, flip angle=90°, acquisition matrix= 320×224, FOV=180 mm, reconstructed matrix=512×512. The cervico-dorsal and thoracic spine was performed to look for the B-12 deficiency-related changes in the spinal cord. The flow velocity of the contrast agent was 2 mL per Kg through the vein.

Treatment and follow-up

All the 36 patients were administered 1000 μg of vitamin B-12 intramuscularly for several days after clinically diagnosed as SCD, followed by orally taken vitamin B-12 and folate at home for two to three months depending on their condition. This was supervised by a neurologist who assessed the compliance. All patients were followed for a minimum period of 4 weeks, and only two were re-evaluated on MRI imaging.

Data analysis

The MRI scans were reviewed independently by two experienced radiologists with one having more than 4 years' experience in the field of neuroradiology and the other more than 25 years. There was no inter-observer disagreement in the MRI findings. The sensitivity of conventional MRI in diagnosing SCD was calculated (Sensitivity=number of positive cases/total number).

RESULTS

19 out of 36 patients showed abnormal signal intensity on T2 weighted images with a sensitivity of 52.8%, among which there were 18 in the posterior column of the spinal cord and 1 in the anterior columns of the thoracic spinal cord; lateral column involvement was not apparent. The spinal cord abnormalities were seen at cervical spinal in 12 patients (33.3%) and at thoracic spine in the other 7 patients (19.4%) (Table 1). MRIs also demonstrated adjacent involvement of multiple segments of the cord. For the five patients with cervical spinal cord abnormalities, axial T2-weighted images showed symmetric T2-hyperintensity that appeared as an "inverted V" sign in the posterior column of the cervical spinal cord (Figure 1). For patients with thoracic spinal cord abnormalities, the bilateral paired nodular T2-hyperintensity looked as "binoculars" at axial thoracic spinal cord (Figure 2). Only one out of the 8 patients who had enhanced MRI examinations showed the lesion of spinal cord slightly enhanced after injected with contrast agent.

All patients presented insidious neurological abnormalities such as tingling sensation in distal extremities, joint position and vibration, impaired sensation of fine touch, paresthesia, numbness, and difficulty in walking. 9 patients had positive Romberg signs, 14 patients had a history of gastrointestinal disorders and 5 suffered abnormal psychiatric conditions. After appropriate supplementation of vitamin B-12, out of 36 patients, clinical signs and symptoms persisted in 11 patients, there was complete clinical improvement in 16 patients, while 9 patients lost contact with us. The lesion extent of the two patients decreased on follow-up MRI images.

DISCUSSION

Causes of vitamin B-12 deficiency

Vitamin B-12 acts as a coenzyme in the methyl malonyl-CoA mutase reaction, which is required for myelin synthesis. Its deficiency therefore results in defective myelin synthesis, leading to several central and peripheral nervous system dysfunctions.[3] Vitamin B-12 deficiency is often ignored and may cause several hematological, gas-

Table 1. MRI features and abnormal distribution of the patients

MRI findings	n/total n (%)	Dorsal-cervical spine		Thoracic spine	
		"Inverted V"	Patchy	Anterior	Dorsal
T2-hyperintensity	19/36 (52.8)	5	7	1	6
No abnormal signal change	17/36 (47.2)				
Enhancement	1/36		1		
Follow-up MRIs	2/36	1			1

