ELSEVIER

MORNING GLORY SYNDROME
MR IMAGING

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We present two cases of the Morning Glory Syndrome (MGS), with the most detailed MR images to date of this rare congenital optic nerve dysplasia. Though the embryology of this syndrome remains controversial, we feel the MR appearance can be diagnostic of the non-familial syndrome and be reliably distinguished from the similar appearing optic disc coloboma, which may be genetically inherited. MR imaging also allows the most sensitive detection and characterization of any associated intracranial anomalies, thus enabling more accurate determination of prognosis for the patient and their family.

KEY WORDS:
Magnetic resonance imaging; Morning Glory Syndrome; Optic nerve; Congenital dysplasia

INTRODUCTION

Morning Glory Syndrome is a term that has been used broadly in the medical literature to describe many variations of atypical dysplastic optic discs (1). Though first described in the German literature by Reis in 1908 (2), it was not until Kindler in 1970 (3) that this entity was clinically defined and the remarkable resemblance to the flower of the same name established. Though gradations between the more common optic disc coloboma and MGS warrant consideration for variations of a single condition (4), most authors now consider them as two separate entities (5) and importantly, this has genetic significance for the patient and their family. We present MR findings in two patients with MGS and suggest that the appearance at detailed MR examination can be used to distinguish reliably between optic disc coloboma and MGS.

CASE REPORTS

Case 1

An 8-month-old white female was brought to the ophthalmology clinic by her mother with report of a "wandering eye" since birth. She was the product of a non-consanguineous union with a normal pregnancy and delivery. The mother was primiparous and drank 1–2 beers per day and smoked cigarettes for the first two months of the pregnancy. An amniocentesis had been performed for a positive triple screen, revealing a 46 XX karyotype. There were no other known medical or congenital abnormalities and the child had met all developmental milestones to date, though speech was slightly behind for age.

Physical exam disclosed an alert, awake and happy baby girl. No facial clefting was present, nor hyper- or hypotelorism. The visual acuity was normal OS while she would not fix or follow OD. Unilateral searching nystagmus was noted OD. The pupils were equal, round, and reactive to light. No afferent pupillary defect was detected. Ductions and versions were normal OU. The external and anterior segment examinations were normal, though the corneal diameter horizontally was 10 mm OD and 11 mm OS. Cycloplegic refraction revealed a mild myopia with -1.50 sphere OD and $+1.00 + 0.75 \times 90$ OS. The fundus examination showed a large (3 disc diameters) disc OD with overlying grey gliotic membrane and peripapillary pigmentary changes. The blood vessels arose from the periphery of the disc and ap-

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peared straightened. The fundus and disc were normal OS.

EEG, renal ultrasound, and audiometric testing revealed no abnormality. An MRI was obtained (Figures 1A–H) and revealed findings typical for MGS with an enlarged, funnel-shaped optic disc with overlying fluffy, high T1-signal intensity material noted on the axial and sagittal images within the slightly microphthalmic right eye. Also noted was a small right optic nerve and asymmetry of the optic chiasm and optic tracts, with diminution on the left compared to the normal appearing right-sided structures. The myelination pattern of the nerves and tracts was nonetheless preserved, as visualized on the SPGR high-resolution images.

Case 2

A 4-year-old white female was seen by ophthalmology for a right esotropia present since birth. She was the first child of a non-consanguineous union and the product of a normal pregnancy and delivery. There were no other medical or congenital problems. She had mild development delays and was enrolled in a Head Start program.

