THE VARIETY OF DYSPHAGIA PROGRESSION IN AMYOTROPHIC LATERAL SCLEROSIS (ALS)

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by onset within the upper limb, lower limb, or bulbar musculature. Regardless of site of onset, dysphagia inevitably occurs. This study aimed to examine the course of dysphagia in ALS, and to investigate whether the progression of dysphagia differs by site of onset. Thirty ALS patients were included. For each patient, we collected information on site of disease onset (bulbar or limb onset), duration to initiation of gastrostomy feeding from disease onset, dysphagia onset, course of dysphagia, and course of the respiratory function after dysphagia onset. Patients were divided into two groups based on the site of onset: the bulbar onset group (the BO group, i.e., clinical onset was characterized by dysarthria and/or dysphagia) and the limb onset group (the LO group, i.e., limb weakness was the first symptom). Each survey item was compared between two groups. There were no significant differences in time to initiation of gastrostomy feeding from disease onset between groups (p=0.45). On the other hand, there were significant differences in dysphagia onset, course of dysphagia, and course of the respiratory function after dysphagia onset (p=0.0008, p=0.007, p=0.0002, respectively).Our result suggest that the progression of dysphagia in ALS may differ by site of onset. Compared with bulbar onset ALS patients, progression of dysphagia may be faster in limb onset patients. Moreover, the decline in respiratory function is likely to influence the progression of dysphagia.

Keywords: *Amyotrophic lateral sclerosis; Dysphagia; Bulbar onset; Limb onset*

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1. INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease that is categorized as limb onset type or bulbar onset type (Turner et al. 2010). Both types of the disease inevitably develop dysphagia, presenting major problems such as weight loss, malnutrition, aspiration pneumonia, and reduced quality of life. Weight loss in particular is directly linked to life expectancy (Körner et al. 2013), and thus nutritional intake is an important consideration. Since the outlook for progression of dysphagia is poor, it is difficult to take measures to continue oral intake. Patients whose oral intake becomes impossible are offered percutaneous endoscopic gastrostomy (PEG) as an alternative means of nutrition. However, there are insufficient data to support specific timing of PEG insertion in ALS patients. (Miller et al. 2009). Hence, it is necessary to know how dysphagia progresses in these patients. Although several studies have reported on dysphagia in AlS, little is known about the progress and course of dysphagia after onset. Bulbar onset ALS patients died more rapidly than their limb onset counterparts (Traynor et al. 2003). Moreover dysphagia has an earlier onset and is severe in patients with bulbar onset (Ruoppolo et al. 2013). However, no reports exist on differences in progression of dysphagia by onset type. The aim of the present study is to examine the course of dysphagia in ALS and investigate whether progression of dysphagia differs by onset type.

2. MATERIALS AND METHODS

We conducted a retrospective cohort study of 30 patients who had been regularly followed at the Yoshino Neurology Clinic from April 2008 to May 2012. All patients met the El Escorial' criteria for the diagnosis of definite ALS. The patients comprised 13 women and 17 men (mean age at onset, 58.8 ± 7.7 years; age range 44-75 years). All patients received PEG (PEG was proposed and performed in all patients with forced vital capacity (FVC) >50%). All cases were started to feed gastronomy due to deterioration of dysphagia. Moreover, all patients were treated with noninvasive ventilation (NIV) or tracheostomy invasive ventilation (TIV).

The following information was obtained from medical records: duration to initiation of gastronomy feeding from disease onset (initiation of gastronomy feeding was defined as the time of combination of oral intake and gastronomy feeding due to dysphagia), dysphagia onset (duration to emerging dysphagia from disease onset; dysphagia symptoms include increased eating time, coughing or throat clearing, gurgly voice, and food remnants in the mouth (Kühnlein et al. 2008, Logemann et al. 2009)), course of dysphagia (duration to initiation of gastronomy feeding from dysphagia onset), and course of respiratory function after dysphagia onset (duration to intervention with noninvasive ventilation (NIV) or tracheostomy invasive ventilation (TIV) from dysphagia onset; all patients were treated with NIV when FVC dropped <50%, at the onset of dyspnea, if NIV was unsuccessful, TIV was performed immediately)

Patients were categorized into the bulbar onset group (the BO group) of clinical onset was characterized by dysarthria and/or dysphagia or the limb onset group (the LO group) if limb weakness was the first symptom. Each survey item was compared between the

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two groups. The Mann-Whitney U test was used for analyses between the two groups. SPSS11.0J for Windows (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. $P<0.05$ was considered statistically significant.

