Prediction of Dysphagia Severity: An Investigation of the Dysphagia Patterns in Patients with Lateral Medullary Infarction

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Abstract

Objective  In order to identify the factors that influence the swallowing function in patients who develop Wallenberg syndrome (WS) following lateral medullary infarction (LMI), we examined various patient characteristics, including the passage pattern abnormality (PPA) of a bolus through the upper esophageal sphincter (UES).

Methods  Fifty-four pure LMI patients with dysphagia participated in this study. PPA, defined as the failure of bolus passage through the UES corresponding to the intact side of the medulla, was identified during videofluorographic swallowing evaluations of each patient. On brain magnetic resonance imaging, the subjects’ lesions were classified vertically into three levels and horizontally into seven levels in relation to the involvement of the ambiguous and/or solitary nuclei. Logistic regression analyses were performed for age, sex, PPA and the vertical and horizontal sites of the lesions.

Results  In terms of severity, 15 subjects were categorized as having mild dysphagia, 26 subjects were categorized as having moderate dysphagia and 13 were categorized as having severe dysphagia. Subjects with cephalic lesions, greater vertical spread of the lesion and PPA were more likely to have severe dysphagia. PPA and a greater vertical spread of the lesion were related to the severity of the functional outcome (p<0.01). The horizontal extent of the lesion was not strongly related to the prognosis.

Conclusion  The presence of PPA in LMI patients is suggestive of abnormalities in the swallowing pattern and, in turn, damage to the medullary central pattern generator. The presence of PPA and a greater vertical spread of the lesion can be useful predictors of severe dysphagia.

Key words: dysphagia, lateral medullary infarction, central pattern generator, Wallenberg syndrome, upper esophageal sphincter opening

Introduction

The incidence of dysphagia accompanying Wallenberg syndrome (WS) following lateral medullary infarction (LMI) is reported to be 50-100% (1-3). While the incidence, clinical features, severity and lesions responsible for dysphagia have been investigated, few studies have examined the relationship between swallowing dynamics and the site of the lesion (4-8). Some studies have focused on upper esophageal sphincter (UES) opening (6, 9). It is known that the UES ipsilateral to the unaffected side of the medulla is disturbed in patients with LMI (9).

The motor aspects of dysphagia in LMI patients are char-
characterized by the failure to trigger pharyngeal phase swallowing movements, a reduced motor output and a lack of coordination (i.e., swallowing pattern abnormalities) (9).

Reduced motor output is characterized by vocal cord paralysis, reduced pharyngeal contractions and UES opening failure, all of which are seen on the side ipsilateral to the affected side of the medulla. Because the bolus usually passes through the pharynx and the UES corresponding to the unaffected side of the medulla, head rotation and changes in body position are useful compensatory strategies in these patients (10). These are the typical characteristics of dysphagia in patients with lesions involving the ambiguous nucleus.

In some patients with LMI, however, the UES ipsilateral to the unaffected side of the medulla is disturbed (9). Head rotation is not useful in this type of patient. The present study focused on such disturbances of UES opening. The passage pattern abnormality (PPA) of a bolus is defined as the failure of bolus passage through the UES on the side ipsilateral to the intact side of the medulla. PPA is suspected to be caused by damage to the central pattern generator (CPG).

With careful observation of bolus passage through the UES, three types of PPA were identified (Fig. 1).

In addition to PPA, the site of the lesion was also examined in this study. Horizontal brain MRI images have been investigated in past studies of LMI (2, 3). According to reports by Kim et al., among patients with cephalic lesions, 83% have dysphagia and 74% have severe dysphagia (11, 12). Despite the high prevalence of severe dysphagia in patients with cephalic lesions, some patients have only mild dysphagia.

In this study, lesions were classified vertically into three levels (cephalic, middle and caudal) and horizontally into various regions in relation to the involvement of ambiguous and/or solitary nuclei.

Logistic regression analyses were performed for age, sex, PPA and the vertical and horizontal sites of the lesions to examine the effects of these factors on the severity of the functional outcomes of the subjects’ swallowing.