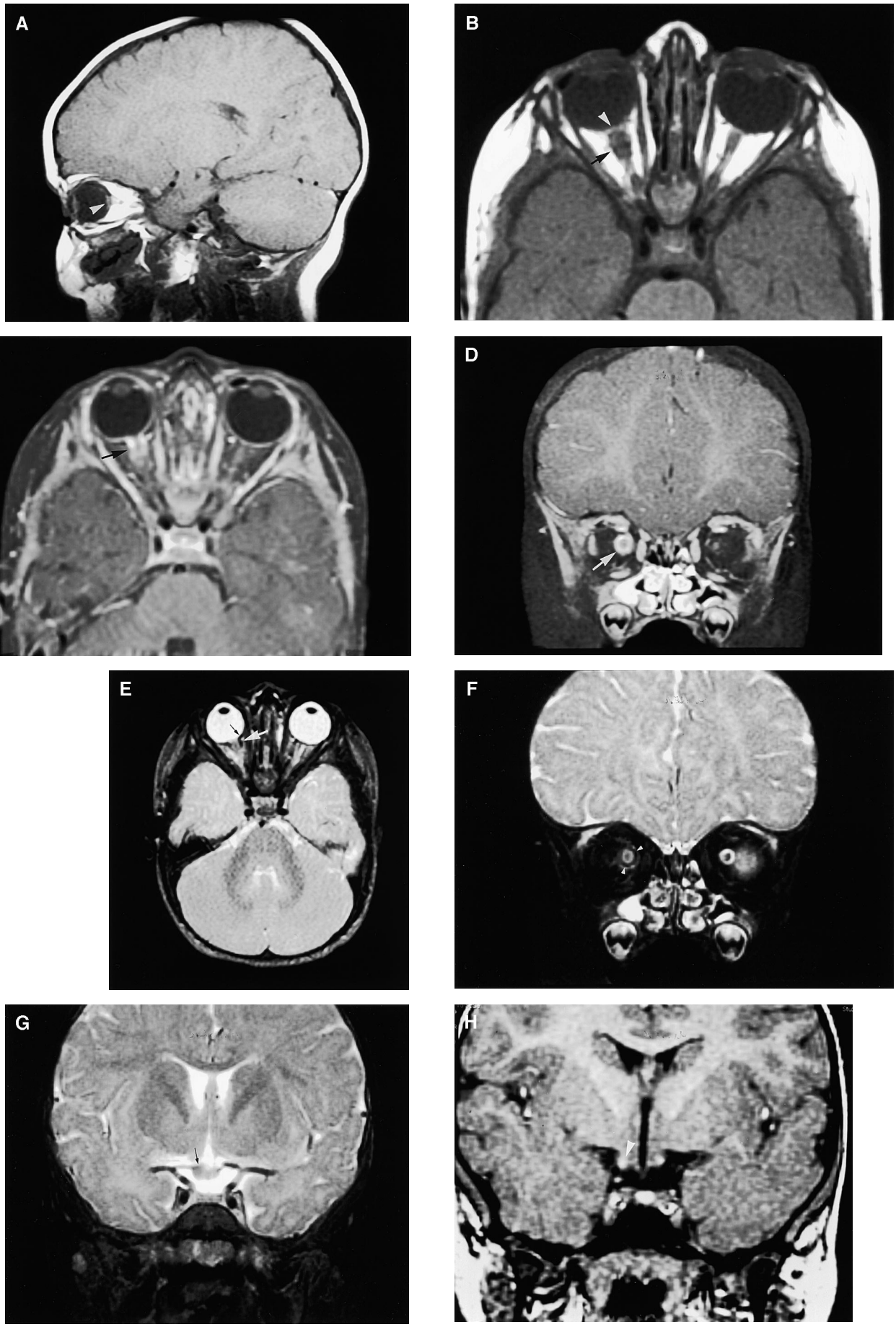
The visual acuity was light perception OD, and 20/20 OS. The pupils were equal, round and reactive with a mild afferent pupillary defect noted OD. A 40-prism diopter right esotropia was present. Ductions and versions were normal OU. The external and anterior segment examinations were normal except for corneal diameters horizontally of 10 mm OD and 11 mm OS. Cycloplegic refraction revealed myopia of −7.00 sphere OD and mild hyperopia of +1.00 sphere OS. Fundoscopy showed an enlarged (three disc diameters) and excavated disc OD with a central gliotic tuft and peripapillary retinal pigment changes (Figure 2A). The macula was incorporated into the excavation. The retinal vessels emerged from the nerve in a straightened, radial fashion. The remaining retinal examination was normal as was the disc and retina OS. A MRI was obtained (Figures 2B and 2C) and disclosed findings similar to those described with our first patient. However, a small focus of fat was noted within the small right optic nerve.

