MEDULLATED NERVE FIBERS
CONFOUNDING OR CONTRIBUTING TO AMBLYOPIA

A CASE REPORT AND REVIEW

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Abstract

Medullated, or myelinated nerve fibers affect between 0.57 to 1% of the population. They are formed by myelination of ganglion cells beyond the lamina cribrosa during embryonic development. Typically, significant visual acuity loss is uncommon. However, reports of amblyopia associated with myelinated nerve fibers have been reported in the ophthalmologic literature.

The following case report illustrates an example of a patient with myelinated nerve fibers and amblyopia in addition to unilateral high myopia and strabismus. The patient was prescribed glasses for full-time wear and given home patching procedures. Over a 2 year period, he has shown significant visual acuity improvement.

Key words

amblyopia, exotropia, myopia, myelinated nerve fibers, strabismus

Von Noorden defines amblyopia as "a decrease in visual acuity in one or both eyes which upon physical examination, appear normal and which, if treated early in life, is completely or partially reversible." He writes that the prevalence of amblyopia is 2-2½% of the general population.[1] He further divides amblyopia based on etiology into the following groups: visual deprivation, anisometropic and strabismic.

The following case illustrates an example where a patient presents with unilateral high myopia, exotropia and amblyopia. In addition to these findings, his retina reveals nerve fiber layer myelination. We questioned how much, if any, these myelinated nerve fibers contribute to the amblyopia.

CASE REPORT

KW, a 5-year-old Asian male, was referred by his optometrist for an amblyopia evaluation. He had no significant systemic or ocular history. The initial examination was conducted during December, 1998. His developmental history was normal. His current prescription, which he received two weeks prior to the evaluation, was OD: -0.50 sphere, OS: -0.50-3.00x003 which yielded a Snellen visual acuity of 20/200 OD and was not improved with pinhole; 20/20-2 OS. The patient became visibly upset when his left eye was occluded by any method.

Cover testing revealed 14 prism diopters of constant right exotropia at distance and near. Extraocular muscles were full and smooth OU with head movement. Color vision was normal OD/OS. Pupils were equal, round, reactive to light with no afferent pupillary defect. Retinoscopy revealed -9.50sph OD, -0.50-2.50x180 OS. A cycloplegic refraction revealed the following: -7.50-0.50x180 OD, -0.50-1.50x180 OS. Dilated fundus examination revealed myelinated nerve fibers emanating superiorly and inferiorly from the optic disc in the right eye, with a clear fundus and foveal reflex. There were no significant retinal findings in the left eye. Testing to determine the fixation status of the OD was not successful because KW became uncooperative.

We diagnosed the patient with anisometropic amblyopia OD. However, because the myelination was extensive, we questioned if there might be an organic component to the amblyopia. We prescribed OD -7.50-0.50x180, OS -0.50-1.00x180 OS for full time wear, basing our prescription for the right eye on the cycloplegic refraction. Additionally, we educated the parent on the importance of patching techniques to help improve the vision in the right eye. The parents were not receptive to a program of in-office vision therapy because of logistic and financial reasons. Consequently, we recommended patching the left eye for a period of four hours a day while doing near activities, such as playing video games, eating, coloring, doing connect the dot books, etc. The patient was scheduled for a two month follow up visit to monitor for visual acuity improvement.

The patient returned during March, 1999. He had been wearing the glasses for

two months. According to the parent, the patient had been patching the left eye but would often remove the patch, so that he actually wore the patch less than the prescribed 4 hours. At this visit, we measured vision with the S-Chart and found it to be 20/274 OD. Laser interferometry, with the patient identifying only the horizontal and vertical stripes, yielded a potential vision of 20/40 OD, 20/25 OS. Based on the results of the normal left eye, we concluded that this test was accurate and that we should expect greater visual acuity improvement in the right eye. A cover test revealed a constant right exotropia of 14 prism diopters at distance and 18 prism diopters at near. A dry over-refraction, yielded -2.50-1.50x020 OD, no change OS. Because of these findings, we changed the right lens prescription to -9.50-2.00x010, splitting the difference between the cycloplegic axis and the current finding. Again, we instructed the parent to have the patient wear the glasses full time and to continue patching four hours a day.

At a visit during June, 1999, KW's parents reported better compliance with the patching. VA, as measured with S-Chart, was 20/120 OD. Lea Symbol VA measured 10/80 OD. Refraction was essentially unchanged. The patient was instructed to continue patching and return for a 1 month follow-up and kept this appointment with further improvement in visual acuity. However, at a visit during August, 1999, acuity had decreased.

