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MRI of the spinal cord in myelopathy complicating vitamin B_{12} deficiency: two additional cases and a review of the literature

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Abstract Focal spinal cord lesions have been present in all previously reported cases of MRI appearances in myelopathy complicating vitamin B_{12} deficiency. We describe two further cases showing mild atrophy only and review the salient features of the previous 11 publications. MRI findings reflect quite closely the known pathological changes in this condition.

Key words Magnetic resonance imaging · Spinal cord · Vitamin B_{12} deficiency

Introduction

In myelopathy complicating vitamin B_{12} deficiency MRI has demonstrated focal abnormal signal in the spinal cord prior to the institution of replacement therapy [1–11]. To our knowledge there are, to date, no descriptions of cases in which MRI abnormalities of this nature were *not* found. We describe two such patients and review the salient features of the 11 previously reported.

Case reports

Case 1

A 34-year-old African woman was referred with a history of inability to walk for 17 months. The problem had first commenced 19 months previously, with a burning sensation in both feet. Progressive weakness and stiffness of the lower limbs followed quite rapidly. Examination showed a spastic paraparesis with absent Achilles reflexes and positive Babinski sign bilaterally. Light touch and pain were diminished in a glove and stocking distribution; vibration and passive movement sense were markedly impaired distally at the feet. Romberg's test was positive.

Laboratory investigations disclosed a red cell count of 3.84×10^{12}/l, haemoglobin 13.3 g/dl and mean cell volume (MCV) 107.7 fl. Serum vitamin B_{12} was < 74 pmol/l (reference range, 118 to 840 pmol/l) and folate 42.8 mmol/l (3.8 to 38.9 mmol/l). The Schilling test gave normal results. Endoscopy revealed no abnormality of the gastric mucosa, but biopsy showed changes of chronic gastritis. Antibody to intrinsic factor was not detected. We found that the patient had a fluctuating intake of the recommended daily allowance of vitamin B_{12}, mainly less than 75 per cent, and we concluded that the low level of serum vitamin B_{12} was caused by inadequate intake.

Nerve conduction studies indicated a severe sensorimotor neuropathy, the underlying pathology appearing to be axonal. Cerebrospinal fluid (CSF) contained no white cells and 0.54 g/l total protein. Tests for syphilis were negative in both blood and CSF. Serum antibody to HIV and to HTLV-I was not detected.