DISCUSSION

Morning Glory Syndrome has also been referred to in the literature as Morning Glory Disc Anomaly, optic nerve coloboma, axial coloboma, congenital optic pit, megalopapilla, and peripapillary scleral staphyloma with posterior ectasia of the papilla (6). Coloboma (from the Greek koloboun, to mutilate) was first described by Walther in 1821 and is defined as an absence or defect of some ocular tissue. This may be complete (when all ocular tissues are involved, i.e., optic nerve, retina, choroid, iris, and lens) or incomplete (7). Classically, three types of optic nerve colobomas have been described: isolated optic nerve, retinochoroidal, and Fuch's. Retinochoroidal coloboma presents a well-defined lesion in the inferior fundus, which may involve the optic disc or be inferior to the disc. Microphthalmos with cyst is considered the primary example of this anomaly. Fuch's coloboma has an inferonasally tilted optic disc in conjunction with an inferonasal crescent along the disc border in the direction of the tilt (8). The optic nerve coloboma has a discrete, focal, white bowl-shaped excavation which is decentered inferiorly within an enlarged optic disc, and minimal if any pigmentary disturbance surrounding the disc (5).

Many authors have considered MGS a variant of optic nerve coloboma (8). Others have suggested placing MGS within the spectrum of disc anomalies from optic nerve coloboma to elevated posterior persistent hyperplastic primary vitreous (9). However, consistent with Kindler's concept (3), present opinion favor MGS as a separate entity from the colobomas and stresses the importance of this distinction in that optic nerve coloboma is often a familial condition and associated with congenital multisystem anomalies while MGS is rarely familial and is never associated with congenital malformation syndromes (2, 5, 8). With more than 70 cases of MGS reported to date in the world literature, some of which are likely more in the spectrum of true colobomas, the reported associations are nonetheless numerous and include agenesis of the corpus callosum (10, 11), porencephaly (11), brain atrophy, and psychomotor retardation (11), progressive hypopituitarism (12), CHARGE syndrome (2), cyst of the optic nerve sheath (8), optic nerve atrophy (10), congenital cataract, persistent hyperplastidc primary vitreous and hemangioma of the ipsilateral eyelid (3), microphthalmos, pupillary membrane remnants, and aniridia (1). Also reported are contralateral congenital ocular anomalies such as coloboma, microphthalmos, anterior chamber cleavage syndrome, microcornea, pupillary membrane remnants and Duane syndrome (1, 13), hypertelorism (10), cleft lip and palate, basal encephalocele (9, 10), dysplastic ears, facial palsy (8), hydronephrosis (12), renal hypoplasia, chronic glomerulonephritis (9), and cardiac defects (8).

