However, an American Society of Retina Specialists 2017 survey showed that ICG remains in use and that retinal specialists, particularly those in the United States, prefer it to other dyes for assisting with epiretinal membrane and/or ILM peeling. This provides further evidence that toxicity of intravitreal ICG is still a relevant issue.

In conclusion, this report demonstrates that ICGA cannot be taken for a certain period after ICG-assisted ILM peeling in an eye with RD secondary to posterior scleritis. The atypical ICGA findings suggest that caution should be used to prevent unnecessary ICG diffusion within the eye (e.g., mixing ICG with viscoelastics[2]).

Appendix A. Supplementary material

Supplementary material related to this article can be found online at http://dx.doi.org/10.1016/j.jcjo.2017.10.025.

Yumi Noguchi, Tatsuhiko Sato, Miho Kumoi, Noriyasu Hashida, Kohji Nishida
Osaka University Graduate School of Medicine, Osaka, Japan.

Correspondence to:
Tatsuhiko Sato, MD, PhD: tatsusatou@gmail.com

References

1. Horiguchi M, Miyake K, Ohta I, Ito Y. Staining of the lens capsule for circular continuous capsulorrhexis in eyes with white cataract. *Arch Ophthalmol*. 1998;116:535-7.
2. Kadonosono K, Itoh N, Uchio E, Nakamura S, Ohno S. Staining of internal limiting membrane in macular hole surgery. *Arch Ophthalmol*. 2000;118:1116-8.
3. Auer C, Herbort CP. Indocyanine green angiographic features in posterior scleritis. *Am J Ophthalmol*. 1998;126:471-6.
4. Tadayoni R, Paques M, Girmens JF, Massin P, Gaudric A. Persistence of fundus fluorescence after use of indocyanine green for macular surgery. *Ophthalmology*. 2003;110:604-8.
5. Ciardella AP, Schiff W, Barile G, et al. Persistent indocyanine green fluorescence after vitrectomy for macular hole. *Am J Ophthalmol*. 2003;136:174-7.
6. Kersey TL, Bolton A, Patel CK. Serial autofluorescence imaging over two years following indocyanine green-assisted internal limiting membrane peel for macular hole. *Clin Exp Ophthalmol*. 2005;33:538-9.
7. Sayanagi K, Ikuno Y, Soga K, et al. Residual indocyanine green fluorescence pattern after vitrectomy for idiopathic macular hole with internal limiting membrane peeling. *Br J Ophthalmol*. 2007;91:939-44.
8. Sayanagi K, Ikuno Y, Soga K, Sawa M, Tano Y. Residual indocyanine green fluorescence pattern after vitrectomy with internal limiting membrane peeling in high myopia. *Am J Ophthalmol*. 2007;144:600-7.
9. Weinberger AW, Kirchhof B, Mazinani BE, Schrage NF. Persistent indocyanine green (ICG) fluorescence 6 weeks after intraocular ICG administration for macular hole surgery. *Graefes Arch Clin Exp Ophthalmol*. 2001;239:388-90.
10. Cekic O, Morimoto T, Ohji M, et al. Nonaxoplasmic transfer of indocyanine green into the optic nerve after intravitreal application. *Retina*. 2004;24:412-5.
11. Hisatomi T, Enaida H, Matsumoto H, et al. Staining ability and biocompatibility of brilliant blue G: preclinical study of brilliant blue G as an adjunct for capsular staining. *Arch Ophthalmol*. 2006;124:514-9.
12. Paques M, Genevois O, Regnier A, et al. Axon-tracing properties of indocyanine green. *Arch Ophthalmol*. 2003;121:367-70.

Can J Ophthalmol 2018;53:e158–e162
0008-4182/18/$-see front matter © 2017 Canadian Ophthalmological Society.
Published by Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.jcjo.2017.10.025

Central serous chorioretinopathy probably associated with isotretinoin in a keratoconus patient

Isotretinoin (13-cis-retinoic acid) is one of the most prescribed and efficacious treatments for severe acne vulgaris and other various skin disorders. However, it has well-recognized ocular side effects, such as meibomian gland dysfunction, blepharoconjunctivitis, dry eye, and decreased dark adaptation. The retinal side effects other than decreased dark adaptation or colour vision have been rarely reported.[1]

Central serous chorioretinopathy (CSCR) is a chorioretinal disease characterized by serous neurosensory retinal detachment in the posterior pole with an obscure etiology.[2] To the best of our knowledge, here we report the first case of CSCR likely caused by isotretinoin.

