retinal detachment from malignant uveal melanoma: predictors and prognostic significance. Invest Ophthalmol Vis Sci 2001;42:2085–2093.
4. Char DH, Kroll S, Quivey JM, Castro J. Long term visual outcome of radiated uveal melanomas in eyes eligible for randomisation to enucleation versus brachytherapy. Br J Ophthalmol 1996;80:117–124.
5. Journee-de Korver JG, Oosterhuis JA, de Wolff-Rouendaal D, Kemmen H. Histopathological findings in human choroidal melanomas after transpupillary thermotherapy. Br J Ophthalmol 1997;81:234–239.

Central Serous Chorioretinopathy Associated With Administration of Sympathomimetic Agents

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PURPOSE: To report central serous chorioretinopathy associated with excessive use of compounds with sympathomimetic activity.

DESIGN: Observational case series.

METHODS: Four patients presented with clinical and fluorescein angiographic evidence of central serous chorioretinopathy. All patients expressed a concomitant psychogenic stress and high-dose ingestion of pseudoephedrine, oxymetazoline, or 3,4-methylenedioxymethamphetamine, all of which possess sympathomimetic properties.

RESULTS: In all cases, resolution of central serous chorioretinopathy coincided with cessation of the medication.

CONCLUSIONS: Patients afflicted with central serous chorioretinopathy should be notified about its possible association with sympathomimetic medications. (Am J Ophthalmol 2003;136:182–185. © 2003 by Elsevier Inc. All rights reserved.)

CENTRAL SEROUS CHORIORETINOPATHY (CSC) IS A DISorder characterized by serous detachments of the macula primarily afflicting young adults. The serous retinal detachments can involve spontaneous resolution with recovery of visual function; however, a subset of patients may experience permanent deterioration of visual function attributable to multiple recurrences. Exposure to corticosteroids have been implicated as potential risk factors in the development of central serous chorioretinopathy.[1–3] In vivo models have implicated sympathomimetic agents in the development of the disorder; however, no known clinical cases have been reported until now.[4]

This is the first observational case series describing three cases of central serous chorioretinopathy in association with the use of two over-the-counter sympathomimetic agents, pseudoephedrine or oxymetazoline (Table 1). We also describe the second known case of the disorder in association with use of 3,4-methylenedioxymethamphetamine (MDMA), an illicit drug with sympathomimetic properties (Table 1).

• **PATIENT 1:** A 43-year-old woman presented with acute visual complaints characterized as "a green circle in the center of vision" and distortion of central vision of the right eye. For allergic rhinitis, she had been ingesting excessive amounts of pseudoephedrine (that is, 45–75 mg every 4 hours). In addition, she acknowledged work-related stress. Best-corrected visual acuity (BCVA) was $20/25^{-2}$in the right eye (OD) and 20/15 in the left eye (OS). Ophthalmoscopic and angiographic examination revealed a serous elevation of the neurosensory retina located superotemporal to the fovea in the affected right eye consistent with central serous chorioretinopathy. During a follow-up examination (4 weeks later), she denied further use of pseudoephedrine and, coincidentally, experienced an improvement of BCVA to 20/15 OD but continued to observe a pale greenish circle inferonasal to fixation. Funduscopic examination of the right eye showed evidence of resolution with a shallower and smaller area of serous elevation. Three months later, she presented with dramatically worsening vision, distortion, and an exacerbation of the paracentral "green circle" of the right eye, which coincided with her reuse of pseudoephedrine. Best-corrected visual acuity decreased to 20/60 OD, and ophthalmoscopic and angiographic examination revealed an enlarged serous elevation with subretinal fibrinous changes within the superotemporal macula and involving the fovea. In the subsequent follow-up, at which time she had discontinued pseudoephedrine for 2 months, her BCVA had returned to 20/15 OD, and funduscopic examination revealed no subretinal fluid but some hard exudate precipitates with mild pigmentary alteration within the macular area.

• **PATIENT 2:** A 32-year-old man presented with a 3- to 4-day history of blurred vision described as a "central spot" of the left eye. He acknowledged ingesting 900 mg of pseudoephedrine during the past 4 days. Examination revealed BCVA of $20/25^{+3}$ OD and $20/30^{+3}$OS. Ophthalmoscopic and angiographic examination revealed a central serous detachment of the macula in the affected left eye

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TABLE 1. Patients With Central Serous Chorioretinopathy and Sympathomimetic Drug Use

