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Original Article

Survey on the Diagnostic Process of Amyotrophic Lateral Sclerosis

Sundo Kim, M.D., Seong-Woong Kang, M.D., Wonah Choi, M.D., Jung-Hyun Park, M.D., Youngsang Lee, M.D., Su Jin Yu, M.D.

Department of Rehabilitation Medicine and Rehabilitation Institute of Muscular Disease, Yonsei University College of Medicine, Seoul 135-720, Korea

Objective To emphasize the need for precise diagnosis of amyotrophic lateral sclerosis (ALS), a progressive and degenerative disease of upper and lower motor neurons that often present initially with weakness at the upper or lower extremities, and frequently misdiagnosed as myelopathy, radiculopathy, peripheral neuropathy or arthropathy that may ultimately lead to unnecessary treatments including surgical procedures.

Method We retrospectively reviewed medical records of 331 ALS patients who visited our hospital between 1998 and 2008. Symptoms at onset, progression of disease, radiologic findings, surgeries prior to diagnosis of ALS, outcome after surgery or conservative treatments, and electrodiagnostic study results were reviewed.

Results Among the 331 patients with ALS, 34 (10.3%) had a history of surgical procedure and 37 (11.1%) underwent conservative treatment prior to diagnosis of ALS. 34 patients with a mean disease duration at diagnosis of 20.0±14.9 months, had surgery for symptoms that were later attributable to ALS. In 30 of the 34 patients, symptoms did not resolve after the intervention. 37 patients with a mean disease duration at diagnosis of 16.6±14.3 months, underwent conservative treatments such as physical therapy prior to diagnosis of ALS. Only in one patient (2.7%), symptoms improved after conservative treatment.

Conclusion In the absence of a single confirmatory study for the diagnosis of ALS, clinical findings may be misinterpreted, leading to an erroneous diagnosis. Therefore, closer and more careful follow-up is necessary for patients with limb weakness in the absence of sensory symptoms, or bulbar abnormalities such as dysarthria and dysphagia.

Key Words Amyotrophic lateral sclerosis, Diagnosis, Electrodiagnostic study, Conservative treatment, Surgical procedure

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a progressive neurological disorder accompanied by the degeneration of upper and lower motor neurons, which is characterized by upper or lower extremities weakness and respiratory muscle paralysis. The patients meet their deaths within several years.[1] The problem is that early clinical presentation of ALS is similar to radiculopathy, myelopathy, mononeuropathy and arthropathy, and

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Corresponding author: Seong-Woong Kang
Department of Rehabilitation Medicine and Rehabilitation Institute of Muscular Disease, Yonsei University College of Medicine, 146-92, Dogok-dong, Gangnam-gu, Seoul 135-720, Korea
Tel: +82-2-2019-3492, Fax: +82-2-2019-3499, E-mail: kswoong@yuhs.ac
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moreover there is no accurate way to diagnose it. Such being the case, there are many cases where patients undergo unnecessary treatments or operations.[2,3] In particular, surgical interventions may accelerate neuromuscular dysfunction.[4] Meanwhile, the lifespan of patients is expected to be extended by the control of respiratory complications, *i.e.*, the principal cause of death in ALS. In case noninvasive ventilation is performed in a timely fashion, respiratory complications may be effectively controlled. In such a case, the quality of patients' lives may be improved.[5,6] Accordingly, accurate diagnosis is of great importance to patients with ALS, which decreases unnecessary treatments and enables patients to undergo proper treatments.[7-10] The diagnosis of ALS involves a detailed inquiry into medical history and neurologic examinations including a check of the manifestation of upper and lower motor neurons. Ordinarily, the diagnosis is performed in accordance with El Escorial Criteria,[11,12] electromyography (EMG), neurophysiological examinations, radiography and blood tests should be performed to differentiate ALS from other diseases. In foreign countries, many studies have been conducted on the diagnosis of ALS,[2,7,13] but in Korea, there has been no study due to the lack of cases. The purpose of this study is to review treatments that patients with ALS underwent before definitely diagnosed, by extension, to present points to be considered in initial examinations.