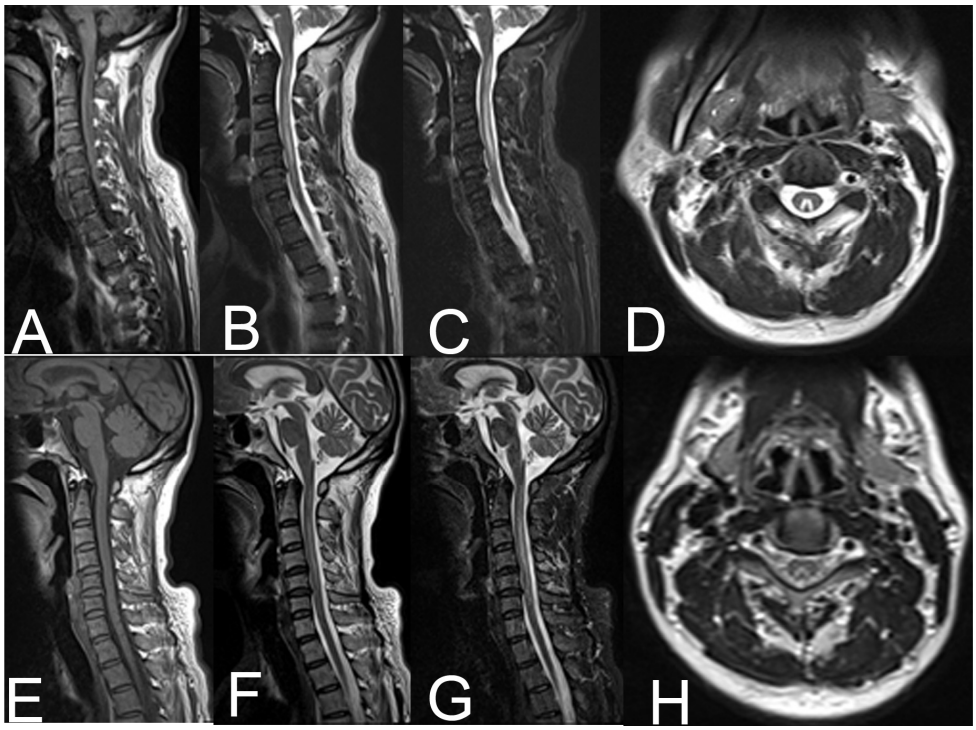

Figure 1. MR findings baseline as well as follow-up in a 44-year-old man with vitamin B-12 deficiency. (A) T1W-FLAIR sagittal image did not show any alteration in signal intensity. (B, C) T2-weighted sagittal images show increased signal intensity in the cervical spinal cord extending from C1 to C6 level. (D) T2-weighted axial image shows abnormal signal involving the posterior columns of cervical cord with inverted V sign. On 4 weeks follow-up, while patient was receiving treatment, patially resolution of abnormal cord hyperintensity was observed in T2-weighted sagittal, T1-FLAIR sagittal and T2-weighted axial images (E, F, G, H).

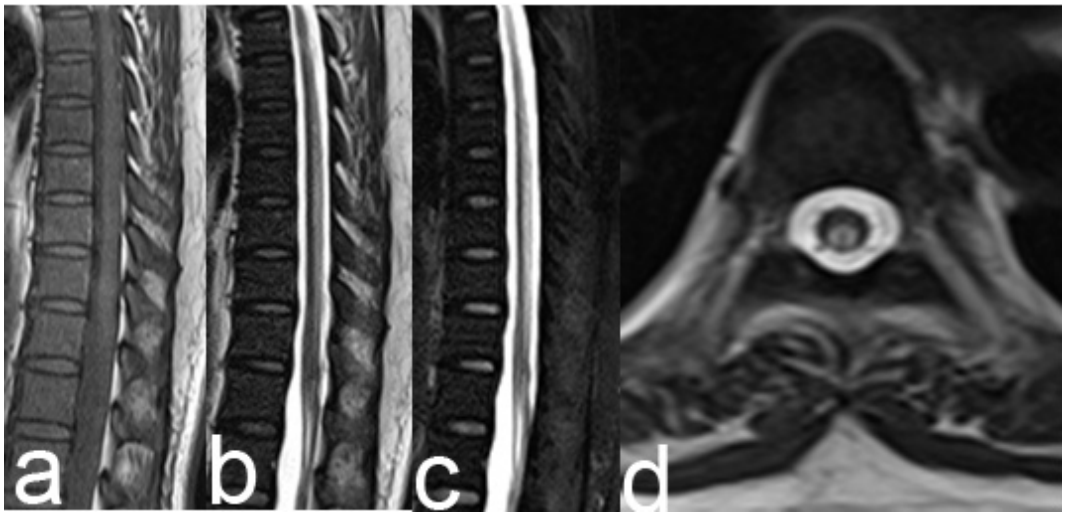

Figure 2. MR findings in a 47-year-old woman with symmetric dysesthesia in the lower extremities for half a month. (a) T1-weighted sagittal image did not show any alteration in signal intensity. (b, c) T2-weighted sagittal images show increased signal intensity in the cervical spinal cord extending from T7 to T11. (d) The abnormal signal intensity looked bilateral paired nodular T2-hyperintensity as "binoculars" at thoracic spinal cord on axial T2 weighted images through the 7th thoracic spinal cord level.

trointestinal, psychiatric and neurological manifestations, which is usually caused by pernicious anaemia, congenital or acquired malabsorption conditions (achlorhydria in elderly patients, long-term alcoholism, gastric or ileal resection, coeliac disease, chronic pancreatic insufficiency, Zollinger Ellison syndrome, Crohn's disease), medications (colchicine, neomycin, and p-aminosalicylic acid), disorders of intracellular cobalamin metabolism (methylmalonic aciduria and homocystinuria), increased requirement (in hyperthyroidism and alpha thalassemia), or inadequate intake (e.g. vegetarian diet).[4] Determination of methylmalonic acid and homocysteine are particularly recommended in cases of diagnostically unclarified vitamin B-12 deficiency.[5]

Clinical manifestation and MRI findings

Vitamin B-12 deficiency due to malabsorption syndrome is frequent in elderly people. In this study 14 patients had gastrointestinal disorders, and 5 had psychiatric manifestations. Subacute combined degeneration is clinically characterized by symmetric dysesthesia, disturbance of position sense and spastic paraparesis or tetraparesis, which may be caused by the involvement of the posterior and lateral columns of the cervical and upper thoracic

parts of the spinal cord. The first abnormality is usually sensory impairment, most often presenting as distal and symmetrical paraesthesiae at lower limbs frequently associated with ataxia. Almost all patients have loss of vibratory sensation, often associated with diminished cutaneous sensation and proprioception and nine of them had positive Romberg signs. Corticospinal tract involvement is common in the more advanced cases, with abnormal reflexes, motor impairment and, ultimately, spastic paraparesis.[6,7] Only 16 out of 36 patients had completely clinical recovery and we lost contact with 9 patients which may be explained by the poor compliance of the patients and the different disease course of the patients.