The patient returned four months later for a follow-up visit. His parents reported that the patient was wearing the patch after school, even when playing outdoors. The refraction was essentially unchanged.. Cover test revealed 12 prism diopters of constant right exotropia at near and 9 prism diopters of constant right exotropia at distance. The parents were again instructed on appropriate activities when KW wore the eye patch and a visit was scheduled for one month , but did not appear until four months later.

At this visit, approximately one year after his first visit, the patient's vision improved to 20/80 with the S-Chart. And two months later, his vision improved to 20/65 with the S-Chart, 20/80+ with the Snellen Chart. The visual acuity level has remained stable since that time, as have the binocular findings and refraction.

Table 1. Incidence of Amblyopia and Visual Acuity

Refractive Status	50% Incidence of Amblyopia	100% Incidence of Amblyopia	Median Visual Acuity
Hyperopia	+2.00 or greater	+3.50 or greater	20/70
Myopia	-5.00 or greater	-6.50 or greater	20/200
Astigmatism	-1.50 or greater	May be amblyogenic	

Table Modified from data in [5,7,8]

DISCUSSION

Anisometropic Amblyopia

The prevalence of amblyopia varies according to the subject group studied and the cutoff visual acuity used. Values range from 0.7 to 2.5% of the population.[1,2] Flom and Neumaier defined amblyopia as VA less than 20/40 in one eye with a one line difference between the eyes. They found that 28% of elementary school children with amblyopia had both anisometropia and strabismus, 34% had anisometropia of 1 diopter or greater and 38% had strabismus.[2]

In the case of refractive amblyopia, one retinal image is clear, the other is blurred. The blurred image may also be smaller or larger, depending on the degree of the refractive condition and the presence of aniseikonia. Researchers agree that blurred or dissimilar retinal images present an obstacle to sensory fusion, which can affect the development of the visual system.[2,3]

Some studies have found that blurred retinal images cause changes at the cellular level in the visual pathway. Amos writes of visual deprivation studies on cats, which resulted in histological changes to the x and y-cells in the retinae.[3] These cells normally respond to clear stimuli. As the images become more blurred, the response of the x and y-cells decreases. At higher cortical levels, such as the lateral geniculate nucleus, similar changes occur when a retinal image is blurred or occluded.[2,3]

Some researchers have concluded that there is not a strong relationship between the amount of anisometropia and the level of amblyopia.[4] Kilvin and Flynn investigated some other aspects of anisometropia and amblyopia. They researched a sample of anisometropic amblyopes with refractive conditions ranging from -18 to +8 diopters. Their sample was comprised of 40% each of hyperopic and myopic anisometropic patients. The authors found an initial median visual acuity of 20/200 in the myopic patients and 20/70 in the hyperopic patients, leading them to conclude that amblyopia was deeper in myopes than hyperopes. In hyperopic and myopic patients with similar amounts of anisometropia, they found equal amounts of amblyopia.[5] In both cases, as the amount of anisometropia increased, the level of amblyopia became deeper, and binocularity was compromised. However, Jamplosky et al. found that as the amount of anisometropia increased, the degree of amblyopia increased for hyperopes, but not for myopes.[6]

The amount of anisometropia necessary to result in amblyopia has been established. (See Table 1). A difference in hyperopia greater than or equal to 1.25D is often significant to result in amblyopia in the more hyperopic eye.[7] According to Ciuffreda et al., a 50% incidence of amblyopia results from hyperopia of 2D. The incidence increases to 100% with hyperopia of 3.5D.[8] Conversely, in myopia, a greater difference in refractive error between the eyes is needed before amblyopia develops. According to Ciuffreda et al., a 50% incidence of ambylopia results from myopia of 5D. The incidence increases to 100% with myopia of 6.5D.[8] With astigmatism, or meridional amblyopia, cylinder amounts greater than or equal to 1.50D can be amblyogenic.[7] The American Optometric Association's guidelines take a more conservative approach; it considers the following potentially amblyogenic: 1 D of hyperopia, 1.5 D of astigmatism, 3 D of myopia.[9]

In conditions where there is both a strabismus and anisometropia, there is disagreement on which condition is primary and which is secondary. Some researchers believe that the uncorrected refractive error is the primary condition with the strabismus being the result.[3,4] However, often it is impossible to determine what is primary or secondary.[4]

Medullated Nerve Fibers

Medullated, or myelinated, nerve fibers are found in 0.57 to 1 % of the population.[10,11]

Studies disagree on whether or not there is a gender predilection.[10,12,13]

Myelinated nerve fibers appear as white to gray-white areas of retina, obscuring underlying retinal detail. In most cases, they radiate peripherally from the optic disc, most commonly superior and inferior temporally, but can appear isolated in the posterior pole.[10,13] Ellis et al. divide myelination into three forms: type one affects one temporal arcade, type two affects both temporal arcades and type three is not contiguous with the disc.[14]