MATERIALS AND METHODS

Subjects

The subjects of this study were defined as ones who were diagnosed with ALS at Gangnam Severance Hospital between January 1998 and December 2008 (11 years) and who were followed up. The diagnoses were based upon history taking, physical examinations, electrodiagnoses and radiologic evaluations. A total of 331 subjects met the inclusion criteria. The subjects were divided into two groups. One was composed of subjects who underwent surgical interventions within 5 years before being definitely diagnosed with ALS (the SI group), and the other was constituted of ones who experienced conservative treatments during the same period (the CT group). Subjects, who received surgical interventions at least 5 years before being diagnosed or who did not show the early clinical characteristics of ALS, were excluded from the SI group.

Methods

Investigations were made into initial symptoms, the time of onset, initial examinations, initial radiological data, the results of initial EMG, initial surgical treatments, treatments performed at other hospitals, the period taken to diagnose, preoperative diagnosis and postoperative improvement (limited to subjects who underwent surgical treatments). Telephone interviews were performed when necessary. All the results were analyzed in percentage terms.

RESULTS

Subjects' information

General information: The subjects of this study were defined as ones who were diagnosed with ALS at Gangnam Severance Hospital between January 1998 and December 2008 and who were followed up. The diagnoses were based upon history taking, physical examinations, electrodiagnoses and radiologic evaluations. A total of 331 subjects met the inclusion criteria. Their mean age was 55.2±11.1 years. Males and females were 211 and 120 respectively. Out of 331 subjects, 71 (21.4%) underwent surgical operations or conservative treatments within 5 years before being diagnosed, 34 (10.3%) and 37 (11.1%) of whom received surgical operations and conservative treatments respectively (Table 1). The other 240 subjects were diagnosed after receiving EMG test at other hospitals or this hospital. Their medical records showed that they did not undergo treatments unrelated to ALS itself including surgical interventions.

SI group: The principal symptoms of 34 subjects, who received surgical interventions before being diagnosed, were upper extremities weakness (15; 44.1%),

Table 1. Demographic Characteristics of Patients with Surgical Procedure Group and Conservative Care Group

	Surgical procedure group	Conservative care group
Number of patients	34	37
Sex (male : female)	24 : 10	18 : 19
Onset age (years)	57.9±10.6	55.5±10.0
Duration from symptom to diagnosis (months)	20.0±14.9	16.6±14.3

Values of average are mean±standard deviation.

Table 2. Distribution of Initial Symptoms in the Surgical Procedure Group (n=34)

Symptom	Number of cases	%, in group
Upper extremities weakness	15	44.1
Lower extremities weakness	13	38.2
Lower back pain	3	8.8
Foot drop	2	5.8
Muscle atrophy	1	2.9

Values are number of patients and percentage.

Table 3. Distribution of Initial Diagnosis in Surgical Procedure Group (n=34)

Diagnosis	Number of cases	%, in group
Herniated lumbar disc	12	35.3
Herniated cervical disc	8	23.5
Lumbar stenosis	4	11.8
OPLL	4	11.8
Tardy ulnar syndrome	2	5.9
Cervical stenosis	1	2.9
Cervical myelopathy	1	2.9
Carpal tunnel syndrome	1	2.9
Rotator cuff tear	1	2.9

Values are number of patients and percentage.
OPLL: Ossification of posterior longitudinal ligament

