Objective: To investigate lower urinary tract function in spinocerebellar ataxia type 6 (SCA6).

Methods: We recruited, without bias, nine SCA6 patients with a mean cytosine-adenine-guanine repeat length of 24.3 (21–26, normal <18). They were four men, five women; mean age 58.6 years; mean disease duration 8.2 years. We performed a urinary symptom questionnaire and a urodynamics.

Results: Urinary symptoms were observed in five of nine patients (56%) and urinary frequency in three of nine patients (33%), and none had urinary retention. Urodynamic abnormalities included detrusor overactivity in one (11%) and weak detrusor on voiding in two, but none had postvoid residual urine. Sphincter electromyography revealed, while mild in degree, neurogenic change in five of the eight patients (63%) on whom the test was performed.

Conclusion: We observed urinary frequency in 33%; detrusor overactivity in only 11%; and neurogenic change in the sphincter electromyography in 63% of our nine SCA6 patients. These findings might be relevant to the cerebellar and spinal cord pathologies of this disease.

Key words cerebellum, detrusor overactivity, lower urinary tract, Onuf’s nucleus, spinocerebellar ataxia type 6

1. INTRODUCTION

Spinocerebellar ataxia type 6 (SCA6) is a rare but well documented familial disease. The responsible gene is the alpha-1A subunit of voltage-gated CaV2.1 (P/Q-type) Ca\(^{2+}\) channels (CACNA1A), where prolonged cytosine-adenine-guanine (CAG, coding glutamine) repeat is found. While it is believed that SCA6 has a pure cerebellar phenotype recent studies indicated that 31% of patients have lower urinary tract symptoms (LUTS). However, no urodynamic reports were available, to our knowledge. We here describe our urodynamic results of nine unselected, genetically-diagnosed SCA6 patients.

2. METHODS

In the present study we recruited, without bias, nine SCA6 patients with a mean CAG repeat length of 24.3 (range 21–26, normal <18) during a 2-year period at our neurology clinic. They were four men, five women; mean age 58.6 (range 36–69) years; mean disease duration 8.2 (range 3–15) years. In one patient (case 3) the gene analysis was performed at another institute; therefore we had only a positive result. Three patients had positional vertigo; all had cerebellar ataxia and none was bedridden with a moderate SARA\(^{3}\) (The Scale for Assessment and Rating of Ataxia) mean score of 23 (range 0–38); none had pyramidal disorder, extrapyramidal disorder, cognitive disorder, sensory abnormality, peripheral neuropathy, or autonomic disorder except for bladder dysfunction, (e.g. postural dizziness/syncope, Horner syndrome, or decreased sweating) (Table 1). All patients underwent brain magnetic resonance imaging scans, showing cerebellar atrophy alone (Fig. 1). None had abnormalities in blood chemistry or urinalysis. We analyzed the relation between LUTS with patients’ age, CAG repeat length, scores of SARA and disease duration. Statistical analysis was made by Student’s \(t\)-test and Spearman’s rank correlation coefficient test.

We performed LUTS questionnaire that was devised for assessing neurologic lower urinary tract function, including questions about daytime frequency (>8 abnormal), night-time frequency (>2 abnormal), urinary urgency, urinary incontinence and voiding difficulty. Each question had four graded choices: none, mild (>once a month), moderate (>once a week) to severe (>once a day). Urodynamics was performed according to the International Continence Society standard methods. After free flowmetry, we measured the postvoid residual by transurethral catheterization, and their volumes were

*Correspondence: Ryoji Sakakibara, MD, PhD, Neurology Division, Department of Internal Medicine, Sakura Medical Center, Toho University, 564-1 Shimoshizuh, Sakura 285-8741, Japan. Tel: +81-43-462-8811 ext. 2323; Fax: +81-43-487-4246. Email: sakakibara@sakura.med.toho-u.ac.jp

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**TABLE 1.** Patients and lower urinary tract symptom

<table>
<thead>
<tr>
<th>No.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>CAG repeat length</th>
<th>Vestibular Ataxia</th>
<th>Urinary incontinence</th>
<th>Illness Duration (years)</th>
<th>Lower urinary tract symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>F</td>
<td>3</td>
<td>Vestibular</td>
<td>24</td>
<td>24</td>
<td>Daytime Frequency: &lt;8</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>F</td>
<td>9</td>
<td>Vestibular</td>
<td>26</td>
<td>26</td>
<td>Night-time Frequency: &lt;2</td>
</tr>
<tr>
<td>3</td>
<td>33</td>
<td>M</td>
<td>15</td>
<td>Vestibular</td>
<td>28</td>
<td>28</td>
<td>Urge and stress</td>
</tr>
<tr>
<td>4</td>
<td>61</td>
<td>M</td>
<td>15</td>
<td>Vestibular</td>
<td>23</td>
<td>23</td>
<td>Monthly Urge</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>M</td>
<td>11</td>
<td>Vestibular</td>
<td>26</td>
<td>26</td>
<td>Monthly Urgency</td>
</tr>
<tr>
<td>6</td>
<td>67</td>
<td>M</td>
<td>8</td>
<td>Vestibular</td>
<td>27</td>
<td>27</td>
<td>Monthly Stress</td>
</tr>
<tr>
<td>7</td>
<td>69</td>
<td>M</td>
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<td>Vestibular</td>
<td>22</td>
<td>22</td>
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<td>8</td>
<td>67</td>
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<tr>
<td>9</td>
<td>69</td>
<td>F</td>
<td>4</td>
<td>Vestibular</td>
<td>20</td>
<td>20</td>
<td>Stress</td>
</tr>
</tbody>
</table>

Abnormal data are indicated as hatched area. CAG, cytosine-adenine-guanine; F, female; M, male; N, normal; SARA, Scale for Assessment and Rating of Ataxia.