**Materials and Methods**

**Subjects**

The subjects included 54 patients with dysphagia (42 men, 12 women; age range: 32 to 82 years; mean age: 60.4 years) who had been diagnosed with WS following pure LMI. The patients were admitted to our hospital. This study is a retrospective study. The patients were diagnosed with WS by neurologists based on neurological findings as well as the presence of lesions on MRI. Subjects with supranuclear lesions in the corticobulbar tract or a history of previous stroke were excluded from the study.

**Assessment of swallowing disturbance**

The presence of dysphagia in the 54 patients was identified using the modified water swallowing test (MWST). Profile scores of 3 or less were considered to be indicative of dysphagia (13). The Functional Oral Intake Scale (FOIS) ranged from the nothing by mouth level (level 1) to the modified diet level (level 6) (14).

**Videofluoroscopic swallowing study (VFSS)**

VFSS was performed using 2, 3 or 5 mL of liquid contrast medium depending on the patient’s swallowing ability. In addition to the liquid material, pureed foods were introduced to the subjects when the examiners confirmed their safety. Aspiration, pharyngeal contraction asymmetry and the movement patterns of the UES opening were evaluated in each patient. A physician and a speech-language-pathologist analyzed the MWST, FOIS and VFSS findings.

**Definition of PPA and classification of the UES opening type**

We examined the UES opening on the frontal and lateral views of VFSS. When the bolus passed through the pharynx and UES, the UES opening of the side ipsilateral to the unaffected side of the medulla was examined. Sometimes, the UES opening was examined while rotating the head to the
affected medullary side to allow the bolus to pass through the unaffected side of the UES. Theoretically, the UES corresponding to the unaffected side of the medulla should open for every pharyngeal swallow. Failure to open at least once during VFSS was diagnosed as PPA (Fig. 1). Triggering of the pharyngeal stage of swallowing was confirmed using videofluoroscopy with laryngeal elevation and contraction of the lateral pharyngeal wall.

The subjects were divided into three groups based on the movement patterns of the UES opening (Fig. 1). If the UES on the unaffected medullary side opened and the contrast medium smoothly passed through the pharynx and UES on this side during every swallow, the subject was classified as having Type 1 passage. If the UES of the unaffected medullary side did not open and the UES of the affected medullary side opened at least once, the subject was classified as having Type 2 passage. If both sides of the UES were disturbed and the bolus could not pass through the UES, the subject was classified as having Type 3 passage.

In some cases, the side of the UES opening changed over time during the observation period (15, 16). For example, Type 2 passage, which is usually observed during the acute stage of stroke, may change to Type 1 passage in the chronic stage. In such cases, the initial classification was used (i.e., Type 2 during the acute stage).

**Topographical subgroups**

The medullary lesions were detected on diffusion-weighted imaging in the acute phase or T2-weighted magnetic resonance imaging (MRI; 1.5T) with 3-mm slices. According to the methods of Kim et al., the lesions detected on brain MRI were classified into three categories: medullary cephalic (at the posterolateral bulging level), middle (at the olivary nucleus level) or caudal (17). Horizontally, the lesions were divided into several regions: A-C and D (Fig. 2). In addition to these four regions, lesions that included both areas A and B were classified as “typical,” while lesions that included both areas B and C were classified as “ventral” and lesions that included areas A-C were classified as “large.” Lesions corresponding to area D were classified as “dorsal.”

Since the lesions observed in our subjects did not fit the classification of Kim et al., we divided the lesions into three groups according to the structure of ambiguous and solitary nuclei. We also used the anatomical atlas Cytoarchitecture of the Human Brain Stem to determine the extent of the lesion and to judge whether the lesion included these nuclei (18). The lesions were vertically classified as medullary cephalic (at the posterolateral bulging level: atlas slice No. 1701 and No. 1801), middle (at the olivary nucleus level: atlas slice No. 1901 and No. 2051) or caudal (atlas slice No. 2301) (19).

We considered the characteristic structures, including the anterior median fissure, inferior cerebellar peduncle and olive as indexes for MRI. Then, we compared these characteristics with those in the anatomical atlas with respect to the aspect ratio and front-to-back ratio.

