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MRI of spinal cord and brain lesions in subacute combined degeneration

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Abstract Subacute combined degeneration is a rare cause of demyelination of the dorsal and lateral columns of the spinal cord and even more rarely of the pyramidal and spinocerebellar tracts and cerebellum. We present the initial and follow-up MRI appearances in a patient with subacute combined degeneration of the spinal cord, brain stem and cerebellum, due to vitamin B_{12} deficiency. The lesions in these structures were demonstrated clearly as pathologically high-signal areas on T2-weighted images. These lesions, except those of the brain stem and cerebellum, disappeared 4 months after therapy. MRI 14 months after the patient's discharge on vitamin B_{12} therapy showed the same picture.

Key words Degeneration subacute combined · Spinal cord · Brain · Magnetic resonance imaging · Vitamin B_{12} deficiency

Introduction

Vitamin B_{12} deficiency can induce subacute combined degeneration (SCD) of the spinal cord. The brain and optic and peripheral nerves may be involved. There is degeneration of myelin and axons and, at a later stage, axonal loss and Wallerian degeneration of the posterior and lateral columns of the spinal cord, typically beginning in the thoracic region and ascending or descending. The neurological disturbances consist of dysaesthesiae and disturbance of deep sensation, mainly affecting the legs and typically manifest as sensory ataxia.

MRI gives us the opportunity to demonstrate such lesions in the spinal cord and to follow their progress while vitamin B_{12} is administered. To our knowledge there are only four previously reported patients with SCD in whom signal abnormalities of the dorsal columns of the spinal cord have been documented on MRI. All showed lesions on MRI restricted to the spinal cord.

We present the MRI findings in a patient with SCD not only of the spinal cord, but also in the brain stem and the cerebellum, including the follow-up, in which the spinal and brain lesions differed.

Case report

A 60-year-old woman was admitted with gradual gait disturbance following a cholecystectomy 2 months previously, during which nitrous oxide was administered. Since then, she had been unable to walk unaided and in the last week could neither stand nor walk at all. Her husband said she showed a gradually increasing memory disorder. During the past year she had felt numbness in both hands. Because of a thrombosis in the legs she was on anticoagulant therapy.

The patient was alert, but with impaired orientation for time and place and impaired memory. She showed horizontal gaze-evoked nystagmus, predominantly to the right. There was a reduction of the deep tendon reflexes of the arms; the knee and ankle reflexes were increased with a Babinski sign on the right. The abdominal reflexes were absent. The patient had a spastic paraparesis. Vibration sense was markedly reduced in the legs, and position sense was absent. There was glove and stocking reduction of sensation to pinprick and light touch. The finger-nose test was normal. The patient was unable to walk und to stand without support.

Electroneurography, electromyography and evoked potentials confirmed severe damage of peripheral and central afferent fibres, responsible for the severe gait disturbance due to sensory ataxia. The electroencephalogram showed mild general slowing without focal abnormalities.

