

# A Pediatric Patient with

## OPTIC NERVE COLOBOMAS and LACRIMAL ABNORMALITIES

### Does This Constitute A Syndrome?

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#### Abstract

*This case report describes a child who presented with a seemingly routine history of esotropia. Our evaluation found that there were bilateral optic nerve colobomas and the atresia (absence) of both puncta. Since both of these conditions are fetal developmental disorders, a literature search was performed to determine whether there was a syndrome connecting the two conditions. It did not result in finding an association between them. The further optometric evaluations are presented along with detailed discussions of optic nerve coloboma and punctal atresia. These findings and the detailed discussions indicate there is still the possibility of an underlying systemic condition or mental retardation. Treatments of optic nerve coloboma and punctal atresia are presented.*

#### Key Words

*esotropia, optic nerve coloboma, punctal atresia, amblyopia*

#### INTRODUCTION

**B**oth optic nerve coloboma and punctal absence (atresia) are conditions that represent fetal developmental disorders. Optic nerve colobomas have been associated with a variety of ocular conditions including decreased visual acuity, corneal anomalies, iris coloboma, lenticular anomalies, strabismus and retinal defects.<sup>1-8</sup> Additionally, optic nerve colobomas have been associated with a variety of systemic multisystem disorders and mental retardation.<sup>3,5,6,8</sup> Lacrimal system disorders have been associated primarily with craniofacial anomalies.<sup>9,10</sup> The following case report raises the question of whether the presence of optic nerve colobomas and a bilateral lacrimal abnormality represent a previously unreported syndrome, or are two unrelated congenital anomalies.

#### CASE REPORT

##### Initial optometric pediatric examination

A 6-year-old African American male, presented to the pediatric clinic at the State University of New York, State College of Optometry (SUNY) for a routine eye examination. His ocular history was significant for a left esotropia and amblyopia since approximately the age of three. He had been patching the right eye for three hours a day for the past year. The patching was discontinued one month prior by his previous eye doctor. According to the patient's mother, the doctor felt

that the patient would need glasses, but deferred prescribing them. The patient's medical history was significant for asthma, for which he was not taking any medications. His family ocular history was significant for glaucoma in his maternal grandmother, and esotropia in his maternal aunt. Birth was by Caesarian section because of maternal bleeding during pregnancy. Birth weight was 7 lbs, 5 oz. Developmental milestones were reported as normal; walking at 14 months and talking at 10 months. The child was at grade level in kindergarten.

Entering visual distance acuities were OD: 20/40 and OS: 20/200. The pinhole did not improve vision in either eye. At near, acuities were OD:20/30 and OS: 20/200. Gross external evaluation showed a constant left esotropia of approximately 30 prism diopters at distance and near. Extraocular motilities revealed a mild abduction difficulty in the left eye. The patient also appeared to have difficulty with up gaze. Confrontation field testing did not indicate restrictions with both eyes open. Pupils were equal, round and reactive to light with a questionable afferent pupillary defect OS. Dry retinoscopy revealed a variable refraction: OD: -3.00 DS to -5.00 DS; OS: -1.00-2.00x100. Retinoscopy with cyclopentolate spray in each eye, revealed a refraction of OD:-3.50-1.00x180 and OS :-0.75-1.50x 180 OS. However, because the patient

was crying, it was possible that he was not fully cyclopleged. Additionally, the magnitude of the myopia OD was not consistent with the entering acuity. Because of these reasons glasses were not prescribed.

Slit lamp examination revealed a bilateral absence of the inferior puncta. Superior puncta were present. There was no history of epiphora. Because of poor patient cooperation, we were unable to perform Goldman applination tonometry. Finger tension pressures were soft and equal. A dilated examination revealed a healthy posterior segment in the OD; while the optic nerve was distinct and pink it was slightly anomalous. In the OS, a large inferior optic nerve coloboma was present. Based on the size of this coloboma, we believed that the vision loss and esotropia in the left eye might have an organic component.

The patient's mother reported that she had never been told that there was a problem with her son's tear ducts or optic nerves. We recommended he be evaluated in SUNY's neurological eye clinic for further assessment. We felt that, based on the findings of the optic nerve heads and the absence of the puncta, the child might have an ocular syndrome with possible systemic and/or neurological associations.

### **Optometric neurological evaluation**

At this visit the child's ocular and systemic history were unchanged. However, the mother now remembered that her obstetrician had recommended additional testing on the fetus (possibly an amniocentesis) but that she had declined. The child's last physical was two weeks prior to this visit and everything was reported as normal. The child appeared more at ease than during the previous visit.

