Pathogenic Implications of Subretinal Gas Migration Through Pits and Atypical Colobomas of the Optic Nerve

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Objective: To describe subretinal migration of gas and silicone oil in a series of patients with congenital cavitary optic disc anomalies and to further clarify the pathogenesis of the associated maculopathy.

Methods: Medical records of 4 female patients, aged 8 to 34 years, who developed subretinal gas migration after vitreous surgery for macular detachment associated with cavitary optic disc anomalies were reviewed. A theoretical model was used to calculate the pressure differential required to induce subretinal gas migration through an optic pit.

Results: The 4 patients had bilateral atypical optic nerve colobomas or a unilateral large optic pit. A definite defect in the tissue overlying the disc excavation could be seen in one eye, and intraoperative drainage of subretinal fluid through the disc anomaly was possible in all cases. Subretinal migration of gas or silicone oil was seen intraoperatively in one case and first appeared between 1 and 17 days postoperatively in the remaining cases. Theoretical calculations suggest that the pressure differential required for migration of gas through a small defect in the roof of a cavitary disc lesion is within the range of expected fluctuations in cerebrospinal fluid pressure.

Conclusions: These observations provide clinical confirmation of a defect in tissue overlying cavitary optic disc anomalies and imply interconnections between the vitreous cavity, subarachnoid space, and subretinal space. We theorize that intermittent pressure gradients resulting from normal variations in intracranial pressure play a critical role in the pathogenesis of retinopathy associated with cavitary disc anomalies.


C ongenital cavitary anomalies of the optic nerve that may be associated with serous detachments of the macula include optic disc pit, optic nerve coloboma (typical and atypical), and morning glory disc anomaly.1-3 Frank macular detachment appears to be preceded by the accumulation of intraretinal fluid emanating from the disc anomaly and constituting an unusual form of retinoschisis-like separation.3 Subsequently there is breakthrough of fluid into the subretinal space leading to detachment of the macula and occasionally larger areas of the retina. The origin of the fluid and precise pathogenesis of macular detachment associated with cavitary optic disc anomalies remain unclear.

We present 4 cases of retinal detachment associated with excavated optic disc anomalies in which vitreous surgery was complicated by subretinal migration of gas and silicone oil. This rare and unexpected event cannot readily be explained by the principles known to govern the behavior of intraocular gas and silicone oil. We believe that our clinical observations, coupled with recent optical coherence tomographic findings and consideration of cerebrospinal fluid (CSF) dynamics, provide important new insights into the pathogenesis of the maculopathy complicating optic pits and related disc anomalies.

METHODS

We retrospectively identified 4 patients who developed subretinal gas migration after vitreous surgery for macular detachment associated with cavitary optic disc anomalies. The patients were derived from the practices of 4 retina specialists at 3 centers. One patient (case 1) was described in a previous report.4 The medical records and available fundus photographs were reviewed. Although institutional review board oversight was not required for this chart review, each patient gave written informed consent before undergoing surgical intervention. Using the physical principles governing the behavior of intraocular gas, we calculated the...
theoretical pressure differential required for gas migration into an optic pit and compared this with information derived from a model of CSF pressure dynamics.

REPORT OF CASES

CASE 1

A 24-year-old woman was examined because of decreased and darkened vision in the central visual field of the right eye. The ocular history was significant for mild myopia. The maternal family history was notable for glaucoma.

The visual acuity measured 6/200 OD and 20/20 OS. The anterior segment was normal in each eye. Examination of the right fundus demonstrated retinal detachment involving the macula and superotemporal midperiphery and extending to the temporal border of the optic nerve (Figure 1). A stellate outer foveal defect was present, with a tiny full-thickness defect at the center of the fovea. The retina between the optic nerve and the fovea had an appearance suggesting retinal thickening or schisis. Examination of the optic disc demonstrated nasization of the vessels with a deep, large, horizontally oval cup and a notch in the temporal neuroretinal rim. The left disc was anomalous, with a large cup and nasization of disc vessels but no evidence of associated maculopathy (Figure 1). B-scan ultrasonography of the right eye showed no evidence of posterior vitreous detachment. Orbital ultrasound and computed tomographic scans were normal bilaterally.

