Kennedy Disease: The First Case Report in Malaysia

Nor Azimah Abdul Azize¹, Yusnita Yakob¹ and Kavitha A/P Rethanavelu²

¹ Molecular Diagnostics & Protein Unit, Institute for Medical Research, 50588 Jalan Pahang, Kuala Lumpur.
² Genetics Department, Hospital Kuala Lumpur, 50586 Jalan Pahang, Kuala Lumpur.

Abstract

Spinal and bulbar muscular atrophy also known as Kennedy Disease (KD) (MIM #313200) is a gradually progressive neuromuscular disorder, in which degeneration of lower motor neurons resulting in muscle weakness, muscle atrophy and fasciculation. These symptoms usually begin in adulthood and worsen slowly over time. KD is inherited in an X-linked pattern, caused by abnormal expansion of CAG repeat in exon 1 of Androgen Receptor (AR) (NM_000044.3) gene. Normal individual has CAG repeats up to 36, whereas KD patient’s has more than 40 repeats. We reported here a 61 years old male patient with progressive nasal speech, impairment of speech clarity, facial asymmetry and generalised weakness for over 3 years. These symptoms were noticed by his family and friends and he was advised to seek medical attention. The aim of this study is to characterize the pattern of CAG repeats in AR gene of this patient by PCR and fragment analysis. Clinical examination of this patient confirmed palatal muscle weakness, velopharyngeal insufficiency, proximal myopathy, facial myokinesia and gynecomastia. The nerve conduction study showed absent sensory and smallest motor response with diffuse neurogenic changes of chronic nature and MRI brain showed no significant changes. He was then referred to Hospital Kuala Lumpur for diagnosis of Kennedy disease and whole blood EDTA was sent to our laboratory for molecular testing. DNA was extracted using a standard protocol. PCR amplification was carried out using primers flanking the trinucleotide repeat region, followed by capillary electrophoresis and sizing of the PCR products. Genemapper software was used to determine the number of CAG repeats. One expanded allele was detected in our first KD patient in Malaysia with approximately 46 CAG repeats. Family screening was suggested for all asymptomatic male relatives as KD is an X-linked disease. As a conclusion, we have successfully determined the CAG repeats expansion in KD patient for confirmation of the disease. Capillary electrophoresis has provided accurate sizing of fragment which is very important in determination of repeats.

Keywords: Kennedy Disease; CAG repeats; neuromuscular disorder

*Author for Correspondence