

## Closure of stage 2 macular hole with a low-dose intravitreal injection of perfluoropropane

*Cierre de agujero macular estadio 2 con inyección intravítreo a dosis baja de gas perfluoropropano*

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### Abstract

**Background:** *Idiopathic macular holes (IMH) are common and affect central vision. We demonstrate the effectiveness of 0.2 ml intravitreal perfluoropropane (C3F8) in Stage-2 IMH. Case:* A 61-year-old woman presented with blurred vision OD. Best-corrected visual acuity (BCVA) was 20/125 OD and 20/20 OS. Biomicroscopy of OD evidenced a Stage-2 IMH. Intravitreal C3F8 was injected and postural measures prescribed. Optical coherence tomography 1 week after revealed posterior vitreous detachment and vitreomacular traction resolution. Full anatomical and functional recovery was achieved at week 4 and remained stable during a 6-month follow-up (BCVA 20/20 OD). Conclusion: Intravitreal C3F8 as initial therapy for Stage 2 IMH represents a good alternative to vitrectomy for patients with IMH.

**KEY WORDS:** *Idiopathic macular hole. Vitreomacular traction. Intravitreal inert gas. Anatomical closure.*

### Resumen

**Introducción:** Los agujeros maculares idiopáticos (AMI) son comunes y afectan la visión central. Demostramos la efectividad de 0.2 ml de perfluoropropano (C3F8) intravítreo en AMI en estadio 2. **Caso:** Una mujer de 61 años presentó con visión borrosa súbita OD. Mejor agudeza visual corregida (MAVC) 20/125 OD y 20/20 en el OS. La biomicroscopía del OD evidenció un AMI en estadio 2. Se inyectó C3F8 intravítreo y se prescribieron medidas posturales. Una semana después, la tomografía de coherencia óptica reveló desprendimiento de vítreo posterior. La resolución de tracción vitreomacular con recuperación anatómica y funcional completa se logró a la semana 4 y se mantuvo estable durante un seguimiento de 6 meses (MAVC 20/20 OD). **Conclusión:** El C3F8 intravítreo como terapia inicial para AMI en estadio 2 representa una buena alternativa a la vitrectomía vía pars plana en pacientes con AMI.

**PALABRAS CLAVE:** *Agujero macular idiopático. Tracción vitreomacular. Gas inerte intravítreo. Cierre anatómico.*

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## Background

Idiopathic macular holes (IMH) are around full-thickness discontinuity of the foveal neurosensory retina and represent a common macular disease that affects central vision<sup>1</sup>. According to the clinical classification of Gass, IMH's can be divided into four stages; Stage 1 being impending macular holes and Stages 2-4 full-thickness macular holes<sup>2,3</sup>. As supported by current Level I evidence, pars plana vitrectomy (PPV) with or without internal limiting membrane peeling and gas endotamponade is considered the treatment of choice for Stage 2-4 macular holes<sup>4,5</sup>. Despite its excellent success rate, adverse consequences as the acceleration of nuclear sclerosis<sup>6</sup>, retinal pigment epithelium alterations, retinal detachment (RD), persistence and reopening of the hole, cystoid macular edema, visual field defects, choroidal neovascularization, and endophthalmitis cannot be ignored<sup>7-9</sup>. The intravitreal injection of inert expansile gas is a safer, minimally invasive alternative to PPV. The success rate depends on the stage of the IMH and their individual presentation<sup>8,10</sup>. We report the case of an IMH Stage 2 successfully treated with an intravitreal injection of perfluoropropane (C3F8) at a previously unreported dose as initial therapy.

## Clinical case

A 61-year-old woman with a previous history of hypothyroidism, cataract surgery on both eyes (OU) and broad vitreomacular traction (VMT) on the right eye (OD) (Fig. 1A), presented to the retina and vitreous clinic with a 10-day history of sudden-onset metamorphopsia and blurred vision OD. Best-corrected visual acuity (BCVA) was 20/125 OD and 20/20 on the left eye (OS). Anterior segment biomicroscopy revealed no alterations OU. Posterior segment examination by means of indirect ophthalmoscopy of OD showed around xanthophylllic circle with evidence of a small retinal defect in the center of the macula and a partial perifoveal posterior vitreous detachment (PVD) consistent with a Stage 2 IMH according to Gass' classification. Diagnosis confirmation with macular optical coherence tomography (OCT) demonstrated a primary small macular hole with VMT in agreement with the International Vitreomacular Traction Study classification system for macular hole<sup>11</sup> (Fig. 1B). The rest of the posterior segment examination was unremarkable OU.

