

## Corneal imaging with optical coherence tomography assisting the diagnosis of mucopolipidosis type IV



Mucopolipidosis type IV (MPS-IV, OMIM #252650), a lysosomal storage disorder caused by dysfunctional mucopolipin-1, is characterized by neurologic and visual impairment, developmental delay, and achlorhydria. *MCOLN1* gene mutation identification is diagnostic but requires clinical suspicion. The latter is challenging, however, because most systemic and ocular findings are nonspecific and rarely evolve simultaneously.<sup>1</sup> Bilateral corneal clouding is the earliest hallmark sign of MPS-IV. Unlike in other metabolic causes of corneal opacification, it is owing to preferential accumulation of abnormal material in the corneal epithelium as opposed to other corneal layers.<sup>1</sup> Slit-lamp recognition of isolated epitheliopathy however is difficult owing to limited collaboration in children.

Herein, we report the case of a 12-year-old boy with developmental and intellectual delay, subcortical neurodegeneration, periventricular leukomalacia, and hypoplastic corpus callosum. His ocular findings included progressive bilateral diffuse corneal clouding with normal intraocular pressures, optic atrophy, and retinal degeneration. Anterior segment optical coherence tomography (OCT; Bioptigen Envisu™, Leica Microsystems, Wetzlar, Germany; anterior segment probe) revealed increased corneal thickness of 636  $\mu\text{m}$  (normal: 540  $\mu\text{m}$ ), increased epithelial thickness of 7  $\mu\text{m}$  (normal: 3–4  $\mu\text{m}$ ), and epithelial hyperreflectivity bilaterally (Fig. 1A–B). The stroma and Descemet’s membrane/endothelial complex were unremarkable. OCT findings raised our clinical suspicion and helped the medical genetics team orient their diagnostic evaluation toward MPS-IV. Metabolic work-up revealed hypergastrinemia (550 ng/L; normal: 0–115 ng/L), suggesting achlorhydria. Exome sequencing and Sanger confirmation in the trio identified 2 *MCOLN1* gene compound heterozygote

variants (NM\_020533.2:c.694A>C; NM\_001008537.2:c.964C>T), consistent with MPS-IV.

Anterior segment OCT is a fast, noninvasive test that can be performed at bedside or in an office to capture cross-sectional images of the cornea, allowing easy visualization and measurement of the different corneal layers. In children with corneal clouding, OCT can facilitate the identification of specific pathologic changes, especially in cases with challenging slit-lamp examination. Corneal epithelial thickening and hyperreflectivity in an overall thickened cornea with normal stroma and endothelium corresponds to the histopathologic findings described in MPS-IV.<sup>1</sup> Their recognition can guide genetic testing, enable timely diagnosis, and prevent unnecessary corneal transplantation. Indeed, these patients’ visual potential is frequently limited by poor retinal and optic nerve function, and corneal clouding tends to rapidly recur in the graft.<sup>1</sup> In other causes of progressive bilateral diffuse corneal opacification in an older child, including mucopolipidosis type II and mucopolysaccharidoses types I-H, I-S, IV, and VI, abnormal material predominantly accumulates in stromal keratocytes, with relative sparing of epithelial and endothelial cells.<sup>2</sup> These corneas also appear thickened on OCT but have a normal-appearing epithelium and granular hyperreflectivity confined to the corneal stroma.<sup>3,4</sup> Of note, we previously reported similar corneal OCT findings to those described here in a 2-year-old child with MPS-IV.<sup>5</sup> This suggests that anterior segment OCT can be useful in distinguishing this disease entity from other causes of corneal clouding with normal intraocular pressures in younger children as well. Unlike MPS-IV, these pathologies—including congenital stromal corneal dystrophy, corneal hereditary endothelial dystrophy, posterior polymorphous corneal dystrophy, Peter’s anomaly, and forceps injury—all demonstrate normal corneal epithelial thickness and reflectivity.<sup>2</sup>

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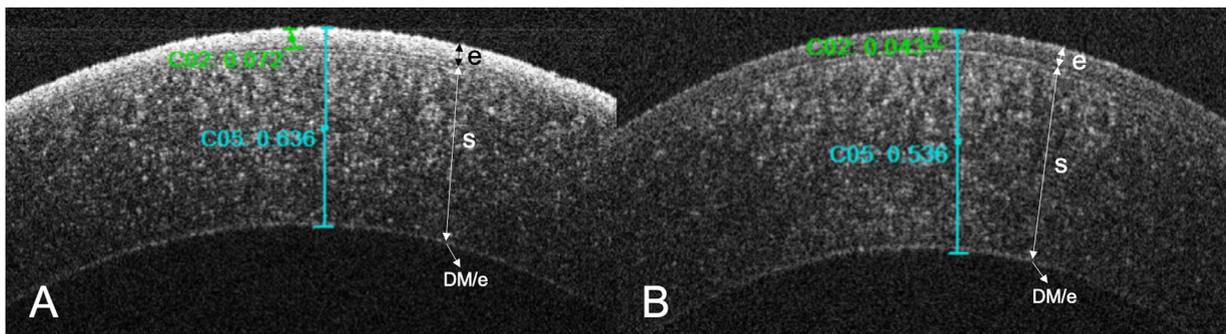


