1 de Dezembro **08h30 | 10h00 – Sala 1**

Retina Médica | Medical Retina

Moderadores | Chairs: Maria Luz Cachulo (CHUC), Diogo Cabral (HGO), Luis Mendonça (HB)

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PHENOTYPIC AND GENOTYPIC SPECTRUM OF BIETTI CRYSTALLINE DYSTROPHY IN A PORTUGUESE COHORT

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Introduction: Bietti crystalline dystrophy (BCD) is an extremely rare inherited retinal dystrophy (IRD) caused by biallelic variants in the CYP4V2 gene. It is characterized by the presence of crystalline deposits in the retina, and sometimes in the cornea, associated with retinal pigment epithelium (RPE) and chorioretinal atrophy. There is considerable variation in genotype, clinical phenotype and disease progression reported in the literature and no clear genotype-phenotype correlations have been found. The aim of this study is to identify the spectrum of disease-causing CYP4V2 variants and describe the phenotypic findings in Portuguese patients with a clinical diagnosis of BCD.

Methods: Cross-sectional study conducted at an IRD referral center in Portugal. Eligible patients were identified using the IRD-PT registry. Patients' medical history and examination, including best corrected distance visual acuity (BCDVA), ultra widefield color fundus photography (UW-FCP), near-infrared reflectance (NIR), UW fundus autofluorescence (UW-FAF), spectral domain optical coherence tomography (SD-OCT) and OCT-Angiography (OCT-A) were analyzed. Genetic testing consisted in Sanger sequencing of the CYP4V2 gene. Variants were classified according to the guidelines of the American College of Medical Genetics and Genomics. All patients were granted genetic counseling by a clinical geneticist.

Results: Six Portuguese patients (5 families) were included. History of consanguinity was reported in 1 family. Genetic testing revealed homozygous variants in 4 families: one class V variant (1 patient), c.694C>T p.(Arg232*); one class IV variant (1 patient), c.1090+1del p.?; and two variants of uncertain significance (VUS) class III (3 patients, 2 families). One patient is still waiting for genetic results. Mean age at first visit was 38.8 years. Mean follow-up was 10.5 years. Symptoms included decreased VA, photophobia, hemeralopia, nyctalopia and visual field defects. Mean BCDVA significantly decreased between the first and last visits, from 0.38 to 0.68 logMAR (p=0.01). On clinical examination none of the patients presented anterior segment changes. NIR confirmed the presence of multiple retinal hyperreflective spots in all patients. Most patients (n=4) exhibited extensive RPE atrophy, focal chorioretinal atrophy, pigment clumping at the periphery and crystalline deposits throughout the retina. Confluent patches of hypoautofluorescence affecting the whole retina were demonstrated by UW-FAF. SD-OCT showed disruption of the ellipsoid zone (EZ), atrophy of the RPE and choriocapillaris, thin choroid, hyperreflective foci in the outer retina as well as outer retinal tubulations. Using OCT-A, areas of choriocapillaris blood flow deficit could be observed. Two patients presented a milder phenotype restricted to the macula and characterized by speckled hypo- and hyperautofluorescence on UW-FAF, focal extrafoveal disruptions of the EZ, preservation of foveal outer retina and intraretinal hyperreflective foci on SD-OCT.

Conclusion: This study described the spectrum of CYP4V2 variants and the range of phenotypic characteristics associated with BCD in Portuguese patients. Molecular testing is essential for a reliable diagnosis given the phenotypic variability. In this case series, genetic testing yielded 2 solved and 3 unsolved cases, pending reclassification of VUS. Multimodal imaging allows for detailed phenotypic descriptions of BCD, facilitating diagnosis and follow-up.