

## Severe Dysarthria Developed in a Carrier of Spinobulbar Muscular Atrophy

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### Abstract

Spinobulbar muscular atrophy (SBMA) is a rare neurodegenerative disorder resulting in distal muscular atrophy with prominent bulbar sign. The pattern of inheritance is X-linked, so most affected patient was male. We present a 78-year old woman with severe dysarthria who was diagnosed as a carrier of SBMA.

**Keywords:** Spinobulbar Muscular Atrophy; Dysarthria; X-Linked Carrier

### Introduction

Spinobulbar muscular atrophy (SBMA) known as Kennedy's disease is a debilitating neurodegenerative disorder resulting in progressive weakness due to degeneration of lower motor neurons in the brainstem, spinal cord, and skeletal muscle, which is inherited in an X-linked recessive manner [1]. Symptoms include dysarthria, dysphagia, fasciculations, tremor, and gait disturbances [2].

The prevalence of SBMA is estimated to be approximately 1 in 400,000, with a proportionally greater number of cases in Japan and Finland. However many patients are tend to be misdiagnosed due to similar clinical features of amyotrophic lateral sclerosis and other, more common motor neuron diseases [3]. In SBMA, there is an expansion of the CAG (polyglutamine) repeat region within exon 1 of the androgen receptor (AR) gene. Generally, females are rarely affected and female carriers tend to have a relatively mild expression of the disease [4].

Here, we report a case of progressive severe dysarthria developed in the female carrier of SBMA.

### Case

A 78 year-old right-handed female presented with 2-year history of progressive dysarthria. She had a history of hypertension and old pontine cerebral infarction at 66 years without any sequelae. At the beginning of dysarthria, she complained of excessive saliva, but had no difficulty with swallowing. As dysarthria worsen, she could speak just a few words, and she swallowed slowly with occasional choking. Recently, phonation became impossible. Relatively, comprehension was maintained. She expressed her thought as gestures. Frequent choking became aggravated. There was no ptosis, double vision, motor weakness, paresthesia in extremities, bladder disturbances, or gait difficulties. On neurologic examination her buccofacial muscles showed normal bulk and tongue showed no fasciculation. Jaw occlusion and tongue protrusion showed symmetric flaccid weakness. Manual motor testing showed normal strength in whole extremities. Fasciculation was not seen. Deep tendon reflexes were decreased. There were no other upper motor signs. Phonation time decreased profoundly and severely strangled voice during phonation. She could hardly pronounce a consonant. Western Aphasia Battery (WAB) test showed inability of spontaneous speech, repetition, naming but, relatively preserved auditory comprehension. In the performance-domain areas, writing was impossible because she was illiterate. Serum CPK was within normal limits. Brain MRI and angiography showed no definite lesion that could contribute dysarthria. Perfusion MRI showed bilateral oligemia. FDG PET showed decreased glucose metabolism in bilateral fronto-parieto-temporal cortex.

EMG/NCS showed prolonged terminal latencies and decreased CMAP amplitude in bilateral median nerves; slow motor nerve conduction velocities in bilateral tibial and left peroneal nerve; slow sensory nerve conduction velocities in bilateral median, right ulnar and bilateral sural nerves. Every limb and facial muscle examined by needle EMG showed normal insertional activities and denervation potential in right FDI and TA muscles. Motor Evoked Potential (MEP) showed suggestion of central conduction block in corticospinal tract. Repetitive nerve stimulation (RNS) test was normal.

Family history was that her son was diagnosed with SBMA 20 years ago. Genetic testing showed that she had 46 and 24 CAG repeats in the androgen receptor on Xq11-12, which suggested heterozygote female carrier. Although NCS and EMG on extremities showed no denervation potential, dysarthria and bulbar weakness were considered as manifestations of SBMA carrier. The patient's neurological symptom and electrophysiologic study will be traced for detection of motor neuron disease.

### Discussion

Lower motor neuron and neuromuscular dysarthria (flaccid dysarthria) is caused by weakness or paralysis of the articulatory muscles, the result usually of disease of the motor nuclei of the medulla and lower pons or their intermedullary or peripheral extensions (lower motor neuron paralysis). If dysarthria progresses slowly, the possibility of neurodegenerative disorder including motor neuron disease increased.

The pathological features of SBMA result from loss of lower motor neurons, particularly of anterior horn cells of the spinal cord, and of the cranial nerves of the brain stem [5].

Female carriers for SBMA typically do not show symptoms because the androgen receptor must bind to its ligand, testosterone, to translocate to the nucleus and perform its functions. As females have low circulating levels of testosterone, Kennedy disease female carriers do not activate their mutant androgen receptors, thus rendering the mutant state of the androgen receptor protein innocuous [4].

Heterozygous female carriers have been reported to display subclinical manifestations of the disease. The majority of carrier women presented signs of chronic denervation at neurophysiological examination and a few women developed mild signs of bulbar motor neuron impairment later in life, which supported the hypothesis that an enlarged polyglutamine mutation within the AR gene has a dominant pathogenic effect and inactivation of the X-chromosome, by preventing the expression of the mutated AR protein in a proportion of motor neurons, may display the rate of neuronal cell damage and the full manifestations of the disease in women [6-8].

Previous report presented that a 75 years old heterozygote female carrier of SBMA had a feature of motor neuron disease. Contrary to our case, the patient had dominant features of upper motor neuron signs (generalized spasticity in the upper and lower limbs bilaterally, positive bilateral Babinski reflex), so the author suggested possibility that coexistence of motor neuron disease in a carrier of SBMA may be a coincidence, or the presence of CAG repeats in the AR may have played some role [5].

We report severe dysarthria and bulbar weakness in old female carrier. These features suggest that selective bulbar symptom can be manifesting in carrier woman. Further electrophysiological test will be performed to evaluate the involvement of extremities. In this report, we described a severe dysarthria developed in a carrier of SBMA.

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