Lesions that included ambiguous nuclei were classified as “NA,” lesions that included solitary nuclei were classified as “NS” and lesions that included both ambiguous and solitary nuclei were classified as “NAS,” respectively.

The subjects were also divided into two groups based on the extent of the lesion: the localized lesion group (L), in which the lesions were localized within one section, and the vertically spread lesion group (V), in which the lesions covered two or three sections (Table 1).

**Classification of the functional outcome**

The subjects were divided into three groups based on the long-term outcome of the swallowing function: severe, moderate or mild dysphagia (Table 1). Patients who received swallowing training for three months or more from admission, alternative nutrition, such as tube feeding, for three months or more and those who underwent botulinum toxin injection or surgery were assigned to the severe group, whereas patients whose oral intake was initiated after three weeks from admission were assigned to the mild group. The subjects were divided into three groups based on the severity of functional outcome: severe, moderate or mild dysphagia (Table 1).

**Table 1. Classification of Cases according to the Vertical Lesion Characteristics**

<table>
<thead>
<tr>
<th>Extent of Lesion</th>
<th>Site of Lesion</th>
<th>Severity of functional outcome</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>L/V</td>
<td>Cephalic</td>
<td>Middle</td>
<td>Caudal</td>
</tr>
<tr>
<td>L</td>
<td>+</td>
<td>-</td>
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L: localized lesion, V: vertically spread lesion, ( ), PPA: passage pattern abnormality

![Figure 2. Lesion location (horizontal section). A+B: typical type, B+C: ventral type, A+B+C: large type, D: dorsal type, E: lateral type, NA: ambiguous nucleus, NS: solitary nucleus](image-url)
were performed.

section and PPA) on the severity of the functional outcome. The spread of the lesion, the extent of vertical spread of the lesion and MRI severity were examined. Logistic regression analyses of the relationship between PPA and horizontal and vertical lesions and severity of the functional outcome were performed. Statistical analysis

The frequency of PPA was investigated, and the relationship between PPA and horizontal and vertical lesions and LMI severity were examined. Logistic regression analyses of the effects of five factors (age, sex, the extent of horizontal spread of the lesion, the extent of vertical spread of the lesion and PPA) on the severity of the functional outcome were performed.

Results

Severity of the functional outcome

A total of 41 of the 54 subjects successfully achieved oral intake within three months after the onset of disease. During videofluoroscopy, all patients exhibited aspiration. All patients reduced the pharyngeal contractions of the affected medullary side. In terms of the severity of dysphagia, 15 cases were categorized as mild, 26 cases were categorized as moderate and 13 cases were categorized as severe (Table 1). Botulinum toxin injection was performed in two severe cases. Surgery to improve the swallowing function was performed in five severe cases. MRI lesion topography and severity of the functional outcome

Of the 15 patients in the mild group, seven (46.7%) had cephalic lesions. Of the 26 patients in the moderate group, 15 (57.7%) had cephalic lesions. Of the 13 patients in the severe group, 12 (92.3%) had cephalic lesions. LMI occurred on the right side in 25 cases and on the left side in 29 cases.

On the other hand, four (26.7%) of the 15 patients in the mild group had vertically spread lesions reaching two or three sections (Table 1). Nine (34.6%) of the 26 patients in the moderate group had vertically spread lesions. Ten (76.9%) of the 13 patients in the severe group had vertically spread lesions.

Of the 34 patients with cephalic lesions, seven (20.6%) had mild dysphagia, 15 (44.1%) had more than moderate dysphagia and 12 (35.3%) had severe dysphagia (Table 2).

With respect to the horizontal classification according to Kim, 45 patients (83.3%) had A+B lesions. All 54 patients had A or B lesions. With respect to the horizontal classification according to the Cytarchitecture of the Human Brain Stem, 48 patients (88.9%) had NA lesions, 20 patients (37.0%) had NS lesions and 19 (35.2%) patients had NAS lesions.

