The spectrum of optic nerve hypoplasia: The importance of a careful nerve head evaluation

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Abstract
Optic nerve hypoplasia is a relatively common, non-progressive, congenital anomaly of the optic nerve causing impaired vision, often manifesting as strabismic amblyopia. It is thought to be a failure of ganglion cell axon migration during embryological development of the eye as a consequence to any insult to the CNS resulting in damage to the developing optic nerve. Three cases of optic nerve hypoplasia are presented demonstrating variable visual profiles. The first case is a 22 year old female with esotropia and Tilted Disk Syndrome. The second is a 6 year old female with esotropia and bilateral optic nerve hypoplasia where occlusion patch therapy was unsuccessful due to the hypoplasia. The final case is a 53 year-old female without strabismus, but a largely reduced visual field consequently causing a functional vision loss. Tips for diagnosis and testing are also offered, stressing the importance of a thorough vision exam. Particularly close attention should be made to Disk-Macula/Disc Diameter ratio, optic nerve head evaluation (pallor with double-ring sign,) visual fields and diagnostic patching.

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THE SPECTRUM OF OPTIC NERVE HYPOPLASIA:
THE IMPORTANCE OF A CAREFUL NERVE HEAD EVALUATION

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Jessica wishes to dedicate her portion of this thesis to her husband, Conley J. Lynch. Ara wishes to thank her fiancé, Tim, for all of his support and encouragement throughout the last several years. She would also like to thank Jessica for doing most of the work on the thesis and still allowing Ara to put her name on it.
ABOUT THE AUTHORS

Jessica Lynch is a native of Ryegate, Montana. After finishing high school in 1993, she started her freshman year at Carroll College in Helena, Montana. She also attended Seattle University, and then graduated in 1997, with honors, from North Dakota State University in Fargo, North Dakota with a BS degree in biology. While attending PUCO, Jessica participated in the Student Optometric Association and is a member of Beta Sigma Kappa Optometric Honor Society. Jessica has been married to her husband, Conley, for six years and together they have two children. Upon graduation, Jessica will be looking for a job in the Portland area.

Ara Sudtelgte grew up in Elkton, South Dakota where she graduated high school in 1993. She attended Northern State University in Aberdeen, SD and South Dakota State University in Brookings, SD, graduating with a BS degree in chemistry in 1998. She was the recipient of the Koczon Chemistry scholarship at NSU and is a member of Beta Sigma Kappa Optometric Honor Society. While attending optometry school, Ara participated in organizations including Amigos Eyecare Organization and Student Optometric Association. Ara hopes to work within the Indian Health Services or somewhere in the Minneapolis area after graduation.
ABSTRACT

Optic nerve hypoplasia is a relatively common, non-progressive, congenital anomaly of the optic nerve causing impaired vision, often manifesting as strabismic amblyopia. It is thought to be a failure of ganglion cell axon migration during embryological development of the eye as a consequence to any insult to the CNS resulting in damage to the developing optic nerve. Three cases of optic nerve hypoplasia are presented demonstrating variable visual profiles. The first case is a 22 year old female with esotropia and Tilted Disk Syndrome. The second is a 6 year-old female with esotropia and bilateral optic nerve hypoplasia where occlusion patch therapy was unsuccessful due to the hypoplasia. The final case is a 53 year-old female without strabismus, but a largely reduced visual field consequently causing a functional vision loss. Tips for diagnosis and testing are also offered, stressing the importance of a thorough vision exam. Particularly close attention should be made to Disk-Macula/Disc Diameter ratio, optic nerve head evaluation (pallor with double-ring sign,) visual fields and diagnostic patching.
The Spectrum of Optic Nerve Hypoplasia:
The Importance of a Careful Nerve Head Evaluation

Introduction

Optic nerve hypoplasia is a relatively common, non-progressive, congenital anomaly of the optic nerve causing impaired vision. Histologically, it is thought to be a failure of ganglion cell axon migration during embryological development of the eye. The result is a small optic nerve with normal central vessels and a pathologically thin nerve fiber layer. Damage to the optic nerve was once thought to occur between the 6th or 7th week of embryonic development (1-4). More recent studies have attributed hypoplasia to any insult to the CNS causing damage to the developing optic nerve during any phase of embryological development (1).