lower extremities weakness (13; 38.2%), lower back pain (3; 8.8%) and others (3; 8.8%) (Table 2). It averagely took 8.9±8.2 months for subjects to undergo surgical treatments after initial symptoms appeared, and took 20.0±14.9 months to be diagnosed with ALS. Preoperative diagnoses were herniated lumbar disc (12; 35.3%), herniated cervical disc (8; 23.5%), lumbar stenosis (4; 11.8%), ossification of posterior longitudinal ligament (4; 11.8%), tardy-ulnar syndrome (2; 5.9%) and others (4; 11.8%) (Table 3). Out of 34 subjects who received surgical operations, 30 (88.2%) did not show improvements. The other 4 (11.7%) showed slight improvements of symptoms, 3 and 1 of whom showed the improvement of muscle weakness and the relief of pain respectively. All of the 4 subjects experienced spinal decompression surgeries for herniated Lumbar discs. In the SI group, 32 (94.1%) had initial examinations from surgeons such as neurosurgeons and orthopedists, just 4 (11.8%) of whom underwent preoperative EMG. One of them was scheduled to be followed up under suspicion of multifocal motor neuropathy or motor neuron disease, but wanted to go through the spinal decompression surgery before being definitely diagnosed with ALS. By request, the surgery was performed on the subject. Two of them were diagnosed with radial nerve injuries on EMG and underwent decompression surgeries. The other was diagnosed with lumbar radiculopathy on EMG and underwent a spinal decompression surgery.

Table 4. Distribution of Initial Symptoms in Other Conservative Care Group (n=37)

Symptom	Number of cases	%, in group
Four extremities weakness	3	8.1
Upper extremities weakness	8	21.6
Lower extremities weakness	9	24.3
Hand muscle weakness	8	21.6
Dysarthria	4	10.8
Foot drop	2	5.4
Dysphagia	1	2.7
Lower back pain	1	2.7
Shoulder pain	1	2.7

Values are number of patients and percentage.

CT group: Out of 331 subjects, 37 had experience of conservative treatments such as physiotherapy, injection therapy and conventional therapies (acupuncture, moxibustion, cupping therapy, etc.) before being diagnosed with ALS. Their initial symptoms were four extremities weakness (3; 8.1%), upper extremities weakness (8; 21.6%), lower extremities weakness (9; 24.3%), hand muscle weakness (8; 21.6%), dysarthria (4; 10.8%) and others (5; 13.5%) (Table 4). It averagely took 16.6± 14.3 months for them to be diagnosed with ALS after initial symptoms appeared. In the case of 28 subjects, it was difficult to identify their diagnoses because they were not written down on their medical records. They showed the above-mentioned symptoms but did not show peculiarities on examinations. It may be because they were treated only for their symptoms. The diagnoses of the other 9 were lumbar radiculopathy (3; 8.1%), herniated cervical disc (2; 5.4%), cervical radiculopathy (1; 2.7%), cervical stenosis (1; 2.7%), diabetic neuropathy (1; 2.7%) and herniated lumbar disc (1; 2.7%). In the CT group, 8 underwent EMG, 3, 1, 1 and 1 of whom were diagnosed with lumbar radiculopathy, cervical radiculopathy, diabetic neuropathy and multifocal motor neuropathy respectively. The other 2 did not show peculiarities. A subject with lower back pain and foot drop showed the improvement of lower back pain.

DISCUSSION

Ordinarily, it is difficult to diagnose amyotrophic lateral sclerosis (ALS) early as distinct characteristics are not observed during its initial stage. In 1990 Belsh and Schiffman[2] reported that approximately 40% of patients with ALS were given wrong diagnoses at the initiatory stage, but in this study just 21% were given wrong diagnoses or underwent conservative treatments without being diagnosed. There is a strong possibility that the subjects were included in the SI or CT group even though they received other treatments before being definitely diagnosed, but such matters might be missed from their medical records. But in practice, more patients would experience other treatments before being definitely diagnosed with ALS. In this regard, Srinivasan et al.[13] reported that out of 260 patients with ALS, 55 (21%) underwent surgical treatments within 5 years before receiving definite diagnoses, just 34 (13%) of whom showed initial symptoms suspected of being from ALS. According to a study conducted on 1,131 patients diagnosed with ALS,[14] 47 (4.2%), who showed symptoms suspected of being from ALS, underwent spinal decompression surgeries before receiving definite diagnoses, 86% of whom did not show any improvements. Slight or significant improvements were observed in 9% and 5% respectively.