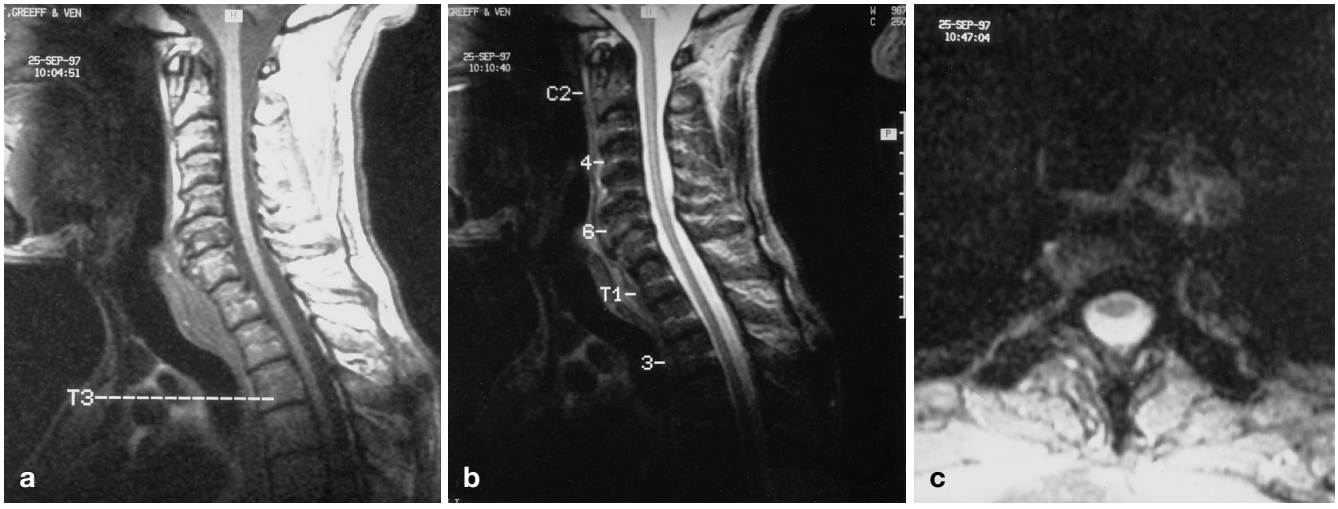

Fig. 1 a–c Case 2. MRI showing mild atrophy of the thoracic spinal cord. **a** T1-weighted **b** proton density and T2-weighted sagittal image. **c** T2-weighted axial spin-echo image at T3

MRI of the spinal cord at 1 T with T1-weighted, proton density-weighted and T2-weighted sequences showed the cervical spinal cord to be of normal calibre, with normal signal intensity. The thoracic spinal cord appeared thin, but its signal intensity was normal.

Treatment with parenteral hydroxycobalamin was followed by modest recovery, with ability to walk returning after approximately 6 months.

Case 2

A 68-year-old African man was admitted with a 21-month history of progressive difficulty in walking. He had been unable to get about on his own for the last 9 months. Examination disclosed wasting of small hand muscles and weakness of all limbs. Tone was increased in the legs, while deep tendon reflexes were hyperactive at the knee and absent at the ankle; plantar responses were both mute. Sensory testing gave inconsistent findings. Support was required to stand and the patient could not walk.

Laboratory tests disclosed a red cell count of 3.07×10^{12}/l, haemoglobin 10.6 g/dl and MCV 111.9 fl. Serum vitamin B_{12} was < 74 pmol/l and folate 8.64 mmol/l. The Schilling test gave results consitent with (intestinal) malabsorbtion. Normal values were obtained for serum albumin, calcium, cholesterol and iron. Endoscopy revealed no abnormality of the gastric mucosa. An upper gastrointestinal barium series was incomplete and could not be repeated.

Nerve conduction studies showed a severe sensorimotor neuropathy, the underlying pathology appearing to be axonal. The CSF contained no white cells and 0.31 g/l total protein. Tests for syphilis were negativ in both blood and CSF. Antibody to HIV and to HTLV-I was not detected.

On MRI of the spinal cord at 1.5 T with T1-weighted, proton density-weighted and T2-weighted spin-echo sequences the cervical region appeared normal. The thoracic spinal cord appeared thin. No other abnormality was evident (Fig. 1).

Treatment with parenteral hydroxycobalamin resulted in rapid recovery. After 3 weeks the patient could walk with a frame.

Discussion

The pathological changes known to occur in myelopathy complicating vitamin B_{12} deficiency provide the basis for interpretation of the MRI appearances found so far (Table 1).

Microscopically, the earliest event is swelling and ballooning of myelin sheaths, caused by formation of intramyelinic vacuoles and separation of myelin lamellae. Progressive enlargement of these lesions imparts a spongy appearance to the affected white matter. The changes begin in the posterior columns of the lower cervical and upper thoracic segments of the spinal cord, spreading thereafter longitudinally and transversely. Eventually, axis cylinders and myelin sheaths are involved and undergo degenerative changes. Phagocytosis of the debris by macrophages is followed by reactive astrocytosis. The degree of fibrous gliosis tends to correlate with duration of the disease and the rate of its progression, becoming pronounced in the more slowly progressive cases or when considerable tissue has been destroyed. Atrophy of the posterior and lateral columns may develop in longstanding, severe cases [12–14].

Demyelination, wallerian degeneration and gliosis are all seen as high-signal lesions on T2-weighted images. In the eight cases where such findings were present initially and subsequently resolved or reversed, *after* B_{12} therapy, it is reasonable to argue that demyelination was the underlying pathology [1–3, 5, 7–11]. In two of these cases there was also evidence of cord expansion [8, 10]. There was no evidence of enhancement in the one patient given contrast medium [8]. MRI was performed in these cases between 2 weeks and 2 months after the onset of symptoms. Possibly, therefore, those appearances could still be reflecting the early changes of myelin-sheath swelling.