Fig. 1 Brain magnetic resonance imaging of the representative case of spinocerebellar ataxia type 6. Axial and sagittal views of T1-weighted images show marked cerebellar atrophy. Pons and midbrain is intact.

regarded normal at <30 mL. We performed standard electromyography (EMG)-cystometry (medium-fill [50 mL/min.], liquid [saline]) using a urodynamic computer (Urovision; Lifetech Inc., Houston, TX, USA) and an EMG computer (Neuropack M2; Nihon Kohden Inc., Tokyo, Japan). Normal values for first sensation and bladder capacity are estimated as 100–300 and 200–600 mL in our urodynamic laboratory. We performed the pressure-flow analysis in all subjects. Using Schäfer’s nomogram, we classified detrusor contractility as: strong, normal, weak, or very weak; a detrusor that was weak or very weak was designated a weak detrusor. Outlet obstruction was designated as Schäfer’s obstruction grade 3 or more. After inserting a concentric needle electrode in the external anal sphincter muscles, we analyzed the motor unit potential (MUP) using the same EMG computer. Neurogenic change was diagnosed according to published criteria, for example, when at least one of the following abnormalities was seen: (i) more than 20% MUP with a duration >10 msec; or (ii) average duration of MUP >10 msec, particularly including the late components. None had prostatic hypertrophy by ultrasound echography of the prostate gland. None had taking drugs that might interfere with lower urinary tract function. We also excluded multiparous women by history taking, diabetes by laboratory data, and degenerative changes in the spine by lumbar magnetic resonance imaging. All patients gave informed consent before participating in the study. This study was approved by the local Ethics Committee.

**3. RESULTS**

LUTS was observed in five of nine patients (56%) (Table 1). LUTS had no relation with CAG repeat length, scores of SARA or disease duration. LUTS was more common in subjects older than 60 years, although there was no statistical significance. The most frequent symptom was daytime urinary frequency (three patients) and urinary incontinence (three patients), followed by urinary urgency (two patients), night-time urinary frequency (one patient), and voiding difficulty (one patient). None had episodes of urinary retention.
Urodynamic abnormalities were seen in three of nine patients (33%) (Table 2), which included increased bladder sensation in two patients, detrusor overactivity in one (11%) and weak detrusor on voiding in two. None had postvoid residuals. Sphincter EMG abnormalities included detrusor-sphincter dyssynergia in none, and neurogenic change in five of the eight patients (63%) on whom the test was performed, although the grade of chronic denervation was mild (only two patients had average MUP duration [10.36 and 11.44 ms]) (Fig. 2).

4. DISCUSSION

In the present study we found the following: (i) LUTS was observed in five of nine patients (56%) and urinary frequency was observed in three (33%) of nine patients, which had no relation with CAG repeat length, scores of SARA, or disease duration; (ii) urodynamics showed detrusor overactivity in only one patient (11%); and (iii) sphincter EMG revealed neurogenic change in the external sphincter muscle in five of eight patients (63%) although the grade of chronic denervation was mild. To the best of our knowledge, this is the first urodynamic report in genetically diagnosed SCA6 patients. Others are considered as not disease-specific findings.

Detrusor overactivity (noted in one patient) indicates an exaggerated micturition reflex during bladder filling. Since this patient had no pyramidal signs or sensory abnormality, it seems unlikely that detrusor overactivity might originate from cervical/thoracic spinal cord disorder. In experimental animals, it is known that cerebellum has inhibitory influences on the bladder function.9,10 There are fiber connections between the bladder and the cerebellar vermis both morphologically11 and electrophysiologically.9 Therefore, it is likely that cerebellar pathology might have led to detrusor overactivity in this case. The low frequency of detrusor overactivity and lack of postvoid residual urine in SCA6 may help in differentiating SCA6 from multiple system atrophy (MSA), in which detrusor overactivity and large postvoid residual are common.12 Although we did not examine other muscles, neurogenic change in the external anal sphincter muscle (noted in 63% of patients) indicates a sacral spinal cord disorder, since the external anal sphincter muscles are innervated by the S2-4 sacral anterior horn cells (Onuf's nucleus). Recent pathology studies in SCA6 indicated that SCA6 involves not only the cerebellum and brainstem olivary nucleus, but also the spinal anterior horn.13–15 Although the grade of chronic denervation in SCA6 was milder than that of MSA,6–8 we have to be careful to distinguish SCA6 from MSA using sphincter EMG. Limitation of the present study includes a small number of subjects, and lack of control. However, some SCA6 patients seek medical care for their lower urinary tract dysfunction. The present study results can help manage bladder dysfunction in SCA6 patients in the future.

In conclusion, we observed urinary frequency in 33%; detrusor overactivity in only 11%; and neurogenic change in the sphincter EMG in 63% of our nine SCA6 patients.
These findings might be relevant to the cerebellar and spinal cord pathologies of this disease.

**Disclosure**

None of the authors have a conflict of interest.

**REFERENCES**