P 2-126

Delayed Diagnosis of A female Carrier Spinal & Bulbar Muscular Atrophy with Proximal Limbs Weakness

Hyun-sung Lee [1,1*], Chang-Hwan Kim[1,1†], Chang-Beom Kim[1,1], Han-Young Jung[1,1], Myeong-Ok Kim[1,1], Kyung-Lim Joa[1,1], Chan-Hyuk Park[1,1]

Inha University Hospital, Department of Rehabilitation Medicine[1]

Introduction

Spinal and bulbar muscular atrophy (SBMA, Kennedy's disease) is an X-linked, adult onset lower motor neuron disease characterized by slowly progressive weakness of the bulbar and extremity muscles. SBMA is caused by a CAG-repeat expansion in the first exon of the androgen receptor (AR) gene on the X-chromosome. Gene analysis can provide a diagnostic basis for this disease. The size of CAG repeats is one of the determinant factors of the severity of SBMA phenotypes. Heterozygous female carriers are generally asymptomatic, and even homozygous females had only mild symptoms. It makes delayed or misdiagnosis of SBMA in female patients. We report a case of symptomatic SBMA female patient who had not been diagnosed correctly for 13 years.

Case report

In 2005, a twenty two year-old female visited our clinic with difficulty in going upstairs and intermittent nonspecific joints pain for several months. She had shown no facial, bulbar weakness and sensory symptom. In family history, her father was hard working person, and had a very mild limbs weakness and mild dyspnea on working without any evaluation. On physical examination, strength of shoulder girdle and proximal lower limbs were grade 4/5 Medical research council (MRC) scale, although distal upper and lower limbs were intact. Tendon reflexes were normoactive. Pathologic reflex was negative. In laboratory test, CPK, Anti-Ach-R Ab, Antinuclear ab and Anti-CCP were negative. Multiple joints x-rays and whole spine MRI showed no specific findings. Nerve conduction study was within normal limits, electromyography (EMG) showed a low proportion of small amplitude and short duration of motor unit potentials in predominantly proximal muscles. Considering the evidence of EMG and proximal limbs upper weakness, we had suspected of subclinical familial myopathy and studied dystrophin gene, however it was negative. We consulted to psychologist for depressed mood and multiple unexplained joints pain. She was diagnosed with somatoform disorder and taken anti-depression drugs. In 2019, she visited our hospital again due to aggravating fatigable proximal and distal limbs weakness and difficulty in opening the lid since two years before. Tongue fasciculation was newly found. The result of Follow-up EMG was similar to the initial test. The patient's uncle who had

shown progressive dysarthria was recently diagnosed with SBMA by AR gene study. Considering her family history, she also got AR gene study revealing high CAG repeats expansion on X-chromosome. Finally, she was diagnosed with SBMA as a heterozygous female carrier.

Conclusion

Female gene carriers of X-linked recessive SBMA can be rarely symptomatic. Because of this genetic nature, it is uneasy to diagnose SBMA with clinical symptoms and electrophysiologic study in symptomatic female SBMA patient. Therefore, in the X-linked genetic disorders, more detailed history taking and aggressive gene study are important for diagnosis and treatment

Table 1. Androgen receptor gene study

Disease/Gene	Results	Reference
SBMA/AR	CAG 26 / 51 repeats , heterozygous type	Repeats in normal repeats 6-34 Repeats in reduced penetrance 36-37 Repeats in full-penetrance ≥38

SBMA: Spinal and bulbar muscular atrophy, AR: androgen receptor