23rd International conference on preimplantation genetics (PGD-IS 2026)
Poster
Shanghai,China, 2026.4.24-27

Anticipation in Embryos Revealed by Preimplantation Genetic Testing for Dentatorubral–Pallidoluysian Atrophy (DRPLA)

Yoshiharu Nakaoka、Michiko Ammae, Tatsuya Nakano, Haruhisa Konishi, Daisuke Kadogami, Yoshiharu Morimoto*

IVF Namba Clinic, Osaka, Japan
*HORAC Grand Front Osaka Clinic, Osaka, Japan

[Objective] Dentatorubral–pallidoluysian atrophy (DRPLA) is an autosomal dominant neurodegenerative disorder caused by the expansion of CAG repeats in the ATN1 gene.
A characteristic feature of DRPLA is genetic anticipation, in which neurological manifestations such as cerebellar ataxia become more severe in subsequent generations, particularly through paternal transmission. Although CAG repeat lengths have been reported in affected offspring, there are no reports documenting changes in CAG repeat numbers at the embryonic stage.
Here, we investigated anticipation in embryos from a male DRPLA carrier by analyzing ATN1 CAG repeat lengths using preimplantation genetic testing for monogenic disorders (PGT-M).

[Case] The husband (32 years old) is a presymptomatic carrier of DRPLA with 57 CAG repeats in the ATN1 gene. The wife is 28 years old. The husband’s affected father had 55 CAG repeats, and his sister, who died at 27 years of age, had 67 CAG repeats.

[Results] Ovarian stimulation was performed using a progestin-primed ovarian stimulation (PPOS) protocol, yielding 10 oocytes and 6 biopsied embryos. Genetic analysis identified two unaffected embryos and four embryos carrying the pathogenic variant. The CAG repeat numbers in the affected embryos were 72, 68, 65, and 59. All exceeded the paternal repeat length of 57, and notably, three of the four embryos had ≥65 repeats, a range associated with a severe phenotype.

[Conclusion] The extent of CAG repeat expansion in embryos from a male DRPLA carrier

was revealed for the first time using PGT-M. All embryos inheriting the pathogenic variant demonstrated further expansion of CAG repeats. These findings serve as valuable objective evidence for genetic counseling, highlighting the significant risk of anticipation in paternal transmission.

Key Words: PGT-M, Dentatorubral–pallidoluysian atrophy (DRPLA), anticipation

We are willing to accept either an oral or a poster presentation.

Topics: PGT-M