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MRI and clinical features in amyotrophic lateral sclerosis

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Abstract MRI of the brain and spinal cord was performed in 21 patients with amyotrophic lateral sclerosis (ALS), 8 normal volunteers and 16 neurological disease controls. High signal was seen in the intracranial corticospinal tract in 16 of the 21 patients on T2-weighted and in 10 on proton density (PD)-weighted images. In one patient, the high signal on T2-weighted images became less marked with progression of the disease. Low signal intensity was seen in the motor cortex in 12 of the 21 patients. High signal in the anterolateral column of the spinal cord on T1 weighted images was seen in 14, and high signal in the lateral corticospinal tract on T2 weighted images was seen in 7 of the 21 patients. The relationship between the abnormal images and upper motor neurone signs remained unclear. High signal intensity was seen in the corticospinal tract in the brain on T2-weighted images in two normal volunteers and four disease controls, and on PD weighted images in three disease controls. Low signal intensity in the motor cortex on T2 weighted images was seen in three normal volunteers and four disease controls. However, high signal intensity was seen in the intracranial corticospinal tract on T1 weighted images in five patients with ALS who showed pronounced upper motor neurone signs including spastic paraparesis, but not in controls. Thus, abnormalities on MRI in the brain and spinal cord should be considered in the diagnosis of ALS, and high signal intensity of the intracranial corticospinal tract on T1-weighted images may reflect the severe pathological changes of the upper motor neurones in ALS.

Key words Amyotrophic lateral sclerosis · Magnetic resonance imaging

Introduction

Abnormalities on MRI of the brain and spinal cord have been reported in amyotrophic lateral sclerosis (ALS) [1]. T2-weighted images may disclose high signal in the corticospinal tract of the brain and spinal cord, which reflect the degeneration of the corticospinal tract [1–6]. Lesions in the motor cortex in ALS are often seen as low signal on T2-weighted images [1, 7, 8].

However, some of these findings are also seen in normal controls or in other diseases and are not necessarily specific to ALS [1, 9, 10]. Moreover, the correlation between abnormalities on MRI and clinical features such as severity of the upper motor neurone signs in ALS is controversial [1]. In this study, MRI findings in the brain and spinal cord are compared with the clinical features of ALS.

Table 1 Clinical and MRI features in patients with amyotrophic lateral sclerosis

Case	Age (years)	Sex	Duration* (months)	Initial symptom[a]	Bulbar signs	Upper motor neurone signs[b]	Lower motor neurone signs	MRI					
								intracranial corticospinal tract			motor cortex T2 low	spinal cord	
								T1 high	PD high	T2 high		T1 high	T2 high
1	27	F	5	SP	−	++	+	+	+	+	−	+	+
2	45	M	6	SP	+	++	±	+	+	+	+	+	+
3	50	M	6, 48	SP	+	++	+	+	+	+	+	−	−
4	53	F	8, 14	SP	−	++	±	+	+	+	−	+	+
5	56	F	12	SP	−	++	+	+	+	+	−	−	−
6	60	M	10	U/p	−	+	+	−	+	+	−	+	+
7	48	F	10	U/p	−	+	+	−	+	+	−	+	−
8	57	M	10	U/p	−	+	+	−	−	+	−	−	−
9	71	F	12, 24	U/p	+	±	+	−	−	+	+	+	−
10	66	M	6	U/d	+	±	+	−	−	+	+	+	−
11	52	M	13	U/d	+	+	+	−	+	+	−	+	+
12	60	M	14	U/d	+	+	+	−	+	+	−	+	+
13	58	M	18	U/d	+	+	+	−	−	−	+	+	+
14	75	M	24	U/d	−	±	+	−	−	−	+	+	−
15	70	F	36	U/d	+	±	+	−	−	−	+	+	−
16	68	F	4	L/p	−	+	+	−	+	+	+	−	−
17	52	M	24	L/p	−	+	+	−	−	+	+	+	−
18	54	M	8	L/d	+	+	+	−	−	+	−	−	−
19	60	M	12	L/d	+	+	+	−	−	−	+	−	−
20	66	M	6	B	++	±	+	−	−	−	+	+	−
21	71	M	12	B	++	+	+	−	−	+	+	−	−

* interval between the onset of symptoms and MRI

[a] intial symptom: *SP* spastic paraparesis *U/p* proximal dominant muscular atrophy of the arms *U/d* distal dominant atrophy of the arms *L/p* proximal dominant muscular atrophy of the legs *L/d* distal dominant muscular atrophy of the legs *B* Bulbar symptoms

