Isolated aniridia caused by a novel *PAX6* heterozygous large deletion mediated by multi-exon complex rearrangement

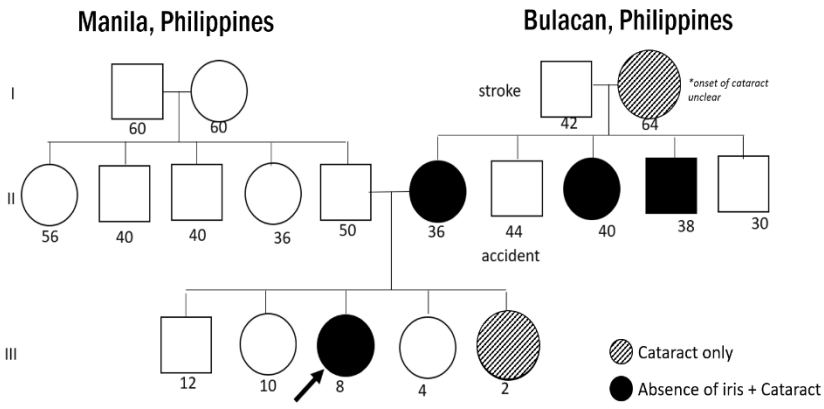
Aramis B. Torrefranca Jr.[1] *Suzanne Marie Carmona*[2,3] *Alvina Pauline D. Santiago*[1] *Michelle D. Lingao*[1] *Eva Cutiongco-dela Paz*[2,3]

[1] *Department of Ophthalmology and Visual Sciences, University of the Philippines – Philippine General Hospital*
[2] *Institute of Human Genetics, National Institute of Health, University of the Philippines Manila*
[3] *Division of Clinical and Metabolic Genetics, Department of Pediatrics, University of the Philippines – Philippine General Hospital*

Purpose: Mutations in *PAX6* gene (chromosome 11p13) encoding a transcriptional regulator involved in oculogenesis mostly present with aniridia. Aniridia is not uncommon in the Philippines but only limited information is available as yet. The purpose of this study was to present a novel, large deletion mediated by complex rearrangement in *PAX6* gene causing an isolated aniridia in a Filipino female.

Case Report: The patient is an 8-year-old female who underwent comprehensive ophthalmologic evaluation. Family history reveals presence of the aniridia and cataract with the mother and a sibling. Systemic work-up was performed including whole abdomen, renal ultrasound, blood chemistry and urinalysis. Targeted cataract panel with *WT1* and *PAX6* genes was performed to determine potential pathogenic mutations.

Results: The patient consulted due to blurring of vision bilaterally. Patient presented with subnormal vision, nystagmus, aniridia and cataractous lenses in both eyes. Patient underwent lens extraction without intraocular lens implantation bilaterally, where patient subsequently underwent intraocular lens implantation on her left eye. Repeat evaluation of posterior pole after cataract removal was unremarkable. Systemic evaluation was unremarkable. Molecular analysis revealed a novel, heterozygous *PAX6*-inherited mutation from the mother. This variant is a complex rearrangement in *PAX6* involving partial deletions of exons 3-4 and part of exon 5, including the initiator codon. Deletions of *PAX6* are part of a contiguous gene deletion syndrome: Wilms tumor, aniridia, genitourinary anomalies and intellectual disability (WAGR) syndrome, and therefore evaluation of the *WT1* gene was necessary to rule out this life-threatening syndrome.



Conclusion: This study was able to report a rare, complex rearrangement of multiple exons and deletions in *PAX6* causing an isolated aniridia phenotype. Patient was managed by a multi-disciplinary team and the guardians were counseled regarding the prognosis and complications.