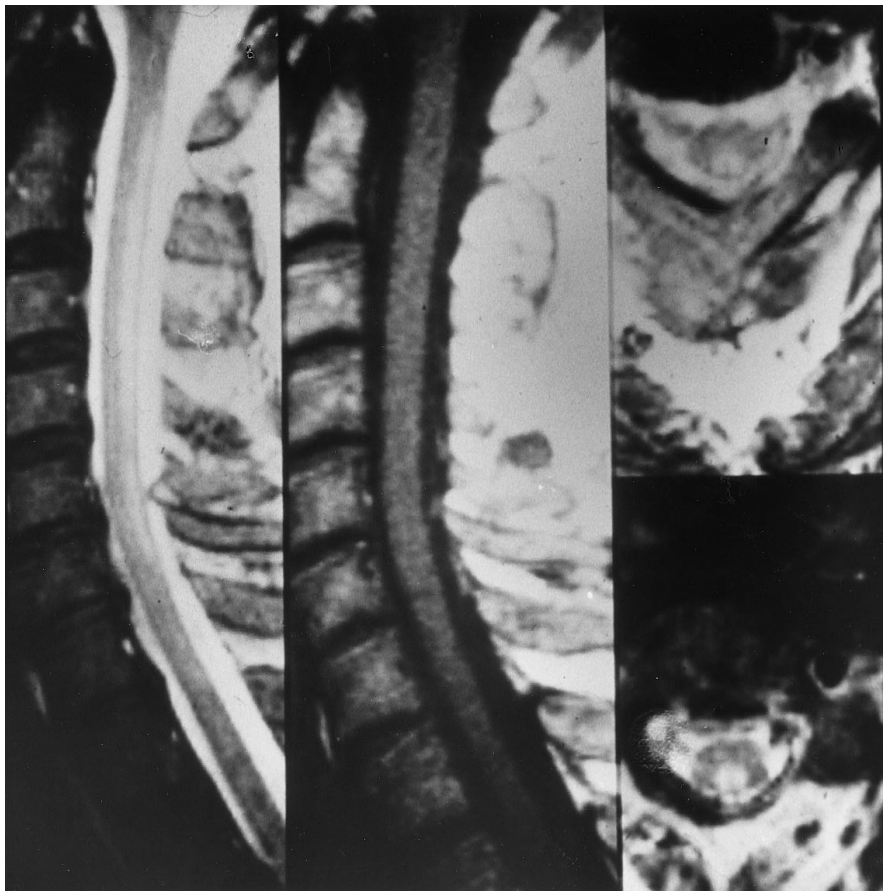

Fig. 1 Second MRI study of the cervical spinal cord showing the demyelination of the dorsal columns as high intensity lesions on T2-weighted images

Laboratory studies demonstrated a decreased haemoglobin level and a normal haematocrit (13.1 g/dl and 51.5 %, respectively), elevated mean corpuscular volume (117.7 fl) and haemoglobin (37.1 pg), decreased thrombocytes (182 000/µl), parietal-cell antibodies and low serum vitamin B_{12} (< 100 pg/ml). Cerebrospinal fluid analysis, including an assay for oligoclonal bands, was normal. Gastroscopy showed atrophic gastritis. A Schilling test could not be performed because treatment with vitamin B_{12} was begun directly after admission.

Initial whole-spine MRI excluded a spinal tumour and showed mild spondylosis without cord compression. An examination of the cervical spinal cord 2 weeks later demonstrated increased signal intensity within the dorsal columns on T2-weighted images (Fig. 1). The lateral columns were not involved. Suspected involvement of the brain stem and cerebellum was confirmed by cranial MRI. This also revealed abnormal signal on T2-weighted images in the medulla oblongata, pons and mesencephalon (Fig. 2). A lesion of similar intensity was demonstrated in the right crus cerebelli. Given the combination of atrophic gastritis, encephalopathy, myelopathy and peripheral neuropathy, as well as the prompt effect of vitamin B_{12} substitution, a diagnosis of SCD or funicular myelosis was made.

Because of the patient's severe condition, treatment with vitamin B_{12} was begun directly after admission, administration being first intramuscular, then intravenous. During therapy the neurological deficits rapidly resolved and she could walk without support at the end of her stay in hospital (2.5 months).

Four months after hospital discharge, she was much improved, with a persistently increased right patellas reflex. Electrophysiological studies showed mild damage to central afferent fibres. MRI of the cervical spinal cord and brain revealed persistent high signal in the pons, mesencephalon and cerebellum but not in the dorsal columns (Fig. 3). At 14 months' follow-up the patient demonstrated continued clinical improvement. MRI of the brain showed no change, suggesting that the intracranial lesions were irreversible (Fig. 4).

Discussion

There are many conditions in which vitamin B_{12} deficieny may develop. Their aetiology can be divided into three main categories: inadequate intake (vegetarians – rare), malabsorption; and other conditions (nitrous oxide anaesthesia, transcobalamin II deficiency – rare), malabsorption being the most important. The most common cause of malabsorption is pernicious anaemia, followed by gastrectomy, intestinal infections and ileal abnormalities (tropical sprue).

Although the clinical manifestations are those of each condition, certain features involving the blood, gastrointestinal tract and nervous system, are common to all.