[b] upper motor neurone signs: ± only increased tendon reflexes + increased tendon reflexes and Babinski's sign without marked spasticity ++ spastic paraparesis

Materials and methods

MRI was performed on 21 patients with ALS (14 men, 7 women aged 27–75 years); serial studies were in cases 3, 4 and 9 during the course of their illness. The duration of illness ranged from 4 months to 4 years, mean 18.8 months. The diagnosis of ALS was established clinically on the basis of the history and physical and electrophysiological examinations. In five patients (cases 1–5), the initial symptoms were spastic paraparesis. Their upper motor neurone signs, including spasticity, increased tendon reflexes and Babinski's sign, were manifest during the course of their illness, especially cases 2 and 4; lower motor neurone signs such as muscular atrophy and electromyographic evidence of denervation were equivocal at the initial stage of the disease.

MRI was also performed on 8 normal volunteers (5 men, 3 women, age 28–72 years, mean 56 years) and 16 neurological disease controls (9 men, 7 women, age 32–75, mean 57 years): cervical spondylotic myelopathy (4 cases), bulbospinal muscular atrophy (4), HTLV-1-associated myelopathy (2), adrenomyeloneuropathy (AMN) (2), leukoencephalopathy of unknown aetiology presenting as spastic paraparesis (2) and Binswanger's disease with dementia and spastic paraparesis (2).

A 1.5 T imager was used in all cases. T1-weighted images of the brain were obtained by a fast spin-echo (FSE) pulse sequence, repetition time of 400 ms echo time 19 ms. FSE T1-weighted images of the cervical spinal cord were obtained with repetition time 500 ms and echo time 25 ms. FSE T2- and proton density (PD)-weighted images of the brain and cervical spinal cord were obtained with repetition time 3000 ms and echo times of 100 and 40 ms; echo-train length was 8, with one excitation, 256 × 192 matrix, field of view 20 cm, and contiguous 5 mm axial slices. The images were analysed visually by two radiologists blind to the patients' histories.

Results

The clinical and MRI findings in the 21 patients with ALS are shown in Table 1.

Cases 1–5 who presented with spastic paraparesis and other prominent upper motor neurone signs showed high signal on T1-weighted images in the centrum semiovale, corona radiata and posterior limb of the internal capsule which corresponded to the large myelinated fibres of the corticospinal tract (Fig. 1). There was also high signal extending from the corona radiata to the cerebral peduncle on the T2-weighted and PD-weighted images.

Of the other 16 patients with ALS whose upper motor neurone signs were not so manifest (cases 6–21), high signal was seen in the corticospinal tract on T2-weighted images was seen in 11 (cases 6–12, 16–18 and 21); five (cases 6, 7, 11, 12 and 16) of these also showed high signal on the PD-weighted images.

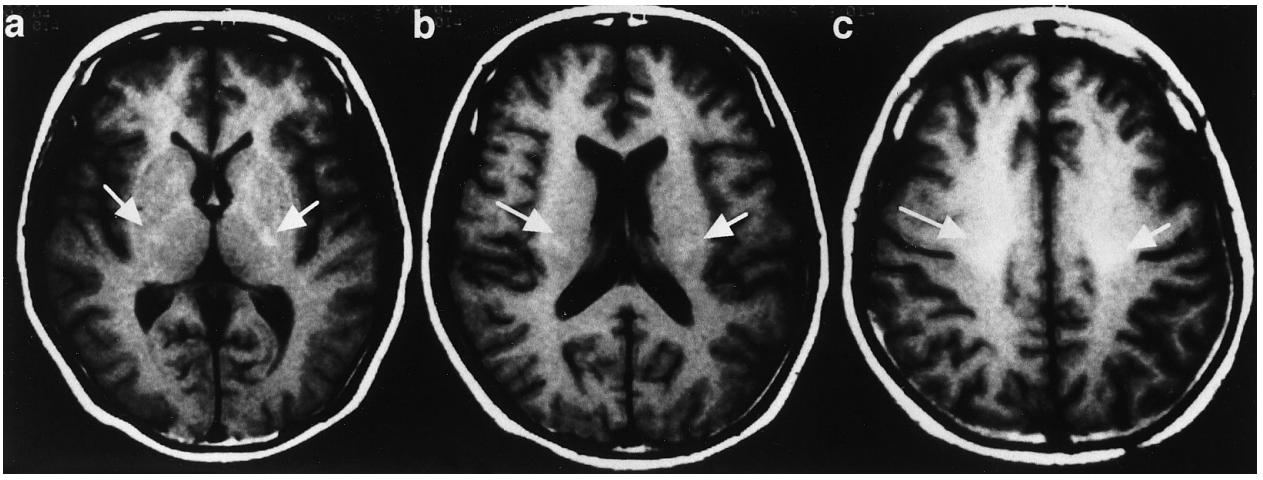

Fig. 1 Axial T1-weighted images of Case 4 disclose symmetrical high signal intensity areas along the course of the corticospinal tract *(arrows),* at the level of the posterior limb of the internal capsule **a**, corona radiata **b** and centrum cemiovale **c**