Predictors of dysphagia

A univariate analysis showed that the patients with PPA, extended vertically spread lesions and cephalic lesions were significantly more likely to have severe dysphagia (Table 3). Age, sex and the site of the lesion (laterality) were not significantly related to severe dysphagia in the univariate analysis. According to a multivariate analysis, patients with pattern abnormalities and lesions involving multiple vertical sections were significantly more likely to have severe dysphagia (Table 3). The horizontal extent of the lesion was not related to the severity of the functional outcome.

Discussion

PPA

The subjects were divided into three groups based on the movement pattern of the UES opening (Fig. 1). Type 1 is typical dysphagia of LMI. In this type, the contrast medium smoothly passes through the pharynx and UES of the una-
affected medullary side. The output patterns of the pharyngeal phase swallowing movements are highly repeatable, and the stereotypic movements are controlled by the CPG (22, 23). With an intact CPG, Type 1 patients with unilateral medullary lesions have a disturbance on the affected side of the medulla.

In cases of Type 2 and 3, PPA is observed. The presence of PPA indicates that the unilateral LMI lesion has disturbed both sides of the UES.

PPA involves failure of the stereotyped motor sequence. Swallowing mechanisms involve not only the medullary nuclei, but also swallowing-related neurons, including the reticular formation, in a complex manner (24). We suggest that the presence of PPA indicates CPG damage, as acute disconnection can occur between the ipsilateral dorsal swallowing center and the contralateral side of the swallowing center in the medulla oblongata (9). Measurement of CPG damage has not been established.

This study showed that patients with PPA are significantly more likely to have severe dysphagia (Table 3). Based on the above findings, dysphagia becomes severe when the CPG is damaged. In this sense, PPA is a useful predictor of severe dysphagia.

In addition, PPA can be detected on electromyography (EMG) of the cricopharyngeal (CP) muscle (25). Among our severe patients, two underwent diagnostic EMG of the CP muscle. The CP muscle of the unaffected medullary side did not relax during swallowing movements. A disturbance of the UES opening indicates the presence of CP relaxation on EMG. Although EMG of the CP is an accurate examination of the UES opening, it is not a general examination. PPA was detected using videofluoroscopic examinations in this study. However, the detection rate of PPA was not apparent. During the course of recovery of dysphagia, the UES of the unaffected side is able to open, and PPA disappears in some cases.

Although the UES of the unaffected medullary side is not open, the UES of the affected medullary side can open in Type 2 passage. The water-drinking examination with body positioning (e.g., lying down one side with head rotation) is a useful rehabilitation tool for this type of dysphagia. Type 3 passage cases exhibit complete UES opening failure with triggering of the pharyngeal stage of swallowing. Such patients exhibit severe dysphagia and are candidates for electric stimulation, botulinum toxin injection or surgery (20).

**Correlations between the severity of the functional outcome and the topography of medullary lesions**

As to the relationship between vertical spread lesion location and severity, Kim stated that patients with cephalic lesions have more severe dysphagia. In the present study, 12 of 13 patients with severe dysphagia had cephalic lesions. However, seven patients (20.6%) with cephalic lesions had mild dysphagia (Table 1). The presence of cephalic lesions alone was not related to severity. The statistical analysis indicated that large lesions (NAS group) were not significantly