Patient	Age	Eye	Sex	BCVA		Agent	Receptors		Recurrence
				Pre	Post		α−	β-	
1*	43	OD	F	$20/25^{-2}$	20/15	Pseudoephedrine	+	+	+
				20/60	20/15				
2	32	OS	M	$20/25^{-2}$	20/20	Pseudoephedrine	+	+	−
3	34	OD	M	20/20	n/a	Oxymetazoline	+	−	−
4	30	OD	M	$20/25^{-2}$	20/20	3, 4-MDMA	+	+	−

BCVA = best-corrected visual acvity; MDMA = methylenedioxymethamphetamine; n/a = not available; OD = right eye; OS = left eye.
*Patient 1: BCVA from initial and recurrent presentations.

consistent with central serous chorioretinopathy. During a follow-up examination, he denied further use of pseudoephedrine, experienced improvement of symptoms, and returned to his baseline visual function. Five months later, his BCVA was 20/20 OS and funduscopic examination revealed no subretinal serous fluid but a residual pigmentary alteration of the retinal pigment epithelium.

• **PATIENT 3:** A 34-year-old man presented with a 2-month history of decreased vision of the right eye. For 1 month before the examination, he had been experiencing sinus congestion and used oxymetazoline nasal spray (3 to 4 times a day). In addition, he had been taking fexofenadine hydrochloride. Approximately 2 weeks after using oxymetazoline, he began to experience visual changes of his right eye. Best-corrected visual acuity was 20/20 OD and 20/60 OS. Ophthalmoscopic and angiographic examination revealed a small disciform serous elevation within the macula of the right eye consistent with central serous chorioretinopathy (Figure 1A).

• **PATIENT 4:** A 30-year-old man presented with a 2-day history of blurred central vision of the right eye. Upon questioning, the patient admitted to the use of approximately six doses (100 mg/dose) of an illicit amphetamine, MDMA, 1 week before the emergence of visual symptoms. In addition, he had recently been promoted to what he considered a significantly more stressful employment responsibility. BCVA was $20/25^{-2}$ OD and 20/20 OS. Ophthalmoscopic and angiographic examination revealed a small serous detachment within the macula of the right eye consistent with central serous chorioretinopathy (Figures 1B and 1C). On the subsequent 4-month examination, during which time he had denied use of MDMA, his vision had improved to 20/20 OD, and the serous macular detachment had resolved, although a residual pigmentary alteration at the level of the retinal pigment epithelium was noted.

In vivo experimental models have implicated sympathomimetic agents in the development of central serous chorioretinopathy.[4] This is the first clinical case series defining a potential association between sympathomimetic use and the disorder. This is particularly important, because pseudoephedrine and oxymetazoline are available as over-the-counter medications. Pseudoephedrine and MDMA are α- and β-adrenergic receptors agonists, whereas oxymetazoline functions as an α-1a- and partial α-2a-adrenergic receptor agonist. Pseudoephedrine also induces the release of norepinephrine. Although the mechanism is unclear, an increase in choroidal blood flow induced with sympathomimetics may be influential in the development or exacerbation of central serous chorioretinopathy, because patients with the disorder exhibit hyperperfusion of choroidal lobules.[4,5]

The four patients presented here were diagnosed with central serous chorioretinopathy in association with acute sympathomimetic use. The emergence of visual symptoms occurred approximately 1 to 2 weeks after the excessive use of sympathomimetics. In one case, we observed a pattern of spontaneous resolution with discontinuation and recurrence with reuse of psuedoephedrine. Furthermore, in that particular case, discontinuation for 3 to 4 weeks was associated with spontaneous visual improvement and partial resolution of the serous elevation. We were unable to identify the precise resolution time in the other cases because the resolution of symptoms occurred before their subsequent examination. However, all patients experienced resolution of visual symptoms after discontinuation of the sympathomimetics. There was no evidence of subclinical cystoid macular edema in either the affected or unaffected eye, based on late-phase fluorescein angiograms in all cases.

At present, we have not identified bilateral central serous chorioretinopathy in association with sympathomimetic use. Although the cases presented here were unilateral, a previous report reporting MDMA use with central serous chorioretinopathy identified unilateral disease, similar to our findings. We do not suggest that unilateral disease is the rule; however, because the inhalation or ingestion of the drug should distribute equally to both eyes, similar to the systemic distribution of corticosteroids. Furthermore, unilateral or bilateral central serous chori-