The patient underwent pars plana vitrectomy with removal of the attached posterior hyaloid, subretinal fluid drainage through a small retinotomy, fluid-gas exchange with 20% sulfur hexafluoride, and 10 days of postoperative face-down positioning. Two months postoperatively, a moderate posterior subcapsular cataract was evident, along with a small macular hole and shallow subretinal fluid in the macula extending nasally to the optic disc. Contact lens examination demonstrated a defect in the tissue overlying the temporal aspect of the disc cavitation.

When the subretinal fluid persisted 2 months later, krypton red laser burns were placed in 3 rows in the temporal juxtapapillary area. The patient then underwent phacoemulsification with placement of an intraocular lens followed by repeat vitrectomy with fluid-gas exchange and postoperative prone positioning. Seven days postoperatively, several gas bubbles were noted in the subretinal space between the optic disc and central macula (Figure 2). There was also gas trapped under neural tissue overlying the deep optic disc cavitation. The gas resolved during the subsequent 3 weeks.

Two months later, the patient noted an abrupt decline in vision in the right eye. Examination showed extensive detachment of the macular region and fluid communication with the small hole in the neural tissue over the optic disc. A 50% fluid-gas exchange using 20% perfluoropropane was performed. After 7 days of face-down positioning, the macula was flat and supplemental krypton laser was applied to the temporal aspect of the optic disc. After 10 additional days of face-down positioning, the patient noted an abrupt decline in vision and was found to have recurrent detachment of the posterior retina. Numerous small subretinal gas bubbles were located in the superior aspect of the detachment (Figure 3). An additional cluster of bubbles appeared to be located within the schisis cavity in the papillomacu-
lar bundle area. No intraocular pressure measurement greater than 25 mm Hg was recorded at any postoperative examination.

Two months later, a total and highly bullous retinal detachment developed, obscuring a view of the optic disc and macula. No peripheral retinal breaks were found. The patient underwent repeat vitrectomy. During fluid-air exchange, subretinal fluid was drained through a small macular hole and over the optic disc. Moderately heavy laser photocoagulation was applied around the entire optic nerve, and lighter burns were placed in the papillomacular bundle and at the edge of the macular hole. Two weeks postoperatively, the visual acuity had improved to 20/100 and the retina was completely flat (Figure 4). During the subsequent 10 years, the visual acuity remained stable and the retina remained attached in the right eye.

**CASE 2**

An 8-year-old girl was diagnosed as having an optic pit in her left eye on routine ophthalmologic examination. The visual acuity was 20/20 OU. Several months later, she returned for evaluation of central visual blurring in the left eye. The ocular and medical histories were notable only for mild myopia. The visual acuity was 20/20 OD and 20/70 OS. The anterior segment was normal bilaterally. Fundus examination of the right eye showed a normal optic disc and retina, with a cup-disc ratio of 0.5. Examination of the left eye showed detachment of the macula associated with a deep excavation in a large optic disc (Figure 5). No Weiss ring was present.

The patient underwent pars plana vitrectomy with removal of the posterior hyaloid. During fluid-air exchange, subretinal fluid was drained through the optic pit. Argon green laser was placed around the temporal juxtapapillary area. The vitreous cavity was filled with 10% perfluoropropane gas and the patient was positioned face down. One week postoperatively, a subretinal gas bubble was noted in the macular region. This was allowed to resorb spontaneously.

One month later, a bullous retinal detachment was noted superiorly, with shallow detachment of the macula. Repeat vitrectomy with lensectomy, fluid-gas exchange, and scleral buckle was performed. No retinal breaks could be found. Recurrent retinal detachment inferiorly was noted 2 weeks postoperatively and treated with repeat vitrectomy followed by injection of silicone oil.