The neurological manifestations are the most worrying, because they often fail to remit completely on

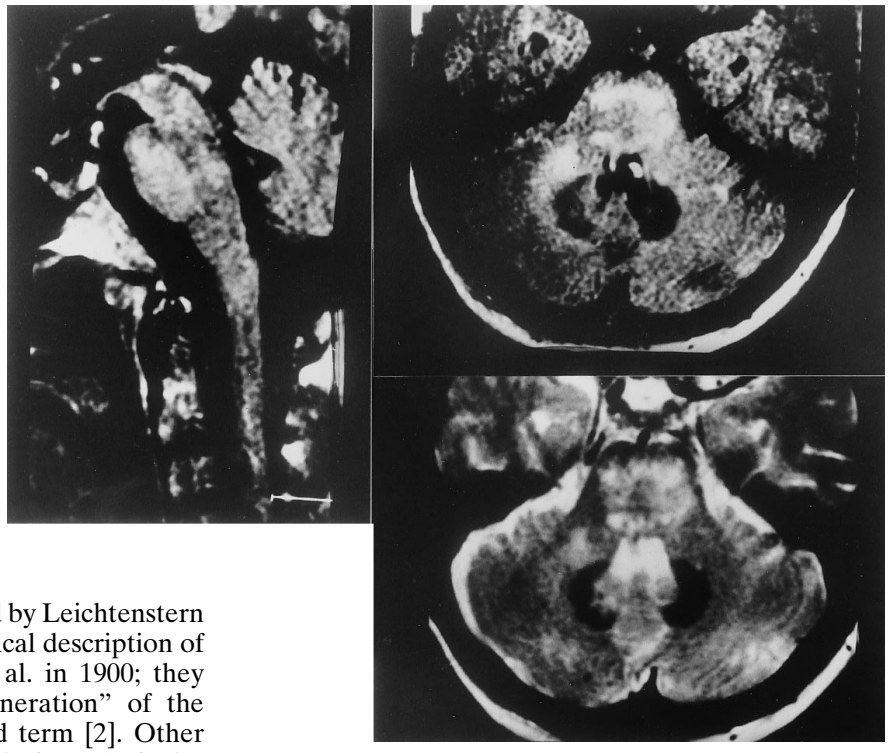

Fig. 2 Demyelination of the medulla oblongata, pons, mesencephalon and crus cerebelli

treatment [1]. They were first reported by Leichtenstern in 1884. The full clinical and pathological description of the disease was given by Russell et al. in 1900; they named it "subacute combined degeneration" of the spinal cord, the most commonly used term [2]. Other terms proposed were "funicular myelosis", "funicular spinal disease" (in the German-speaking area) and "vitamin B_{12} neuropathy" [3]. The term "subacute" describes the course of the clinical features, in which functional disturbances increase fairly rapidly and can cause severe disability in a few weeks or months [2]. Patients experience paraesthesiae, stiffness, numbness or tingling of the limbs (the earliest neurological manifestation), slight sensory ataxia and loss of posterior column function.

SCD is an uncommon cause of myelopathy today. Clinical presentation of patients with vitamin B_{12} deficiency is different today, and less advanced than in the past, possibly due to improved treatment. Clinical improvement and full recovery from myelopathy can occur when treatment is started in the early stages of the disease [4].

Neuropathological findings initially include swelling of myelin sheaths with little change in the axons in the posterior columns of the upper cervical segments (funiculus gracilis and spinocerebellar tracts) and in the lateral columns, which typically commences in the thoracic cord, but can extend to involve other levels. Later, myelin sheath and axonal degeneration and loss are seen, leading to Wallerian-type degeneration of the long tracts. Sites of involvement also include peripheral nerves, cerebrum and optic nerves, although a relatively small number of cases of the latter have been reported [2].

The specific biochemical mechanisms causing demyelination of the spinal cord in SCD are not clear. Deficiencies of methionine and *S*-adenosylmethionine are found in association with demyelination due to defective methylfolate metabolism [5, 6]. Vitamin B_{12} is a coenzyme which, together with folate, is essential for the formation of methionine from homocysteine. Methionine is converted to *S*-adenosylmethionine, which serves as a donor of methyl groups for reactions including methylation of myelin basic protein [7].

