48th BRAVS Meeting RETINA 2024 CONNECTING SCIENCE TO REAL WORLD

COMPARISON OF GENOMIC COMPOSITION AND PHENOTYPIC EXPRESSION VIA MULTIMODAL ANALYSIS IN RETINITIS PIGMENTOSA

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INTRODUCTION

Retinitis pigmentosa (RP) is the most common form of hereditary retinal dystrophies[1]. At least 79 genes have been reported as responsible, with the majority of mutations found in seven main genes: CYP4V2, RHO, USH2A, RPGR, CRB1, RP2, and CHM[1,2]. However, there is currently no multimodal analysis of this disease in the literature using broad line fundus imaging technology, including autofluorescence, as well as genotype-phenotype comparative studies studies[1,3]

PURPOSE

We describe RP cases through multimodal analysis using broad line fundus imaging technology (fundus photography and autofluorescence with green and blue wavelengths), SD-OCT, and SLO-NIR, comparing findings between identified genotypes and phenotypes.

METHODS

This is an observational and descriptive study conducted through a review of the retina department's database at the Leitão Guerra Eye Clinic in patients with confirmed genetic testing associated with RP phenotype from 2021 to 2022.

RESULTS

Eleven patients were identified, of which eight were female and three were male, with a median age of 43 years. Eight genes were identified: USH2A, ABCA4, EYS, MYO7A, MFRP, AM161, CLN3GNAT2, and CRB1. We described the profile and location of pigmentation, presence of bone spicules, atrophy, and macular involvement.

IDENTIFIED GENES

USH2A	ABCA4	EYS	MYO7A
MFRP	AM161	CLN3GNAT2	CRB1

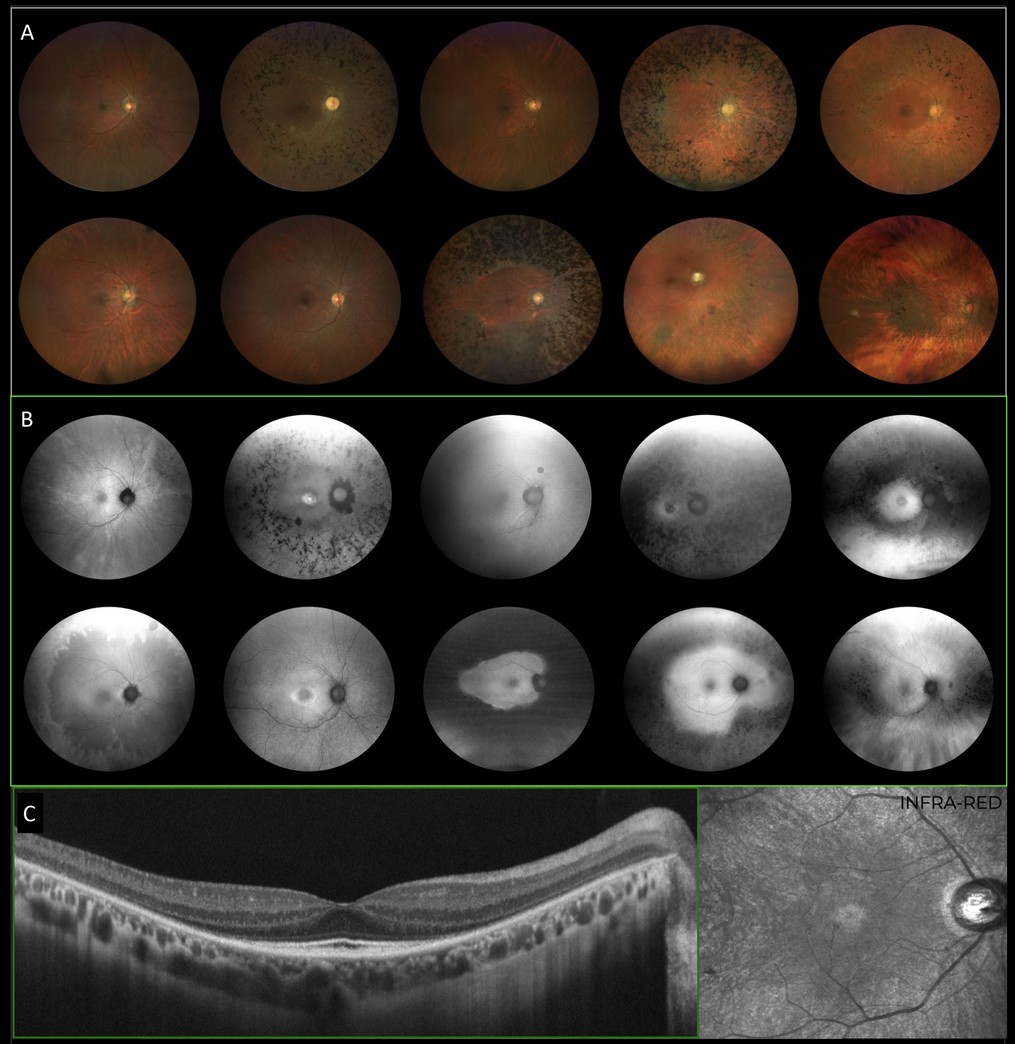

Figure A: Color fundus scans of 11 patients showing the presence the various RPE mobilization (" spikes "), in addition to changes typical of retinitis pigmentosa such as vascular attenuation and pale disc.

Figure B: SW-GREEN autofluorescence (500—585 NM) of the 11 patients with different phenotypes showing hyperaufluorescence in the macular region (hyperautofluorescent ring).

Figure C: SD-OCT of a patient showing a reduced ellipsoid zone that coincides with the area of hyperaurofluorescent ring formation in SW-GREEN autofluorescence

DISCUSSION

The significance of the correlation between genetics and phenotype in retinitis pigmentosa (RP) is underscored by the inherent genetic diversity and the array of clinical presentations[1,3] This ongoing investigation is poised to comprehend the profound implications of this correlation, aiming to augment disease understanding, refine clinical management approaches, provide guidance for familial counseling, and propel advancements in therapeutic modalities, which are making continuous progress[4]. The comprehensive nature of this investigative methodology fosters an extensive comprehension of RP, laying the groundwork for future implementations of personalized precision medicine and elevating standards in patient care.

A nuanced understanding of the genetic underpinnings of RP and its phenotypic expressions is imperative for manifold reasons. Furthermore, it facilitates synchronization with the advancing landscape of targeted genetic therapies, gene augmentation strategies, and the formulation of personalized interventions tailored to specific genetic subtypes[5].

In summary, the correlation between genetics and phenotype in RP encompasses multifaceted implications, spanning disease comprehension, strategies for clinical management, practices in familial counseling, and strides in therapeutic modalities[2,4]. This integrative approach not only contributes to broad comprehension of RP but also establishes a sturdy foundation for the eventual implementation of personalized precision medicine, thereby culminating in an elevated standard of patient care.

Shortwave fundus autofluorescence (SW-FAF) is a diagnostic imaging technique that allows non-invasive access to metabolic changes in the retina. In FAFgreen, the absorption of green light by the luteal pigments is negligible and a round area of hyperautofluorescence occurs, reducing the contrast that depicts a hyperautofluorescent ring[4].

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