Embryologically, the optic pits appear as two indentations, one on each side of the neural groove, by the 3rd week of gestation. They then deepen to form the optic vesicles, the distal part of which expands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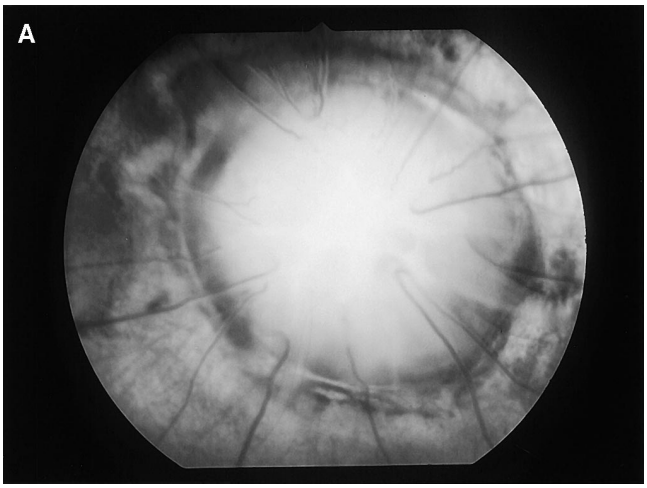
while the proximal part becomes the tubular optic stalk. Two types of invagination subsequently occur (7). The outer layer invaginates onto the inner layer at 4 weeks to form the optic cup. The sensory retina forms from the former outer wall of the vesicle, while the outer wall of the cup becomes the retinal pigment epithelium (8). A concomitant inferonasal invagination occurs along the optic stalk and cup which is the fetal cleft. The inner (sensory retina) lags behind the outer (pigment epithelium) layer and there is thus a normal slight protrusion of the inner layer through the fetal cleft while it is still open (7). The mesenchyme carrying the hyaloid artery extends into the optic stalk and cup via this cleft (8). The fissure then closes during the 5th week. The primitive epithelial papilla where the optic nerve head will develop can be identified at this time (8). Isolated optic nerve head colobomas arise from failure of closure of only the most superior end of the fetal cleft. Failure to close other parts of the cleft cause iridic, lenticular, and retinochoroidal colobomas (8). During the 7th week of gestation axons of the retinal ganglion cells start to form the optic nerve which is complete by 27 weeks (8). The optic nerve hypoplasia of MGS is believed etiologically due to either retrograde axonal degeneration from intracranial lesions or to an antegrade process from ganglion cell deficit within the developing retina (4). Our cases lend credence to the latter mechanism, as our patients had no intracranial abnormalities. The sclera begins forming at the end of the 2nd month in an anterior-to-posterior manner and is complete at the 5th month (3). The choroid is formed by the surrounding mesoderm, with the pigment epithelium exerting an essential influence on its development. This process is complete by the 7th month.

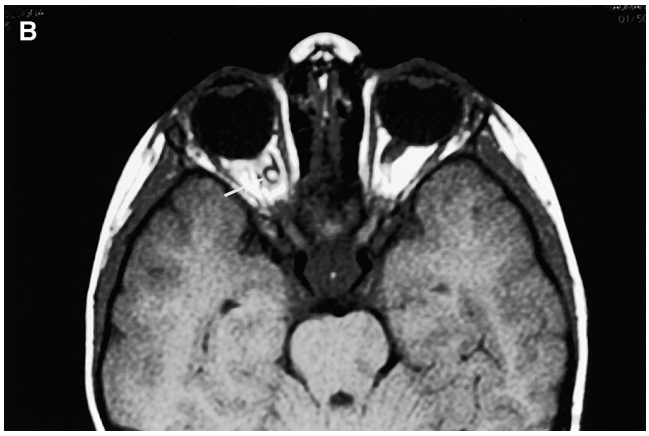
The etiology of MGS is disputed (1, 12). It may be that a simple optic nerve dysplasia is the etiology of MGS, while more extensive posterior segment colobomas, with or without optic disc involvement, are due to abnormalities of fetal fissure (cleft) closure (4). A combined defect of ectodermal and mesodermal dysgenesis has been proposed as distinguishing MGS from the typical coloboma (1, 3, 9). Goldhammer (10) however, suggested the two optic nerve anomalies represented respective ends of a wide spectrum.

Kindler (3) claimed that the tissue lying within the optic cup in patients with MGS is related to remnants of the hyaloid system. In support of this are several reports in the literature of MGS patients with persistent hyaloid elements (13). There are also reports of basal encephalocele in MGS patients, believed to result from a failure of induction of formation/migration of the neural crest ectomesenchyme of the midline craniofacial structures secondary to a failure of fetal cleft closure (2, 10). This may also be implicated in the faulty closure of the posterior scleral wall with retinal and neural tissue extending into the funnel-shaped dysplastic optic disc (1). Optic nerve coloboma has been reported in an infant of a mother treated with Thalidomide (7), though no definite teratogenic link has been established in any case of MGS. Dysplasia of the corpus callosum has also been reported in MGS patients and may again be an induction failure as this structure develops from the 7th to the 20th weeks of gestation (10).

Three distinguishing ophthalmoscopic features are required for the diagnosis of MGS: an enlarged optic disc with a funnel-shaped scleral defect; an elevated peripapillary tissue annulus referred to as chorioretinal pigmentary disturbance and considered by some the most characteristic single anomaly (14); and pale, whitish, fluffy tissue of glial hyperplasia overlying the optic disc. Additional characteristic features in-

FIGURE 1. An 8-month-old girl noted to have a "wandering right eye" since birth. **(A)** T1-weighted (616/16/1) sagittal 4 mm MR image through the right globe shows a fluffy tissue tuft isointense with white matter and located at the optic nerve head papilla (*arrow*). This is consistent with either the glial hyperplasia or the elevated peripapillary annular tissue seen with MGS. **(B–D)** T1-weighted (600/16/2) pre- **(B)** and post- **(C)** contrast axial 4 mm images through the optic nerve are shown with a post-contrast coronal fat-saturated 4 mm image **(D)** through the optic nerve head and demonstrate mild microphthalmia and an abnormally enlarged proximal right optic nerve (*arrows*) with marked peripheral enhancement. The optic papilla is again subtly thickened and irregular **(B,** *arrows***)**. **(E** and **F)** T2-weighted (2500/80/0.75) 4 mm axial image **(E)** of the optic nerve head shows an abnormally enlarged optic disk with marked hypointense signal of the thickened proximal optic nerve sheath (*arrows*) which is similar in thickness and signal to the adjacent sclera (*tiny black arrow*), consistent with the colobomatous choroidoscleral ballooning of MGS. Coronal 4 mm fast spin-echo (3500/95/2/8) fat-saturated image **(F)** through this enlargement demonstrates a target appearance to the complex with the outer hypointense choroidoscleral balloon (*white arrowheads*) and the central optic nerve, surrounded by hyperintense CSF within the optic nerve sheath. **(G** and **H)** Coronal FSE (3500/95/2/8) fat-saturated 4 mm **(G)** at the optic chiasm shows an asymmetric diminution on the left which is otherwise isointense in signal compared to the normal appearing right (*tiny black arrow*) chiasm. This diminution extends posteriorly from the enlarged optic nerve head on the right through the right optic nerve, to the left chiasm and left optic tract **(H)**. The coronal 1.5 mm spoiled gradient recalled (SPGR) (43/13/35) image **(H)** demonstrates identical, normal hyperintense central myelin signal (*white arrowhead*) within each optic tract. This suggests that the diminutive nerve caliber is secondary to a reduction in axon number, not structure.





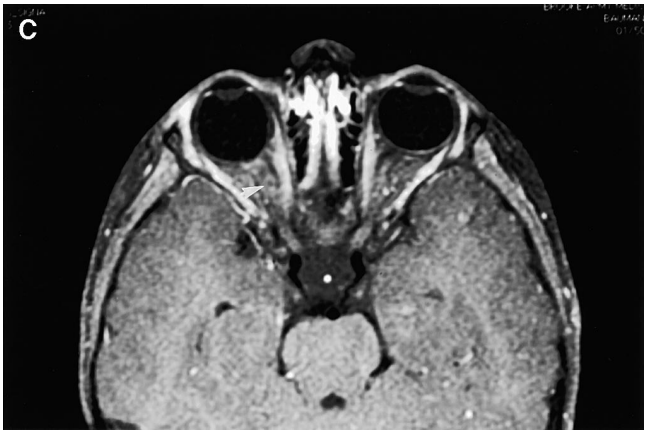


FIGURE 2. A 4-year-old girl with a right esotropia since birth. **(A)** Photograph of the right optic disc demonstrating the characteristic appearance reminiscent of the bloom of the *Ipomoea sp* from which the MGS appellation is borrowed. **(B** and **C)** T1-weighted (600/15/2) pre- **(B)** and post **(C)** contrast axial 3 mm images through the optic nerve. A small hyperintense signal focus is present **(B**, *white arrow***)**, situated centrally within the right optic nerve on multiplanar images (not shown). This focus produces a nonenhancing signal void on the fat-saturated post-contrast image (*white arrowhead*), consistent with fat within the nerve.

clude radially arranged strait and narrow retinal vessels, the origins of which may be obscured by the central tissue tuft overlying the optic disc (1, 12). Heterotopic elements, including myofibroblasts and adipose tissue, have been described and may alter the appearance of the disc at fundoscopy (1, 7). Our second patient had fat within the optic nerve (not the disc) and is the first reported MGS patient imaged with this anomaly (Figures 2B and 2C).

Patients with MGS present at an early age with poor vision and/or strabismus. A frequent myopic refractive error is noted. Though patient's visual acuity is often disturbed, only rarely is blindness noted (8, 12, 13). In addition, no definite correlation has been found between fundus morphology and visual acuity (1). Leukocoria may be elicited with congenital cataract. Non-rhegmatogenous retinal detachments are seen in 25–38% of eyes with MGS (4, 14) and 25% of these cases progressed to blindness. Retinal detachment is usually of the serous variety. This suggests that CSF may accumulate under the retina through a communication between the optic nerve sheath and the subretinal space in the malformed papilla (1).

Beyer et al. (9) reported on ten eyes with MGS in 8 patients with an average age of 13.5 years. He described one father-son pair with bilateral disease. The visual acuity ranged from 20/30 to 20/400. An afferent pupillary defect was present in all patients with unilateral disease. Goldmann perimetry most commonly demonstrated a central scotoma. Clinically, an enlarged optic nerve disc was seen in 8 eyes (9). Elevated hyperplastic glial tissue overlying the disc was noted in all eyes and was pronounced in 4, while peripapillary pigment changes were also seen in all eyes, with macular capture in four. Interestingly, the papilla was enlarged in only 8 eyes. Bilateral disease has been reported in several cases (1, 9, 10, 15) but is apparently rare (3), with an overall symmetric visual acuity which is slightly better than reported in unilateral involvement, and without an increase in associated non-ocular anomalies.

In children, the M:F ratio of MGS is 1:2 and the condition is described more often OD (60%) (2). It is rare in Blacks (4). The incidence of optic nerve coloboma in the general population is less than 0.1%. It is inherited as an AD trait, with a variable penetrance

(30% overall) and expression. It has a bilateral incidence of 60%, and is found equally in males and females (7). In distinction, all reported cases of MGS to date have been sporadic (10). However, this does not exclude an autosomal recessive cause. Also, with no reports of reproduction by these patients, a dominant mutation is also possible.

The diagnosis of MGS is usually made clinically. However, cross-sectional imaging enables confirmation of the diagnosis, as well as further characterization of the extent of the syndrome, and can enable evaluation of a globe with congenital cataract or vitreal opacities (8, 16). Modalities utilized in the imaging evaluation of patients with MGS have included ultrasound, CT and MR. Ultrasound can demonstrate not only the presence and size of a colobomatous defect, but a marked prominence of the intraocular portion of the optic nerve (6, 8–10). No brain or skull base information can be assessed with ultrasound, however, and retroocular information is limited. The CT appearance of MGS has been described as quite characteristic (8), with several reports in the literature on orbital findings with MGS (7–9, 13, 16). In addition, CT is useful for concurrent evaluation of the intracranial anatomy and any associated anomalies (11, 13). CT has disclosed microphthalmos and widening of the optic nerve head which is of water density and continuous with the vitreous humor (7, 8). Also described is an increased thickness of the intraocular nerve and enhancement with contrast administration, seen in 50% of the patients in Beyer's series (9). The contrast enhancement, described as scleral-based, is at the apex of the optic nerve defect (8). The contrast enhancement pattern that we observed in our patients is quite similar to that described in the CT literature, however we believe it is more likely choroidal-based, as the sclera is a relatively avascular tissue. Importantly, Beyer's series found no abnormality of the intraorbital optic nerve.

Despite recent claims that "MR imaging provides no information that is not readily available at CT" and that CT is the technique of choice in children (7), several authors have already described MR findings in patients with MGS (2, 12, 15, 16). These reports describe the skull base findings with associated encephalocele, rather than the primary visual apparatus abnormalities (2, 12, 15). However, one report (16) describes the abnormal orbital anatomy in MGS, utilizing a 0.5 T magnet and demonstrating only axial T1 and T2-weighted images. Our findings agree with the results of this study, and the results of the previously published CT studies of the globe and orbit in MGS. However, no previously published example at either CT or MR has traced the optic nerves back through the chiasm and into the optic tracts, disclosing the abnormally small nerve and contralaterally small tract. Additionally, we now describe the cross-sectional imaging appearance of the fluffy tuft of glial hyperplasia at the optic nerve head. Our cases thus demonstrates the most detailed imaging in patients with MGS to date by any modality and our described findings, if reproducible in other MGS patients, could allow definitive differentiation of MGS from other related ocular anomalies. Though sedation is often necessary for pediatric patient compliance with MR and was utilized in our cases, decreased eye movement will often result and may allow more detailed images of the globe to be obtained. The need for sedation must also be contrasted with the real advantages of MR over CT to include lack of ionizing radiation, multiplanar capabilities, and the superior contrast-to-noise ratio with MR imaging.

Differential diagnostic considerations which may mimic MGS at imaging include staphyloma of the posterior globe, retrobulbar duplication cyst, and microphthalmia with cyst (7, 17). Staphyloma is an inflammatory condition with localized globe ectasia that may be posterior in some cases. A duplication cyst will not involve the optic nerve head, rather lying perineurally adjacent the papilla. Microphthalmia with cyst is a severe congenital malformation with gross scleral ectasia. The cyst in this condition may be larger than the parent globe. The differentiating feature is the neck of the cyst where it connects with the globe, which is much smaller than the actual cyst (7). There should be no fundoscopic findings compatible with MGS in these patients. High-resolution MR or CT imaging may also be helpful in determining these differential features.

The prognosis in MGS patients revolves around the full constellation of congenital anomalies present and any occurrence of retinal detachment. Treatment options are limited. Significant refractive errors are corrected and occlusion therapy is utilized to reverse any amblyopia in infants. Strabismus is corrected surgically if good fixation is achieved with the affected eye, or if the deviation is cosmetically undesirable (1). Some authors have advocated optic nerve sheath fenestration to decompress the subretinal space via the (proposed) abnormal communication in the nerve head thereby preventing recurrent retinal detachment (1).

Evolution and progression of the abnormal fundoscopic features of MGS has been described (9, 14). The macula and its xanthophyllic pigment may become partially or totally contained within the scleral defect, a phenomenon called macular capture. In Beyer's report (9), 2 patient's exhibited a marked

progression in their abnormal fundoscopic exam, and in Steinkuller's (4) review of 22 cases there were two documented instances of progression. One of these patients underwent enucleation for a suspected growing mass. Here again detailed imaging could obviate the need for unnecessary surgery, or at least allow for more reliable and detailed follow-up of difficult cases.

CONCLUSION

We have reported the most detailed MR findings in MGS to date in two patients. This may allow for an accurate diagnosis of this syndrome and differentiation from closely related conditions. This in turn may carry significant genetic and prognostic significance for the patient and their family.

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