

Visual Observations of an American Patient With Leber Hereditary Optic Neuropathy After Purported Injections of Stem Cells in China

We describe our clinical observations of a patient with Leber hereditary optic neuropathy and acute vision loss. She received what she was told were umbilical cord blood stem cells by a clinic in Qingdao, China.

Report of a Case. A 42-year-old woman noted vision loss in August 2009. Visual acuity was 20/80 (55 Early Treatment Diabetic Retinopathy Study [ETDRS] let-

ters) OD and 20/40+ (71 ETDRS letters) OS. Automated visual field testing revealed bilateral central scotomas, with mean defects of -2.31 dB OD and -0.80 dB OS (**Figure 1**). The optic nerve heads were swollen with peripapillary telangiectasias characteristic of acute Leber hereditary optic neuropathy. The mean thicknesses of the retinal nerve fiber layers were substantially increased to $130\ \mu\text{m}$ OD and $134\ \mu\text{m}$ OS (**Figure 2**). The level of serum phosphorylated neurofilament heavy chain, a biomarker of axonal injury, was elevated at $0.29\ \text{ng/mL}$ (normal, $0.07\ \text{ng/mL}$). Genetic analysis showed homoplasmy for mutated G11778A ND4 mitochondrial DNA.

Three months later, the patient went to the Chengyang People's Hospital, Qingdao, China, where she received 4 intravenous and 2 intrathecal infusions of

