Characteristics of Anal Sphincter Electromyography in Patients with Multiple System Atrophy

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Abstract: In this study, the characteristics of external anal sphincter electromyography (EAS-EMG) in patients with multiple system atrophy (MSA) were analyzed, and its value in the diagnosis of MSA was discussed. The data of 23 patients with MSA who underwent EAS-EMG examination between January 2019 and December 2021 were selected to analyze examination data such as the average duration of motor unit potentials (MUPs), average amplitude, satellite potentials, and the percentage of polyphasic waves, and to explore the correlation between the results of EAS-EMG and autonomic dysfunction in patients with MSA based on their data characteristics. The results of data analysis showed that the most common symptoms in 23 patients with MSA were urination and defecation disorders, sleep disorders, and unsteady walking, the most common signs were increased muscle tone, postural hypotension, and ataxia, and the most common autonomic dysfunction was rectal and bladder dysfunction, orthostatic hypotension, and sexual dysfunction. The average duration of MUPs was 11.6 (10.1-13.9) ms, the average amplitude was 885 (683-1198) μV, and the percentage of polyphasic waves was 26.2 (12.5-50.0)%. Patients with satellite potentials had longer disease duration. There were no significant differences in parameters between different types of autonomic dysfunction. The results suggested that abnormal changes in EAS-EMG may indicate an impaired autonomic function in patients with MSA, and this conclusion may not limit to patients with urination and defecation disorders.

1 Introduction

Multiple system atrophy (MSA), first named in 1969 [1], is a neurodegenerative disease characterized by autonomic dysfunction, Parkinson's symptoms, cerebellar ataxia symptoms, and pyramidal tract signs. The characteristic pathological changes are the discovery of intracytoplasmic inclusion bodies in oligodendrocytes [2, 3]. Autonomic dysfunction in patients with MSA is mainly manifested as dysuria, orthostatic hypotension, and sexual dysfunction [4].

In 1978, Sakuta et al. [5] first reported abnormalities in external anal sphincter electromyogram (EAS-EMG) in patients with MSA. Since then, the diagnostic value of this examination in MSA has been increasingly confirmed by international scholars. Clinical studies have shown a high incidence of abnormal EAS-EMG in patients with MSA [6]. This study aimed to analyze the characteristics of EAS-EMG data in patients with MSA in our laboratory, and further explore the diagnostic value of EAS-EMG data in MSA.

2 Materials and methods

2.1 Analytical method

The Mann-Whitney U test was adopted for data acquisition and analysis in this study [7, 8], and the method is described briefly as follows.

Two independent random samples were selected randomly, and the observations were ranked by size and weight. The weight of the minimum observation was 1, and the weight of the second-ranked observation was 2. For the same observations, the average rank order of the observations was taken as the weight, and the weight sum of the samples was calculated.

$$U_1 = A_1 - \frac{B_1*(B_1+1)}{2} \quad (1)$$

$$U_2 = \mathrm{A}_2 - \frac{B_2*(B_2+1)}{2} \quad (2)$$

where A_1 is the weight sum of sample 1, A_2 is the weight sum of sample 2, B_1 is the number of items in sample 1, and B2 is the number of items in sample 2.

$$U_1+U_2=\mathrm{A}_1 - \frac{B_1*(B_1+1)}{2}+\mathrm{A}_2 - \frac{B_2*(B_2+1)}{2} \quad (3)$$

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N is the total number of items in the two groups of samples.

$$N=B_1+B_2 \quad (4)$$

$$A_1+A_2=N\,(N+1)/2 \quad (5)$$

The following equation was obtained by substituting equation (3) with (5).

$$U_1+U_2=B_1*B_2 \quad (6)$$

If $U_i < U_j$ ($i,j \in B_1, B_2$), U_i was taken as a test statistic, and table lookup was adopted for small samples.

2.2 Patient population

In this retrospective study, patients who underwent EAS-EMG examination and were clinically diagnosed as MSA between January 2019 and December 2021 were selected as research objects to analyze their clinical symptoms and the characteristics of EMG data and to explore the correlation between examination data and autonomic dysfunction.

2.3 Detection method of EAS-EMG

The Nicolet Edx myoelectric evoked potentiometer (Natus Corporation, the United States) was used for the EAS-EMG examination. The sensitivity was 100μV/d, the scanning speed was 5ms/d, and the filtering frequency band was 20-10 kHz. During the examination, a patient was in the left decubitus position with bent hips and knees. The buttocks were separated, and the needle electrode was inserted at a mirror angle with the mucosa on the medial side of the junction of the sphincter skin and mucosa. The depth of needle insertion was about 0.5-1.0 cm. The position of the needle electrode was adjusted until the continuous tensional electrical activity was detected.

2.4 Data collection

The general information and clinical characteristics of patients, including age, gender, disease duration, symptoms, and signs, were collected retrospectively from the electronic medical record system. EMG-related data included the average duration of motor unit potentials (MUPs), average amplitude, the percentage of polyphasic waves, and satellite potentials [9].