A 19-year-old male patient presented to our clinic with blurred vision in his right eye for 6 weeks. He was a medical student. He had been using oral isotretinoin 40 mg/day for the last 6 months, as prescribed by his dermatologist to treat acne vulgaris. He had keratoconus, and 2 years previously both eyes were operated on for corneal collagen crosslinking. On examination, the best-corrected visual acuity (BCVA) was 20/28 OD, with −1.50 spherical and −3.00 cylinder axis at 70° correction. BCVA was 20/20 OS with −2.25 spherical and −2.00 cylinder axis at 125° correction. There was no Vogt's striae, scar, or haze on slit-lamp examination. Dilated fundus examination revealed lobulated shallow serous retinal detachment in the right macula and yellow deposits at the central fovea (Fig. 1A).

Corneal topography was consistent with keratoconus, showing paracentral corneal thinning: 401 μm OD and 384 μm OS.

On fundus fluorescein angiography (FFA), multiple hyperfluorescent spots were seen in the temporal and inferior side of the fovea in the early phases. Late phase of the angiography revealed persistent and increased hyperfluorescence and serous macular detachment (Fig. 1B). Optical coherence tomography (OCT) through the right macula demonstrated neurosensory retinal detachment

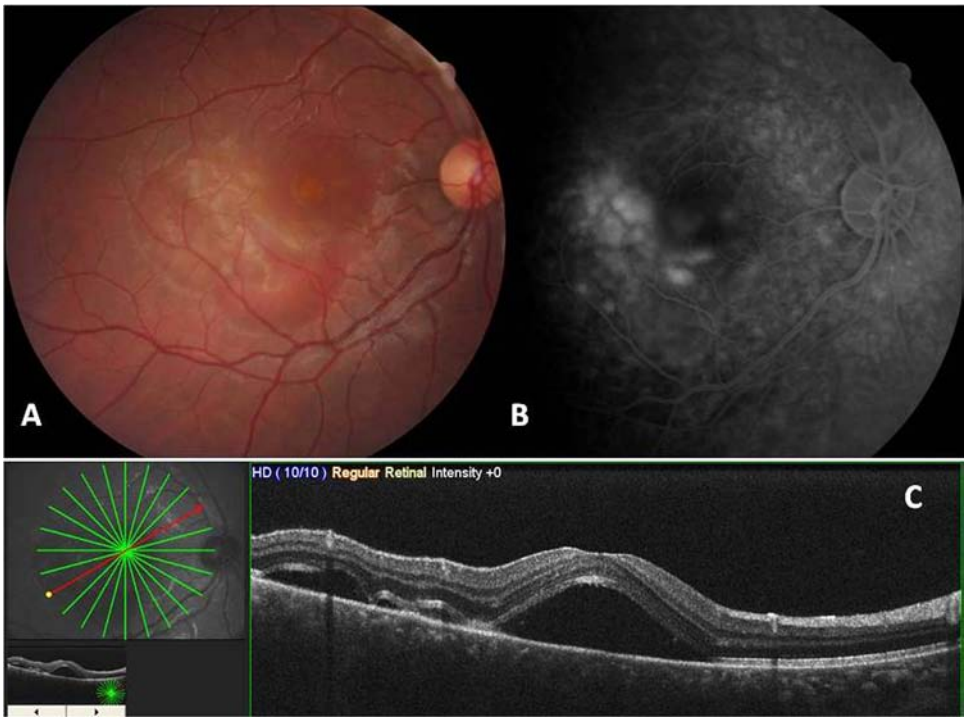

Fig. 1—(A) Fundus photograph of the right eye showing lobulated shallow serous retinal detachment in the right macula and yellow deposits at the central fovea. (B) Fundus fluorescein angiography of the right eye with persistent and expanded hyperfluorescence and serous macular detachment. (C) Optical coherence tomography of the right eye demonstrating neurosensory retinal detachment with subretinal fluid in a multifocal manner.

with subretinal fluid in a multifocal manner (Fig. 1C). The FFA and OCT findings were consistent with CSCR. Lifestyle changes were recommended. Oral isotretinoin treatment was discontinued because it was thought to be a possible causative agent.