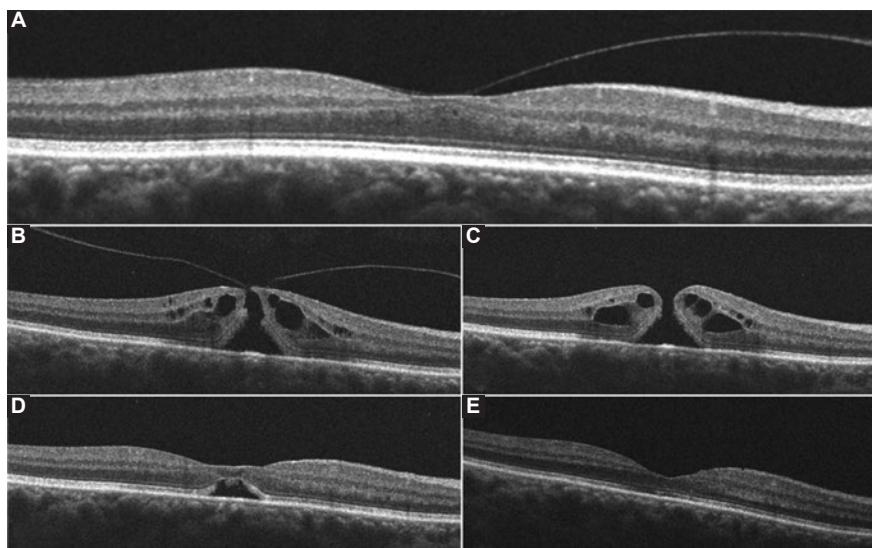
Intravitreal injection through pars plana of 0.2 ml of 100% C3F8 gas was offered to our patient and performed in an operating room using the sterile technique, topical anesthesia, povidone-iodine, topical antibiotics, eyelid speculum, and a 27-gauge needle with a 3-ml syringe. Uncorrected visual acuity was verified to be at least of count fingers and arterial pulse of the central retinal artery confirmed to be present by means of indirect biomicroscopy. Broad-spectrum antibiotic eye drops 4 times a day for 4 days, and posture measures were prescribed: 1 week in sitting position (to achieve PVD) and 1 week in reading position (to achieve anatomic closure). Intraocular pressure was normal on the 1<sup>st</sup> post-operative day.

One week after the procedure, a macular OCT evidenced PVD and resolution of VMT with a subsequent increase in the maximal foveal thickness, intraretinal cysts and a decrease of the hole aperture size (Fig. 1C). By week 2 postoperatively, OCT evidenced anatomic closure, with a remaining subfoveolar neurosensory RD (Fig. 1D); and a BCVA of 20/100. Regular follow-up demonstrated progressive morphologic improvement with full neurosensory reattachment, restoration of normal foveal contour and preservation of cytoarchitecture of the inner and outer retinal layers with a BCVA of 20/20 OU 4 weeks postoperatively (Fig. 1E). After a 6-month follow-up, morphologic and functional stability were maintained. No adverse events due to the intravitreal injection of C3F8 were presented.

## Discussion

Intravitreal injection of 0.2 ml of C3F8 proved to be effective in producing PVD, the release of VMT and anatomic closure of Stage 2 IMH with long-term stability. Gass hypothesized that IMH's begin with tangential traction of the perifoveal vitreous cortex that results in foveal dehiscence and progress from foveolar detachment to full-thickness IMH<sup>3</sup>. The serial high-definition OCT images obtained in our patient support the current theory that the course of the condition begins with perifoveal PVD and is continued by anteroposterior and dynamic VMT<sup>12,13</sup>. The prevalence of IMH's has been estimated in 0.1-0.8% of adults aged >40 years with an age-adjusted incidence of 7.8/100,000 of the general population per year<sup>13</sup>. Two-thirds of patients are females and unilateral involvement is seen in about 80% of the cases<sup>14</sup>.