Visual acuities at distance were OD:20/50 and OS:20/400. The pinhole did not improve acuity in the OD, but improved vision to 20/100 in the OS. Confrontation visual field testing was full in the OD, but there was a suspected superior restriction in sensitivity in the OS. Pupils were equal, round and reactive with a grade 1+ APD in the left eye, which we attributed to the extent of the optic nerve coloboma in that eye. Goldmann applination tonometry was OD: 18mm Hg and OS: 20 mmHg. The patient was diagnosed with optic nerve head colobomas

OS > OD, a constant left esotropia with an APD and a superior visual field defect, secondary to the coloboma. He was referred to the unit's attending neurologist for further evaluation.

### **Neurological evaluation**

This visit occurred one month later. History and entering visual acuities were essentially unchanged from the prior visits. Dry retinoscopy done at this visit was OD:-1.75-1.25x30 and OS:-2.50-0.50x150. The dry manifest refraction was OD:-1.75-1.00x30 (20/50-2) and OS:-2.25-1.00x160 (20/100). The cranial nerve evaluation was normal. Motor testing revealed full strength throughout. The neurologist noted that the patient had difficulty standing on one foot and difficulty with tandem (i.e. walking a straight line). This could indicate poor coordination or motor tone, and does not necessarily indicate a neurological problem. The neurologist did not feel that further systemic and/or neurologic testing was indicated. She advised the patient's pediatrician of her findings and opinion; the pediatrician concurred. The neurologist referred the patient back to the pediatric clinic for follow up.

### **Optometric pediatric clinic subsequent examinations**

The patient returned to the pediatric clinic one month later. He was not responsive to visual acuity testing at this visit. Dry retinoscopy OD was -1.00-1.25x60 and OS was -1.50-1.50x120. We felt these findings to be the most accurate retinoscopies, as the child was engrossed in watching a video during the testing. Based on this fact, and on the variability of the previous findings, it was decided to prescribe: OD:-1.00-1.00x60; OS:-1.00-1.00x120 in polycarbonate lenses for full time wear. We also hypothesized that the previous variabilities in retinoscopic findings could relate to the optic nerve anomalies in both eyes, creating retinal irregularities, and by the variable fixation by the child. Thus, if retinoscopy were performed along the axis of the coloboma, because of the child's inability to visually fixate on the desired straight ahead target, there would be apparently increased myopia.

The patient returned to the clinic for a follow up two months after wearing the glasses and was easily distracted and poorly attentive. He did not tolerate an

eye patch or occluder over either eye. Corrected binocular acuities were 20/50 at distance and 20/40 at near. Color vision was 14/14 OU with Ishihara plates. Although difficult to perform, keratometry revealed slight astigmatism in each eye; the mires in each eye appeared clear and regular.

We decided not to change the prescription, but to monitor visual acuity and retinal health on a regular basis. We explained that at a future visit we might change the prescription and, if the patient's attention and ability to tolerate a patch improved, we would reinstitute patching the OD and add active vision therapy, in an attempt to improve the visual acuity in the OS. However, prior to again instituting patching, we would attempt laser interferometry to differentiate the extent of the organic visual acuity loss from any functional visual acuity loss.

Both examining optometrists concurred that because this child had bilateral optic nerve colobomas, greater in the left than right eye, the likelihood of attaining 20/20 acuity in either eye was not good. We also felt that the size of the coloboma in the left eye and the esotropia, were responsible for the visual acuity loss in that eye.

### **DISCUSSION**

My further interest in this patient was to determine whether there was an existing syndrome or other reports that connected optic nerve colobomas and the bilateral atresia of the inferior puncta. My literature search identified only one report of a patient with both punctal and optic nerve hypoplasia.<sup>11</sup> Additionally, that patient presented with corneal abnormalities. The authors proposed that it is unusual to find both anterior and posterior ocular abnormalities that are the result of fetal developmental disorders. They suggested that patient's conditions constituted a "novel syndrome."<sup>11</sup> Nevertheless, I was compelled to extend my research on optic nerve coloboma and punctal atresia in order to eliminate the possibility of a syndrome that has not been reported. Further, I wished to gain knowledge on treatments for each condition in order to provide optimal management of this patient. The following is the cogent information for each of these conditions.

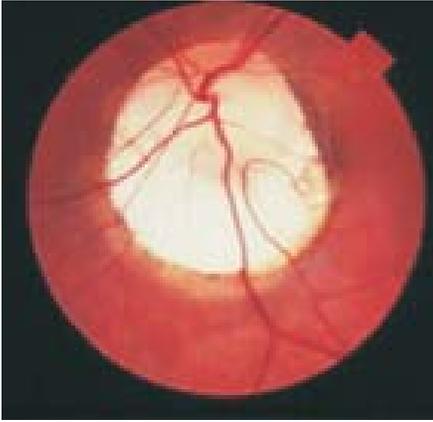


Figure 1. Optic Nerve Coloboma. The patient's visual acuity in this eye was 20/20. Courtesy of Dr. Sherry Bass, State University of New York, State College of Optometry.

### Optic Nerve Coloboma

This condition presents as an enlarged and vertically elongated disc with a thin or absent inferior neuroretinal rim and an intact superior rim.<sup>12</sup> The coloboma is often a sharply demarcated, inferior bowl shaped excavation of the disc, 2-8 diopters in depth.<sup>12</sup> See Figure 1.

Embryologically, colobomas result from an incomplete closure of the fetal fissure at the 5<sup>th</sup> to 7<sup>th</sup> week of fetal life.<sup>1</sup> Failure of the fetal fissure to close can affect a variety of ocular structures including the cornea, iris, ciliary body, lens zonule, choroid, retina, optic disc, or optic nerve.<sup>1,2</sup> Typically, colobomas occur inferonasally; if the location is not inferonasal, it is termed "atypical."<sup>1,2,13</sup> Some suggest that atypical colobomas may result either from a rotation of the fissure, which fails to close in its new position, or a break in another area.<sup>1</sup>

Optic nerve colobomas have been associated with a variety of ocular findings, including: decreased visual acuity, visual field loss, nystagmus, retinal detachments, retinal pigment epithelial changes, persistent hyperplastic primary vitreous, microphthalmos, microcornea, iris or eyelid colobomas, macular hypoplasia, anterior segment abnormalities, corneal neovascularization, cataracts, strabismus and aphakia.<sup>1-8</sup>

Visual acuity in these patients is variable and can range from 20/30 to no light perception (NLP).<sup>8</sup> Berk found that visual acuity loss was related to the degree of ocular malformation and microphthalmia.<sup>3</sup> Olsen et al reported that out of four factors: coloboma size turbance, optic nerve color, extent of foveal involvement, and

degree of subfoveal retinal pigment epithelial disturbance, the only feature predictive of decreased visual acuity was the degree of foveal involvement.<sup>14</sup> However, it is important to note that there are reported cases when a coloboma of the optic nerve resulted in a decrease in visual acuity, in spite of the fact that the fovea was spared.<sup>3,7</sup>

In patients with optic nerve colobomas, decreased visual acuity may also be attributed to functional amblyopia, i.e., refractive or strabismic. Refractive conditions in eyes with optic nerve colobomas have ranged from -12.00 to +11.00 D with astigmatism ranging from zero to -7.00D.<sup>6,14</sup> There has also been an association with high myopia (>10D) and steep corneal curvature in the eye with less severe disc involvement.<sup>7</sup> One study reported 50% of patients with optic nerve colobomas also were strabismic; there was an equal distribution between esotropia and exotropia.<sup>3</sup>

Sixty six percent of patients with autosomal dominant optic nerve colobomas have nonrhegmatogenous retinal detachments, although the incidence varies with the type of optic nerve coloboma.<sup>15</sup> Patients may also have serous macular detachments, which may spontaneously reattach.<sup>16</sup>

### Multi system coloboma syndromes

Systemically, optic nerve colobomas have been associated with developmental delays, congenital forebrain anomalies, deafness, midline facial defects, agenesis of the corpus callosum, microcephaly, renal disease, cleft lip and palate, capillary hemangiomas, epilepsy, mental retardation, multi system syndromes and chromosomal anomalies.<sup>3,5,6,8</sup> For colobomas associated with systemic syndromes, inheritance can be autosomal dominant, autosomal recessive or X-linked recessive, although many syndromes have no determined inheritance pattern.<sup>13</sup>

The most common multi system syndrome involving coloboma is the CHARGE syndrome.<sup>17</sup> CHARGE is an acronym for: colobomatous microphthalmia, heart defects, choanal atresia, retarded growth and development, genital hypoplasia, and ear anomalies or hearing loss. At least four features are needed for a diagnosis.<sup>13,17</sup> Most patients will present with retinochoroidal colobomas with op-

tic nerve involvement.<sup>18</sup> CHARGE may be due to a genetic defect or insult during the second month of pregnancy.<sup>13</sup>

Another multi system syndrome involving coloboma is the renal-coloboma, also known as papillorenal syndrome. Patients with this syndrome have renal hypoplasia which leads to renal failure.<sup>19</sup> Parsa et al recommend not using the term "coloboma" in these patients, because "there is no evidence that the optic fissure fails to close."<sup>20</sup> Instead, they propose that the renal-coloboma syndrome is a vascular dysgenesis resulting in optic nerves with multiple cilioretinal vessels, anomalous central retinal vessels and choroidal circulatory anomalies.<sup>20</sup> A defect in the Pax2 gene has been associated with this condition.<sup>5,19,20</sup>

There are also a variety of chromosomal abnormalities, such as trisomy 13-15 (Patau's syndrome), trisomy 18 (Edward's syndrome) and trisomy or tetrasomy 22 (cat eye syndrome) that have been associated with optic disc coloboma.<sup>5,6,21</sup>

Environmental causes, specifically the use of thalidomide, LSD, anti-convulsants or alcohol during pregnancy, intrauterine vitamin A deficiency and perinatal infections have also been associated with ocular colobomas.<sup>13</sup>

### Treatment of optic nerve colobomas

Patients who present with an optic nerve coloboma require a thorough ocular and visual evaluation. Precise refraction is imperative since these patients may have an amblyogenic refractive error. If amblyopia is found, and if there is any question regarding foveal involvement, amblyopia therapy should be attempted, especially if an amblyogenic refractive error is present.<sup>14</sup> If multiple systemic malformations are present, family and genetic testing may be indicated to determine if there is a defect, that may be passed on to offspring.<sup>12</sup>

### Punctal atresia

Punctal atresia is an unusual condition, often associated with craniofacial anomalies, including: dysmorphism, oro-ocular-clefting syndrome, and ectrodactyly-ectodermal dysplasia-clefting (EEC).<sup>9,10</sup> Patients may be asymptomatic, or present with epiphora, conjunctivitis or dacryocystitis.<sup>9,10</sup> There have been reports that the absence of lacri-

mal puncta has been associated with a decrease or absence of salivary gland function.<sup>9,10</sup>

The nasolacrimal system and face develop at the same time. An early nasolacrimal apparatus develops from a thickening of a cord of surface ectoderm, located between the nose and the medial canthus, at around 5 to 6 weeks of gestation.<sup>22</sup> Between weeks 6 to 12 of gestation, the bud of ectoderm extends towards the inner canthus and nasal cavity. By 12 weeks of gestation, two distinct horizontal sections (canaliculi) along with a vertical lacrimal sac and duct are present.<sup>1</sup> At the same time, the core cells of the bud begin to degenerate and form a lumen, which completely opens between 6-7 months of gestation.<sup>1,22</sup>

A variety of developmental mechanisms can be responsible for anomalies of the nasolacrimal system. In some cases, the development of the channels themselves can be incomplete. In other cases, a part of the system may not form, creating an incomplete nasolacrimal system.<sup>1</sup> Agenesis of the canalicular system can result from a failure of cells to proliferate during weeks 6-12 of gestation, or from a failure of the cords to canalize.<sup>22</sup>

### Treatment of punctal atresia

Treatment is based on the patient's symptoms. For chronic conjunctivitis and discharge, treatment with topical antibiotics is preferred.<sup>10</sup> In symptomatic patients, a probing of the intact structure of the nasolacrimal system may also be indicated, and nasolacrimal intubation should be considered.<sup>10</sup> In children with atresia of both puncta who manifest with symptoms, a dacryocystorhinostomy (DCR) is indicated; however, this procedure should be delayed until the child is at least 10 years old.<sup>10</sup>

### CONCLUSION

This report presents a patient with anterior and posterior segment anomalies which have not previously been reported to be in association with each other. It is also noteworthy that these defects had not been diagnosed by previous health care professionals.

Given the prenatal history of this patient, it is possible that an insult around the fifth week of gestation could have affected the closure of the fetal fissure, and early formation, or opening, of the nasolacrimal system. However, since the optic nerve

and lacrimal system develop from different embryonic origins, neuroectoderm and surface ectoderm respectively, it is not possible to develop a mechanism for this patient's anomalies. Additionally, the lacrimal system develops over a longer time period, and later in gestation, than does the optic nerve. This could suggest that two different insults occurred in this patient, further indicating that the two conditions are not related. Furthermore, we do not know the extent of the patient's lacrimal system dysfunction; i.e. does he have an inferior canaliculus or only a punctal anomaly?

Based on a review of the literature regarding both ocular conditions, it is also possible that this patient may have an underlying systemic condition and/or mental retardation. The patient will continue to be monitored for changes, at which time, further testing may be warranted. At a future visit, retinal tomographic imaging will be conducted to further assess the extent of the coloboma and any associated retinal defect. Visual acuities will also continue to be monitored for changes, and laser interferometry will be attempted to determine the potential acuity.

Based on the magnitude of the esotropia, surgical correction is an option, but in this case, surgical correction would be primarily for cosmetic and not functional reasons. Ideally, the patient would benefit from surgical correction and active vision therapy, if the vision could be improved. However, because we are unsure of the magnitude of potential visual acuity improvement, and because of this patient's variable attention during testing, he is a poor therapy candidate. Consequently, we did not recommend surgical intervention.

### Acknowledgements

Sherry Bass, O.D., provided the photo in Figure 1 and Harry Wyatt, Ph.D., provided expertise in anatomy.

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Date accepted for publication:  
December 16, 2005