

Structural and Functional Retinal Phenotype in Mucopolysaccharidosis Type I Hurler and I Hurler-Scheie

Deepika C Parameswarappa¹, MD, Anupreet Tumber¹, MS, Stephanie N Kletke¹, MD,
Thomas Wright¹, PhD, Alaa A Tayyib¹, MD,

¹Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada

Introduction: Visual prognosis in mucopolysaccharidosis (MPS) type I may be guarded despite timely management of corneal cloudiness and glaucoma in the presence of retinal degeneration. Systemic hematopoietic stem cell transplantation and enzyme replacement therapy have largely been considered to have no effects on retinal degeneration. We aim to define the structural and functional retinal phenotype in MPS I subjects by analyzing spectral-domain optical coherence tomography (SD-OCT) and full-field electroretinogram (ERG) features.

Methods: Eighteen children (55% males) with MPS I Hurler (I-H, n=15) and Hurler-Scheie (I-H/S, n=3) who had SD-OCT and ERG from 2005 to 2023 were included in this retrospective review. The diagnosis of MPS was confirmed by the presence of biallelic variants in IDUA and/or α -L-Iduronidase enzymatic deficiency. Descriptive and qualitative analysis of the SD-OCT parameters were performed. Age-wise Pearson's correlation of the a-wave amplitude and b/a ratio of the dark-adapted (DA)3 and DA10 ERGs was performed.

Results: The median age of presentation was 5 years (range 2 to 9) with a mean visual acuity of $0.6 \pm 0.3 \log \text{MAR}$. All children had diffuse ground glass-like stromal opacities with 21/36 eyes requiring deep anterior lamellar keratoplasty. Fifteen patients (83%, 15/18) had bilateral normal fundus appearance whilst three had peripapillary subretinal yellowish deposits in one eye. Maculopathy defined as parafoveal loss of the ellipsoid zone on SD-OCT was noted in four patients (mean age 13.5 ± 2 years). SD-OCT demonstrated foveal external limiting membrane (ELM) thickening in 17/18 patients with a median thickness of 36 μm (range 26 to 43 μm). Foveal ELM thickening was observed in the absence of clinically apparent retinal changes in all patients. One patient without ELM thickening was the youngest (2 years) and had normal retinal exam. Baseline ERGs at the mean age of 11 years (range 2 to 18) showed a reduced average b/a ratio of 0.9 (range: 0.3 to 1.6) and 0.8 (range 0.2 to 1.2) to the DA 3 and DA10 ERGs, respectively. 11 and 14 patients had an electronegative ERG to DA 3 and DA10 ERGs respectively. Significant correlation was noted between age - b:a ratio ($p = 0.0075$, DA 3; $p = 0.0094$, DA 10) and age - visual acuity ($p = 0.0272$).

Conclusions: ELM thickening is the most consistent finding in MPS 1 eyes noted in 94% of individuals within our study group. SD-OCT is an important investigative tool for MPS 1 patients, despite unremarkable retinal examination. The changes in b/a amplitude ratio in DA 3 and DA 10 ERGs appear to be a good biomarker of the progression of retinal degeneration.