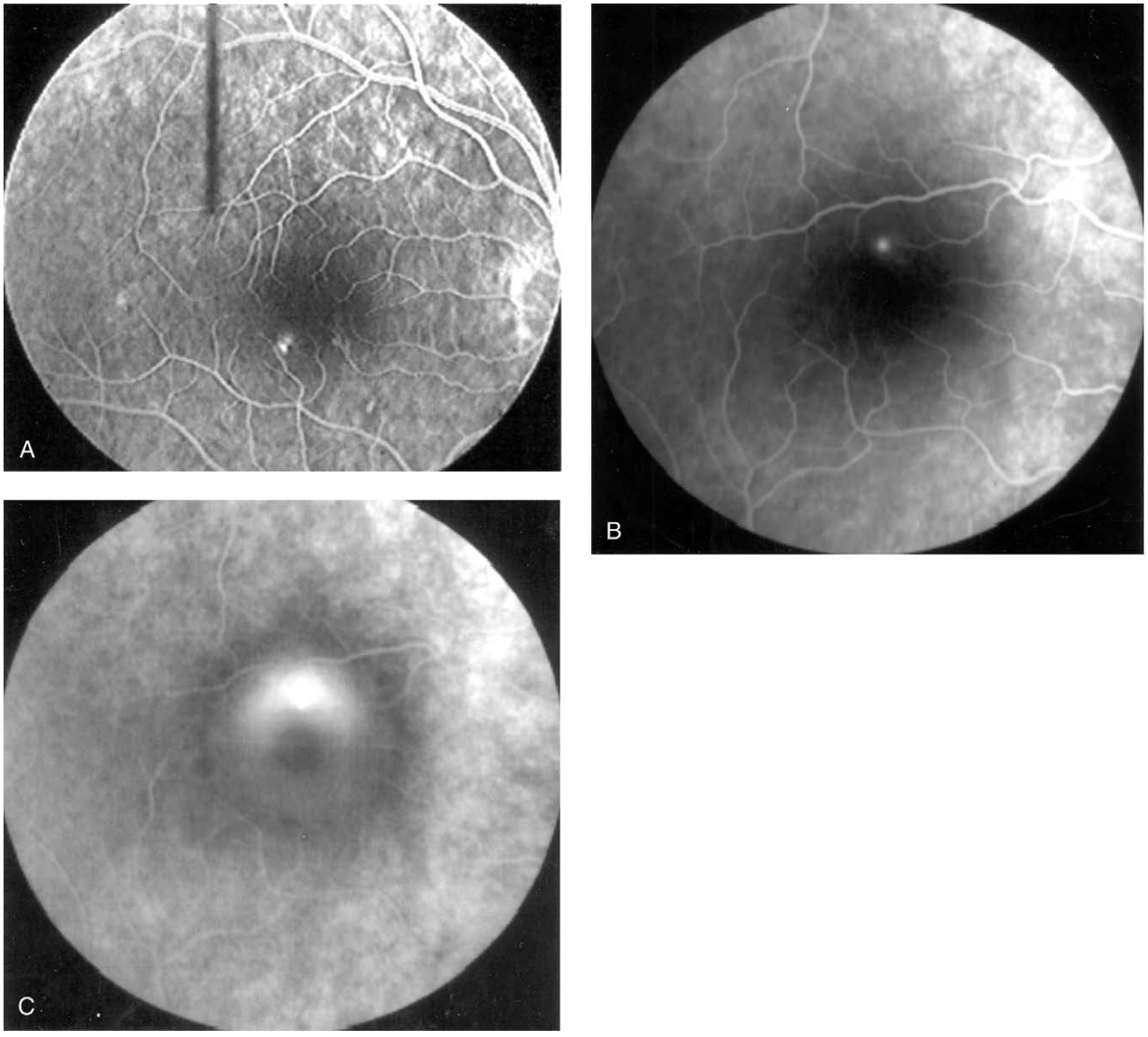

FIGURE 1. (A) Patient 3: Mid-phase fluorescein angiogram demonstrating a small hyperfluorescent focus of retinal pigment epithelium leakage in the inferotemporal aspect of the foveal avascular zone in a patient using oxymetazoline spray. (B) Patient 4: Mid-phase fluorescein angiogram demonstrating a single sharply circumscribed hyperfluorescent focus of retinal pigment epithelium leakage in a patient using MDMA. (C) Patient 4: Late-phase fluorescein angiogram showing fluorescein dye filling the area of the serous neurosensory retinal detachment in a patient using MDMA.

oretinopathy cases have been identified with the use of corticosteroid. The molecular mechanism that dictates unilateral or bilateral distribution in this disorder is not understood, but the choroidal tissue and the retinal pigment epithelium may have different susceptibilities to these agents and, therefore, to the development of either unilateral or bilateral central serous chorioretinopathy.

This observational case series represents the first report documenting a possible association between the excessive use of sympathomimetic agents and central serous chorioretinopathy, particularly in susceptible individuals. It may be prudent to question patients about sympathomimetic use and advise patients with central serous chorioretinopathy to discontinue use of these medications.