Low signal was seen in the motor cortex on T2-weighted images in 12 of the 21 patients (cases 2, 3, 9, 10, 13–17 and 19–21).

In one of the three patients who underwent serial MRI (case 3), the high signal in the corticospinal tract on T2-weighted images gradually became less marked with progression of the disease, and had almost disappeared when the patient became bed-ridden (Fig. 2), there was no remarkable change on T1- or PD-weighted images.

High signal was also seen in the corticospinal tract on T2-weighted images in two of the eight normal volunteers and four of the 16 disease controls: two each with AMN and leukoencephalopathy presenting spastic paraparesis. High signal was also seen on PD-weighted images in one with AMN and both with leukoencephalopathy). High signal in the corticospinal tract on T2-weighted images in normal volunteers was seen as either low or isosignal intensity on T1- and PD-weighted images.

Low signal was also seen in the motor cortex on T2-weighted images in three of the eight normal volunteers and four of the 16 disease controls: one with a bulbospinal muscular atrophy, two with leukoencephalopathy and one with Binswanger's disease.

High signal was seen in the anterolateral columns of the cervical spinal cord on T1-weighted images in 14 patients (cases 1, 2, 4, 6, 7, 9–15, 17 and 20) (Fig. 3 a), but not in controls. High signal intensity in the lateral part, which corresponded to the lateral corticospinal tract of the cervical spinal cord was seen on T2 weighted images in 7 patients (cases 1, 2, 4, 6 and 11–13) (Fig. 3 b). However, high signal was also seen on T2-weighted images in two patients with cervical spondylotic myelopathy.

Discussion

The abnormalities on MRI correspond to the sites of degeneration found in previous pathologial studies [11–13], and may reflect degeneration of the upper motor neurones in patients with ALS. Low signal intensity in the motor cortex on T2 weighted images in ALS may reflect excessive iron deposition following degeneration of the upper motor neurones [7, 8]. Recently, we indicated that high signal intensity on T1 weighted images of the anterolateral column of the spinal cord was frequently seen in patients with ALS, and suggested that this new observation may be useful for the diagnosis of this disease [14].

In the present study, high signal in the corticospinal tract on T2- (16 of 21) and PD- (10 of 21) weighted images and low signal in the motor cortex on T2 weighted images (12 of 21) were seen frequently in patients with ALS. However, they could be also seen in normal and disease controls as others have also found [1, 9].

In contrast, high signal intensity on T1 weighted images of the anterolateral column of the cervical spinal cord which includes the corticospinal tract was seen only in patients with ALS (14 of 21) as previously indicated [14], but there was no clear relationship between these abnormalities and clinical features such as severity of the upper motor neurone signs.

In addition, five patients with ALS with severe upper motor neurone signs such as spastic paraparesis showed high signal in the intracranial corticospinal tract on T1-weighted images as well as on T2- and PD-weighted images. This was not seen in other patients with ALS whose upper motor neurone signs were not so manifest, nor in controls.

