CASE REPORT

Imaging diagnosis of upper motor neuron compromising in a patient with Chiari 1 malformation

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SUMMARY

We report a case of a typical MRI from a patient with bulbar-onset sporadic amyotrophic lateral sclerosis associated with Chiari type 1 malformation. Our report reinforces the conventional neuroimaging appearance associated with each condition and the associated abnormalities on a clinical and advanced imaging techniques basis. The MRI signal intensity was useful for detecting upper motor neuron degeneration based on corticospinal tract signal intensity, while diffusion tensor imaging parameters were limited to this purpose. Our description reinforces the relevance of the T1 magnetisation transfer sequence to demonstrate corticospinal tract degeneration and corroborate an amyotrophic lateral sclerosis diagnosis in an individual participant, when there is a potential concurrent 'amyotrophic lateral sclerosis mimic syndrome'. To our knowledge, this is the first description of the non-conventional MR techniques applicability to distinguish the impact of amyotrophic lateral sclerosis from Chiari 1 malformation.

BACKGROUND

Bulbar onset of amyotrophic lateral sclerosis (ALS) has rarely been associated with Chiari 1 malformation.

We present a report of this rare association in which recently developed imaging techniques were used to estimate the impact of the disorders and to demonstrate corticospinal tract degeneration.

This description reinforces the relevance of the T1 magnetisation transfer sequence to demonstrate corticospinal tract degeneration and corroborate an ALS diagnosis in an individual participant, when there is a potential concurrent 'amyotrophic lateral sclerosis mimic syndrome'.

CASE PRESENTATION

A 49-year-old man, who had been working as a manual labourer stacking boxes in a warehouse for the past 30 years, presented with a 6-month history of progressive slurred speech and moderate dysphagia. He had progressive asymmetric weakness and wasting (right to left) that had spread from his lower limbs to his upper limbs over the previous 3 months. Discrete amyotrophy of his right hand and myofasciculations in different regions (thorax, limbs and tongue) were also present. He had no cognitive impairment. The diagnosis of sporadic ALS with bulbar onset was confirmed according to

the current criteria. In order to exclude its mimics, the patient was submitted to a brain MRI.

INVESTIGATIONS

The patient was submitted to a brain MRI study in order to exclude diseases that could simulate amyotrophic lateral sclerosis.

A Philips 1.5 T MR scanner was used to acquire comparative multiplanar sequences with identical parameters in a healthy age-matched control and a patient with ALS, which include three-dimensional sequences MPRAGE T1-weighted (repetition time/echo time, 7.6/3.8 ms) and fluid-attenuated inversion recovery (repetition time/echo time/inversion time, 7700/261/2300 ms). Diffusion tensor imaging (DTI) data were acquired with a synergy-L sensitivity encoding (SENSE) head coil using a single-shot spin echoplanar imaging pulse sequence. For each of the 32 non-collinear and non-coplanar sensitised to water diffusion gradients (p Value=700 mm²/s), we acquired 70 contiguous slices parallel to the anterior commissure–posterior commissure line (matrix, 232×232; field of view, 256×256 mm; echo time, 70; repetition time, 10 894; SENSE factor, 1; EPI factor, 47; number of excitations, 2; slice thickness, 2.2 mm; and predefined regions of interest of 26 mm²). Axial T1-weighted images with additional magnetisation transfer sequence (MTC) were also obtained (TR, 600 ms; TE, 12 ms; magnetisation transfer pulse on resonance).

The raw diffusion tensor data were transferred to a workstation (MR Philips workspace 2.6.3.3) and processed with dedicated software. Fractional anisotropy and mean diffusivity values were compared on predefined regions of cortical spinal tract (CST) (table 1). Ectopic cerebellar tonsils (6 mm below the foramen magnum) with minimal medullar compression were observed in this symptomatic patient, in whom selective bilateral hyperintensity along the corticospinal tract was also characterised on T1 magnetisation transfer sequence images. Neither hydrosyringomyelia nor any additional brain abnormalities were identified (figure 1).

DIFFERENTIAL DIAGNOSIS

A confident ALS diagnosis requires the exclusion of its mimic syndromes to avoid misdiagnosis and for adoption of the appropriate approach to the uniformly fatal outcome of this motor neuron disease. A few disorders can simulate ALS symptoms, including craniocervical junction malformations,

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To cite: Nunes RH, Littig IA, Rocha AJ da, *et al.* *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201302

Table 1 Comparative analysis of DTI parameters (fractional anisotropy and mean diffusivity values) on predefined regions of bilateral CST.

