When is Onuf’s nucleus involved in multiple system atrophy? A sphincter electromyography study

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Background: External anal sphincter (EAS) electromyography (EMG) abnormalities can distinguish multiple system atrophy (MSA) from Parkinson’s disease in the first five years after disease onset. However, the prevalence of the abnormalities in the early stages of MSA is unknown.

Objectives: To present EAS-EMG data in the various stages of MSA.

Methods: 84 patients with “probable” MSA were recruited (42 men, 42 women; mean age 62 years (range 47 to 78); mean disease duration 3.2 years (0.5 to 8.0; <1 year in 25%); 50 cerebellar form (MSA-C), 34 parkinsonian form (MSA-P)). EAS motor unit potential (MUP) analysis and EMG cystometry were carried out in all patients.

Results: The overall prevalence of neurogenic change of the EAS MUP was 62%—52% in the first year after disease onset, increasing to 83% by the fifth year (p<0.05); it also increased with severity of gait disturbance (p<0.05), storage and voiding disorders, and detrusor sphincter dyssnergy (NS). The neurogenic change was not correlated with sex, age, MSA-P/C, postural hypotension, constipation, erectile dysfunction in men, underactive or acontractile detrusor, or detrusor overactivity. In 17 continent patients without detrusor overactivity or low compliance, urinary incontinence was more severe in those with neurogenic change than in those without (p<0.05).

Conclusions: Involvement of Onuf’s nucleus in MSA is time dependent. Before the fifth year of illness, the prevalence of neurogenic change does not seem to be high, so a negative result cannot exclude the diagnosis of MSA.
Results

Patients’ functional ability and urinary disorders were as follows. Gait disorder (as measured by the international cooperative ataxia rating scale, walking capacities subscale19) was absent (score of 0) in none, independent walking (score 1–3) in 23, walking with one stick (score 4–5) in 22, walking with aid (score 6–7) in 28, and wheelchair bound (score 8) in 11. All patients except for two had urinary symptoms. Urinary incontinence (storage disorder) was never experienced in the study. Statistics were analysed using the \( \chi^2 \) test.

Discussion

Results of the EAS EMG in over 500 MSA patients have already been reported, with an abnormality rate of more than 70% in many studies.7–15 Compared with those findings, the overall prevalence rate of neurogenic change in the present study was slightly lower (62%). This is presumably because up to 25% of our patients had a disease duration of one year or less, as early referral to our department has increased recently, and patients are able to come to us without referral. Thus the diagnosis of MSA in such early cases should be made with extreme caution. In addition to the clinical diagnostic criteria,16 we added an imaging study to ensure the diagnosis in all patients, and we carried genetic analyses as far as possible. Although the EAS MUP abnormalities allow one to distinguish MSA from Parkinson’s disease in the first five years after disease onset,16 the prevalence of the abnormalities in the early stages of MSA (or, conversely, the false negative rate) has not been established up to now. We report here for the first time that in our patient cohort the prevalence of neurogenic change was 52% in the first year after disease onset, increasing to 83% by the fifth year (p<0.05). Among the patients who underwent repeated studies, many were normal or had only mild abnormality at the initial examination, but the abnormality became marked during the course of their illness. Therefore, as expected, the involvement of Onuf’s nucleus in MSA is time dependent. In the early stages of illness, the prevalence of neurogenic change in MSA does not seem to be high. In two patients who underwent repeated studies, the EAS EMG findings remained normal. We do not know whether there are some
MSA patients who never develop neurogenic change during the course of their illness. However, Wenning et al reported three patients with normal EAS EMG and necropsy confirmation of MSA. Thus the negative result cannot exclude the diagnosis of MSA.

The prevalence of neurogenic change also increased with the severity of gait disturbance (p<0.05) in the present study. However, it was not related to postural hypotension (reflecting adrenergic nerve dysfunction), erectile dysfunction in men (presumably reflecting cholinergic and nitrate oxidergic nerve dysfunction), detrusor overactivity (reflecting central type of detrusor dysfunction), constipation (presumably reflecting both peripheral and central types of autonomic and somatic dysfunctions), or sex. Changes in the EAS MUP were slightly more common in patients with detrusor sphincter dyssynergy (reflecting central type of sphincter dysfunction). It has previously been reported that neurogenic change does not correlate directly with a clinically obvious functional deficit. Patients with marked abnormalities of the EAS MUP may have no faecal incontinence although in such patients anal sphincter weakness is not uncommon. In the present study, the prevalence of neurogenic change slightly increased with the severity of storage disorder (incontinence) and voiding disorder (large PVR). The latter may only reflect a parallel and not a causative relation. In the former, the most common urinary incontinence in MSA is urge incontinence, which mostly results from the detrusor (bladder) overactivity. However, we noted urinary incontinence in 17 patients without detrusor overactivity or a low compliance detrusor, which might have a sphincter aetiology. Urinary incontinence was more severe in the patients with neurogenic change than in those without (p<0.05). These results are in agreement with observations by Beck et al, and with our previous findings that neurogenic change of the EAS MUP led to a low urethral pressure and sphincter incompetence, particularly in women in the middle to advanced stages of MSA (inability to hold urine, “intrinsich sphincter deficiency”, or stress urinary incontinence type 3). The function of Onuf’s nucleus is not confined to the innervation of the EAS—that is, it innervates external urethral sphincter as well. As we do not carry out EMG of the external urethral sphincter routinely, the present study results may represent only one aspect of the nucleus. However, our findings may contribute to the differential diagnosis of Parkinsonism and ataxic cerebellar disorders.

In conclusion, the results of the present study suggest that the involvement of Onuf’s nucleus in MSA is time dependent.

Table 1 Neurogenic sphincter EMG and clinical variables other than duration of illness

<table>
<thead>
<tr>
<th>Patients with neurogenic sphincter EMG</th>
<th>Patients with neurogenic sphincter EMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
<td>Age &gt;60 years</td>
</tr>
<tr>
<td>MSA-C</td>
<td>MSA-P</td>
</tr>
<tr>
<td>Independent walking (1–3)</td>
<td>Wheelchair bound(6–7)</td>
</tr>
<tr>
<td>Postural hypotension</td>
<td>Postural hypotension +</td>
</tr>
<tr>
<td>Constipation</td>
<td>Constipation +</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>Erectile dysfunction +</td>
</tr>
<tr>
<td>Continent</td>
<td>Incontinent</td>
</tr>
<tr>
<td>RU &lt;200 ml</td>
<td>RU &lt;200 ml</td>
</tr>
<tr>
<td>Detrusor overactivity</td>
<td>Detrusor overactivity +</td>
</tr>
<tr>
<td>UD/AD</td>
<td>UD/AD +</td>
</tr>
<tr>
<td>DSD</td>
<td>DSD +</td>
</tr>
</tbody>
</table>

*International cooperative ataxia rating scale, walking capacities subscale.

AD, acontractile detrusor; DSD, detrusor sphincter dyssynergy; MSA, multiple system atrophy; RU, residual urine volume; UD, underactive detrusor.

In the early stages of the illness, the prevalence of neurogenic change does not seem to be high, so a negative result cannot exclude a diagnosis of MSA.

REFERENCES

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