2.5 Statistic analysis

SPSS 26.0 software was used for statistic description and analysis. For continuous variables, the Kolmogorov-Smirnov single sample test was used to test whether data were normally distributed. Continuous variables conforming to normal distribution were expressed as mean ± standard deviation, and continuous variables not conforming to normal distribution were expressed as median and upper and lower interquartile ranges. Categorical variables were expressed as the numbers of cases and percentages. The Levene test was used to compare the homogeneity of variances between the two groups of data. For continuous variables with normal distribution and equal variances, the independent sample t-test was used for inter-group comparisons. For non-normally distributed data or continuous variables with the homogeneity of variances, the Mann-Whitney U test was used for inter-group comparisons. $P<0.05$ was considered statistically significant (bilateral).

3 Results

3.1 General information of patients

A total of 23 patients with MSA, including 18 males and 5 females, with an average age of (64.63±13.05) years and an average disease duration of (3.3±2.6) years, were admitted to the neurology outpatient clinic and ward from January 2019 to December 2021. Patient data are shown in Table 1.

Table 1 General information of patients

Variables	N(%) (Total number of cases: 23)
Age (years)	64.63±13.05
Gender	
Male	18 (78.3%)
Female	5 (21.7%)
Disease duration	
Disease duration (mean ± standard deviation, years)	3.3±2.6
＞5 years	2 (9%)
≤5 years	21 (91%)
Diagnosis	
Most likely MSA	22
Possible MSA	1

3.2 Symptoms and signs of patients

Among the 23 patients with MSA, the main symptoms were constipation in 12 cases and urination disorders in 17 cases. Among them were 19 cases of urination and defecation disorders, 15 cases of sexual dysfunction, 6 cases of dizziness, 14 cases of unsteady walking, and 4 cases of weakness in both lower limbs. The abnormal signs were dystonia in 23 cases and postural hypotension in 14 cases. The data are shown in Table 2.

Table 2 Symptoms and signs of patients

Variables	N(%) (Total number of cases: 23)
Symptoms	
Urination and defecation disorders	19 (82.6)
Abnormal defecation	12 (52.2%)
Abnormal urination	17 (73.9%)
Abnormal defecation and urination	10 (43.5%)

Variables	N(%) (Total number of cases: 23)
Dizziness	6 (26.1%)
Unsteady walking	14 (60.9%)
Weakness in both lower limbs	4 (17.4%)
Hypomnesis	10 (43.5%)
Sleep disorders	16 (69.6%)
Dysphagia	4 (17.4%)
Signs	
Dystonia	23 (100%)
Postural hypotension	14 (60.9%)
Fremitus	7 (30.4%)
Ataxia	12 (52.2%)

3.3 EAS-EMG findings

The EAS-EMG in 23 patients showed the non-normal distribution of duration, amplitude, and percentage of polyphasic waves, and the data are shown in Table 3. Satellite potentials were detected in 3 patients (14.3%), with an average disease duration of 6.0 years for patients with satellite potentials and 3.1 years for patients without satellite potentials.

Table 3 EAS-EMG in 23 patients

Variables	Detection result
Duration (ms)	11.6 (10.0-13.9)
Amplitude (μV)	885 (683-1198)
Percentage of polyphasic waves (%)	26.2 (12.5-50.0)

All 23 patients had autonomic dysfunction, of which urination and defecation disorders (urinary frequency, urinary urgency, urinary incontinence or constipation) accounted for 87.0% (20 cases), orthostatic hypotension accounted for 60.9% (14 cases), and sexual dysfunction accounted for 83.3% (15 cases) of male patients. The EAS-EMG in patients with or without urination and defecation disorders, and with or without orthostatic hypotension, was analyzed using the Mann-Whitney U test. The data are shown in Table 4 and Table 5.

Table 4 EAS-EMG analysis for urination and defecation disorders

Parameters	Patients with urination and defecation disorders (N=19)	Patients without urination and defecation disorders (N=4)	*P*
Duration (ms)	11.4（10.0-13.6）	13.85（11.225-16.475）	0.366
Amplitude（μV）	932.0（683.0-1198.0）	848.5（454.25-1204.5）	0.667
Percentage of polyphasic waves (%)	28.6（12.5-55.6）	25.6（15.25-29.05）	0.286
Disease duration (years)	3.0 (2.0-5.0)	2.25 (0.3125-4.0)	0.667

Table 5 EAS-EMG analysis for postural hypotension

Parameters	Patients with postural hypotension (N=14)	Patients without postural hypotension (N=9)	*P*
Duration (ms)	11.5（9.9-14.225）	13.1（10.45-15.25）	0.516
Amplitude（μV）	908.5（422.0-1251.0）	858.0（774.5-1213.0）	0.734
Percentage of polyphasic waves (%)	19.2（11.5-61.7）	28.6（22.5-47.8）	0.25
Disease duration (years)	4.0（1.0-5.0）	3.0（1.5-3.5）	0.6