REFERENCES

1. Haimovici R, Gragoudas ES, Duker JS, et al. Central serous chorioretinopathy associated with inhaled or intranasal corticosteroids. Ophthalmology 1997;104:1653–1660.
2. Iida T, Spaide RF, Negrao SG, et al. Central serous chorioretinopathy after epidural corticosteroid injection. Am J Ophthalmol 2001;132:423–425.
3. Hassan L, Carvalho C, Yannuzzi L, et al. Central serous chorioretinopathy in a patient using methylenedioxymeth-

amphetamine (MDMA) or "ecstasy." Retina 2001;21:559–561.
4. Yoshioka H, Katsume Y, Akune H. Experimental central serous chorioretinopathy in monkey eyes: fluorescein angiographic findings. Ophthalmologica 1982;185:168–178.
5. Spaide RF, Hall L, Haas A, et al. Indocyanine green videoangiography of older patients with central serous chorioretinopathy. Retina 1996;16:203–213.

Observation of Idiopathic Full-thickness Macular Hole Closure in Early Postoperative Period as Evaluated by Optical Coherence Tomography

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PURPOSE: To report the optical coherence tomography (OCT)-determined progressive changes in a macular hole (MH) following vitreous surgery with a gas tamponade.
DESIGN: Observational case report.
METHODS: A 60-year-old woman with an idiopathic full-thickness MH (Gass, Stage 2) in the left eye underwent vitreous surgery with a gas tamponade. The progressive closure of the MH was followed by OCT because an unplanned decrease of the gas tamponade made the macula accessible to OCT examination.
RESULTS: On day 1, the tissue surrounding the MH extended into the center, and on day 2, the subretinal fluid and foveal cysts decreased and the retinal separation was reduced. On the third postoperative day, the MH was closed and the foveal contour was similar to that of normal retinas.
CONCLUSION: These results demonstrated that a small MH appears to be closed by 3 days after vitrectomy with gas tamponade. Although we cannot generalize to all sizes of MH, our findings suggest that small MHs are closed much earlier than reported and that the duration of maintaining a prone position can be shortened.

MACULAR HOLES (MHS) ARE CONSIDERED TO BE closed on the first few postoperative days, but it is recommended that patients maintain a prone position for 4 to 14 days[1] to keep the retina flattened by the gas tamponade. Needless to say, maintaining this position for any length of time is uncomfortable and inconvenient for the patient, and knowledge of the time required for the MHs to be sealed would be important for the comfort of patients.

Optical coherence tomography (OCT) images of the closing of a MH obtained through the silicon oil tamponade, and also images of impending MHs have been reported.[2,3] We describe a patient with a full-thickness MH who underwent vitrectomy with gas tamponade and in whom we were able to follow the closure process serially by OCT images, because the gas tamponade decreased inadvertently in the very early postoperative period.

The procedures used were approved by the Institutional Review Board of the Yamagata University School of Medicine and conformed to the tenets of the Declaration of Helsinki. An informed consent was obtained from the patient after an explanation of the procedures were presented.

A 60-year-old woman had a 1-month history of metamorphopsia in her left eye with a best-corrected visual acuity of 0.4 (corresponding to 20/50 on ETDRS scale). A MH (Gass, Stage 2) was detected by OCT and slit-lamp contact lens biomicroscopy (Figure 1, left; Figure 2, top). She consented to vitrectomy with SF6 gas tamponade and underwent vitreous surgery with internal limiting membrane (ILM) peeling.

On the first postoperative day, the SF6 gas bubble had decreased to approximately 20% of the vitreous space, probably due to leakage from one or more of the ports used for vitrectomy. We elected to inject additional gas to accelerate the healing, and a second gas injection (0.4 ml of pure SF6 gas) was performed 1 day after securing informed consent from the patient.

The preoperative and the postoperative OCT images through the fovea are illustrated in Figure 2 to demonstrate the changes in the foveal contour during the recovery process. On the first postoperative day, the tissue surrounding the macular hole was folded toward the center, but the cystic changes and retinal separation were still present (Figure 2, middle left). On the second day, the MH was closed and the cystic retinal changes were not present (Figure 2, middle right). A foveal depression was present on this second day after surgery, and the visual acuity was 0.4 (20/50).

On day 3, the MH was closed, and the foveal configuration was very similar to the normal state (Figure 2, bottom left). The visual acuity recovered to 0.8 (20/25) 3 months after the surgery. The MH has remained closed during the 1 year follow-up period (Figure 1, right), and the visual acuity was 1.0 (20/20) at the last visit.

Macular holes are considered to be closed in the first few postoperative days after vitrectomy with ILM peeling after a short period of gas tamponade (within 1 day) by the OCT images.[4] We present an interesting case in which it

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