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

T. Mark Johnson, MD, FRCSC; Mark W. Johnson, MD

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.


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. 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 and silicone oil, 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 nasulation 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 nasalization 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 papillomacular-
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 decented 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 disc.
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.

### RESULTS

#### 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. 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 the bubble is the surface-tension force, which is the product of 3 factors: the coefficient of surface tension ($\gamma = 0.073$ N/m for a gas-water interface), the length of the margin of prolapase (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 $\Delta p = 2\gamma/R$. Assuming a hole 200 µm in diameter, $\Delta p = 2(0.073 \text{ N/m})/0.0001 \text{ m} = 1460 \text{ Pa} = 148 \text{ mm H}_2\text{O}$. 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. 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. Intracranial pressure also appears to vary significantly over time. Studies of patients with pseudotumor cerebri have demonstrated intracranial pressures varying from 50 to 500 mm H$_2$O during 24-hour periods. There are few studies examining intracranial pressure over time in otherwise normal patients.

Cerebrospinal fluid pressure is dependent in part on body position. The CSF can be modeled as a closed tube 700 mm in length with a pressure of 140 mm H$_2$O in the horizontal position. When the tube is reoriented vertically, the pressure within different parts of the tube is altered substantially. 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 abnormalities that are often referred to as atypical optic nerve colobomas.1-3,10 The embryologic basis for atypical optic nerve head colobomas, including optic pits, is unclear. Although our patients had negative family histories, their disc abnormalities 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.1,3,10 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 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 cavitary
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 cavitary disc anomalies similar to human
optic pits demonstrated leakage of ink from the vitreous
cavity (but not from the subarachnoid space) into the sub-
retinal space via the optic pit.15 (2) During vitrectomy, in-
traoperative drainage of subretinal fluid through cavitary
disc anomalies was possible in our cases and in previ-
ously reported cases.6,16,17 (3) In addition to the cases re-
ported in this study, rare cases of subretinal migration of
vitreous substitutes through anomalous disc excavations
have been reported previously. These include the migra-
tion of gas through an optic pit after outpatient perflu-
oroxypropene injection,19 the migration of both gas and sili-
cone oil through a morning glory disc after vitrectomy,10
and the intraoperative migration of perfluorodecalin through a morning glory disc.19

Vitreous fluid is thought to gain access to anomalous
disc cavitations through small holes or breaks in overly-
ing diaphanous membranes or neuroectodermal tissue. In
our case 1, a gas bubble was observed trapped within the
disc excavation, having passed through a small visible break
in overlying neural tissue (Figure 2). Similar breaks have also been documented in other series.6,16-18,20 The possi-
ability of vitreous traction associated with these breaks has been suggested by clinical observations in several
cases.6,17,18,21 But its pathogenic role remains unclear. Ob-
viouly, vitreous traction played no role in the subretinal
gas migration seen in our patients, since the migration oc-
curred in each case after vitrectomy and peeling of the pos-
terior cortical vitreous layer.

Several authors have suggested that CSF from the peri-
nuclear subarachnoid space may be responsible for the reti-
nopathy complicating optic pits and related anomali-
ies.22-25 Histologically, optic nerve pits are herniations of
dysplastic retina into a collagen-lined sac or pocket, which
often extends posteriorly into the subarachnoid space
through a defect in the lamina cribrosa.22,26 The posterior
aspect of the sac is typically a multiloculated fluid-filled
space. Optical coherence tomographic studies have sug-
gested a communication between the schisis-like intrareti-
nal space and a periretinal space associated with the optic
pit.12,23 Furthermore, communications between the sub-
arachnoid space and subretinal space and between the sub-
arachnoid space and vitreous cavity have been proved clini-
cally in patients with the morning glory anomaly. In one
case, metrizamide dye injected into the subarachnoid space
migrated into the subretinal space but not into the vitre-
ous.23 In a second case, gas injected into the vitreous at the
time of optic nerve sheath fenestration for extensive reti-
nal detachment was noted to migrate into the periretinal
subarachnoid space.24 Finally, the finding of relative hy-
potony in an eye with an optic pit was attributed by the
authors to drainage of intraocular fluid through the pit and
into the subarachnoid space.25

Our cases of gas and silicone oil migration from the vitreous into the subretinal space clearly prove a com-
munication between these 2 spaces through the cavitary
disc anomalies. However, this phenomenon also sug-
gests an unusual and complex pathogenesis, since sur-
face tension considerations dictate that migration of a large
intravitreal gas bubble through a small defect is impos-
sible without a large pressure gradient. Assuming a gen-
erous hole in the roof of an optic pit of 200-μm diam-
er, we calculate that a pressure differential across the
defect of at least 148 mm H2O (11 mm Hg) is necessary
to force a gas bubble into the optic pit and then subreti-
nal space. However, a significant pressure differential be-
tween the vitreous cavity and subretinal space does not
normally exist. We propose that the pressure differen-
tial required for the subretinal migration of gas ob-
served in our patients derives from pressure fluctua-
tions in CSF that are transmitted to the optic pit via the
periretinal subarachnoid space.

Large fluctuations in intracranial and CSF pressure have
been measured in both normal and pathologic situations.
Factors such as changes in body position and venous pres-
sure contribute to these fluctuations. Our calculations,
based on the simplified models described in this report,
suggest that the pressure differential required for migra-
tion of gas through a small defect in the roof of a cavitary
disc lesion is well within the range of expected fluctua-
tions in CSF pressure. Such pressure alterations would be
transmitted to the sac of the pit by CSF migration across
the connective-tissue capsule in cases where the porous
capsule is permeable to fluid (Figure 10). In pits with an
impermeable capsule, we speculate that pressure trans-
mission could occur by small pressure-induced move-
ments of the capsule causing deformation of the pit sac
(Figure 10). Thus, the pit conceivably functions like a bulb
syringe, “sucking” fluid (or gas or silicone oil) into the pit
sac during a drop in intracranial pressure and then, with
a rise in pressure, ejecting it from the sac. The fluid or gas
exiting the pit would be expected to divide, part into the
vitreous cavity and part into the retinoschisis cavity and
eventually the subretinal space (Figure 3). The existence
of such transient pressure gradients is suggested by the
observation in one patient that vitreous debris overlying an
optic pit was intermittently sucked into the pit and later
dislodged back into the posterior vitreous.25

Our model demonstrates that normal fluctuations in
intracranial pressure can theoretically produce forces that
are capable of exceeding the surface tension of gas at a
small break overlying an optic pit. The pressure gradi-
ent required for subretinal migration of materials with
lower surface tension, such as silicone oil, perfluorocar-
bon liquid, and hyaluronic acid,25 is lower, such that sub-
retinal migration could occur more easily and through
smaller defects in the dysplastic tissue overlying the pit.
Furthermore, since intravitreal gas can occasionally mi-
grate through cavitary disc anomalies into the subarach-
noid space,24 silicone oil or perfluorocarbon liquid could
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 periorbital 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 postoperatively 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-

**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. \(^\text{5,18,20}\) 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 cavitory disc anomaly functioning as a mechanical pump driven by fluctuations in CSF pressure might also explain the peculiar retinoschisis-like separation 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 alternations in CSF pressure, transmitted to the pit sac as pressure might also explain the peculiar retinoschisis-like separation and associated retinal detachment seen in these cases.


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