4 Conclusions

The data we collected showed that there were more male patients than female patients. All patients showed impaired autonomic function and increased Parkinson's-like muscle tone. And 69.6% of the patients were complicated with sleep disorders, most of whom had sleep disorders several years before the onset, mainly manifested as decreased overall sleep time, early wakening and sleep fragmentation, etc. Some patients had stridor, obstructive apnea, rapid eye movement sleep behavior disorder and central sleep apnea. This may be associated with the degeneration of neurons in the hypothalamus and brainstem. Some studies have shown that sleep deprivation can lead to the activation of immunoinflammatory response in the brain and

pathological changes in neurodegenerative diseases [10,11]. Sleep disorders may be caused by diseases, and sleep disorders may also accelerate the progression of diseases. Therefore, targeted sleep intervention treatment at an early stage may provide new means to delay disease progression.

In this retrospective study, we found that memory loss occurred in 43.5% of patients, and most patients had a disease course of less than 5 years, suggesting cognitive decline early in the onset of MSA. Previous studies have shown that it takes about seven years for patients with MSA to experience obvious cognitive dysfunction from definite diagnosis [12], and about 50% of patients with MSA who have survived more than eight years have obvious symptoms of cognitive dysfunction [13]. Therefore, the early diagnosis and timely intervention of cognitive dysfunction in patients with MSA should be carried out to improve the quality of life of patients.

Previous studies have shown that in patients with MSA, autonomic dysfunction will greatly affect the quality of life, resulting in a significant decline in patients' daily living ability and frequent medical visits [14]. Data analysis showed that about 75% of patients diagnosed with MSA had complaints related to autonomic dysfunction, which mainly manifested in postural change-related symptoms and directly reflected in rectal and bladder dysfunction. However, these symptoms are often not taken seriously by patients for various reasons or are identified as corresponding diseases due to the diagnosis and treatment of gastroenterology or urology. There are even the misdiagnosis and mistreatment of surgery based on prostate diseases, causing great physical and mental health harm to patients [15]. In order to evaluate, diagnose and differentiate autonomic dysfunction in patients with MSA early, the choice of methods is very important, which will greatly determine the accuracy of diagnosis, and then greatly affect the speed of recovery and promote the recovery of quality of life [16]. In this study, it was found that 73.9% of patients developed autonomic dysfunction at an early stage, while only 17.4% of patients presented this as the main complaint. The analysis of male patients in this study showed that sexual dysfunction accounted for 83.3% of male patients, indicating that this is a common and important manifestation of autonomic dysfunction in patients with MSA.

The proportion of patients with urination disorders was shown to be greater than the proportion of patients with postural hypotension, and bladder dysfunction tended to occur earlier if both symptom indicators were present [17]. A European study on 71 male patients with MSA showed that 76% of them had dysuria prior to postural hypotension, and 91% of them had sexual dysfunction prior to orthostatic hypotension [18]. In this study, 75% of patients without orthostatic hypotension were shown to have constipation, and 87.5% of patients without orthostatic hypotension had urination disorders. And urinary frequency, urinary urgency, and decreased force of urination was shown to be more common than urinary incontinence, indicating that abnormal urinary symptoms besides urinary incontinence should also be paid sufficient attention to in clinical examination. Therefore, the EAS-EMG examination for patients with abnormal urination at a certain stage is of positive significance for the diagnosis and treatment process. If patients are further found to have neurogenic damage and other problems, it should be followed up closely. Previous studies showed that, in general, some indicators of EAS-EMG in patients with abnormal urinary symptoms were significantly different from those without corresponding symptoms, indicating that the loss of Onuf's nucleus was closely related to the occurrence of urination disorders in patients with MSA [19, 20]. However, this consistent conclusion was not obtained in this study, which was considered an insufficient sample size. In the future, we will continue to expand the sample size for further research.

Studies have shown that 90% of patients with MSA have abnormal EAS-EMG, with a sensitivity of 80% [16]and specificity of 93%-100% [21-23]. There is no consensus on the abnormal criteria for EAS-EMG due to the difficulty of obtaining normal value data from the special location of the anal sphincter, which has become a major problem limiting the progress in this research area. Most scholars believe that most patients with MSA can be distinguished from other causes of Parkinson's syndrome with an average duration of more than 10 ms [16, 21, 24]. If the same criteria were applied in this study, the abnormal rate of EAS-EMG in 23 patients with MSA would be 100%, which was basically consistent with previous studies. At present, domestic and foreign experts and scholars are still making unremitting explorations on the pathogenesis, diagnosis, and treatment of MSA, hoping to overcome it completely in the future. The early clinical manifestations of MSA have poor specificity, and imaging features are not obvious. Therefore, it is particularly important to reduce misdiagnosis, diagnose early and give appropriate treatment. In subsequent studies, we will further explore the differences between EAS-EMG in patients with MSA and those with other neurodegenerative diseases to guide clinical application and diagnosis.

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