Mean diffusivity ($\times 10^{-6}$ mm ² /s)	Healthy control				Patients with ALS			
	Centri semiovalis	Internal capsules	Peduncles	Pons	Centri semiovalis	Internal capsules	Peduncles	Pons
Right	613.6 $\pm$ 85.9	734.7 $\pm$ 91.1	730.8 $\pm$ 128.8	697.5 $\pm$ 67.5	537.2 $\pm$ 96.9	664.1 $\pm$ 84.4	629.8 $\pm$ 74.5	713 $\pm$ 149.8
Left	555.7 $\pm$ 83.8	743.6 $\pm$ 75	795.8 $\pm$ 104.1	730.2 $\pm$ 102.3	565.5 $\pm$ 91	761.8 $\pm$ 116.7	680.0 $\pm$ 102.1	710.8 $\pm$ 148.9
Fractional anisotropy ($\times 10^{-3}$)								
Right	747.6 $\pm$ 78.6	713.4 $\pm$ 136.6	749.0 $\pm$ 123.2	706.1 $\pm$ 117.1	810.2 $\pm$ 50.9	785.5 $\pm$ 74.4	754.7 $\pm$ 174	779.2 $\pm$ 58
Left	756.2 $\pm$ 83.8	703.3 $\pm$ 111.9	745.1 $\pm$ 143.3	707.7 $\pm$ 135	835.9 $\pm$ 98.2	752.5 $\pm$ 110	786.8 $\pm$ 137.9	776.2 $\pm$ 104

ALS, amyotrophic lateral sclerosis; CST, cortical spinal tract; DTI, diffusion tensor imaging.

requiring neuroimaging examination. Chiari type 1 is an uncommon malformation that has been reported to be an important differential diagnosis in patients with adult-onset dysphagia.

We believed that in our patient the Chiari 1 malformation was a fortuitous imaging finding because he was asymptomatic

until the onset of the progressive brainstem dysfunction. We also believed that the whole neurological manifestation could not be attributed to Chiari 1 malformation. Furthermore, the selective corticospinal tract abnormality observed on T1 magnetisation transfer sequence images was identical to that seen in

Figure 1 Amyotrophic lateral sclerosis associated with Chiari 1 malformation versus age-matched healthy control. Ectopic cerebellar tonsils can be observed on the sagittal T1 image (asterisk) with minimal medullar compression estimated on superimposed MR tractography (A). Asymmetric hyperintensity along CST (left>right) was documented on a T1 MTC image (B) (arrowheads). Bilateral normal hypointense signal on the CST is observed on comparative T1 MTC from a healthy control (C). CST, cortical spinal tract; MTC, magnetisation transfer sequence.

previously reported patients with ALS, reinforcing the upper motor neuron impairment.

DISCUSSION

A confident 'amyotrophic lateral sclerosis' ALS diagnosis requires the exclusion of 'ALS mimic syndromes' to avoid misdiagnosis and to adopt the appropriate approach to the uniformly fatal outcome of this motor neuron disease.¹ MRI is only accepted to exclude diseases that could simulate ALS.¹ A reproducible MRI protocol was recently proposed with the aim of establishing a consensus on the various applications of MRI to the study of ALS and to explore the possibility of multicentre collaboration.² However, the demonstration of an associated mimic syndrome in a patient with ALS is unpredictable and the application of the new MR techniques in this setting has been long required.

The current diagnostic criteria were recently introduced to better define lower motor neuron (LMN) degeneration.¹ However, paraclinical evidence of upper motor neuron (UMN) compromise is still lacking, particularly in the early stages of the disease. A broad spectrum approach using conventional and non-conventional MRI techniques has been used in the search for UMN biomarkers with variable success.²⁻⁶

A few disorders can simulate ALS symptoms, including craniocervical junction malformations. Chiari type 1 is an uncommon malformation that has been reported to be an important differential diagnosis in patients with the adult-onset dysphagia requiring MRI examination.^{5 7 8} In this setting, dysphagia has been attributed to the pressure exerted by ectopic cerebellar tonsils on the hypoglossal nuclei and possibly also on the central pattern generators for swallowing, which are situated in the dorsal region of the medulla.⁵

We believed that in our patient the Chiari 1 malformation was a fortuitous imaging finding because he was asymptomatic until the onset of the progressive brainstem dysfunction. We also believed that all the neurological manifestations could not be attributed to Chiari 1 malformation. Conversely, ALS might explain our patient's entire disorder, including the concurrent indicators of UMN and LMN deficits in the limbs and bulbar territories, which were associated with progressive symptoms in the absence of sensory or cerebellar signs. Furthermore, the selective CST abnormality observed on T1 MTC images was identical to that seen in previously reported patients with ALS.^{6 9}

A previous report suggests that the long-term medullar compression observed in Chiari 1 malformation might play a role in the region-specific onset of ALS.⁷ Considering his occupation, this might have occurred in our patient, but MR tractography did not confirm significant medullar compression in a supine position. The authentication of this proposed mechanism awaits further studies with larger case numbers.

The early diagnosis of sporadic ALS with bulbar onset associated with Chiari 1 malformation is a challenge. Our report is in agreement with previous arguments,^{7 8} but added information using newer MR techniques. MR tractography was useful to estimate the medullar effect of Chiari 1 malformation, while sagittal MRI has only been able to demonstrate cerebellar ectopic tonsils.^{7 8} On the other hand, our results of fractional anisotropy (FA) and mean diffusivity (MD) were not sufficient to distinguish a patient with ALS from a healthy control.

Cosottini *et al*¹⁰ have confirmed DTI potential for detecting CST impairments in patients with ALS with a good diagnostic accuracy, and a significant difference in FA and MD values along the CST has been shown in a series of patients with ALS with either limb-onset or bulbar-onset of symptoms.¹¹ Recent

reports have suggested that DTI represents an emerging neuroimaging technique to quantitatively assess CST pathology in patients with ALS, functioning as a promising imaging biomarker.^{2 4 12} However, it is important to be aware of how to transfer research results and the limitations of their reproducibility in clinical practice, mainly while addressing the needs of an individual patient.³ Recent arguments realise that this quantitative technique cannot be retained a surrogate marker of ALS pathology in a single participant because of the overlap of DTI indexes between patients and control participants. It is assumed that the quantitative analysis of CST compromise using DTI parameters may be limited by many factors, such as individual differences in the extent and severity of involvement and even asymmetry of CST compromise. Moreover, the analysis may be affected by intraobserver and interobserver variability, since the region of interest in the CST within the internal capsule and brainstem is rather small and may be affected by partial volume averaging.

The selective degeneration depicted on T1 MTC images of our patient confirmed previous reports as a distinct finding for the ALS diagnosis.^{6 9} We believe that this sequence is useful and reliable for the diagnosis of ALS even in patients with early evidence of UMN involvement.

To our knowledge, this is the first description of the application of the non-conventional MR technique to distinguish the impact of ALS from Chiari 1 malformation. We believe that early diagnosis of this rare association is close. While DTI parameters were limited to this purpose our description reinforces the relevance of the T1 MTC sequence to demonstrate CST degeneration and corroborate an ALS diagnosis in an individual participant, even if there is a potential concurrent 'ALS mimic syndrome'.

Learning points

- ▶ Chiari type 1 is an uncommon malformation that has been reported to be an important differential diagnosis in patients with the adult-onset dysphagia requiring MRI examination.
- ▶ The early diagnosis of sporadic amyotrophic lateral sclerosis with bulbar onset associated with Chiari 1 malformation is a challenge.
- ▶ Although diffusion tensor imaging represents an emerging neuroimaging technique to quantitatively assess corticospinal tract pathology in patients with amyotrophic lateral sclerosis (ALS), it is important to be aware that this quantitative technique cannot be retained a surrogate marker of ALS pathology in an individual participant because of the overlap of DTI indexes between patients and control participants.
- ▶ The MRI signal intensity was useful for detecting upper motor neuron degeneration based on corticospinal tract signal intensity, reinforcing the relevance of the T1 magnetisation transfer sequence to demonstrate corticospinal tract degeneration and corroborate an ALS diagnosis in an individual participant, when there is a potential concurrent 'amyotrophic lateral sclerosis mimic syndrome'.

Contributors AJR was responsible for the study concept, writing the manuscript and interpretation of the data. RHN and IAL were responsible for writing the manuscript and for interpretation of data. BCOV was responsible for the clinical study concept and critical revision of the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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