Optic nerve hypoplasia can be particularly difficult to detect due to a variety of subtle, segmental forms and presentations. The importance of distinguishing optic nerve hypoplasia (ONH) from other causes of amblyopia is significant and should be questioned or evaluated when traditional amblyopia therapy (occlusion therapy) shows no improvement of visual function.

This article looks at three cases of subtle optic nerve hypoplasia where the diagnosis was made only after thorough examination and a persistence to determine the etiology of monocularly decreased vision. Included in the article are examination and diagnostic techniques meant to aid in the identification of optic nerve hypoplasia.

Case 1

W.N.

A 22-year-old female presented to the Pacific University Family Vision Center at Pacific University College of Optometry for a routine vision exam. Her chief complaint was of blur at
distance and near. She had been diagnosed with strabismus at the age of five and had been wearing glasses and presently wears RGP's. Her medical history was unremarkable.

During entrance skills, the patient displayed a 10\(^{\text{A}}\) right esotropia with a 4\(^{\text{A}}\) right hypertropia at distance. An 8\(^{\text{A}}\) right esotropia was present at near. Pupils were equal, round and displayed a brisk reaction to light with no evidence of an afferent pupillary defect. EOMs were normal and confrontational visual fields were full OU. An undilated Humphrey's central 30-2 threshold visual field was conducted on both eyes. The reliability of the test was good and the results showed decreased sensitivity in the inferior field. Scattered points were reduced to <2%; OD affected more than OS. A refraction of \(-8.75-4.00\times177\) OD and \(-10.75-4.75\times175\) OS resulted in best-corrected visual acuities of 20/30 OD, 20/20 OS.

An anterior segment evaluation revealed scattered cortical and nuclear cataracts OU. Open angles OU were noted by gonioscopy. Intraocular pressures with Goldmann tonometry were 15 mmHg OD, 16 mmHg OS. A dilated fundus examination performed revealed 0.1/0.1 cup-to-disc ratio with tilted optic nerve heads, a "double-ring" sign and scleral crescents 360 degrees OU. The right disc was slightly smaller than the left and both were located approximately 6.0-6.5 disc diameters away from the macula. Retinal vessels appeared normal OU. Macula's were flat with a bright foveal reflex OU. Vitreoretinal condensation was also evident OU with vitreal fluid pockets OS>OD. No apparent retinal detachment was found. Dilated stereo fundus photographs were taken and appear below.

W.N. was diagnosed with Tilted Disk Syndrome, high myopia and congenital cataracts. The patient was given a distance spectacle prescription and educated on the signs and symptoms of retinal detachment. She was told to return to the clinic in one year or sooner if needed. No
treatment was recommended for her esotropia due to the likelihood of underlying segmental hypoplasia as the primary causal factor.

Case 2

M.R.

A 6-year-old female was referred to the Pacific University Family Vision Center for a second opinion regarding decreased visual acuity. Her prenatal history had been unremarkable. She had been delivered full term with a birth weight of 5 pounds 11 ounces. It was reported that at the age of 6-8 months the baby was treated for bronchitis and was incubated due to a sedative overdose. She also suffered from ear infections during infancy. Personal ocular history was unremarkable. Developmental history was also unremarkable including school performance at grade level. Entering distance visual acuities were 20/60 OD, 20/25 OS, 20/25 OU. Near visual acuities were 20/100 OD, 20/40 OS. Pupils were equal, round, and reactive to light with no evidence of an afferent pupillary defect. EOM's were full and comitant. Cover test revealed a comitant 20\(^{A}\) right esotropia in the distance. An A-pattern was revealed at near with a cover test showing 15-20\(^{A}\) right esotropia in upgaze, 10-15\(^{A}\) RET in primary gaze, and 6-8\(^{A}\) RET in downgaze. A variable 8-10\(^{A}\) right hypotropia was also noted at near. Dry retinoscopy revealed
low hyperopia of +0.50 sphere OD, OS. No response was noted with Lang I or II stereo acuity with and without a trial framed prescription of +0.50 OD, OS with 11° BO. Cycloplegic retinoscopy revealed +1.25 sphere OD, OS. Anterior segment evaluation was unremarkable by gross observation. A dilated fundus examination revealed 0.1/0.1 cup-to-disc ratio with mild hypoplasia of the right optic nerve head and nondistinct margins nasally OD. The determined diagnoses were: amblyopia with esotropia and variable hypotropia OD, hypoplastic disc possibly causing decreased visual acuity OD, and hyperopia OU. No prescription was given at that time, but a diagnostic patching regimen of 2 hours per day OS was recommended.