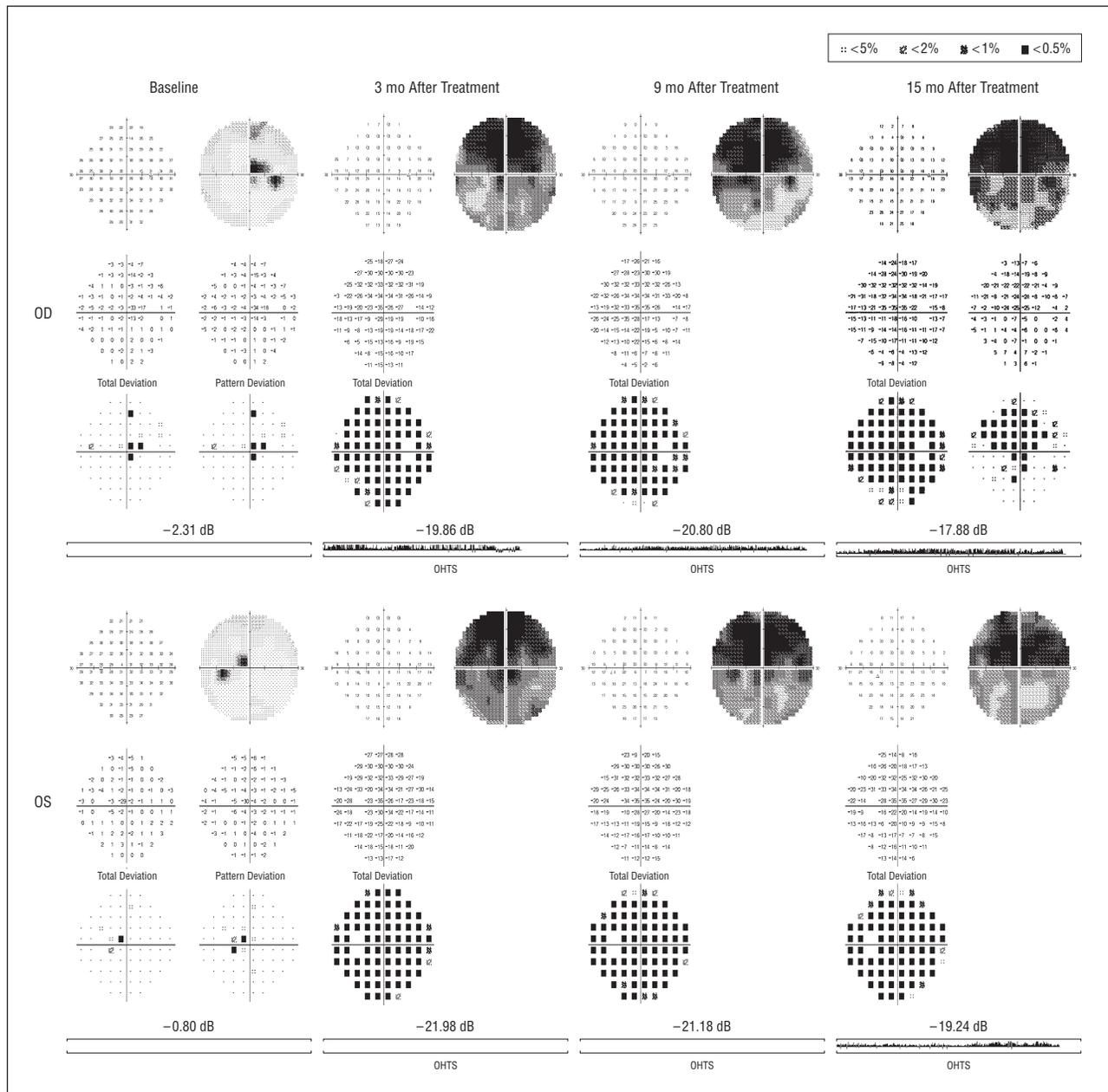


Figure 1. Humphrey visual field (30-2 threshold) changes are shown in both eyes at the baseline visit before treatment, 3 months after purported stem cell therapy (the fields show dense central scotomas), 9 months after purported stem cell therapy, and 15 months after purported stem cell therapy.

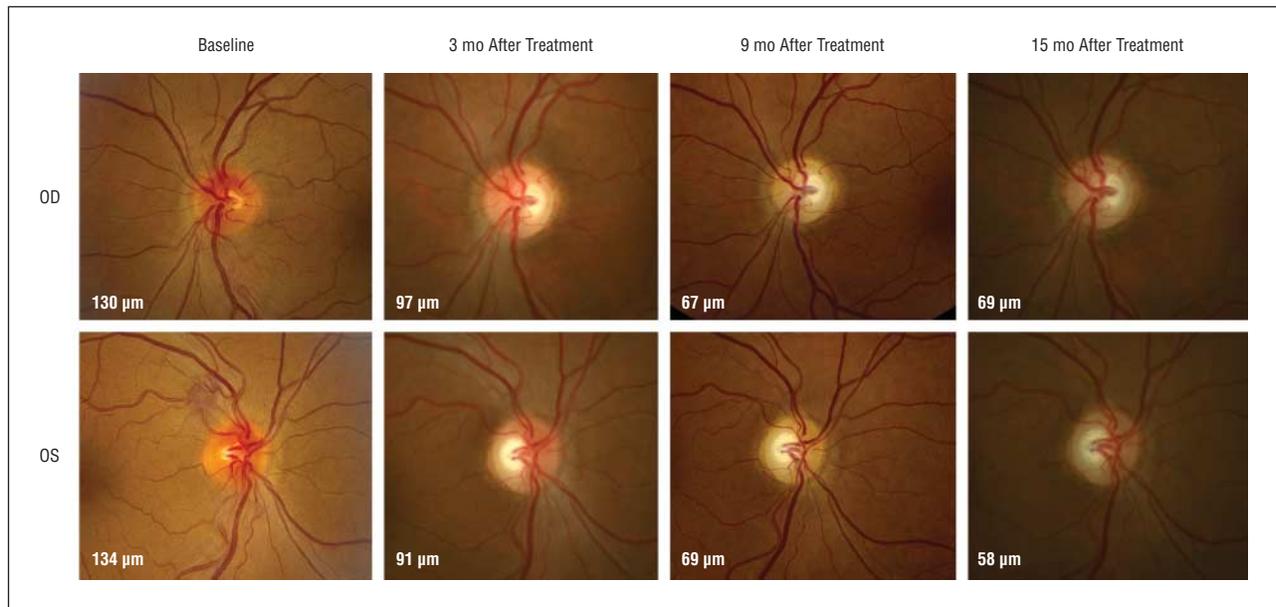


Figure 2. Fundus photographs. Bilateral optic disc edema was present with peripapillary telangiectasias at the baseline visit before treatment. The optic disc edema had resolved 3 months after purported stem cell therapy. Optic atrophy was prominent 9 months and 15 months after purported stem cell therapy.