During embryonic development, myelin formation begins at the lateral geniculate nucleus and progresses anteriorly to the lamina cribrosa. An error in either this process, or in the formation of the sclera, is hypothesized to be responsible for the myelin's reaching the retina.[15]

Based on this information, myelin would be expected to be found only over the optic nerve head. However, Williams argues that isolated patches of myelin can be explained because myelin can move through the retinal nerve fiber layer. It is able to "settle" in an area with low nerve fiber layer density and become visible.[15]

Systemically, myelinated nerve fibers have been associated with conditions such as oxycephalia and forms of dyscrania.[11,13] There are also reports that associate myelinated nerve fibers with ocular conditions such as exotropia, esotropia, hyperopia, nystagmus, keratoconus, polycoria, prominent Schwalbe's line, tilted lens, aniridia, polycoria, coloboma, afferent pupillary defects and visual field defects.[10,11,15,17,19]

According to Moore,[17] it is uncommon to have significant central visual acuity loss with myelinated nerve fibers. However, various reports of amblyopia associated with myelinated nerve fibers have been published.[11-16,18] Studies have also found a relationship between myelinated nerve fibers and myopia.[12,18,19] Holland and Anderson reviewed German and French studies on myelinated nerve fibers which reported that between 35-58% of eyes with this condition are myopic.[16] Similarly, Ellis et al. found that 83% of patients with myelinated nerve fibers had myopia greater than 6 diopters.[14] In all cases, the myopia progressed. The authors postulated that medullated nerve fibers may contribute to myopia by creating axial enlargement. In contrast, other authors argue that the greater axial length of myopic eyes puts them at a greater risk for damage secondary to myelination.[18]

Table 2. Literature Review of Myelinated Nerve Fibers, Amblyopia and Strabismus

Study	Age	Binocularity	Rx	BVA	Patching
Buys[12]	3-10	No Info	No Info **+0.25-2.50x180**	**20/200**	7mos @ 3.5 yrs
Straatsma[11]	13	35 LXT'	Plano **pl-4.50x105**	20/20 **20/200**	1 mo @ 5.5yrs
Straatsma	7.5	40 LET'	+0.50 **-7.50-4.00x095**	20/20 **1/200**	None
Straatsma	32	15 LXT' 25 LH'	+1.00-0.75x180 **-5.75-3.75x045***	20/20 **20/400**	None
Straatsma	50	4 RXT	**+1.50-3.00x105** +0.25	3/200 20/20	None
Lee et al [18]	16mo	20 RET	**-8.00-0.50x180** +0.50	20/200 20/20	Yes ? Time
Lee et al	6	4 LET	+1.25-0.75x180 **-5.00-0.50x180****	20/25 **20/400**	Yes ? Time
Lee et al	6	4 LET	+1.50 **-4.00**	20/25 **20/100**	Yes ? Time
Lee et al	3	4 LET	-1.25-0.50x180 **-13.00-2.00x075**	20/20 **5/200**	Yes ? Time
Holland & Anderson[16]	4	20 LET	+4.75 **-12.50**	18/30 **FC 2'**	None
Holland & Anderson	4-5	Small < ET	+0.75 **-10.00-1.00x180**	20/30 **20/200**	None
Ellis et al[14]	2.5-3	45 RXT	**-15.50** plano	**FC 5'** 20/30	6 mos @ 30 mos
Ellis et al	2	No Info	**-12.00** +1.00	**20/400** 20/30	4 mos
Ellis et al	2-7	None	**-1.75-2.25x075** +0.50	**6/400** 20/15	Yes ? Time
Ellis et al	7.5-10	No Info	-0.25-0.25x180 **-10.50-4.00x165***	20/20 *20/200*	6 wks @ 7.5 yrs
Ellis et al	5-10	20 RET	**-9.50** -1.50	*20/200* 20/20	7mos @ 5 yrs
Ellis et al	4-10.5	No Info	**-6.25-1.00x110** -3.25-1.00x165	**20/200** 20/20	1 yr @ 4 yrs

**Macular Pucker, ** APD. The age for each patient indicates the time of best visual acuity (BVA), or BVA over a period of years.*

The relationship between the extent of myelination and the refractive error or degree of amblyopia has also not been determined. Ellis et al. reported on six patients with amblyopia, strabismus and myopia.[14] All patients had "fairly extensive" myelination. The amount of myelination ranged from extending along both temporal arcades and nasally off the optic nerve head, to isolated patches in the posterior pole. The best visual acuity found in any patient after extensive patching was 20/200. However, in all cases, in addition to myelination, the patients had an abnormal macular area, with 67% displaying a delayed response to the macular photostress test. One patient also had nerves that were described as "pale." This raises the question of whether or not in some cases, the decreased visual acuity is secondary to an underlying retinal or optic nerve pathology instead of to the myelinated nerve fibers themselves.