Diagnosis is based on the clinical features and laboratory estimation of vitamin B_{12} levels [1]. MRI has recently been used for detecting SCD. It is the imaging method of choice for showing the demyelination of the spinal cord, seen as high-signal lesions on T2-weighted images. The typical distribution of the lesions in the dorsal and dorsolateral region, visible in axial sections, may confirm the diagnosis of SCD. MRI is the only imaging modality by which these appearances can be demonstrated [8]. However, the final diagnosis can be established by the best clinical and laboratory correlation.

In our patient, symptoms began after administration of nitrous oxide during surgery. Nitrous oxide enhances oxidation of vitamin B_{12}, thereby rendering it ineffective. In a patient with borderline B_{12} levels in serum, such exposure can precipitate the complications of B_{12} deficiency [8].

The first MRI study of our patient showed no abnormality in the dorsal columns, presumably because of the subacute course of the disease. The later stages of

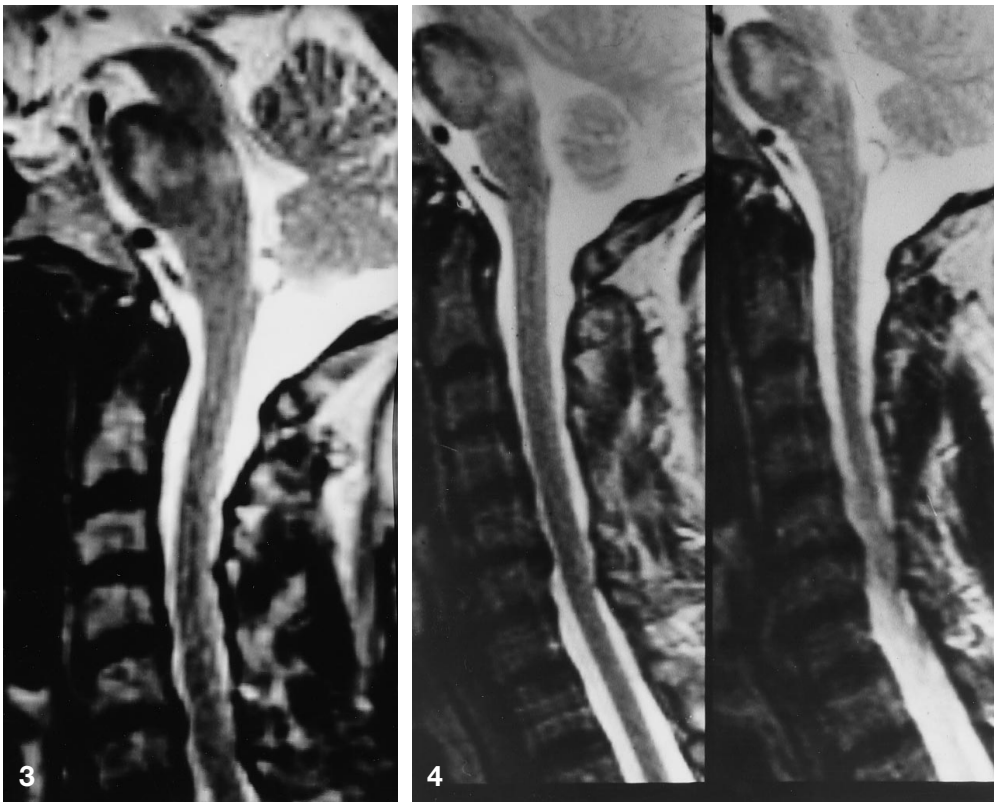

Fig. 3 Follow-up study 4 months after administration of vitamin B_{12}

Fig. 4 Follow-up study 14 months after starting therapy showing the irreversibility of the brain lesions in contrast to the reversible spinal cord lesions

the disease may show on MRI. This could be why the MRI examination of the cervical spinal cord became abnormal 2 weeks later. This case demonstrates that MRI can show the exact location and extent of lesions caused by vitamin B_{12} deficiency, and be used to assess the response to vitamin B_{12} therapy. To the best of our knowledge there are only four previous reports in the literatur [7, 9–11] on MRI abnormalities in SCD, all referring only to the myelopathy. We showed the intracranial extension of this severe complication of vitamin B_{12} deficiency for the first time on MRI, indicating that the intracranial damage may be irreversible.

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