Fig. 1—Corneal optical coherence tomography images. (A) The right cornea of our patient with mucopolipidosis type IV displays a thickened hyperreflective epithelium measuring 7.2  $\mu\text{m}$  (normal:  $\sim 4 \mu\text{m}$ ). (B) The epithelium in a normal cornea displaying normal reflectivity and thickness is shown for comparison. E, epithelium; s, stroma; DM/e, Descemet/endothelium complex.

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## Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

## Biopsy of a diffuse anterior chamber angle melanocytoma using a Kahook Dual Blade



A 68-year-old female was referred to the emergency ophthalmology clinic with a pigmented iris lesion and an intraocular pressure (IOP) of 38 in her left eye. Initial clinical assessment revealed the presence of a localized, flat, plaque-like peripheral and midperipheral iris lesion in one quadrant. Pigmented seeding on the rest of the iris surface and associated mild corectopia were observed. There were no notable episcleral sentinel vessels, and there was no iris neovascularization. On gonioscopy, heavy pigment invaded 8 clock hours of the angle (Fig. 1). The ciliary body was normal. Fundus examination, visual field testing, and optical coherence tomography all showed severe glaucomatous damage in the left eye (with normal testing in the right

eye). The patient was initially managed medically using 4 topical glaucoma medications and systemic acetazolamide.

Evaluation by the ocular oncology service was highly suspicious for a diffuse melanoma. The patient initially refused any diagnostic surgical procedure. She finally agreed to undergo a fine needle aspiration biopsy (FNAB). However, it did not yield a sufficient specimen for adequate diagnosis.

Given the unsuccessful FNAB, additional options for incisional biopsies were discussed. The patient agreed to proceed with a goniotomy using the Kahook Dual Blade (KDB; New World Medical, Rancho Cucamonga, Calif.). Through a clear corneal temporal 1-mm incision, an ophthalmic viscosurgical device (OVD) was injected in the anterior chamber and used to inflate the nasal angle. The patient's head was turned away from the surgeon and the microscope was tilted to 40 degrees. Under gonioscopic visualization, the KDB was used to obtain a trabecular meshwork biopsy of approximately 2 clock hours (Fig. 2). The

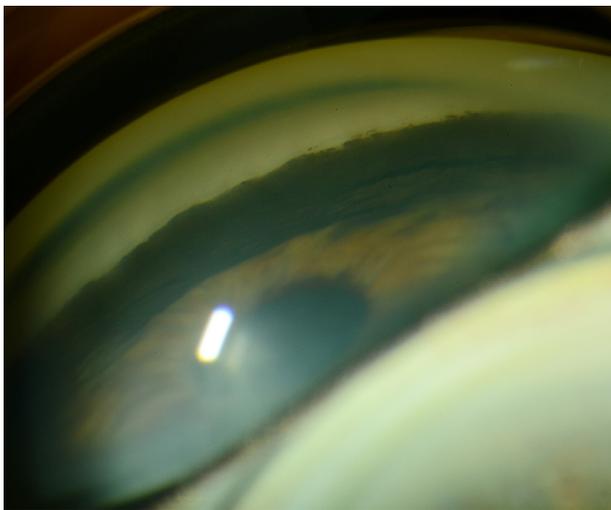


Fig. 1—Nasal gonioscopic view of the left eye, showing prominent dark pigment invasion.

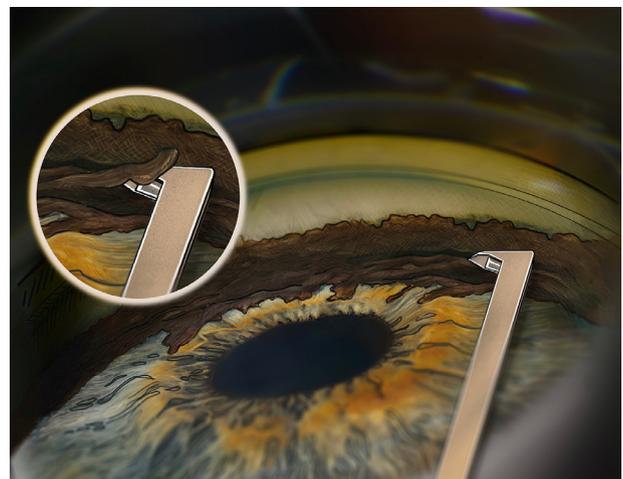


Fig. 2—Artist rendering illustrating incisional biopsy using the Kahook Dual Blade.