This study was approved by the Ethics Committee of the Tokyo Medical and Dental University Faculty of Dentistry (Approval No. 786).

3. RESULTS

3.1 Demographic data

The demographic characteristics of the ALS patients are shown in Table 1. The BO group consisted of 14 patients (nine males, five females, mean age of symptom onset, 62.0 ± 5.6 years), and the LO group consisted of 16 patients (eight males, eight females; mean age of symptom onset, 56.0 ± 8.3 years).

Table 1. Patient demographic data

	total (n=3%)	BO group (n=14)	LO group (n=16)
Age at onset (years) (mean ± SD)	58.8 ± 7.7	62.0 ± 5.6	56.0 ± 8.3
Gender			
M	17	9	8
F	13	5	8
PEG after onset (months) (mean ± SD)	30.6 ± 20.0	25.5 ± 14.0	35.1 ± 23.6
Noninvasive ventilation (NIV)	28	14	14
Tracheostomy invasive ventilation (TIV)	2	0	2

3.2 Survey items

The mean number of months of initiation of gastronomy feeding from onset was 28.4 months (SD, 13.0) in the BO group and 37.9 months (SD, 22.5) in the LO group, respectively. Similarly, the mean number of months to emerging dysphagia from onset was 7.5 months (SD, 8.4) in the BO group and 29.3 months (SD, 21.8) in the LO group. The mean number of months to initiation of gastronomy feeding from dysphagia onset was 20.9 months (SD, 13.2) in the BO group and 8.7 months (SD, 3.7) in the LO group. Moreover, the mean number of months to intervention with NIV or TIV from dysphagia onset was 20.8 months (SD, 13.5) in the BO group and -1.6 months (SD, 16.3) in the LO group.

3.3 Comparison each of the items between groups (Table 2)

There were no significant differences in the duration to initiation of gastronomy feeding from disease onset between the two groups ($p=0.45$; Mann-Whitney U test). In contrast, there were significant differences in dysphagia onset, course of dysphagia, and course of respiratory function after dysphagia onset between the two groups ($p=0.0008$, $p=0.007$, $p=0.0002$ respectively; Mann-Whitney U test).

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Table 2. Comparison between groups

	Duration to initiation of gastronomy feeding from disease onset	Dysphagia onset	Course of dysphagia	Course of the respiratory function after dysphagia onset
BO group	28.4 ± 13.0	7.5 ± 8.4	20.9 ± 13.2	20.8 ± 13.5
LO group	37.9 ± 22.5	29.3 ± 21.8	8.7 ± 3.7	-1.6 ± 16.3
p-value	n.s	p<0.01	p<0.01	p<0.01

Data are expressed as mean ± SD (months).

4. DICSUSSION

In this study, we examined the course of dysphagia in ALS, and whether there is a difference in the progression of dysphagia by type of onset. We also assessed factors affecting progression of dysphagia in ALS.

4.1 Course of dysphagia in ALS

A previous study reported that dysphagia began 1.9 years after disease onset (Ruoppolo et al. 2013). Consistent with that report, dysphagia emerged after an average of 2.4 years (29.3 months) in the LO group in the present study. Also consistent with previous reports, dysphagia had an earlier onset in the BO group (Ruoppolo et al. 2013, Wijesekera and Leigh 2009).

There were significant differences in the course of dysphagia (duration to initiation of gastronomy feeding from dysphagia onset) between the two groups. With respect to the course of dysphagia, progression was faster in the LO group compared with the BO group. Although bulbar onset is associated with shorter survival (Gordon et al. 2013), progression of dysphagia is faster in limb onset. Thus, dysphagia shows an opposite tendency to that of survival.