Contrast medium is recorded as being given to three of the 11 patients in whom focal lesions were detected

Table 1 MRI findings in reported cases of myelopathy complicating vitamin B_{12} deficiency

Reference	Age (years)	Sex	Race	Duration of symptoms (months)	Cause of B_{12} deficiency	MRI		
						Initial		Follow-up (months)
						T2-weighted images	T1-weighted images	
1	43	Male	Black	6	Pernicious anaemia	High signal C3-4		Normal (36)
2	36	Female	?	12	Pernicious anaemia	High signal C3-6		Normal (4)
3	69	Male	?	3	Pernicious anaemia	High signal cervical		Improved (10)
4	68	Female	?	7	Pernicious anaemia	High signal whole cord		Unchanged (2)
5	66	Male	?	3	Malabsorption	High signal T9-11		Normal (2.5)
6	10	Male	Hispanic	0.5	Pernicious anaemia	High signal whole cord	Low signal Contrast enhancement C5-6	None
7	65	Female	?	?	Pernicious anaemia	Posterior high signal C2-7		Improved (2.5)
8	38	Male	?	2	Pernicious anaemia	High signal C1-5	Swollen upper cervical cord	Normal (6)
9	50	Female	?	5	Malabsorption	High signal thoracic cord	Contrast enhancement Cervical and thoracic cord	Normal (18 days)
10	73	Female	?	0.5 +	Chronic atrophic Gastritis	High signal posterior, lateral cord	Cervical and thoracic swelling	Improved (8)
11	54	Male	?	6	Chronic atrophic Gastritis, enteritis	High signal cervical, thoracic cord		Normal (36)
This report								
	34	Female	Black	20	Diet	Normal signal	Slight atrophy thoracic cord	None
	66	Male	Black	21	Malabsorption	Normal signal	Mild atrophy thoracic cord	None

[6, 8, 9]; pathological contrast enhancement was seen in two [6, 9]. This would suggest either a significantly different vascularity of the lesion compared to the surrounding tissues, or, more likely, an increase in the permeability of the blood spinal cord barrier [15]. Support for the latter interpretation is given by the occasional occurrence in subacute combined degeneration of an elevated CSF total protein concentration [16]. However, the CSF findings were not recorded for the patient described by Wolansky et al. [6], while normal values were reported by Küker et al. [9]. Contrast enhancement of the lesion therefore remains to be explained in these instances.

Persistence of high signal intensity *following* treatment with B_{12} was recorded in four of the 11 cases [3, 4, 7, 10]. The final MRI was done in these patients between 10 weeks and 10 months after treatment had commenced. Insofar as one only of the eight patients in whom the abnormal signal regressed or resolved after therapy was restudied earlier than 10 weeks [5], demyelination, wallerian degeneration, gliosis or a combination of all three have to be considered as an explanation for persistence of abnormal signals after appropriate therapy.

Atrophy of the spinal cord is a late change in the myelopathy of vitamin B_{12} deficiency. Our two patients gave a history of symptoms beginning at least 20 months before the MRI. The appearance in both cases of cord thinning may thus be explained by the length of time a pathological situation had existed. Absence of such changes in each of the other ten patients for whom relevant information was recorded can be interpreted similarly: namely, that symptoms had been present for 12 months or less in all of them.

Animal experiments have shown that gliosis can in fact occur *without* change in signal intensity on T2-weighted images [17]. This finding may be invoked to explain the resolution of high signal after therapy in six of the previously reported cases and evidence only of atrophy in our own patients. However, the experimental lesions were produced acutely by cold injury while nerve fibres within the affected tissue, as well as their

myelin sheaths, showed no obvious pathological change. The two situations may therefore not be sufficiently analogous for sound inferences to be drawn.

MRI findings so far reported in the myelopathy complicating deficiency of vitamin B_{12} thus reflect rather closely the known pathology of this condition. Several types of abnormality are seen, apparently depending on the duration of symptoms. Early lesions can show cord swelling, with or without contrasts enhancement. These also manifest as areas of high signal on T2-weighted images and tend to disappear after replacement therapy. The cord may be atrophied in patients who present a long time after symptoms first commence.

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