In this study, 71 subjects (21.4%) out of 331 underwent inappropriate treatments within 5 years before receiving definite diagnoses, 34 of whom (10.3%) got surgical treatments. It is not much different from other studies. Out of 34 subjects who received surgical operations, just 4 (11.7%) showed slight improvements. Their diagnoses were lumbar stenosis (2), ossification of posterior longitudinal ligament (1) and cervical myelopathy (1). Three of them showed the improvement of muscle weakness, and the other showed the relief of pain. They were assumed to contract ALS concurrently with spondylosis. Similarly, Yoshor et al.[14] reported that 81.9% of patients, who underwent surgical operations before being diagnosed, were clearly connected with ALS. 14.5% were accompanied by other diseases, and the other 3.6% contracted other diseases.

In this study, 14 subjects (41.1%) got cervical decompression surgeries before receiving definite diagnoses; 15 (44.1%) lumbar decompression surgeries; 1 (2.9%) cervical and lumbar decompression surgeries; 4 (11.7%) other surgeries. In comparison with the study of Srinivasan et al.[13] in which 3 (8.1%) and 11 (29.7%) were operated on for cervical vertebrae and lumbar vertebrae respectively, more subjects were operated on for them in this study. It may be because they mostly complained of symptoms related with the herniated intervertebral disc, such as upper limb muscle weakness (15; 44.1%), lower limb muscle weakness 913; 38.25) and lower back pain (3; 8.8%).

In this study, out of 34 subjects who underwent surgical operations, just 4 (11.8%) underwent EMG. The percentage was lower than that of a previous study in which 11 (32.3%) out of 34 had EMG test.[13] It is deemed that they received initial examinations from surgeons or at hospitals that were not equipped with EMG instruments or where intersectional joint treatment was not implemented. As a result, they might miss the opportunity to have electrodiagnostic examinations. Sostarko et al.[4] represented that it is not advisable for patients with ALS to undergo operations for the spine because such operations seriously damages neuromuscular function. Contrarily, Yoshor et al.[14] maintained that surgical operations might be helpful to relieve the symptoms of spondylosis but did not worsen ALS. The reason why symptoms were improved after surgical treatments might be that preoperative diagnoses were muscle weakness or pain. But in the case of symptoms that were not improved after surgical operations, there is a strong possibility that symptoms such as muscle weakness were initial symptoms of ALS. Taken altogether, it may be advisable to confine surgical operations to cases where ALS is accompanied by spondylosis and the pain is not relieved by nonsurgical treatments and has been undoubtedly caused by the spine.[13] Also in this study, improved symptoms were confined to spine-related diseases. In addition, only some subjects showed slight improvements of symptoms, which implies that a decision should be made on whether to perform surgical operations. There is no biological marker to clinically diagnose ALS, but EMG can partially substitute for it. It can reveal the injury of the lower motor neuron and thus can be a part in the diagnosis of ALS. In this study, cases where EMG was performed before treatments stood at 11.8% and 21.6% in the SI group and the CT group respectively. The reason why EMG was not performed on patients with ALS may be that ALS is similar in initial symptoms to other spinal diseases and medical staffs lack experience in ALS. Thus for cases where muscle weakness is not accompanied by pains or paresthesia, where weakness cannot be lucidly explained by radiologic examinations

and where dysarthria or dysphagia is observed, in-depth neurologic examinations and EMG need to be performed to check muscular fasciculation and diagnose other diseases early. However, fasciculation may not be observed during the early stage of ALS but may be observed even in cervical spondylosis. Thus, EMG has the demerit of low diagnostic sensitivity in relation to the incipient stage.[15,16] There is a need to perform neurologic examinations and EMG for diseases whereon physiotherapy or conservative treatments cannot have an effect and weakness that takes a turn for the worse contrary to radiodiagnosis, though they were not diagnosed as ALS at the initiatory stage.

CONCLUSION

There has been no medical examination to definitely diagnose amyotrophic lateral sclerosis (ALS) yet, and also electromyography (EMG) and radiologic examinations have limitations in accurately diagnosing it. Such being the case, it is imperative to pay close attention to clinical symptoms and progress, especially bulbar dysfunction such as muscle weakness, dysarthria and dysphagia. In addition, there is a need to periodically follow up patients in order that they should not receive inappropriate treatments but could undergo proper treatments in timely fashions.

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