A Case of Hereditary Retinoblastoma that Changed the Indications for Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) in Japan

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Background: In Japan, the implementation of preimplantation genetic testing for monogenic disorders (PGT-M) targets severe hereditary diseases, requiring case-by-case approval from the Japan Society of Obstetrics and Gynecology (JSOG). Since the JSOG issued its ethical guideline in 1998, it took nearly a quarter-century until 2022 for its first revision. The definition of severity was previously "a disease that manifests symptoms severely impairing daily life or posing a threat to life before reaching adulthood." With the revision, the criteria were changed to "in principle, before reaching adulthood," and additionally included diseases "for which there are currently no effective treatments to prevent the condition, or for which highly invasive treatments are necessary."
This report covers a case of retinoblastoma (RB) from our clinic that prompted this revision.

Methods: The wife in this case had hereditary RB and had one eye removed. Their second child, conceived through IVF at our clinic, was diagnosed with RB. Although the child avoided enucleation, he suffered severe visual impairment (corrected visual acuity below 0.1) and motor developmental delays. In 2018, they applied for PGT-M, but JSOG denied the application as it did not meet the criteria. Dissatisfied with this decision, they strongly desired PGT-M and reapplied. As a result, JSOG held the PGT-M Ethics Review Committee, where experts in medicine and sociology, patient associations, and the general public engaged in open discussions, leading to the revision of their ethical guidelines.

Results: This case was reviewed by the Individual Clinical Ethics Review Committee following the revision of JSOG's guidelines. The results are expected to be made public by JSOG from August onwards.

Conclusion: Moving forward, discussions on the indications for PGT-M are anticipated to include not only retinoblastoma but also hereditary cancers such as Lynch syndrome and familial adenomatous polyposis, as well as hereditary breast and ovarian cancer syndrome, particularly those preserving fertility through oocyte or embryo cryopreservation.