Clinical Neurophysiology 125 (2014) 1906–1911

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Thinning of cervical nerve roots and peripheral nerves in ALS as measured by sonography

Hiroyuki Nodera [a,*], Naoko Takamatsu [a,b], Yoshimitsu Shimatani [a], Atsuko Mori [a], Kenta Sato [a], Masaya Oda [b], Yuka Terasawa [a], Yuishin Izumi [a,b,*], Ryuji Kaji [a]

[a] *Department of Neurology, Tokushima University, Tokushima, Japan*
[b] *Department of Neurology, Vihara Hananosato Hospital, Hiroshima, Japan*

See Editorial, pages 1719–1720

A R T I C L E   I N F O

Article history:
Accepted 11 January 2014
Available online 24 February 2014

Keywords:
ALS
Nerve root
Sonography

H I G H L I G H T S

- Sonography is a bedside test to visualize morphology of peripheral nerves at various segments including at the nerve root level.
- The patients with ALS had smaller nerve diameters or areas in the peripheral nerves or nerve roots in the upper extremity than those of normal subjects.
- Sonographic evaluation of cervical nerve roots might be more sensitive to detect nerve atrophy in ALS than peripheral nerves.

A B S T R A C T

Objective: Progressive atrophy and loss of motor axons is a hallmark of amyotrophic lateral sclerosis (ALS). Limited sonographic data are available on potential detection of atrophy of peripheral nerves and nerve roots in ALS.

Methods: Patients with either definite or probable ALS and control subjects underwent sonographic evaluation of the cervical roots (C5, C6, and C7) and peripheral nerves (median and ulnar nerves) on the right. These diameters and cross-sectional areas (C6, median, and ulnar nerves) were compared.

Results: The diameters and cross-sectional areas were consistently smaller in ALS than in controls. No correlation was present between the sonographic parameters and the disease severity, disease duration, age, or gender. The overall sensitivity and specificity tended to be greater in the cervical nerve roots than in the peripheral nerves.

Conclusions: This study shows atrophy of cervical nerve roots and peripheral nerves in ALS detected by sonography. Cervical nerve roots might be more appropriate to detect motor axon loss than peripheral nerves.

Significance: Sonographic evaluation of nerve roots and peripheral nerves may be a useful disease marker in ALS to confirm the diagnosis and to potentially monitor the disease progression.

Abbreviations: ALS, amyotrophic lateral sclerosis; ALSFRS-R, ALS Functional Rating Scale-Revised; AUC, area under the curve; CMAP, compound muscle action potential; CSA, cross-sectional area; MMT, manual muscle testing; ROC curves, receiver operating characteristic curves.

* Corresponding authors. Address: Department of Neurology, 3-18-15 Kuramotocho, Tokushima City 770-8503, Japan. Tel.: +81 88 633 7207.
E-mail addresses: hnodera@tokushima-u.ac.jp (H. Nodera), yizumi@clin.med.tokushima-u.ac.jp (Y. Izumi).

http://dx.doi.org/10.1016/j.clinph.2014.01.033
1388-2457/

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that predominantly affects the upper and lower motor neurons. Neuropathological studies have shown atrophy of peripheral nerves and preferentially ventral nerve roots in ALS (Atsumi and Miyatake, 1987; Blackwood et al., 1949; Dyck et al., 2005; Sobue et al., 1987, 1981). To evaluate potential loss of lower motor neurons in patients with suspected ALS, invasive neuropathological evaluation is not always possible; thus, alternatively, manual muscle testing (MMT) and the amplitudes of the compound muscle action potential (CMAP) have been traditionally used as clinical measures. However, because reinnervation can compensate for neuronal loss, MMT and CMAP may be preserved, at least in the early disease phase. The compensatory reinnervation masks the neuronal loss and may limit identification of motor axon loss in a timely manner. Therefore, a measure to potentially detect early axon loss should be clinically useful.

High-resolution sonography has been utilized in various neurological diseases (Hobson-Webb, 2013; Pillen and van Alfen, 2011). Swelling and compression of peripheral nerves can be assessed by measuring axon diameters and areas, as seen in conditions such as demyelinating polyneuropathy and carpal tunnel syndrome, respectively (Cartwright et al., 2012; Matsuoka et al., 2004). Little sonographic data had been available on the size of the axons in degenerative nerve diseases such as ALS. Cartwright et al. recently showed nerve atrophy in the median and ulnar nerves in ALS (Cartwright et al., 2011). Because ALS is a clinically heterogeneous disease that may have variable degrees of involvement in each body segment, widespread sonographic assessment would be more informative to identify potential axon loss. For this purpose, cervical nerve roots may be adequate in assessing innervations to proximal muscles. Thus, the aim of the present study is to evaluate the cervical nerve roots and peripheral nerves in patients with ALS to find whether pathologically proven thinning of peripheral nerves and nerve roots can be identified in vivo by sonography.