Authors cannot agree on the etiology of the amblyopia in patients with myelinated nerve fibers. Many of the eyes in the studies reviewed would be suspected of being amblyopic on the basis of refractive or binocular status alone. Ophthalmologic authors have assumed that there is an organic etiology to the decreased visual acuity. Williams proposes that the retinal myelination causes a decrease in the number of ganglion cells

which causes optic nerve hypoplasia, resulting in decreased visual acuity.[15] Holland and Anderson, postulated that the myelinated nerve fibers result in an elevation of the optic disc which may lead to an overall disorganization of neural elements. This disorganization of visual pathways is responsible for amblyopia development.[16]

The work of Tansley tends also to support an organic etiology for the amblyopia.[20] On histological studies of mammals, he noted that animals such as mice and rabbits, with deep cups and poorly developed lamina, have extensive myelination. These animals also have pure rod retinas and generally poor visual acuity. Conversely, animals such as cats and monkeys have shallower cups with well developed lamina and no retinal myelination. These animals have pure cone retinas and good visual acuity. Tansley postulates that the eye must be rigid to keep the retina undistorted and to maintain sharp vision.[20]

TREATMENT

A guideline for amblyopia treatment is first to prescribe the full correction based on a cycloplegic refraction, especially in cases of hyperopia.[7,8] Glasses might be preferred to contact lenses if there is a difference in refractive error between the eyes. With glasses or contact lenses alone, complete visual acuity improvement occurs in only 10% of patients.[7] The remaining 90% require other methods to help improve visual acuity.

The second step after full optical correction would be direct occlusion for 2-6 hours a day.[7] During the time of patching, the patient should do fine motor work such as coloring, bead stringing, connect the dots, etc. He/she should not be engaged in outdoor tasks because of a decrease in depth perception. Similarly, he/she should not read or do homework, partly because the vision is not optimal for cognitive tasks.

The third and final step or treatment is active vision therapy designed to first improve the visual acuity in the affected eye and then to improve binocular fixation.[7,8]

Compared to other forms of refractive amblyopia, myopic amblyopia generally has a poorer prognosis for visual improvement. Good prognostic indicators include: a younger age at time of treatment, no strabismus and central fixation.[11] In the ophthalmological literature, there are reports of visual acuity improvement with orthoptics in myopic amblyopes. Sen found 58% of myopic amblyopes treated with either full time occlusion alone or full time occlusion with pleoptics (Cuppers Afterimage) improved by two lines or better, with 31% achieving 20/40 or better as a final visual acuity.[21]

Table 3. Evaluation of a Patient with Myelinated Nerve Fibers and Amblyopia

S-Chart Visual Acuity
Retinoscopy including Cycloplegia
Pupils
Color Vision
Amsler Grid
Macular Photostress Test
Laser Interferometry
Neutral Density Filter
Dilated Fundus Examination

CONCLUSION

In our case study, there are three factors that can contribute to the amblyopia: myopia, exotropia and the myelinated nerve fibers. Unfortunately, we do not know what factor is primary and what is secondary or tertiary.

The purpose of this paper was to examine what percentage, if any, of the decrease in vision is secondary to the myelinated nerve fibers. Based on our experience with this patient, the decrease in visual acuity cannot fully be attributed to "organic amblyopia," as the patient has shown a visual acuity improvement with optometric means. Our patient would not be remarkable if he did not have the myelinated nerve fibers. Without this condition, he would be a strabismic and refractive amblyope.

Although a triad of myelinated nerve fibers, myopia and strabismus has been reported in the literature, it does not appear to be the norm. In some studies, patients had abnormal macular areas, which could also be responsible for the decrease in vision. Additionally, the decrease in vision could be attributed to the high refractive error or the strabismus of some patients. In order to fully rule out an organic etiology, when patients present with myelinated nerve fibers and amblyopia/ strabismus, a cycloplegic exam is indicated. Additionally, careful attention should be paid to tests of optic nerve and macular function, such as color vision, pupils, Amsler grid and macular photostress test. As with other amblyopes, laser interferometry/ retinometry should be considered to determine if visual acuity improvement is possible.[8] Furthermore, neutral density filters can also be considered to determine if there is an organic component to the amblyopia. Table 3. Contains the tests I recommend to be done on patients with myelinated nerve fibers and amblyopia.

We have educated this patient's parents on his visual and ocular conditions and explained that we will continue to patch as long as his visual acuity, as measured with S-Chart, continues to improve. Based on our laser interferometry findings, we would predict a final visual acuity of around 20/40. We would also recommend a program of in office vision therapy to help improve the patient's binocular and accommodative skills.

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