Conventional MRI in diagnosing SCD has a relatively high sensitivity of 52.8% in our retrospectively study. Patients with cervical spinal cord abnormalities showed symmetric linear T2-hyperintensity as an "inverted V" sign at cervical spinal cord on axial T2-weighted images. While for patients with thoracic spinal cord abnormalities, bilateral paired nodular hyperintensity looked as "binoculars" on axial T2-weighted images. Follow-up MRIs after vitamin B-12 treatment showed decreased abnormalities in the two patients. Symmetric T2-hyperintensity within dorsal column of spinal cord is commonly seen in SCD patients with a linear pattern in the cervical spine and a nodular pattern in the thoracic spine. The residual patients who showed no abnormal signal intensity on MR images might be explained by the fact that the lesions may gradually increase when serum levels of vitamin B-12 are low for prolonged periods of time.

Treatment and diagnosis

It is important to distinguish B-12 deficiency from other causes of myelopathy, as it is treatable. Early detection is necessary for full clinical recovery as it is critical in the pursuit of improved quality of life and health care cost savings. The present report provides a renewed and more recent rationale for clinicians to use definitions of B-12 deficiency that include homocysteine or MMA. By identifying and treating a B-12 deficiency earlier, it may be possible to prevent some of the functional disabilities common to individuals as they age but possibly responsive to improved nutrition.[4] Andrès suggested a dose of 1000 μg of oral cyanocobalamin for pernicious anemia (during the entire lifetime) and a mean daily dose of 250 μg for food-cobalamin malabsorption.[8]

In the present study, MRI of the spine showed spinal cord signal abnormality in 19 out of 36 patients with a high sensitivity of 52.8%. Classic posterior column involvement was seen in 16 patients, posterior and lateral columns involvement in two patient and involvement of anterior column in one patient each. Cervical or cervicothoracic cord with predominant involvement of posterior columns is usually observed in patients with vitamin B-12 deficiency related SCD and may be more specific for this condition as reported in the literature.[9] Our data is in agreement with the literature with respect to the posterior column involvement, and it is seen in a slightly large percentage of all the patients In a recently published review of observational studies, it was mentioned that MRI findings at the time of diagnosis could have a prognostic value in SCD.[10,11]

It is important to distinguish subacute combined degeneration from copper deficiency myelopathy (CDM) due to vitamin B-12 deficiency and methotrexate-induced myelopathy where the abnormalities of the dorsal and/or lateral columns of the spinal cord are consistent with those described for SCD. Thus, specific laboratory studies are required.[12,13]

Conclusion

Conventional MRI may be a useful tool for the diagnosis of SCD as it has a relatively high sensitivity. The diagnosis of SCD should be based on clinical features and serum vitamin B-12 levels combined with conventional MRI examination.

AUTHOR DISCLOSURES

No author has a conflict of interest.

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脊髓亚急性联合变性的常规 MRI 诊断价值分析

脊髓亚急性联合变性（SCD）常发生于维生素 B-12 缺乏的患者，T2 加权像上通常显示为脊髓后索及侧索的异常高信号。本文研究目的在于评估常规磁共振检查对诊断 SCD 的价值。回顾性分析经临床确诊的 SCD 患者 36 例，所有患者均行脊柱 MRI 扫描，其中 8 例行增强 MRI 扫描。36 例患者中 19 例表现为 T2 加权图像上异常信号，灵敏度为 52.8%，其中 18 例病变位于脊髓后份，1 例病变发生于胸髓前份。所有 MRI 表现异常的患者中，12 例异常信号位于颈髓（33.3%），7 例病变位于胸髓（19.4%）。颈髓出现异常信号者 5 例，在轴位 T2 加权像上呈对称线性高信号，即“倒 V”字征，是 SCD 的典型影像学表现。胸段脊髓异常信号在 T2 加权像上呈对称性“望远镜”样高信号。8 例增强 MRI 检查的患者仅有 1 例病变表现出轻度强化。所有 36 例患者在适当补充维生素 B-12 治疗后临床症状得到改善。2 例 MRI 随访见异常信号范围较前缩小。因此，传统的 MRI 检查对诊断及评估维生素 B-12 缺乏引起的亚急性脊髓联合变性具有价值。

关键词：常规磁共振、脊髓亚急性联合变性、维生素 B-12、缺乏、营养