At the follow-up visit two months later, entering visual acuities were 20/50+2 OD, 20/25 OS using an isolated line, showing a slight improvement. A cover test revealed alternating fixation with preference for the left eye. Performance of Worth 4-Dot showed no suppression, however, suppression was noted during the red lens test. Lang stereo testing was negative. Color vision was unremarkable. A possible slight restriction in confrontational visual field was noted temporally OD. It was recommended at that time to continue with the patching therapy at least 2 hours per day while performing detailed tasks.

A follow-up was performed one year later. Entering visual acuities were 20/50 OD, 20/20 OS. Cover test revealed no change in the angle of esotropia. Suppression was noted on the Worth 4-Dot and no stereopsis was found on Stereo Fly tests. Dry retinoscopy revealed low hyperopia of +0.50 sphere OD, +1.00 OS. Dilated fundoscopy showed a small pale right optic nerve head with indistinct nasal margins OU and mild myelination OS. Stereoscopic fundus photographs were also taken at this visit. Careful side by side comparison of nerve head photos revealed that the right nerve head was approximately 15% smaller that the left and the margin of the right nerve head was indistinct and thin from 6-11 o’clock along the nasal aspect. Also,
automated fields were attempted but proved unreliable due to patient’s age and attention. Repeated confrontation fields were inconclusive. The patient’s parents were educated regarding her condition and no further lenses or therapy were prescribed.

Case 3 D.A.

A 53-year old white female presented to the Pacific University Family Vision Center for a complete vision exam. She had worn glasses since the age of three and was being treated for asthma, hyperthyroidism and angina. D.A. was unable to work because of her impaired vision and was now using a cane, in addition to her glasses, to move around. Cover testing showed 2\(^\circ\) of exophoria at distance and 6-8\(^\circ\) of exophoria at near. EOMs and pupils were unremarkable. Stereopsis was not tested at this exam. Confrontational visual fields revealed an inferior constriction OU. Further testing with a Humphrey central 30-2 threshold test showed decreased sensitivity 360 degrees and absolute inferior hemianopsias OU with macular sparing that respected the vertical midline. D.A.’s left eye was slightly more affected than her right. Her best-corrected distance and near acuities were 20/25 OU with the addition of OD -5.25-0.50\(\times\)160, OS -3.50-1.25\(\times\)171 +1.75 ADD OU.
Slit lamp examination was unremarkable except for mild staph blepharitis OU, Voight's Limbal Girdle OU and mild nuclear sclerotic cataracts OU. Intraocular pressures with Goldmann tonometry were 11mmHg OD and 14mmHg OS. A dilated fundus exam revealed small, pale optic disks with indistinct margins. The disks appeared to be tilted with the inferonasal portion displaced posteriorly. A choroidal crescent was found inferonasally OU. The D-M/DD ratio was 4:1. The A/V ratio was 5/6 OU and no macular reflex was found OU. Stereoscopic fundus photos were taken.

D.A. was found to have tilted and hypoplastic disks OU with resulting inferior visual field loss OU. She was given a spectacle prescription and asked to return to the clinic in six months to monitor the visual field loss. Upon subsequent visits, her visual field loss was found to be stable.

The three cases presented above illustrate the wide spectrum of optic nerve hypoplasia presentations. Optic nerve hypoplasia can be a challenge to diagnose. Strabismic amblyopia, Tilted Disk Syndrome and visual field defects show that the range of accompanying signs are
numerous. Because of the varied phenotypes, it is very important that the clinician be able to correctly diagnose this condition because it is fairly common and the resulting amblyopia relatively impervious to traditional therapy. The following are some helpful tips for detecting optic nerve hypoplasia.

**Tips for Diagnosis of Optic Nerve Hypoplasia**

1. **Nerve Head Appearance**

   The most common clinical presentation of optic nerve hypoplasia is that of a small, gray, or pale optic nerve head, which often is surrounded by a yellowish mottled peripapillary halo, flanked on either side by a ring of pigment (double-ring sign.) The outer ring is the junction of the scleral choroidal pigment with the lamina cribrosa and approximately corresponds to the size of a normal optic nerve head. The inner, darker ring represents the junction of the termination of the retinal pigment epithelium and the hypoplastic optic nerve (1,5.) Although the double ring sign may be helpful in diagnosis, it is often incomplete or absent and therefore, diminishes its diagnostic value (6.) Case #2 presented here exemplifies this point.