Table. Stem Cell Treatment Schedule for 6 Umbilical Cord Blood Stem Cell Injections

Visit No.	Visit Date	Cell Type	Delivery Route	Anesthesia	Adverse Effects
1	November 23, 2009	UCBSC	IV	None	None
2	November 27, 2009	UCBSC	LP	Local	None
3	December 2, 2009	UCBSC	IV	None	None
4	December 7, 2009	UCBSC	LP	Local	None
5	December 11, 2009	UCBSC	IV	None	None
6	December 14, 2009	UCBSC	IV	None	None

Abbreviations: IV, intravenous injection; LP, lumbar puncture to subarachnoid cavity; UCBSC, umbilical cord blood stem cell.

what were purported to be umbilical cord blood stem cells according to the schedule listed in the **Table**; the number of cells infused was not available. Three months after the infusions, visual acuity had worsened to 20/400 (20 ETDRS letters) OD and 20/500 (15 ETDRS letters) OS. Central scotomas were much denser with mean defects of -19.86 dB OD and -21.98 dB OS (Figure 1). Optic disc swelling resolved, with mean retinal nerve fiber layer thicknesses of 97 μ m OD and 91 μ m OS (Figure 2). The serum phosphorylated neurofilament heavy chain (square root) level had increased to 0.54 ng/mL. Nine months after purported stem cell therapy, visual acuity had worsened further to 20/600 (13 ETDRS letters) OD and 20/800 (4 ETDRS letters) OS. Optic atrophy was prominent with mean retinal nerve fiber layer thicknesses of 67 μ m OD and 69 μ m OS. Fifteen months after the infusions, the patient's visual acuity stabilized at 20/600 (14 ETDRS letters) OD and 20/700 (8 ETDRS letters) OS. Optic atrophy persisted with mean retinal nerve fiber layer thicknesses of 69 μ m OD and 58 μ m OS.

Comment. While we do not know for certain that this patient received umbilical cord blood stem cells but assume that she did, this is the first peer-reviewed

report to our knowledge describing the visual results of treatment with intravenous and intrathecal stem cells in China or elsewhere for vision loss from Leber hereditary optic neuropathy or any other optic neuropathy. The progression of vision loss in our patient with initial optic nerve head swelling followed by optic atrophy is characteristic of the natural history of Leber hereditary optic neuropathy.¹⁻³ In this well-documented case, intravenous and intrathecal umbilical cord blood stem cell therapy failed to stop the decline in visual function or to prevent optic atrophy. Notwithstanding website testimonials, there is no medical evidence that this purported therapy works for optic neuropathies. Therefore, patients and physicians should be cautious in seeking an unproven remedy for a disease that at present has no effective therapy.

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1. Sadun AA, Carelli V, Salomao SR, et al. Extensive investigation of a large Brazilian pedigree of 11778/haplogroup J Leber hereditary optic neuropathy. *Am J Ophthalmol.* 2003;136(2):231-238.
2. Seo JH, Hwang JM, Park SS. Comparison of retinal nerve fibre layers between 11778 and 14484 mutations in Leber's hereditary optic neuropathy. *Eye (Lond).* 2010;24(1):107-111.
3. Newman NJ, Biousse V, Newman SA, et al. Progression of visual field defects in Leber hereditary optic neuropathy: experience of the LHON Treatment Trial. *Am J Ophthalmol.* 2006;141(6):1061-1067.

COMMENTS AND OPINIONS

Ciliary Body Clefting Accompanied by Rupture of the Trabecular Meshwork in Congenital Glaucoma

In congenital glaucoma, the exposure to consistently elevated intraocular pressure expands the still-elastic scleral shell and leads to tissue remodeling with iris thinning, zonular stretching, posterior recession of the peripheral uvea, rarefied ciliary body, increased corneal diameter, and increased axial length of the bulbus.¹

As recently demonstrated via ultrasound biomicroscopy by Roche et al,² the well-known breaks of the Descemet membrane in primary congenital glaucoma can also be accompanied by previously unsuspected clefting of the corneal stroma, resulting in its immediate hydration and opacification known as *hydrops*. If the intraocular pressure is quickly normalized with reappositioning of the corneal stromal cleft wound edges, little, if any, stromal scarring then occurs owing to healing by primary rather than secondary intention.²

Using ultrasound biomicroscopy, we demonstrate here another hitherto unsuspected and undetected decoupling of paired tissues and rupture in an infant with congenital glaucoma associated with cutis mar-

morata. Ultrasound biomicroscopy and gonioscopy of the anterior segment of the right eye, which did not undergo operation, demonstrated clefting of the ciliary body from the underlying sclera along with rupture of the trabecular meshwork (**Figure 1** and **Figure 2**); both phenomena were more pronounced in the superior quadrants.

Elongation of the eye secondary to elevated intraocular pressure leads to posterior positioning of the ill-defined ciliary body as well as stretching of the zonules.¹ The limited and differing tissue elasticity of adjacent ocular structures, in this case the choroidal complex and the sclera,³ accounts for their separation, or clefting. This clefting necessarily alters anterior chamber angle morphology and may be facilitated by a rupture of the stretched trabecular meshwork.

Following the normalization of intraocular pressure, these still-elastic tissues may return to their respective anatomical positions, rendering it possible for healing of any ruptured tissue edges to occur by primary rather than secondary intention² and accounting for the scant scarring that ensues (Figure 1).

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1. Gupta V, Jha R, Srinivasan G, Dada T, Sihota R. Ultrasound biomicroscopic characteristics of the anterior segment in primary congenital glaucoma. *J AAPOS.* 2007;11(6):546-550.
2. Roche O, Beby F, Dufier JL, Parsa CF. Descemet membrane rupture accompanied by stromal clefting in congenital glaucoma. *Arch Ophthalmol.* 2008;126(8):1163-1164.
3. Friberg TR, Luce JW. A comparison of the elastic properties of human choroid and sclera. *Exp Eye Res.* 1988;47(3):429-436.

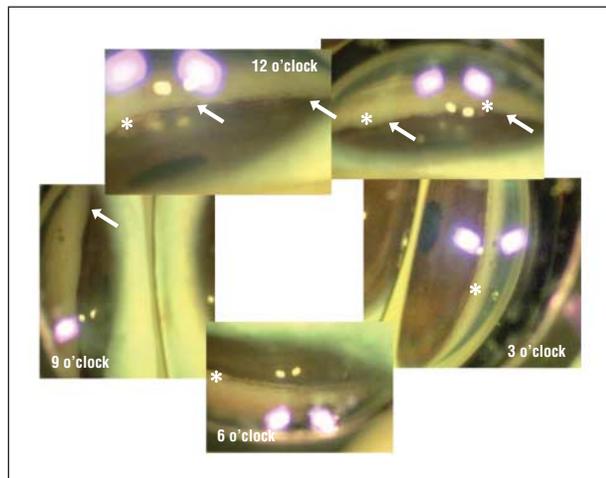


Figure 1. Gonioscopic images of the anterior segment (patient's view) corresponding to the ultrasound biomicroscopy images in Figure 2. The angle is widely open with visualization of the ciliary body band and scleral spur. At the 12-o'clock position, the gonioscopic image conjectures ciliary body clefting from the sclera (asterisks) and multiple ruptures of the trabecular meshwork (arrows); both changes were confirmed by ultrasound biomicroscopy (Figure 2). Note the visible pigmentations on the borders of caverns within the clefting.