Published in final edited form as:

J AAPOS. 2012 December ; 16(6): 534–538. doi:10.1016/j.jaapos.2012.08.006.

Acquired bilateral myelinated retinal nerve fibers after unilateral optic nerve sheath fenestration in a child with idiopathic intracranial hypertension

Sasapin G. Prakalapakorn, MD, MPH and Edward G. Buckley, MD

Department of Ophthalmology, Duke Eye Center, Durham, North Carolina

Abstract

Purpose—To report the unusual development of bilateral myelinated retinal nerve fibers (MRNF) adjacent to the optic nerve in a child after treatment of idiopathic intracranial hypertension (IIH) with unilateral optic nerve sheath fenestration (ONSF) and to discuss the etiology of acquired MRNF.

Methods—The patient's clinical history, including visual acuity, refractive error, ocular alignment, fundus examination, and optic nerve photographs, was retrospectively reviewed. A literature review was performed for acquired MRNF in children using PubMed. The results of the demographic and clinical findings of our patient were compared with those of previously reported cases.

Results—The child developed bilateral MRNF adjacent to the optic nerve 5 months after unilateral ONSF. In reviewing the literature, 8 of 10 cases of acquired MRNF in children had prior abnormalities of the optic nerve, 4 of 10 had associated bilateral optic nerve head drusen, 3 of 10 had associated optic nerve glioma, and 3 of 10 had a history of significant increased intracranial pressure requiring surgical intervention.

Conclusions—While the etiology of acquired MRNF is uncertain, this case plus a review of the literature suggest that it may be related to changes in the lamina cribosa combined with possible optic nerve injury caused by optic nerve head drusen, optic nerve glioma, or elevated intracranial pressure, and that it can occur months to years after intervention.

Acquired myelination of the retinal nerve fibers is an unusual event. Normally, myelination of the optic nerve begins at the lateral geniculate body and ends at the lamina cribosa around the time of birth. Occasionally, myelination can extend anteriorly beyond the lamina cribosa and involve the retinal nerve fibers. This type of myelinated retinal nerve fibers (MRNF) is felt to be congenital and is stable.

We report a case of a young girl with idiopathic intracranial hypertension (IIH) who underwent *unilateral* optic nerve sheath fenestration (ONSF) and later developed *bilateral* MRNF adjacent to the optic nerve months after the surgery. While a case of bilateral ONSF in a child that later led to bilateral acquired MRNF has been reported,¹ we are unaware of a

© 2012 American Association for Pediatric Ophthalmology and Strabismus. Published by Mosby, Inc. All rights reserved.

Correspondence: S. Grace Prakalapakorn, MD, MPH, Duke Eye Center; 2351 Erwin Road, DUMC 3802, Durham, NC 27710 (grace.prakalapakorn@duke.edu)..

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

case of unilateral ONSF leading to bilateral MRNF. This case plus a review of the literature on acquired MRNF in children suggest a possible mechanism for its occurrence.

Methods

This study conformed to the requirements of the Health Insurance Portability and Accountability Act. A retrospective chart review was performed on the patient. The patient's clinical history, including visual acuity, refractive error, ocular alignment, fundus examination and optic nerve photographs, was reviewed. The results of the demographic and clinical findings of our patient were compared with those of previously reported cases.

Case Report

A 17-month-old white girl presented to the Pediatric Ophthalmology service at the Duke Eye Center, Durham, North Carolina, for "prominent" optic nerves in both eyes. She was an otherwise healthy child with a past ocular history of an accommodative esotropia and anisometropia that were corrected with hyperopic spectacles. Her parents denied any irritability or vomiting. On ophthalmological examination, her visual acuity was equal in both eyes by preferential looking test. Cycloplegic refraction was +3.00 sphere in the right eye and +6.25 sphere in the left eye. Dilated fundus examination revealed bilateral disk edema (Figure 1A-B). Aside from prominent optic nerve sheaths bilaterally, her magnetic resonance imaging was within normal limits, showing no hydrocephalus, intracranial mass, or venous sinus thrombosis. A lumbar puncture had an opening pressure of 29 cm H₂O (normal, <20) and normal cerebrospinal fluid studies. The child was diagnosed with idiopathic intracranial hypertension (IIH) and started on oral acetazolamide (10mg/kg/day in divided doses). Over the next 4.5 months (7 months after the papilledema was first discovered), the right optic nerve appeared to develop pallor, and an ONSF was performed on the right eye.

Immediately after surgery, there was decreased disk edema in the right eye, but 2 months after surgery a whitish/yellowish material was noted around the right optic nerve. Over time, this material expanded around the right optic nerve and the disk edema decreased in the left eye. Three months after its appearance was noted in the right eye, a whitish/yellowish material was noted to have appeared around the left optic nerve. Over time, the material around both optic nerves expanded and took on a whitish appearance (Figure 1C-F). At 5 years of age, her best-corrected visual acuity was 20/20 in each eye.

Results

Our literature search identified 10 previously reported cases of acquired MRNF in children. Including our case, 8 of 11 cases (82%) had prior optic nerve abnormalities, 4 of 11 (36%) had a history of increased intracranial pressure (ICP) requiring surgical intervention, 4 of 11 (36%) had associated bilateral optic nerve head (ONH) drusen, and 3 of 11 (27%) had an associated optic nerve glioma (Table 1).

Discussion

Acquired MRNF appear to differ from congenital MRNF based on laterality, associated refractive error, strabismus and potential visual acuity (Table 2). The most well-known ocular abnormalities associated with congenital MRNF is the syndrome of unilateral MRNF, myopia and amblyopia which is associated with exotropia and poor visual acuity.²⁻⁵ In contrast, the 10 reported cases of acquired MRNF in individuals <16 years of age, as was the present case, tended to be bilateral and associated with optic nerve abnormalities, hyperopia, esotropia, and good visual acuity.^{1,6-11}

While acquired and congenital MRNF cases may differ, all MRNF may result from a single common pathway. The most likely theory on the pathogenesis of congenital MRNF is that a defect in the lamina cribosa or the presence of fewer axons at the lamina cribosa result in a structure loose enough to allow oligodendrocytes access into the eye.¹² This same theory can be applied to the acquired cases as well. Damage to the lamina cribosa may be related to increased ICP, ONH drusen or optic nerve glioma in all but 2 cases. These 2 children (cases 2 and 3) may have developed MRNF due to an unappreciated congenital weakness in the lamina cribosa.

The importance of the integrity of the lamina cribosa in the development of acquired MRNF is supported by the fact that there are no reports in the literature of adults with IIH, ONH drusen, or optic nerve glioma who acquired MRNF. Because there is an increase in the total collagen content in the lamina cribosa with age,¹³ children compared to adults may be more susceptible to damage of their relatively weaker lamina cribosa and to injury of their optic nerve. Lepore¹⁴ noted that IIH patients with unilateral papilledema tended to be older and theorized that the age-related proliferation of collagen in the lamina cribosa may be one factor protecting the non-swollen nerve. The pressure gradient across the lamina cribosa may also compromise the lamina cribosa and increase the risk of optic nerve injury. Abegg and colleagues¹⁵ reported the presence of unilateral papilledema in a patient with IIH following trabeculectomy and suggested that the pressure gradient across the lamina cribosa may have induced the collapse of axoplasmatic transport and resulted in unilateral papilledema. We did not measure intraocular pressures (IOP) in our patient, but it would be interesting to see if there is a relationship between the pressure gradient across the lamina cribosa (ICP-IOP) and the development of MRNF.

Despite the above theory, why do only a few individuals with papilledema, ONH drusen or optic glioma develop MRNF? We hypothesize that in acquired cases, in addition to some weakness or defect in the lamina cribosa, there must also be injury to the optic nerve to restart the myelination process. Through reactive microgliosis, axons can remyelinate following injury.¹⁶ Cyclic shear stress on the lamina cribosa and the optic nerve that occur over the course of time from increased ICP or drusen may cause deformation and defects of the lamina cribosa and injury to the optic nerve. In vitro studies have shown that cyclic shear stress compared to steady shear stress were more harmful to neurons¹⁷ and mechanical stretch of neurons resulted in a transient rise in plasma membrane permeability that increased with both the magnitude and rate of mechanical strain.¹⁸ In addition, the abrupt difference in pressure surrounding the optic nerve due to surgery/shunting procedure may cause enough additional stress to damage the lamina cribosa and optic nerve, thereby increasing the risk of MRNF. As unilateral ONSF can affect both optic nerves resulting in bilateral optic nerve improvement,¹⁹ it could theoretically cause stress on both optic nerves to stimulate development of MRNF bilaterally. To our knowledge, this is the first case of unilateral ONSF leading to bilateral MRNF reported in the literature.

Literature Search

The authors searched PubMed (MEDLINE) for English-language only articles for the period 1946 to 2012, using combinations of the following search terms: *acquired, medullated OR myelinated, retinal nerve fiber(s) OR fibre(s), retinal myelination.*

Acknowledgments

Financial support: NIH EY016333 and an unrestricted grant from Research to Prevent Blindness to the Duke Eye Center (SGP). The funding organizations had no role in the design or conduct of this research.