2. **Visual Acuity**

   Visual function is variable and may range from 20/20 to no light perception. Studies have not found a correlation between visual function and the overall size of the disc (7.)
3. **Disc-Macula/Disc Diameter (D-M/DD)**

   The D-M/DD ratio is the ratio of the horizontal distance between the center of the optic disc and the macula to the mean diameter of the optic disc. The D-M/DD ratio is characteristically increased in eyes with optic nerve hypoplasia. A ratio approximately greater than 3:1 is present in 95% of patients with optic nerve hypoplasia (7) and may be considered if in adjunct with reduced visual function (8). Some claim that this ratio is too low and it should rather be 3.7:1 to 4.2:1 (9). The ratio is thought to be falsely lower for younger children and high hyperopes and falsely higher for adults and high myopes (> -4.00) (9).

   This ratio can be seen using direct and indirect ophthalmoscopy, fundus photography, or direct measurements of the optic nerve can be taken by CT scanning, A and B-scanning ultrasonography. Fundus photography may be the simplest, and most reproducible and useful clinical aid to determine the D-M/DD (9). However, the image size of the disc with fundus photography is subject to minifying or magnifying effects associated with optical physiology.

4. **Visual Field Defects**

   Most eyes show variable visual field defects (1). The defects tend to be static and ophthalmoscopically correlated. Patients with diffuse nerve deficits tend to have more or less concentric visual field contraction and those with segmental hypoplasia show field loss associated with the direction of the disc tilt.

5. **Retinal nerve fiber layer (NFL)**

   NFL defects are easily shown only in severe cases, although red-free filters may aid in detecting these defects. These include absence of nerve fiber layer opacity and striations,
exposure of small retinal vessels normally hidden in the nerve fiber layer and the appearance of broad, bright reflexes along major retinal vessels (6.)

6. Tilted Disk Syndrome

Optic nerve hypoplasia can also manifest as segmental hypoplasia, where only part of the optic nerve is affected. Tilted disk syndrome is thought to be one presentation of sector hypoplasia and is exemplified by a scleral crescent (8.) It is a bilateral condition in which the superiotemporal optic disk is elevated and the inferonasal disc is displaced posteriorly, resulting in an optic disc of oval appearance. Situs inversus of the retinal vessels, inferonasal conus, thinning of the inferonasal RPE and choroids, thinning of the NFL entering the underdeveloped disc area and myopic astigmatism are also found (10.) These patients usually show visual field loss corresponding to the direction of the tilt and have vision better than 20/40 (1.)

7. Unilateral vs. Bilateral

Unilateral cases may be mistaken for primary strabismus and amblyopia. Unilateral optic nerve hypoplasia usually presents in early childhood accompanied by strabismus and monocular acuity reduction. Afferent pupil defects are common in more severe unilateral cases (8, 11-12.)

Bilateral cases are more frequent and often are associated with nystagmus and sluggish pupil reactions(1). Although bilateral, asymmetry of the two optic nerve heads is common. In one study, half of patients presenting with bilateral optic nerve hypoplasia (BONH) had visual function at light perception or NLP. In the same study, 29% of patients with BONH also had CNS abnormalities (13.) There are a wide variety of clinical conditions that may be accompanied by optic nerve hypoplasia. One condition that has been widely reported is septo-
optic dysplasia. Septo-optic dysplasia is characterized by BONH, partial or absent septum pellucidum and partial or complete agenesis of the corpus collosum. This condition may also be accompanied by neurological and/or endocrine abnormalities (13-16.) One common anomaly is a growth hormone deficiency (13.) There are varying reports as to the percentage of patients with BONH that also have partial or absent septum pellucidum/corpus collosum. These range from 27% (16) to 46% (13.) Because of these relatively high percentages, the clinician must be able to recognize the infant who presents with BONH combined with jaundice, lethargy, hypothermia, hypotonia, and hypoglycemia as these patients may have septo-optic dysplasia and would be in need of immediate referral (13.) Siatkowski recommends that any infant presenting with BONH be referred for a thyroid and adrenal screen and endocrine consultation.