2. Methods

2.1. Inclusion criteria of the ALS patients and control subjects

The following two groups were recruited and prospectively assessed: (1) ALS: the patients who fulfilled the criteria for definite or probable ALS according to the revised El Escorial ALS criteria (Brooks et al., 2000) combined with the Awaji electrodiagnostic criteria (de Carvalho et al., 2008). Briefly, Awaji electrodiagnostic criteria recognize fasciculation potential as a sign of active denervation along with fibrillation and positive sharp wave, provided that concurrent evidence of reinnervation is present in the same muscle (i.e., long-duration, high-amplitude motor units, late recruitment, polyphasia). Given the potential disagreement of how the Awaji criteria and the revised El Escorial criteria are to be combined, we used both clinically probable and laboratory-supported probable criteria as originally stated in the revised El Escorial criteria. (2) Controls: asymptomatic persons who had no neurological symptom or sign. Specifically, an individual who reported symptoms suggesting cervical radiculopathy (e.g., neck pain, radicular pain, a history of whiplash injury), carpal tunnel syndrome (e.g., hand pain/paresthesia, nocturnal exacerbation, use-related exacerbation), and ulnar neuropathy (e.g., hand pain/paresthesia, elbow injury, elbow pain) was excluded. All the patients with ALS had plain cervical X-ray and showed no clear evidence of significant cervical spondylosis potentially associated with cervical radiculopathy or myelopathy. At the time of the sonography, the ALS patients were assessed according to the ALS Functional Rating Scale-Revised (ALSFRS-R). The study was approved by the Institutional Review Board of Vihara Hananosato Hospital and Tokushima University. The subjects gave written informed consent at the time of the testing.

2.2. Sonography

The sonographic examinations were performed using LOGIQ7 (GE) with an 11-MHz linear-array transducer. A single technician (N.T.) who was not aware of the diagnosis performed the sonography. The participants were tested in the supine position with the arm supinated and abducted at body level. The maximal diameter and the cross-sectional area (CSA) were measured by tracing the nerve just inside the hyperechoic rim, corresponding to the epineurium (Sugimoto et al., 2013b).

For imaging of the cervical nerve roots, a coronal oblique plane was used to visualize the cervical nerve roots longitudinally. By using the previously described methods (Matsuoka et al., 2004), the right C5, C6, and C7 nerve roots were easily identified. To obtain optimal images for measurements of maximal diameter and CSA, the cervical nerve roots were examined in the sagittal oblique plane in addition to the coronal oblique plane in some cases. Of note, CSA was reported only at the C6 level because the cross section was not clear at C5 and C7 in some individuals. Color Doppler imaging distinguished the cervical nerve roots from vessels, confirming no flow signals in the cervical nerve roots. The right median and ulnar nerves were also imaged at the wrist – 3 cm proximal to the wrist crease to avoid a common compression site. The room temperature was maintained at 23–25 °C. The skin temperature at the wrist and the neck was measured and maintained at >32 °C by covering them with a blanket.

2.3. Data analysis

SPSS (version 20.0J; Tokyo, Japan) was used for statistical analysis, using Welch's test, one-way analysis of variance (ANOVA) with Games–Howell post hoc test, Fisher's exact test, chi-square test, and Spearman's correlation coefficient where applicable. A statistically significant P value was set at 0.05.

3. Results

The representative sonographic images of the cervical root are shown in Fig. 1. The diameter and the CSA of the C6 nerve root in the ALS patient were smaller than those in the control subject, suggesting nerve atrophy. Table 1 shows the demographics of the ALS patients and control subjects. The following parameters were similar between the groups: age, height, weight, and body mass index (BMI). The number of female subjects was slightly higher in the control than in the ALS group ($P = 0.1$). There was no difference of either the diameter or CSA in any peripheral nerve/nerve root between the genders in either group ($P > 0.4$). Thus, the slight, non-significant gender difference between the groups was not considered to be relevant for further analysis.

The diameters and CSA of the cervical nerve roots and the peripheral nerves are shown in Fig. 2 and Table 2. The parameters in the control group were similar to those reported by Sugimoto et al. (2013a). The diameters and CSA were smaller in ALS than in control in any of the segments ($P < 0.01$ or less), although these values overlapped between the two groups. There was no age dependency in any of the sonographic parameters in either group. The ALSFRS score or disease duration showed no correlation between the sonographic parameters ($P > 0.1$ or greater). As reported earlier, there was weak, but positive correlation between the weight and some of the sonographic parameters in the control