The intravitreal injection of 0.2 ml of C3F8 as initial therapy for a case of macular hole presenting with BCVA of 20/125, VMT, hole aperture size of 226 µm



**Figure 1.** Horizontal high-definition optical coherence tomography images of the right macula and their correspondent best-corrected visual acuity (BCVA) at the time. **A:** Imaging before the onset of visual symptoms shows a split of the vitreous cortex with broad vitreomacular traction (VMT) and a resultant partial loss of foveal depression with intraretinal fluid (BCVA 20/20). **B:** Imaging after the onset of visual symptoms reveal perifoveal vitreous detachment, focal VMT along with a full-thickness hourglass shape defect of the neurosensory retina, surrounded by a cuff of intraretinal cysts; hole aperture size was 226 $\mu$ m and maximal foveal thickness was 433 $\mu$ m (BCVA 20/125). **C:** One week after gas injection a complete posterior vitreous detachment, rounding off the edges of the retinal defect and a slight increase in the cuff-like thickened zone of intraretinal cysts can be seen. Maximal foveal thickness was 450  $\mu$ m (BCVA 20/100). **D:** 2 weeks after perfluoropropane injection an anatomic closure of the retinal defect with the partial morphological recovery of the foveal depression and a remaining subfoveolar neurosensory retinal detachment are demonstrated (BCVA 20/100). **E:** 4 weeks postoperatively, a full morphologic and functional recovery is shown with full anatomic integrity of inner and outer retinal layers (BCVA 20/20).

and maximal foveal thickness of 433  $\mu$ m has not been described yet. The occurrence of complete PVD 1 week after gas injection in our patient is consistent with previous reports<sup>8,10</sup>. A pilot study made by Chan et al.<sup>10</sup> first demonstrated that the intravitreal injection of 0.3-0.5 ml of C3F8 could produce PVD with release of VMT in 95% of eyes with IMH Stages 1-3 and that a closure rate of 91% of Stage 1, and 50% of the Stage 2 IMH's could be achieved. A more recent study with a larger sample, made by Mori et al.<sup>8</sup> reported a rate of PVD and IMH Stage 2 closure of 95% and 50%, respectively. Sulfur hexafluoride (SF6) was used in this study, arguing a lower rate of the retinal hole, tear, or detachment due to its shorter intravitreal half-life<sup>8</sup>. It was demonstrated that IMH's with aperture sizes <200 and BCVA better than 20/40 achieved anatomic closure more frequently than larger holes<sup>8</sup>.

After PVD and VMT release, we observed in our patient a more even distribution of intraretinal fluid which may have elicited an increase in maximal foveal thickness, a consequent rounding of the hole edges, and a decrease of the hole aperture size (Fig. 1C). Two weeks after this sequence of events, anatomic closure with reabsorption of intraretinal fluid and a small neurosensory detachment were evident (Fig. 1D).

Complete neurosensory reattachment occurred 2 weeks later (Fig. 1E). Intravitreal C3F8 at a dose of 0.2 ml proved to be safe. Significant ocular hypertension after gas injection was absent and, therefore, a paracentesis was not needed. Because the anatomical closure took place in a period of 14 days after the procedure, a shorter intravitreal half-life gas such as SF6 could be used initially; nevertheless, a longer lasting bubble such as that of C3F8 could enhance macular stability and provide a better end-result since a subfoveolar neurosensory RD was present in our patient until week 4 after treatment.

Intravitreal injection of an inert expansile gas as the initial treatment of IMHs is a safe alternative, with minimal morbidity, few adverse events, less discomfort, and potentially great long-term anatomic and functional results. We suggest the use of 0.2 ml of C3F8 for the treatment of primary IMHs Stage 2 with hole aperture size <250  $\mu$ m, regardless of maximal foveal thickness, and even in cases with a presenting BCVA worse than 20/40 as a less invasive and alternative initial therapy. Studies with larger samples are required to enrich current evidence, identify the best-suited cases for intravitreal gas injection as well as the type and dose of the inert gas to be used.

## Conflicts of interest

The authors report no commercial or financial disclosure.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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