8. Case History

A thorough case history should concentrate on possible risk factors. Because optic nerve hypoplasia is a manifestation from damage to the CNS during any time before full development, special attention should be paid to prenatal history. Risk factors for hypoplasia include: young and/or diabetic mothers, premature or postmature birth, Fetal Alcohol Syndrome, and other teratogenic agents (17.) A slightly greater male prevalence with ONH has also been demonstrated (17.)

9. Vessel Evaluation

One study illustrated that those with ONH had a notably greater distribution of tortuosity and a considerably smaller number of branching points of the retinal vasculature (17.)
Testing Tips:

1. Refractive errors: the magnification or minification effect that occurs with the presence of significant refractive errors must be taken into consideration while performing ophthalmoscopy/fundus photography. The most accurate method to determine D-M/DD is to use an A-scan ultrasonography to determine axial length and, then, apply a formula to determine the actual length (18.) This method provides you with only marginal differences in measurement and coupled with the inconvenience to the average practitioner, they prove to be impractical.

2. Diagnostic patching regimen: Previous studies had determined that patching therapy could improve the visual function of some children with unilateral structural defects of the optic nerve, although more recent studies discount those conclusions (19.) A study by Yang and Lambert showed that for children with optic nerve hypoplasia it was the structural changes rather than amblyopia that accounted for vision loss (20.) It is possible, however, to have two disease processes simultaneously. If amblyopia is superimposed on an optic nerve structural defect, occlusion therapy may improve visual function. For this reason, it is best to stick to a very conservative, diagnostic patching regimen.

   A common patching regimen is to treat patients with 6-8 hours/day direct occlusion. Follow-ups are scheduled at an interval of one week for every year of age, not to exceed four weeks. It is advocated that occlusion therapy be discontinued after equal acuity is achieved in the amblyopic eye, or after three consecutive, compliant episodes of full-time occlusion without further visual improvement (19-21.) It is important to note that it is best to avoid full-
time occlusion unless you are certain of a unilateral structural defect, in which case the risk of deprivational amblyopia and strabismus of the “good” eye is minimal.

Conclusion

Optic nerve hypoplasia is a condition that can easily go undiagnosed. This is due to the great variability of the visual profile, optic nerve head presentation and the associated findings with those patients with ONH. Of particular interest to the authors are the pediatric patients who present with unilateral strabismus and decreased acuities. Young patients presenting with esotropia and decreased acuities are a common occurrence in a pediatric practice. Strabismic amblyopia is one of the most common pediatric conditions encountered. The strabismus is most commonly a developmental or neurological imbalance (as in accommodative esotropia), with the accompanying amblyopia as a response to deprivation of the foveal receptors. However, occasionally, presumed strabismic amblyopia is secondary to a structural anomaly or disease of the anterior visual pathway (retina/optic nerve), such as optic nerve hypoplasia.

Two of the cases discussed dealt with this phenomenon of strabismus in conjunction with ONH. The first case that was reviewed was of a young adult female with esotropia and Tilted Disk Syndrome. The diagnosis was fairly straightforward because of the appearance of her nerve heads and the resulting visual field loss. Her strabismus is assumed to be secondary to the segmental hypoplasia. Diagnosis of the second case was not as straightforward as the first. The second case was a young girl with a large degree of esotropia and bilateral ONH. The bilaterality of the hypoplasia made it impossible for the clinicians to compare nerve heads. Other factors, such as the D-M/DD ratio, and optic nerve appearance were utilized in the diagnosis. In such cases where the diagnosis of ONH may not be obvious, it is very important to consider all
causes of strabismus and amblyopia. In the second case, the traditional approach to amblyopia treatment proved to be unsuccessful due to the hypoplasia. The third case was unlike the first two in that it did not involve strabismus or marked amblyopia. This patient had Tilted Disk Syndrome and a large degree of inferior visual field loss. Despite the remarkable visual field loss, the patient had only very mild amblyopia. This is an example of how visual acuities cannot be predicted by the degree of OHN.

Aside from strabismic amblyopia, ONH should also be considered when a young patient presents with small, pale optic nerve heads (sometimes with the characteristic double-ring sign), a large D-M/DD, visual field loss or nerve fiber layer defects. A thorough exam with close attention to the above factors, as well as a diagnostic patching regiment may also aid in the identification of this condition. When diagnosing this condition, as well as others, it is important not to diagnose a patient in a knee-jerk response to a certain constellation of symptoms, but instead to consider other causes. The result of this article will certainly lead these authors to view other similar situations in a more encompassing manner and to more comprehensive treatment decisions.
References: