Congenital Anomalies of the Optic Nerve in One Family

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We present three cases of congenital optic disc anomalies in one family who underwent an extensive diagnostic workup to exclude any intracranial pathology. One patient had elevated optic nerve heads and was hospitalized for multiple diagnostic tests including a lumbar puncture and magnetic resonance imaging scan. This patient had a sister with a previous history of having undergone head and orbital computed tomography to evaluate her symptoms of headaches with anomalous optic nerve heads. The third patient was the father of the other two patients who had previously undergone an extensive evaluation for elevated optic nerve heads and was treated for presumed pseudotumor cerebri with fenestration of the optic nerve sheath. These cases underscore the importance of a detailed family history and examination of family members to exclude congenital abnormalities of the optic nerve head before beginning an extensive workup.

Optic nerve head elevation is often alarming and requires the physician to make a critical distinction whether the disc abnormality is (1) congenital and static or (2) acquired and progressive. The differential diagnosis of an elevated optic nerve head includes increased cerebrospinal fluid pressure (caused by space-occupying intracranial lesions), or abnormalities of the optic nerve, including tumors, pseudotumor cerebri, and other inflammatory or ischemic entities. In addition, the optic disc is the site of various congenital anomalies that may cause optic nerve head elevation and mimic disc edema.[1,2] Congenital anomalies of the optic nerve often are transmitted as an autosomal dominant trait. Therefore, a detailed family history is crucial to the accurate evaluation of these patients, and a careful examination of other family members may help establish the diagnosis and eliminate the need for an extensive workup. We present three cases of congenital disc anomalies in one family who underwent extensive diagnostic procedures to exclude papilledema.

Report of Cases

Case 1

A 21-year-old woman was seen in July 1988 complaining of floaters and blurred vision OS. The patient denied any history of ophthalmic diseases, but her medical history was remarkable for left-sided temporal headaches for ap-

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proximately one year that had been previously diagnosed by her dentist as temporomandibular joint dysfunction. Visual acuities were 20/20 OD and 20/25 OS with no correction and no improvement after pinhole occlusion. Her pupils were symmetric, and no relative afferent pupillary defect was detected. Color vision, motility, and confrontational fields were normal. Amsler grid testing was normal OD, but there was a temporal defect OS. Anterior segment examination was unremarkable. Funduscopic examination showed elevated optic discs (greater OS) with some buried vessels (Figure 1). Spontaneous venous pulsations were absent bilaterally, and no hemorrhages were seen. In addition, a Bergmeister's papilla with epipapillary glial tissue was greater OS. B-mode ultrasonography confirmed elevation of the optic nerve heads but found no evidence of optic disc drusen or excess fluid around the nerve. Additional workup included formal automated visual fields; these showed a diffuse field loss OS that was denser superiorly and temporally but did not respect vertical or horizontal midlines. There were several scattered points of decreased sensitivity OD. Flicker-fusion testing was normal OD and decreased OS, as was contrast sensitivity. Fluorescein angiography showed no sign of optic nerve autofluorescence or leakage.

The patient was admitted for evaluation of her elevated optic nerve heads. The results of head and orbital magnetic resonance imaging scans were unremarkable, revealing no sign of ventricular dilation or mass lesions. A lumbar puncture found an opening pressure of 110mmHg. Cerebrospinal fluid analysis was normal, as were blood chemistries and hematologic and serologic studies. Neurologic examination revealed no focal abnormalities.

After additional questioning regarding the patient's family history, it was discovered that both the patient's sister and father had been diagnosed with "abnormal" optic discs. It was believed that the patient had congenital elevated anomalous discs, and she was discharged from the hospital in stable condition. The most recent follow-up examination (November 1991) showed no change in the patient's condition.

Case 2

This 18-year-old woman, the sister of the patient described in Case 1, was seen initially as a 5-year-old child. Examination at that time revealed visual acuities of 20/30 OD and 20/80 OS. Cycloplegic retinoscopy was −1.25 sphere OD and −6.25 sphere OS. She was diagnosed as having anisometropic amblyopia OS and had been treated in the past by patching OD. She also had anomalous optic discs OU with a large area of peripapillary atrophy and small epipapillary gliotic changes of the optic disc. The overall configuration of the optic nerve heads was consistent with a mild morning-glory configuration (Figure 2). The patient was followed at regular yearly intervals with no change in corrected visual acuity. During that time, however, she had progressive myopic changes in her fundus. She was seen

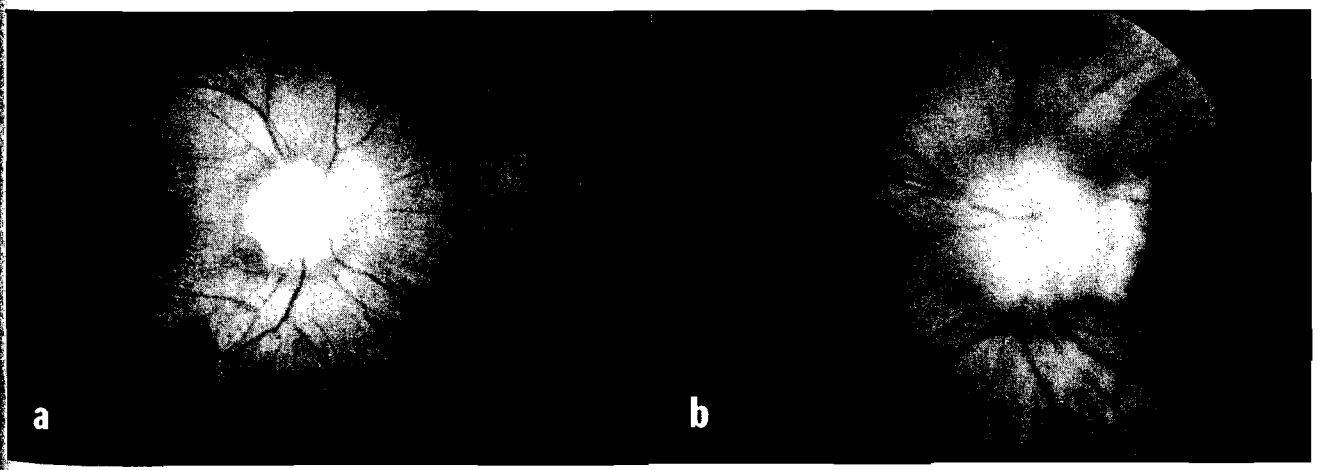

Figure 1. *Case 1.* Optic nerve photographs showing disc elevation and blurring of the disc margins, greater on the left than on the right. In addition, there is a Bergmeister's papilla with some epipapillary glial tissue which is also greater on the left (a, OD; b, OS).

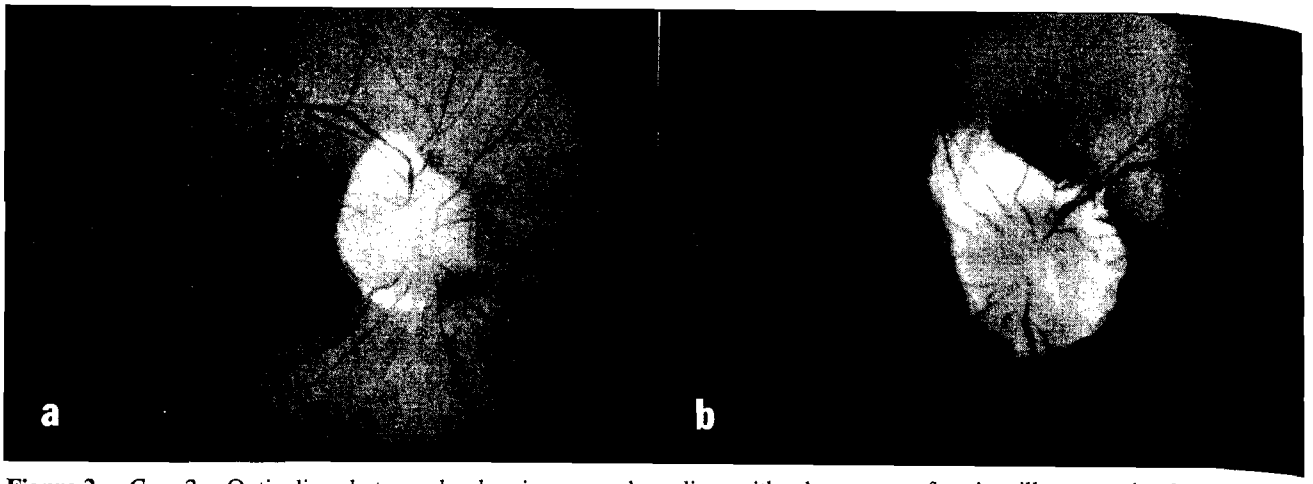

Figure 2. *Case 2.* Optic disc photographs showing anomalous discs with a large area of peripapillary atrophy OU and a small amount of central epipapillary gliotic tissue (a, OD; b, OS).

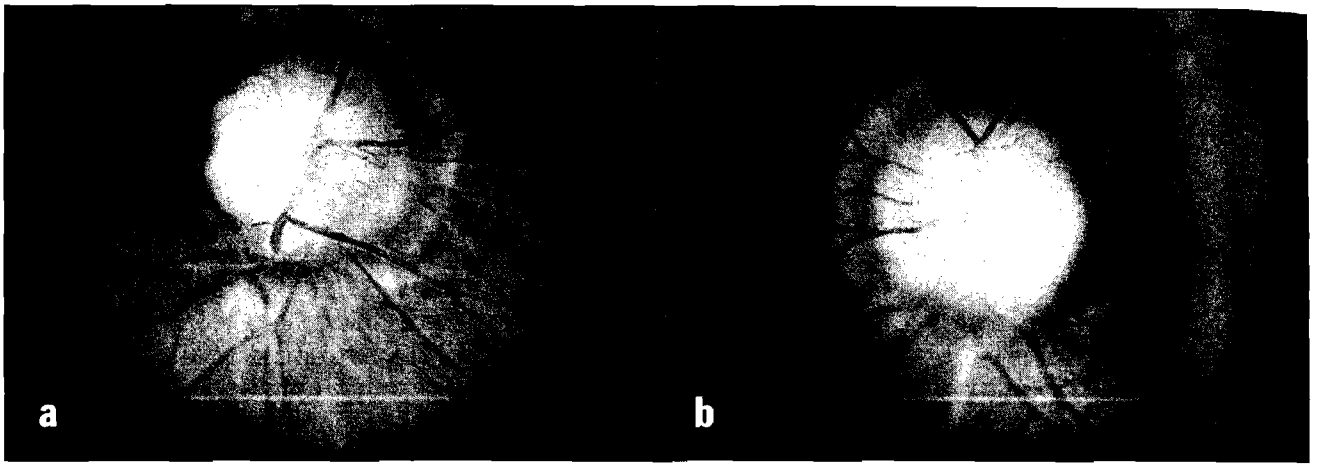

Figure 3. *Case 3.* Photographs taken in 1975 showing a marked elevation of the discs OU with blurring of the disc margins. In addition, there is a small amount of central epipapillary gliotic tissue in OU (a, OD; b, OS).

again in 1986, complaining of a paracentral scotoma OS. Her visual acuities were 20/30 OD and counts fingers OS. Her refractive error was $-7.25 + 3.50 \times 105°$ OD and $-11.50 + 3.50 \times 60°$ OS. Amsler grid testing found a dense central scotoma OS with a relative afferent pupillary defect. The anterior segment OS was essentially normal, but funduscopic examination revealed a serous macular detachment and subretinal neovascular membrane with a Fuchs' spot. Using fluorescein angiography, a neovascular membrane was seen nasal to the fovea that spared the central fovea. Focal laser treatment was done successfully; however, her visual acuity did not improve.

She was seen again several months later, complaining of additional headaches, which had been present for several weeks. Visual-field testing and head and orbital computed tomography showed no intracranial pathology. Her most recent examination (September 1989) revealed no change in her condition.

Case 3

This man was the father of the patients presented in Cases 1 and 2. He was seen initially early in 1975 at the age of 31 years, complaining of severe headaches. He had elevated optic nerve heads bilaterally and underwent an extensive neurologic workup to assess the cause of his "papilledema," including a bilateral carotid angiogram, pneumoencephalography, isotope brain scan, and an electroencephalo-

ram, all of which were unremarkable. A lumr puncture was reported as "normal" (no her details were given) with an unremarkable erebrospinal fluid examination.

The patient was seen again one month later, which time he had visual acuities of 20/20 U with a slight myopic and astigmatic correcon. Goldmann visual fields showed a mild nlargement of the blind spot OU. Anterior gment and external ocular examinations ere unremarkable. Dilated fundus examinaion revealed extremely elevated discs bilaterlly (Figure 3). A fluorescein angiogram at this ime identified a "solid elevation" of both optic discs with disc hyperfluorescence after luorescein injection. It was believed that he had bilateral chronic disc edema secondary to seudotumor cerebri. When the edema did not improve, the patient was treated with oral corticosteroids tapered over several months. The patient's vision remained normal at this time, but there was no improvement in the disc edema.

The patient was seen 30 days later, and his visual acuities were still 20/20 OU with no change in refraction. Goldmann visual fields were unchanged from early 1975. The patient had persistent optic nerve elevation bilaterally and was admitted to the hospital for an additional workup. Bilateral internal carotid angiograms were again normal. Computed tomography found normal intracranial structures with a possible slight enlargement of the optic nerve OS. Lumbar puncture revealed an opening pressure of 190mmHg. Cerebrospinal fluid analysis was unremarkable.

The patient underwent an optic nerve sheath fenestration procedure OS, which released a moderate amount of subarachnoid fluid. The procedure was tolerated well; however, postoperatively, the elevation in his optic nerves did not change. When last seen (July 1977), he had visual acuities of 20/20 OU, with virtually no change in the appearance of his optic nerves (Figure 4). The patient was killed in a motor vehicle accident sometime after this last examination.

Discussion

A sequence of complex embryologic events allow the optic nerve to be the site of many congenital ocular abnormalities.[1-4] The ability to recognize these, and to differentiate the benign entities from the more visually significant ones, is invaluable to the clinician. An understanding of ocular embryology and anatomy is essential in reviewing the categorization, pathogenesis, and ophthalmologic effects of different anomalies. Ocular colobomas, for example, are common malformations that can appear as a notch or fissure in any ocular structure. At about six weeks' gestation, the embryonic fissure begins to close, beginning at the midpoint of the fissure, proceeding in both directions, and ending at the peripapillary tissue and iris.[2] This explains the typical location of the colobomatous lesions. Optic nerve head colobomas tend to be associated with an inferior crescent and, sometimes, a staphyloma in the region of the defect. If the macula is not involved and no other developmental anomalies exist, visual defects may be limited to a scotoma at the site of the defect. An autosomal

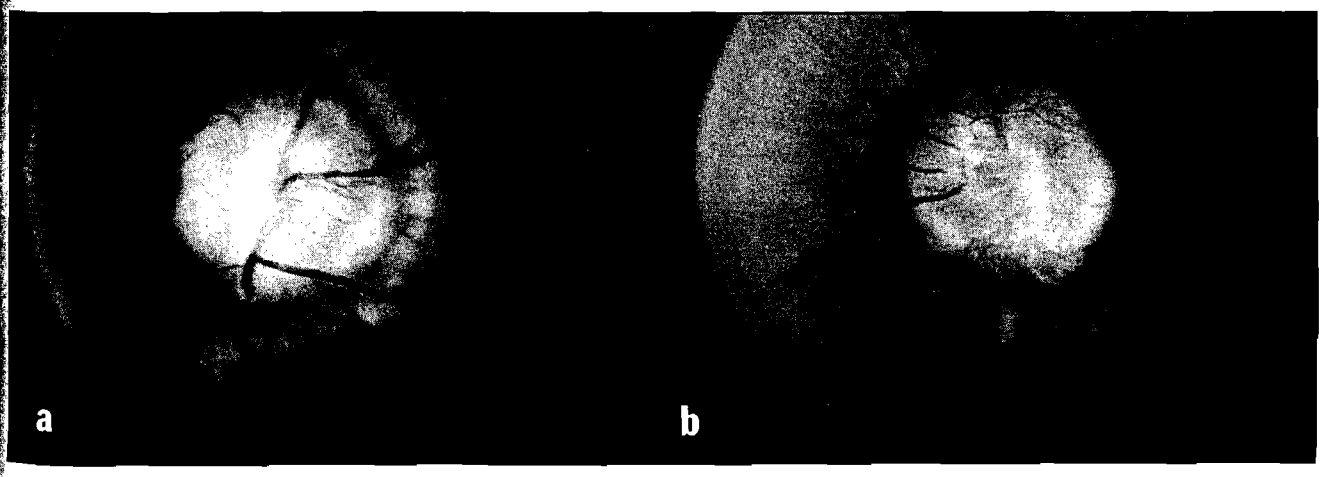

Figure 4. *Case 3.* Disc photographs after optic nerve sheath fenestration OS showing virtually no change 2 years after the photographs shown in Figure 3 (a, OD; b, OS).

dominant pattern is the most common mode of inheritance for ocular colobomas.[3]

Several anomalies may cause an elevation of the optic disc, imitating papilledema or optic disc edema. The term often used for these elevated disc anomalies is pseudopapilledema.[5] In moderate to severe hyperopia, papilledema may be suspected in an elevated disc with indistinct margins. This is seen most commonly in children and young adults. A severely hyperopic disc may be differentiated from true papilledema by a visible physiologic cup and the lack of hemorrhages, venous congestion, or leakage of dye during fluorescein angiography. The elevation of the disc in hyperopia may be caused by a narrowed scleral canal or hyperplasia of glial tissue.[2] None of our patients were hyperopic.

Another entity that may cause an elevated disc anomaly simulating papilledema is buried optic nerve head drusen.[6,7] Drusen consist of cellular deposits of hyalin-like material, which often become calcified. The optic nerve head is elevated and irregular; however, buried drusen usually are not associated with capillary dilation on the disc or exudates. Drusen occasionally may be associated with disc hemorrhages. The cause of drusen is unclear, although aberrant axoplasmic transport has been implicated.[8] Buried drusen can be diagnosed easily using ultrasonography. In addition, drusen may show autofluorescence before fluorescein angiography. Our patients had no evidence of buried drusen by examination or ultrasonography.

Disc elevation can be secondary to persistent epipapillary fibrous glial tissue or Bergmeister's papilla.[9-11] Persistent hyperplastic primary vitreous may be manifested by failure of the glial sheath of Bergmeister, which envelops the posterior portion of the embryonic hyaloid system, to involute completely posteriorly. This may lead to retention of fibrous and glial tissue, forming a mound of tissue on the optic nerve head or an epipapillary membrane. This epipapillary glial tissue can cause elevation of the optic disc, simulating papilledema as seen in Patients 1 and 3.

A more visually limiting optic nerve head coloboma was termed descriptively the morning-glory syndrome.[12-15] On examination, there is a funnel-shaped staphyloma surrounding the posteriorly displaced and distorted disc with tufts of white glial tissue. Encompassing this excavation is an annulus of chorioretinal pigment disturbance. The retinal vessels are atypical and emerge and enter over the edge of the funnel in a radial pattern. An mentioned previously, visual loss is often severe. Retinal detachment is the most common complication. The full-blown syndrome tends to be unilateral, although there is an increased incidence of other associated abnormalities in the fellow eye. Patient 2 had an optic nerve configuration similar to a partial morning-glory syndrome, in addition to progressive myopic retinal changes.

Certain ophthalmoscopic features help distinguish congenital from acquired disc elevation. Peripapillary hemorrhages, vascular congestion, opacification of the peripapillary nerve fiber layer, absence of the optic cup, and lack of spontaneous venous pulsations are signs classically associated with an acquired elevation. Ultrasonography is helpful in imaging drusen and edematous optic nerves. When the clinical and ultrasonic examination does not identify the congenital or acquired nature of the abnormal optic nerve head clearly, an extensive neurologic evaluation is recommended. In 1962, a series of 28 patients were reported who had pseudopapilledema and had undergone various diagnostic testings for brain tumors.[5] Fourteen of these had undergone one to three lumbar punctures. Interestingly, the opening pressure was elevated in three patients, none of which had an intracranial lesion. Four patients underwent carotid arteriography, five patients underwent pneumoencephalography, and four patients underwent placement of burr holes and ventriculography. With the availability of computed tomography and magnetic resonance imaging, the diagnostic workup for intracranial disease has become less invasive. A lumbar puncture with attention to the opening pressure and cerebrospinal fluid chemical analysis may be helpful in differentiating papilledema from other causes of disc swelling.

We presented the cases of three patients from the same family who underwent multiple diagnostic procedures to evaluate optic nerve anomalies that were found to be congenital in origin. In cases of suspected congenital optic nerve head abnormalities, a detailed examination of family members is advised before launching an extensive workup to exclude intracranial pathology. In patients who are asymptomatic or have symptoms that do not suggest intracranial pathology, similar ocular findings in a family member increase the possi-

lity of a congenital anomaly. In these cases, areful follow-up by the physician is an appropriate course of action.

References

1. Brown GC, Tasman WS: *Congenital Anomalies of the Optic Disc*. New York, Grune and Stratton, 1983.
2. Apple DJ, Rabb MF, Walsh PM: Congenital anomalies of the optic disc. *Surv Ophthalmol* 1982;27:3–41.
3. Pagon RA: Ocular coloboma. *Surv Ophthalmol* 1981;25:223–236.
4. Magli A, Greco MC, Alfieri MC, et al: Hereditary colobomatous anomalies of the optic nerve head. *Ophthalmic Paediat Genet* 1986;7:127–130.
5. Hoyt WF, Pont ME: Pseudopapilledema: Anomalous elevation of optic disk: Pitfalls in diagnosis and management. *JAMA* 1962;181:191–196.
6. Friedman AH, Beckerman B, Gold DH, et al: Drusen of the optic disc. *Surv Ophthalmol* 1977;21:375–390.
7. Kamin DF, Hepler RS, Foos RY: Optic nerve drusen. *Arch Ophthalmol* 1973;89:359–362.
8. Spencer WH: Drusen of the disc and aberrant axoplasmic transport. *Ophthalmology* 1978;85:21–38.
9. Apple DJ, Hamming NA, Gieser DK: Differential diagnosis of leukocoria, in Peyman GA, Apple DJ, Sanders DR (eds): *Intraocular Tumors*. New York, Appleton-Century-Crofts, 1977; 235–283.
10. Apple DJ, Rabb MF: *Ocular Pathology: Clinical Applications and Self-Assessment*. St. Louis, CV Mosby, 1985; 323–336.
11. Joseph N, Ivry M, Oliver M: Persistent hyperplastic primary vitreous at the optic nerve head. *Am J Ophthalmol* 1972;73:580–583.
12. Kinder P: Morning-glory syndrome: Unusual congenital optic disk anomaly. *Am J Ophthalmol* 1970;69:376–384.
13. Skeinkuller PG: The morning glory disk anomaly: Case report and literature review. *J Pediatr Ophthalmol Strabismus* 1980;17:81–82.
14. Traboulsi EI, O'Neill JF: The spectrum in the morphology of the so-called "morning-glory disk anomaly." *J Pediatr Ophthalmol Strabismus* 1988;25:93–98.
15. Apple DJ: New aspects of colobomas and optic nerve anomalies. *Int Ophthalmol Clin* 1984;24:109–121.