References

1. Aaby AA, Kushner BJ. Acquired and progressive myelinated nerve fibers. *Arch Ophthalmol*. 1985; 103:542–4. [PubMed: 3985835]
2. Straatsma BR, Heckenlively JR, Foos RY, Shahinian JK. Myelinated retinal nerve fibers associated with ipsilateral myopia, amblyopia, and strabismus. *Am J Ophthalmol*. 1979; 88:506–10. [PubMed: 484678]
3. Hittner HM, Antoszyk JH. Unilateral peripapillary myelinated nerve fibers with myopia and/or amblyopia. *Arch Ophthalmol*. 1987; 105:943–8. [PubMed: 3606454]
4. Kee C, Hwang JM. Visual prognosis of amblyopia associated with myelinated retinal nerve fibers. *Am J Ophthalmol*. 2005; 139:259–65. [PubMed: 15733986]
5. Tarabishy AB, Alexandrou TJ, Traboulsi EI. Syndrome of myelinated retinal nerve fibers, myopia, and amblyopia: a review. *Surv Ophthalmol*. 2007; 52:588–96. [PubMed: 18029268]
6. Kushner BJ. Optic nerve decompression. Presumed postoperative development of medullated nerve fibers. *Arch Ophthalmol*. 1979; 97:1459–61. [PubMed: 464869]
7. Ali BH, Logani S, Kozlov KL, Arnold AC, Bateman B. Progression of retinal nerve fiber myelination in childhood. *Am J Ophthalmol*. 1994; 118:515–17. [PubMed: 7943132]
8. Jean-Louis G, Katz BJ, Digre KB, Warner JE, Creger DD. Acquired and progressive retinal nerve fiber layer myelination in an adolescent. *Am J Ophthalmol*. 2000; 130:361–2. [PubMed: 11020421]
9. Parulekar MV, Elston JS. Acquired retinal myelination in neurofibromatosis 1. *Arch Ophthalmol*. 2002; 120:659–5. [PubMed: 12003622]
10. Duval R, Hammamji K, Aroichane M, Michaud JL, Ospina LH. Acquired myelinated nerve fibers in association with optic disk drusen. *J AAPOS*. 2010; 14:544–7. [PubMed: 21094066]
11. Bothun ED, Kao T, Guo Y, Christiansen SP. Bilateral optic nerve drusen and gliomas in Klippel-Trenaunay syndrome. *J AAPOS*. 2011; 15:77–9. [PubMed: 21315629]
12. Williams TD. Medullated retinal nerve fibers: speculations on their cause and presentation of cases. *Am J Optom Physiol Opt*. 1986; 63:142–51. [PubMed: 3953757]
13. Hernandez, MR.; Neufeld, AH. The extracellular matrix of the trabecular meshwork and the optic nerve head. In: Ritch, R.; Shields, MB.; Krupin, T., editors. *The glaucomas*. C.V. Mosby; St. Louis: 1989. p. 163–78.
14. Lepore FE. Unilateral and highly asymmetric papilledema in pseudotumor cerebri. *Neurology*. 1992; 42:676–8. [PubMed: 1549237]
15. Abegg M, Fleischhauer J, Landau K. Unilateral papilledema after trabeculectomy in a patient with intracranial hypertension. *Klin Monbl Augenheilkd*. 2008; 225:441–2. [PubMed: 18454392]
16. Bellhorn RW, Hirano A, Henkind P, Johnson PT. Schwann cell proliferations mimicking medullated retinal nerve fibers. *Am J Ophthalmol*. 1979; 87:469–73. [PubMed: 109005]
17. Edwards ME, Wang SS, Good TA. Role of viscoelastic properties of differentiated SH-SY5Y human neuroblastoma cells in cyclic shear stress injury. *Biotechnol Prog*. 2001; 17:760–67. [PubMed: 11485440]
18. Geddes DM, Cargill RS 2nd, LaPlaca MC. Mechanical stretch to neurons results in a strain rate and magnitude-dependent increase in plasma membrane permeability. *J Neurotrauma*. 2003; 20:1039–49. [PubMed: 14588120]
19. Alsuhaibani AH, Carter KD, Nerad JA, Lee AG. Effect of optic nerve sheath fenestration on papilledema of the operated and the contralateral nonoperated eyes in idiopathic intracranial hypertension. *Ophthalmology*. 2011; 118:412–14. [PubMed: 20801522]

FIG 1.

Optic nerve photographs of the right eye (A, C, E) and left eye (B, D, F) of a 17-month-old girl showing bilateral disk edema at presentation (A-B) and the presence and expansion of myelinated retinal nerve fibers at 9 (C-D), and at 33 months (E-F) after optic nerve sheath fenestration in the right eye.

Table 1

Acquired myelinated retinal nerve fibers (MRNF) in children

Case	Author	Age ^a	Sex	First eye ^b	Second eye ^{c,d}	Amblyopia history	Strabismus	RE (SE)		BCVA		Notes
								OD	OS	OD	OS	
1	Aaby et al ¹ ; Kushner ⁶	2 yrs (5.5 mos s/p ONSF)	F	OD	+6 yrs	NR	Acc ET	+3.63	+3.75	20/20	20/20	s/p bilat ONSF
2	Aaby et al ¹	5.5 yrs	M	OD	(8.5 yrs)	Yes	Right E(T)	+0.13	+0.75	20/40+2	20/30	
3	Aaby et al ¹	~9 yrs	F	OS	+1 yr	No	E(T)	+4.75	+4.50	20/25	20/20	Turner syndrome
4	Ali et al ⁷	15 mos	M	OD	(9 yrs)	NR	NR	Plano	-0.50	20/20	20/30	Arnold-Chiari malformation; hydrocephalus s/p ventricular shunt; ON dysplasia OS
5	Jean-Louis et al ⁸	7 yrs	M	OS	+7 yrs	No	NR	NR	NR	20/20	20/20	Bilat drusen
6	Parulekar et al ⁹	12 yrs	M	OD	(16 yrs)	NR	NR	NR	NR	20/30	NR	NF1; right ON glioma, proptosis, optic disk edema, opticociliary shunt vessels, RAPD (resolved later)
7	Parulekar et al ⁹	13 yrs	M	OS	(15 yrs)	NR	NR	NR	NR	20/15	20/20	NF1, ON glioma OS extending to ONH; ON atrophy OS
8	Duval et al ¹⁰	10 yrs	F	OD	< +8 yrs ^e	No	NR	+0.75	+0.75	20/20	20/20	Niikawa-Kuroki syndrome; bilat ONH drusen
9	Duval et al ¹⁰	6 yrs	M	OS	+4 yrs	NR	NR	+1.50	+1.50	"normal"	"normal"	Cerebellopontine arachnoid cyst s/p cystoperitoneal shunting at 6 wks + reoperation for shunt malfunction; dysmorphic features; no unifying syndrome; bilat ONH drusen
10	Bothun et al ¹¹	15 yrs	F	Appearance noted same time OU	Appearance noted same time OU	No	V-pattern ET	+4.50	+6.00	20/20	20/25	Klippel-Trenaunay syndrome; bilat ON + chiasmal gliomas; ONH drusen

\$watermark-text

\$watermark-text

\$watermark-text

Case	Author	Age ^a	Sex	First eye ^b	Second eye ^{c,d}	Amblyopia history	Strabismus	RE (SE)		BCVA		Notes
								OD	OS	OD	OS	
11	Current study	26 mos (2 mos s/p ONSF)	F	OD	+3 mos	Yes	Acc ET	+3.00	+6.25	20/20	20/20	IIH; s/p ONSF OD

Acc, accommodative; BCVA, best-corrected visual acuity; *bilat*, bilateral; *ET*, esotropia; *ET*, intermittent esotropia; *F*, female; *IIH*, idiopathic intracranial hypertension; *M*, male; *Mos*, months; *NFI*, Neurofibromatosis type 1; *NR*, not reported; *OD*, right eye; *ON*, optic nerve; *ONH*, optic nerve head; *ONSF*, optic nerve sheath fenestration; *OS*, left eye; *OU*, both eyes; *RAPD*, relative afferent pupillary defect; *RE*, refractive error; *s/p*, status post; *SE*, spherical equivalent; *Sph*, sphere; *yrs*, years.

^aAge at appearance of MRNF on examination.

^bLaterality of first eye affected.

^cTiming of appearance of MRNF in second eye relative to the first eye.

^dAges at last reported examination at which no MRNF was noted in second eye are given in parentheses.

^eDate of presentation unclear.

Table 2

Characteristics of myelinated retinal nerve fibers (MRNF) previously reported compared to those acquired in childhood

	Syndrome of unilateral MRNF, myopia and amblyopia ²⁻⁵	MRNF acquired in childhood ^{a,1,6-11}
Sample size	N = 43 (43 eyes)	N = 11 (18 eyes)
Sex	47% Male ^b 53% Female ^b	55% male 45% female
Location		
• continuous with ON	97%	100%
• discontinuous with ON	3%	0%
Laterality		
• unilateral	100%	36%
• bilateral	0%	64%
Visual acuity	29% 20/30 ^c 6% 20/40-20/100 ^c 65% 20/200 ^c	94% 20/30 6% 20/40
Strabismus	17 XT 10 ET 1 hypertropia 1 with past history strabismus, NOS	5 ET
Refractive error (SE)	Plano to -20.50	Plano to +6.25

ET, esotropia; *NOS*, not otherwise specified; *NR*, not reported; *ON*, optic nerve; *SE*, spherical equivalent; *XT*, exotropia.

^aIncluding findings from the current study.

^bResults reported in 32 of 43 cases.

^cResults reported in 34 of 43 cases.