North Carolina Macular Dystrophy (MCDR1/NCMD): 30-50 Year Follow-up of the Original Family

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Purpose:
The clinical phenotype of NCMD is highly variable and remains poorly appreciated and understood. One of the features of NCMD is the lack of progression in an individual despite its original name by Lefler, Wadsworth and Sidbury who named it “dominant progressive foveal dystrophy” as reported in 1971. We reexamined 25 of the original NCMD family 30-50 years after first being examined by one of us (Kent Small).

Methods:
Dr. Kent Small (KS) examined twenty-five individuals of the original NCMD pedigree during a recent field in an office setting. KS performed standard Snellen visual acuity, slit lamp and fundus examinations on all individuals. Fundus photography was performed with an OPTOS California camera (Marlborough, MA) and SD-OCT was performed with Zeiss Cirrus 5000 (Oberkochen, Germany). These findings were compared with the original data collected by KS in 1988 and images from 1971 by Lefler (HF) et al. SD-OCT was not available during the original ascertainment of the family in 1988. Blood was collected for DNA. IRB approval was obtained.

Results:
The 25 subjects examined were part of the original NCMD family, which we previously found the point mutation CHR6: 99593030 (Hg38) in a non-coding region of a DNASE1 hypersensitivity binding site on chromosome 6. Eight were affected children of those originally examined 30 years ago by KS and were not yet born in 1988 at the time of the original ascertainment. The remaining 17 subjects (34 eyes) had been examined 30 years previously. Dr. Lefler had examined six of these subjects 50 years previously. Of these, 4 eyes showed worsening of vision with fundus photos showing evidence of fibrosis from choroidal neovascularization, some with surrounding atrophy suggesting previously resolved subretinal fluid. One showed improvement in visual acuity for unexplainable reasons.

Conclusions:
Most NCMD patients have stable vision and fundus findings throughout their lives even up to 50 years follow-up. The ones who lost vision did so with grade 2 disease, which developed choroidal neovascularization that spread or leaked into the nasal maculae. With anti-VEGFs now available, some of these patients may benefit from these treatments.