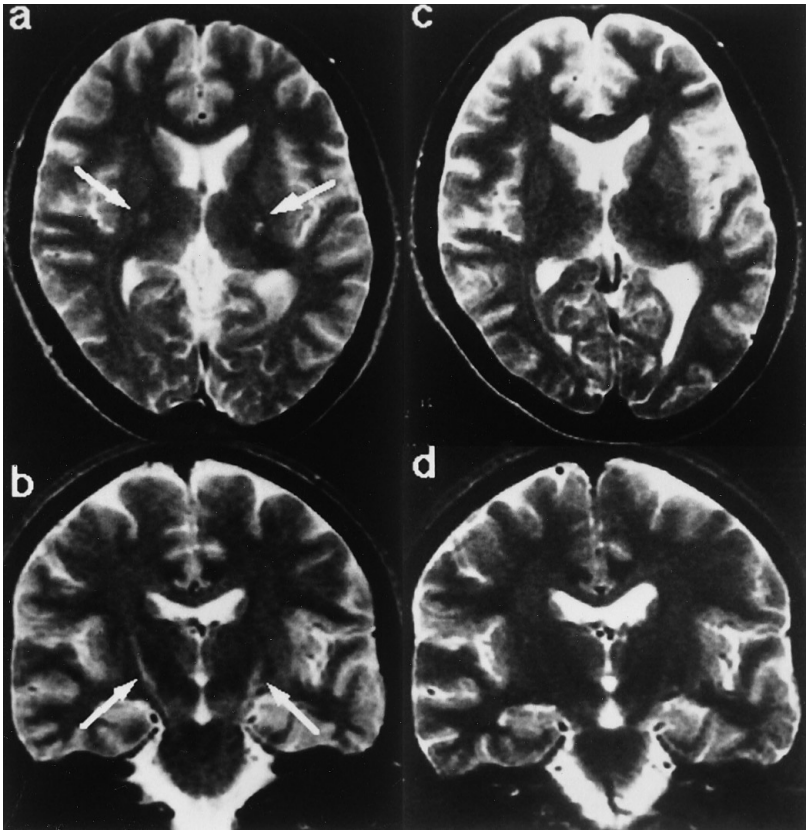

Fig. 2 High signal intensity in the corticospinal tract on T2-weighted images of Case 3. **a** Axial image at the level of the internal capsule **b** coronal image. After 6 months from onset *(arrows)*. These have almost disappeared after 4 years **c, d**

Segawa [10] also demonstrated high signal in the intracranial corticospinal tract on T1-weighted images in patients with ALS but not in normal and disease controls, as in the present study.

Although the cause of the high signal on T1 weighted images (T1-shortening) of the intracranial corticospinal tract and the spinal cord is undetermined, pathological changes seen in ALS, such as lipid-laden macrophages, accumulation of intra-axonal neurofilaments [13, 15] and an increase of intracellular proton density in the corticospinal tract may contribute to T1-shortening [14, 16, 17]. High signal on T1 weighted images in the intracranial corticospinal tract may be specific for ALS and may correlate with the severity of the upper motor neurone lesions.

The high signal in the corticospinal tract on T2-weighted images became less marked with progression of the disease in one patient. Although their cause is unknown, the MRI changes may reflect the decrease of protein-bound proton density due to pathological changes such as the development of fibrillary gliosis in the corticospinal tract as the disease progresses [18]. This

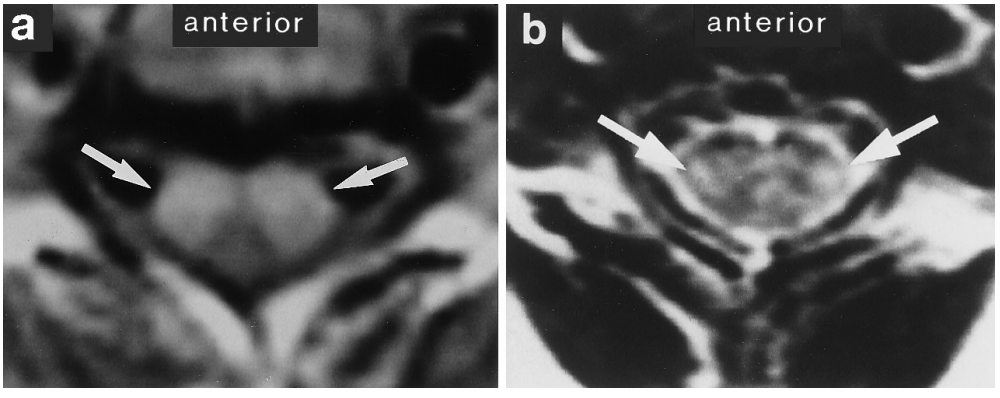

Fig. 3 Axial T1-weighted image of Case 6 showing symmetrical high signal intensity *(arrows)* in the anterolateral column of the cervical spinal cord at C4–5 **a**, and T2-weighted image showing high signal *(arrows)* in the lateral corticospinal tract at the same level **b**

case and a previously reported one [19] suggest that MRI findings may be variable at the stage of the disease, and related to pathological processes during the progression of the disease in ALS.

The findings suggest that examining the corticospinal tract of the brain and spinal cord with conventional T1-, PD- and T2-weighted images, and also serially, may be useful in the diagnosis of ALS. Further study is required to establish whether the high signal intensity in the intracranial corticospinal tract on T1 weighted images correlates with the severity of the upper motor neurone lesion.

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