Abstracts

2 - Corneal manifestations and glaucoma onset with *FOXC1* and *PITX2* variants in Axenfeld-Rieger syndrome

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Purpose: Axenfeld-Rieger syndrome leads to a spectrum of anterior chamber structural changes and glaucoma risk. Variations in *FOXC1* and *PITX2* genes are the main cause for these disorders and can be phenotypically similar. This study compares age of glaucoma onset and corneal abnormalities between *FOXC1* and *PITX2* variants.
Methods: This cross-sectional study involved 54 individuals from 24 families with *FOXC1* or *PITX2* variants in the Australian and New Zealand Registry of Advanced Glaucoma (ANZRAG).
Results: The mean age of the cohort was 39 years (range 3 to 85 years; females, 54%). More than half the patients (n=32) showed variation in *FOXC1* gene. Corneal abnormalities were more common in *FOXC1* variants (16/32, 50%) than *PITX2* variants (4/22, 18%, p=0.017). Megalocornea was the most common corneal abnormality among *FOXC1* variants. Corneal decompensation was more common in individuals with corneal abnormalities (14/20, 70%) than in those without (2/34, 5.9%, p=0.0001). There was no significant difference in the prevalence of glaucoma between the *FOXC1* and *PITX2* variants. However, the median age at diagnosis of glaucoma for *FOXC1* was 3 years (range 0 to 38) and the median age at diagnosis of glaucoma for *PITX2* was 20 years (range 1 to 48). Systemic manifestations were seen in 50% of patients with *FOXC1* variants and all the patients with *PITX2* variants.
Conclusions: Corneal abnormalities are more common in *FOXC1* than *PITX2* variants and often associated with early onset glaucoma. These findings highlight that patients with *FOXC1* variation require close follow-up and monitoring throughout infancy and into adulthood. Genetic diagnosis can provide a useful indicator of the risk of clinical complication.