Our results suggest that dysphagia in bulbar onset ALS may develop early, but follow a long course. Therefore, long-term interventions for dysphagia are required. One of such interventions is Palatal Augmentation Prosthesis (PAP). The purpose of PAP is to reshape of the hard palate to improve tongue/palate contact during swallowing due to impaired tongue mobility as a result of surgery, trauma, or neurologic/motor deficits (The glossary of prosthodontic terms. 1999). Dysphagia in patients with ALS is characterized by impairment of the oral phases of swallowing. These patients present with abnormal lingual movement, which makes swallowing effortful and is therefore inefficient and fatiguing (Easterling et al. 2013). Hence, PAP is likely to improve the oral phase of swallowing in ALS. Moreover, the use of PAP over 3 years in ALS patients was previously reported (Esposito et al. 2000), supporting its utility for long-term intervention. On the other hand, Strand et al reported that patients with ALS who have early eating problems, should be advised of the need for dietary modification, which is required for the continuation of oral intake (Strand et al. 1996). Dietary modification has been shown to be an effective approach for moderate dysphagia (Kühnlein et al. 2008). Furthermore, with compensatory swallowing strategies such as the supraglottic swallow and posture positioning, the ability to swallow safely

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may still be maintained (Watts and Vanryckeghem 2001). Oral feeding for as long as possible is preferable from the perspective of quality of life, some kinds of swallowing rehabilitation methods are useful (Higo et al. 2004).

Meanwhile, the results of this study suggest that compared with bulbar onset ALS, limb onset ALS may be slow onset of dysphagia, but follow a short course. Since rapid progression of dysphagia is expected in limb onset, it is necessary to examine swallowing function immediately once dysphagia presents. Videofluoroscopic swallowing examination (VF) is considered the gold standard for assessing swallowing function. In a previous report (Kuwai et al. 2003), VF was used to quantitatively evaluate and identify ALS-related swallowing disorders, attesting to the utility of this technique for evaluating ALS-related dysphagia. If the evaluation of swallowing function by VF is difficult, videoendoscopic swallowing examination (VE) may present a viable alternative. VE allows for diagnosing dysphagia and timely implementation of dietary changes and/or therapeutic strategies to continue safer oral intake (Leder et al. 2004). VE is also effective for examining swallowing function in patients with ALS.

4.2 Factors that affect the progression of dysphagia

There were significant differences in the course of the respiratory function after dysphagia onset between the BO group and the LO group (p=0.0002). This suggested that dysphagia and respiratory impairment progressed more rapidly in the LO group than in the BO group. In the LO group, 8 of these cases were treated with NIV and TIV before onset of dysphagia or at about the time dysphagia presented. In contract, all patients in the BO group were treated with NIV after dysphagia onset. In the present study, all patients were offered NIV when their FVC drops below 50% or patients had clinical findings of hypoventilation (Melo et al. 1999, Kleopa et al. 1999). If NIV was not tolerated, patients were immediately switched to TIV (NIV, 28 patients; TIV, 2 patients). That is, there was a tendency to decrease respiratory function enough to treat with NIV at the time dysphagia emerged in the LO group. The onset of dysphagia may coincide with the insidious development of respiratory insufficiency in ALS (Miller et al. 1999), and swallowing function deteriorates along with respiratory function (Hopkins et al. 1996). Our results suggest a similar trend with dysphagia in the LO group. Given that swallowing and respiratory function are coordinated when swallow takes place (Costa and Lemme 2010, Pitts et al. 2012), our findings suggest that a decline in respiratory function is associated with the progression of dysphagia in ALS.

4.3 Study limitations

This study has some limitations worth noting. We did not evaluate the swallowing and respiratory function of each patient by VF and spirometer. Furthermore, since swallowing function was assessed by subjective complaints of patients, definition of dysphagia is arbitrary. Hence, further studies are needed to evaluate in detail the swallowing and respiratory function of patients with ALS.

Other limitations include the retrospective nature of data collection, the relatively small sample size and a single-center experience.

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5. CONCLUSIONS

In this study, we examined the course of dysphagia in ALS and investigated whether the progression of dysphagia differed by site of onset. Our results suggest that there is a difference in the progression of dysphagia by site of onset. Compared with bulbar onset ALS, progression of dysphagia is faster in limb onset ALS.

6: ACKNOWLEDGEMENTS

This study was supported by a Grant-in-Aid for Young Scientists (B) (25862074) from the Japan Society for the Promotion of Science.

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