Ten days postoperatively, the patient was found to have extensive silicone oil in the subretinal space (Figure 6). She underwent repeat vitrectomy with silicone oil aspiration through the pit and placement of autologous blood over the optic pit. Endolaser treatment was performed for 360° around the optic nerve. Six months postoperatively, the visual acuity in the left eye was no light perception. The retina was completely attached, but extensive optic atrophy was present.

**CASE 3**

A 34-year-old woman had a 3-month history of central visual distortion and darkening in the left eye. The ocular and medical histories and family ocular history were unremarkable. Visual acuity was 20/20 OD and 20/50 OS. The anterior segments were normal.

The right fundus was normal apart from a large optic cup with a small amount of fibroglial tissue and nasalization of disc vessels. There was a large, deep, sharply delimited, and inferiorly decentered excavation in the left disc, with a possible slitlike defect in the neural rim nasally (Figure 7). Biomicroscopy of the left macula showed evi-
dence of retinoschisis and retinal striae in the papillomacular bundle and fovea, with a small serous outer-layer detachment in the central macula (Figure 8). No evidence of a posterior vitreous detachment was present.

Laser photocoagulation was performed along the temporal aspect of the optic nerve. Four months later, the visual acuity was 20/60 OS and a persistent macular detachment was noted. The patient underwent pars plana vitrectomy. During fluid-air exchange, a portion of the subretinal fluid was aspirated through the optic disc cavitation. At the conclusion of the procedure, subretinal gas was noted. The fluid-air exchange was repeated and the subretinal air was removed.

At the 7-year follow-up examination, the visual acuity was 20/30 OS. The macula was attached with mild residual retinal striae, and laser scars were present along the temporal margin of the optic nerve.

CASE 4

A 33-year-old woman had sudden loss of vision in her left eye. The family history was notable for glaucoma. The visual acuity was 20/20 OD and 20/200 OS. Results of anterior segment examination were normal. Fundus examination showed a large anomalous optic disc with a large cup (cup-disc ratio, 0.7) bilaterally. In addition, there was a small pit in the temporal aspect of the left disc accompanied by a large serous detachment of the macula.

The patient underwent pars plana vitrectomy. During fluid-air exchange it was noted that the subretinal fluid could be aspirated via the optic pit. Endolaser photocoagulation was applied to the temporal juxtapapillary retina. On the first postoperative day, the macula was completely flat and additional laser treatment was performed along the temporal margin of the disc.

Three weeks postoperatively, the visual acuity was 20/30 OS. Recurrent subretinal fluid was noted adjacent
to the optic pit. Pure perfluoropropane gas was injected into the vitreous cavity and the patient was placed in a prone position. One day later, multiple small gas bubbles were noted in the submacular space. The intraocular pressure was 14 mm Hg. The subretinal gas resolved during the subsequent month.

The patient returned 6 weeks later with an acute decline in vision to the level of counting fingers. Examination demonstrated extensive retinal detachment over the temporal half of the fundus, with no peripheral retinal breaks. The patient underwent repeat vitrectomy with fluid-air exchange, laser, and subretinal fluid drainage through a retinotomy. Additional laser treatment was applied along the temporal margin of the optic disc. Two years postoperatively, the visual acuity was 20/50 OS and the retina was completely attached.

**PRESSURE DIFFERENTIAL CALCULATION**

For a bubble of gas to pass through a retinal break, the force pushing the bubble through the hole must exceed the surface tension of the gas bubble on the edges of the hole.\(^7\) The force tending to push the bubble through the hole is the product of the area of the hole (\(\pi R^2\)) and the pressure difference across the hole (\(\Delta p\)). The force opposing prolapse is the surface-tension force, which is the product of 3 factors: the coefficient of surface tension (\(\gamma = 0.073 \text{ N/m for a gas-water interface}\)), the length of the margin of prolapse (circumference of the hole = \(2\pi R\)), and the cosine of the contact angle (\(\theta\)). When a gas bubble is about to pass through the hole, the radius of curvature of the bubble equals the radius of the retinal hole. At this point the angle of contact is \(0^\circ\) and \(\cos\theta = 1\). Therefore, the equation for the pressure difference (in pascals) across the hole at the time of gas migration simplifies to

\[
\Delta p_{\text{required}} = \frac{2R\gamma}{\pi R^2} = \frac{2}{\pi R},
\]

Assuming a hole 200 µm in diameter, \(\Delta p_{\text{required}} = \frac{2(0.073 \text{ N/m})}{0.0001 \pi} = 1460 \text{ Pa} = 148 \text{ mm H}_2\text{O}.\) Thus, the pressure gradient required to push a gas bubble through a hole of this size is at least 148 mm H\(_2\)O (approximately 11 mm Hg).

**MODEL OF CSF PRESSURE**

Normal CSF pressure in the lateral recumbent position typically varies from 100 to 250 mm H\(_2\)O.\(^8\) In a case series of 58 patients ranging in age from 15 to 83 years, the mean CSF pressure was 141 ± 19 mm H\(_2\)O.\(^8\) Intracranial pressure also appears to vary significantly over time.\(^8\) When the tube is reoriented vertically, the pressure within different parts of the tube is altered substantially (Figure 9). Although this model is not an exact replica of the human condition, it demonstrates that changes in body position cause significant alterations in intracranial pressure. The magnitude of these changes easily exceeds the pressure gradient required for gas migration calculated in the previous subsection.

![Figure 9](http://archopht.jamanetwork.com/pdfaccess.ashx?url=/data/journals/ophth/9933/)

Typical coloboma of the optic disc is a congenital excavation, located inferonasally, that is believed to result from malclosure of the embryonic ocular fissure.\(^2,4\) Optic disc pits are classically small and temporally located, but they appear to exist along a spectrum of congenital cavitary disc anomalies that are often referred to as *atypical optic nerve colobomas*.\(^3,10\) The embryologic basis for atypical optic nerve head colobomas, including optic pits, is unclear. Although our patients had negative family histories, their disc anomalies are similar to those previously described in several autosomal dominant pedigrees of atypical optic nerve colobomas and pits that were often associated with nonrhegmatogenous detachments of the macula or more extensive areas of retina.\(^3,10\) The optic disc abnormalities in case 3 also bear some resemblance to those described in the papillorenal syndrome, an autosomal dominant condition occasionally associated with serous retinal detachment.\(^11\) Our patient had no personal or family history of renal disease.

Careful biomicroscopy and optical coherence tomographic imaging have demonstrated that edema or a schisis-like separation in the outer retina appears to be the initial pathogenic step in the development of serous macular detachment complicating congenital cavitary optic disc anomalies.\(^5,12-14\) Fluid from the disc excavation first accumulates within the retinal stroma, most prominently in the outer plexiform layer. When severe, the edema mimics a retinoschisis cavity, but with intact vertical bridging retinal elements. The fluid later enters the subretinal space, either through an obvious outer lamellar foveal hole\(^5,12,13\) or possibly through minute invisible breaks in the outer retina. The schisis-like separation has been
shown both to precede macular detachment and to in-
variably communicate with the optic disc, even when the
associated macular detachment does not.12-14 The pres-
ence of schisis-like outer retinal edema most likely ex-
plains the high frequency of treatment failure after pho-
tocoagulation to the juxtapapillary retina in these eyes,
although separation of the outer retina from the retinal
pigment epithelium may also be a factor.