| Table 3. Relationships between the Severity of the Functional Outcome and Risk Factors |
|-----------------------------------------|---------------|---------------|---------------|---------------|----------------|----------------|
|                                        | Severity of dysphagia | total | Mild | Moderate | Severe | Univariate p | Multivariate p |
| Age (years) <65                       | 25             | 10             | 10             | 5      | 0.114 | -             |
| Age ≥65                                | 29             | 5              | 16             | 8      |        |              |
| Sex                                    |                |                |                |        |        |              |
| female                                 | 12             | 7              | 1              | 3      | 0.07  | -             |
| male                                   | 42             | 8              | 24             | 10     |        |              |
| Passage pattern abnormality            |                |                |                |        |        |              |
| +                                      | 32             | 15             | 16             | 1      | <0.001 | <0.001       |
|                                     | 22             | 0              | 10             | 12     |        |              |
| Vertical lesion                        |                |                |                |        |        |              |
| L                                       | 31             | 11             | 17             | 3      | 0.007  | 0.039         |
| V                                       | 23             | 4              | 9              | 10     |        |              |
| Horizontal lesion                      |                |                |                |        |        |              |
| Dorsal (+)                             | 42             | 14             | 20             | 8      | 0.042  | 0.899         |
|                                         | 12             | 1              | 6              | 5      |        |              |
| Dorsal (-)                             | 39             | 13             | 18             | 8      | 0.133  | -             |
|                                         | 15             | 2              | 8              | 5      |        |              |
| Typical (+)                            | 9              | 1              | 5              | 3      | 0.404  | -             |
|                                         | 45             | 14             | 21             | 10     |        |              |
| Typical (-)                            | 32             | 12             | 15             | 5      | 0.023  | 0.144         |
|                                         | 22             | 3              | 11             | 8      |        |              |
| Ventral (+)                            | 6              | 4              | 1              | 1      | 0.064  | -             |
|                                         | 48             | 11             | 25             | 12     |        |              |
| Ventral (-)                            | 34             | 11             | 16             | 7      | 0.281  | -             |
|                                         | 20             | 4              | 10             | 6      |        |              |
| NAS (+)                                | 35             | 11             | 17             | 7      | 0.283  | -             |
|                                         | 19             | 4              | 9              | 6      |        |              |

According to the multivariate analysis, the patients with pattern abnormalities and lesions involving multiple vertical sections were significantly more likely to have severe dysphagia. Logistic regression analyses revealed that the presence of cephalic lesions in the medulla oblongata is a useful predictor of severe dysphagia. The presence of cephalic lesions alone was not related to severity. The statistical analysis indicated that large lesions (NAS group) were not significantly more likely to have severe dysphagia.
related to severe dysphagia (Table 3).

The authors state that they have no Conflict of Interest (COI).

The patients with PPA had a tendency to have severe dysphagia. Animal studies have identified swallowing-related neurons in the medulla oblongata, thus suggesting that the CPG is located around the lateral reticular formation in cephalic lesions (23, 26). At present, the CPG is thought to be located within the neural network consisting of key components, such as the ambiguous nucleus, solitary nucleus and reticular formation, while the topography of the lesions is indefinite.

Furthermore, by combining the above swallowing dynamics, it is clear that patients with PPA and cephalic lesions are significantly more likely to have severe dysphagia (Table 2).

Severe dysphagia is also more likely to occur in patients with vertically spread lesions (Table 1). Dysphagia caused by vertically spread lesions is more severe than that caused by localized lesions. Because the CPG is thought to be situated vertically in the medulla oblongata in humans, it is possible that the CPG is contained within vertically spread lesions.

The horizontal extent of the lesion was not found to be strongly related to the severity of the functional outcome. Eighty-nine percent of the patients in this study had lesions containing ambiguous nuclei. The size of the lesion and the presence of solitary nuclei were not strongly related to the severity of dysphagia.

Predictors of the prognosis

Age, sex and the site of the lesion (laterality) were not related to the severity of dysphagia. In addition, it was confirmed that the LMI patients with PPA and greater vertical spread of the lesion had poor functional outcomes. In such cases, it is necessary to consider long-term treatment, including botulinum toxin injection or surgery, to prevent aspiration and achieve adequate nutritional management. On the other hand, a nonsurgical approach (rehabilitation) is adequate in mild cases.

Conclusion

Swallowing dynamics, lesion distribution and the severity of the functional outcome were investigated in 54 LMI patients. PPA was identified by examining the UES opening of the unaffected medullary side during pharyngeal phase swallowing, and the vertical distribution of the lesion was investigated in three sections of the medulla oblongata (cephalic, middle and caudal). Patients with PPA and vertically spread lesions were significantly more likely to have severe dysphagia. The presence of PPA and vertically spread lesions including the cephalic level can therefore be useful predictors of severe dysphagia.

The authors state that they have no Conflict of Interest (COI).

References

21. ASPEN Board of Directors and the Clinical Guidelines Task force.


