KENNEDY’S DISEASE PHENOTYPE WITH POSITIVE GENETIC STUDY FOR KUGELBERG-WELANDER’S DISEASE

Case report

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ABSTRACT - We described a patient with clinical findings from Kennedy’s disease and positive genetic study for Kugelberg-Welander's disease. A 24 years old man with negative family history presented with progressive spinal and bulbar muscular atrophy and gynecomastia at the age of 14. He was clinically diagnosed as having Kennedy’s disease. However, a genetic study performed later was found to be negative for this disease and was positive for Kugelberg-Welander’s disease, with deletion of the exons 7 and 8 in the “survival of motor neuron” gene.

KEY WORDS: Kennedy’s disease, Kugelberg-Welander’s disease, genetic test.

Although several hereditary neurodegenerative diseases, among which Kennedy’s disease (KD) also known as X-linked spinal and bulbar muscular atrophy and Kugelberg-Welander’s disease (spinal muscle atrophy type III), are classified as lower motor neuron disease, they usually present with strikingly different clinical features¹. As well as that, they have distinct genetic mutations, allowing a correct diagnosis based on specific and precise laboratory testing²,³. We present a rare case of a patient with clinical features of Kennedy’s disease, whose genetic testing was compatible with spinal muscle atrophy type III (Kugelberg-Welander’s disease). We also highlight the clinical and genetic divergent features of both disorders.

CASE

A 24 years old man presented to our service complain-
cule strength in upper limbs and grade I muscle strength in lower limbs. Deep tendon reflexes were absent, there was generalized muscle atrophy, fasciculations in both tights and myopathic gait.

Laboratory work-up disclosed low serum blood levels of testosterone, FSH and LH. An electromyographic study was abnormal, with findings suggestive of both active and chronic denervation in a diffuse distribution including limbs and the tongue. Nerve conduction study was normal. A muscle biopsy was performed and it also showed signs of chronic denervation. Based on both the clinical features and abnormal laboratory results, he was then diagnosed as having KD.

A blood sample was collected and sent to genetic study. Our patient showed 26 CAG repeats within the first exon of the androgen receptor gene and disclosed a deletion of exon 7 and 8 for the survival motor neuron (SMN) gene, suggestive of spinal muscle atrophy. Those findings were confirm when tested in another different genetic laboratory. Based in the result of genetic test the patient received the diagnosis of Kugelberg-Welander’s disease.

**DISCUSSION**

Kennedy’s disease, also known as X-linked spinal and bulbar muscular atrophy is a rare disease that first presents with symptoms such as proximal muscle weakness, cramps, fasciculations, bulbar palsy and in a few patients, signs of peripheral resistance to androgens. It is an X-linked disease, whose genetic defect is an abnormal repeated expansion of the CAG trinucleotide at the first exon of the androgen receptor gene. Individuals affected with KD have between 40-53 CAG repeats. Normal range is between 17-26 repeats. Conversely, in Kugelberg-Welander’s disease (also known as spinal muscle atrophy type III) symptoms begin during childhood, with symmetrical and proximal muscle atrophy of all four limbs, without either compromise of bulbar muscles or signs of androgen resistance. The genetic mode of transmission is autosomal recessive with a deletion of either the exons 7 or 8 of the survival motor neuron gene. More than 95% of patients with SMA type I and II and 80% of patients with SMA type III have deletions of SMN in the telomeric copy.

Based on genetic findings, our patient was diagnosed as having Kugelberg-Welander’s disease, even though at first his clinical features led to the diagnosis of KD, except for the unusually early onset of disease. Gynecomastia is a major clinical feature in males, suggestive of androgen resistance, and it is probably due to a genetic mutation at the androgen receptor gene. This latter finding, when combined with signs of impairment of lower motor neuron is highly specific for KD, as it was observed in our patient.

There is a handful of published reports of patients with uncommon phenotypic signs, which were later diagnosed as KD. Shaw et al. reported the case of a patient whose main clinical feature was a non-specified personality disorder, initially attributed to pre-senile dementia. Genetic testing disclosed 44 repetitions of the CAG compatible with Kennedy’s disease. In addition to the variant phenotypic presentations of Kennedy’s disease, genetic transmission can also turn out to be abnormal. Ikezoe et al. described a family that tested positive for the genetic marker of KD, despite the fact that genetic inheritance was abnormal with an autosomic dominant pattern instead of a X-linked pattern, but without androgen receptor abnormalities. Schmidt et al. in 2002 described two sisters with KD, who had an expansion of CAG at the androgen receptor gene.

Based in our case and other reports found in the literature, one can infer that several chromosomal changes, some of which the genetic defect remains unknown, can present with the same phenotypic findings, thus partially explaining the myriad clinical presentations of the very same disease. Molecular diagnostic testing may confirm a diagnosis and may avoid the need of more extensive investigation. Genetic advice may be provided correctly.

**REFERENCES**