The most plausible sources of fluid responsible for the
retinopathy associated with optic pits and other cavi-
tary disc anomalies are the vitreous cavity and the subarach-
"noid space. Evidence confirming a communication through
the pit between the vitreous cavity and the subretinal space
includes the following: (1) india ink studies performed on
collie dogs with cavity disc anomalies similar to human
optic pits demonstrated leakage of ink from the vitreous

collie dogs with cavitary disc anomalies similar to human
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potentially do so more easily and with unknown pathologic consequences. It may therefore be prudent to avoid the use of liquid vitreous substitutes in the surgical management of cavitary optic disc anomalies.\textsuperscript{16,19}

A substantial pressure difference between the vitreous cavity and subretinal space cannot develop in an eye with a mobile retina.\textsuperscript{7} However, fluctuations in intraocular pressure do affect the pressure differential between the vitreous cavity and spaces outside the globe, such as the pit sac and perioptic subarachnoid space. Indeed, high intraocular pressure during fluid-air exchange likely contributed to the gas migration observed intraoperatively in case 3. In the remaining cases, migration occurred post-operatively and without an apparent contribution by elevated intraocular pressure.

We believe that a pathogenic model that incorporates transient pressure gradients derived from the subarachnoid space is necessary to explain the unusual phenomenon of subretinal gas migration through cavitary disc anomalies. A unifying model must also include the observation that the anatomy of cavitary disc anomalies varies from one eye to another. On the basis of the studies previously referred to, it seems clear that cavitary lesions communicate openly with the vitreous cavity in some eyes, with the subarachnoid space in other eyes, and with both spaces in yet others. As Irvine et al\textsuperscript{24} suggested, the vitreous, sub-

\textbf{Figure 10.} Schematic illustration of the anatomy of an optic pit and associated maculopathy. The herniated dysplastic tissue and pit capsule vary in porosity from one eye to another. In eyes with an impermeable capsule, the pit functions like a bulb syringe, “sucking” vitreous fluid into the pit sac during a drop in intracranial pressure (ICP) (A) and then, during a rise in pressure, expelling it from the sac (B). In eyes with a permeable capsule, fluctuations in ICP are transmitted to the pit by cerebrospinal fluid migration across the capsule (C).
arachnoid, and subretinal spaces may all be variably inter-connected because of the incomplete differentiation and porous nature of the herniated tissues composing the optic nerve anomaly (Figure 10). It follows that the subretinal fluid in a given case might be vitreous fluid, CSF, or an admixture of the two fluids. We speculate that the age at symptom onset in patients with congenital excavated disc lesions may depend in part on the anatomy of these inter-connections. The typical age at onset, in the third and fourth decades of life, may reflect the age at which sufficient liquid vitreous is available to be drawn into the pit.5,18,20 On the other hand, CSF is more likely involved when the onset occurs in patients too young to have liquefied vitreous, especially when the associated retinal detachment is extensive.

The concept of a cavitary disc anomaly functioning as a mechanical pump driven by fluctuations in CSF pressure might also explain the peculiar retinosischisis-like separa-tion and associated retinal detachment seen in these cases. Fluid moving passively from the vitreous cavity through a pit would unlikely be driven into the retinal stroma with sufficient force to cause a large schisis-like split and subsequent macular detachment. However, it is plausible that alterations in CSF pressure, transmitted to the pit sac as described previously, would pump small aliquots of fluid under pressure into the retinal stroma. This fluid might be expected to gradually dissect a schisis cavity in the outer retina and eventually break into the subretinal space, often through a stellate outer foveal defect that has the appearance of having been created under force.

Subretinal migration of gas or silicone oil through cavi-tary disc anomalies is an uncommon phenomenon. On the basis of our cases and those previously re-ported,16,17,19,24 it appears that patients with large cavi-tary anomalies may be at greatest risk for this complica-tion. Although these eyes tend to develop large and recurrent retinal detachments, anatomic success is ultimately possible with the creation of a sufficient laser barrier in the juxtapapillary retina. Caution must be exercised in the application of this laser barrier, since the optic atrophy and poor visual outcome seen in case 2 may have resulted from overly intense laser treatment extending 360° around the nerve head. A unifying model of patho-genesis that we believe accounts for subretinal gas migra-tion and other peculiar features of the retinopathy associated with cavitary disc anomalies includes 2 critical features: (1) variable interconnections between the vitreous, subarachnoid, and subretinal spaces and (2) transmission of intracranial pressure fluctuations to the pit via the perineural subarachnoid space.

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REFERENCES


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