

## An autopsy case of the Kennedy-Alter-Sung type of familial spinal and bulbar muscular atrophy:

Demonstration of a CAG repeat in the androgen receptor gene  
using whole genome amplification

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### Abstract

Spinal and bulbar muscular atrophy (SBMA) is an X-linked recessive trinucleotide, polyglutamine (polyQ) disease, caused by the abnormal expansion of a polymorphic CAG tandem-repeat in the first exon of the androgen receptor (AR) gene. SBMA was first reported by Kennedy, Alter, and Sung; therefore, this disease is often referred to as Kennedy-Alter-Sung syndrome. Spada, Fischbeck, and colleagues discovered SBMA is caused by an unstable CAG repeat expansion in the first exon of the AR gene. Thereafter, the complete diagnosis of SBMA is generally made possible by genetic analysis of patient-derived tissues or peripheral blood cells; however, when an extremely insufficient amount of unfixed biopsy tissue or postmortem tissue is available, genetic analysis by the standard PCR method reported by Spada, Fischbeck, and colleagues may be impossible. To address this issue, whole genome amplification (WGA) technology was applied. With this technology, we have verified successfully the expansion of a polymorphic CAG tandem-repeat in the first exon of the AR gene, using a trace amount of genomic DNA. This DNA originated from only two sections of unfixed, unstained muscle tissue specimens obtained by biopsy from a patient 24 years prior. The muscle tissue specimens had been subjected to long-term storage at room temperature (RT). They were of 10 micrometer thickness weighing 1–2 mg, and were the only tissue samples available for genetic analysis at that time. For comparison, frozen postmortem brain tissues obtained from another patient with SBMA were processed in a similar manner. Tottori J. Clin. Res. 9(2), 190-204, 2017

Key words: spinal and bulbar muscular atrophy (SBMA), Kennedy-Alter-Sung (KAS) syndrome, androgen receptor (AR), CAG repeat, polyglutamine (polyQ), whole genome amplification (WGA)

### Introduction

SBMA is an adult-onset (third to fifth decade of life), X-linked recessive trinucleotide, polyQ disease, caused by the abnormal expansion of a polymorphic CAG tandem-repeat in the first exon of the AR gene, which is mapped to chromosome Xq11-q12. This disorder was first reported by Kennedy, Alter, and Sung<sup>1)</sup> in 1968; therefore, this disease is often called

Kennedy-Alter-Sung syndrome (also known as Kennedy's disease). SBMA is characterized by the following: proximal limb, facial, masseter, and bulbar muscular atrophy, weakness with contraction fasciculation, fine finger tremor, muscle cramps, hoarseness, rhinolalia aperta, dysphagia, dysarthria, diminished deep tendon reflex without pathological reflex, and an impaired sense of vibration<sup>2)</sup>. The muscle weakn-