One month later, BCVA increased to 20/20 OD, and OCT demonstrated totally recovered right macula with no residual subretinal fluid (Fig. 2).

Four months later, he presented again with blurred vision, this time in the left eye for 2 weeks. The BCVA was 20/25, and OCT showed serous retinal detachment on the left macula (Fig. 3). He reported that he had resumed taking isotretinoin again 5 weeks earlier on his own. His medication was discontinued, and in about 3 weeks the left eye recovered with BCVA 20/20 and no subretinal fluid in either eye on OCT.

The total follow-up time was 25 months, and no recurrence was seen after the discontinuation of isotretinoin. The BCVA is 20/20 OU, and there was no subretinal fluid at the last visit.

CSCR is characterized by detachment of the neurosensory retina due to accumulation of serous fluid between the photoreceptor outer segments and the retinal pigment epithelium (RPE) accompanied by changes in the RPE.[3] Hyperpermeability of choroidal vessels, impairment of choroidal vascular autoregulation, and dysfunction of RPE barrier and pumping play a role in the pathophysiology.[4] It occurs more commonly in

Fig. 2—Optical coherence tomography of the right eye 1 month after quitting isotretinoin, demonstrating totally recovered right macula with no residual subretinal fluid.

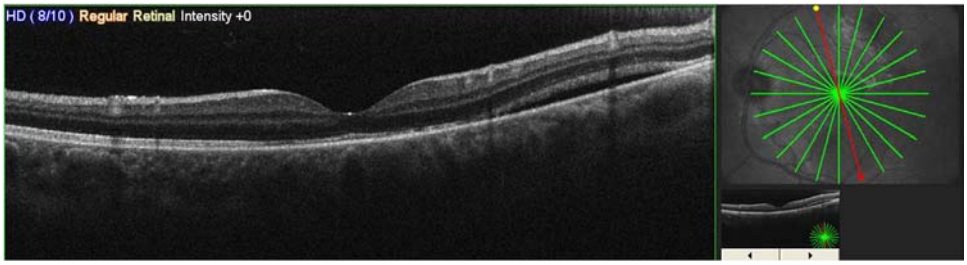

Fig. 3—Optical coherence tomography of the left eye demonstrating serous retinal detachment on the inferior part of the macula.

young men with unilateral presentation of metamorphopsia, micropsia, mild dyschromatopsia, and decreased contrast sensitivity.[2]

CSCR is generally self-limiting with spontaneous resolution of the subretinal fluid. Therefore, in the first 3 months of the disease no additional treatment is suggested, other than avoiding or treating risk factors such as steroid usage, antibiotics, alcohol, endogenous Cushing's syndrome, phosphodiesterase-5 inhibitor use, obstructive sleep apnea, pregnancy, type A personality, and psychosocial stress.[5] There was no known risk factor for CSCR in our patient, so we decided to discontinue isotretinoin and observe the patient.

Isotretinoin has been reported to have certain ocular side effects, such as meibomian gland dysfunction, ocular sicca, blepharoconjunctivitis, corneal abnormalities, decreased vision, decreased dark adaptation, increased tear osmolarity, myopia, and ocular discomfort, mostly involving the ocular surface according to Fraunfelder et al.[1] Decreased colour vision and persistent loss of dark adaptation were probable side effects. Abnormal retinal functions, including impaired night and colour vision, were reported in a number of studies, possibly due to interference with vitamin A metabolism and inhibition of retinol dehydrogenases.[6] Retinal findings other than abnormal night and colour vision, such as pigment disturbances, were conditional or unclassifiable side effects.[1]

The serous macular detachment in our patient appeared after isotretinoin administration and improved with discontinuation. Later, it appeared in the other eye with resumption of the drug and recovered after discontinuation. Therefore, we believe our patient's clinical situation is associated with isotretinoin. Moreover, according to the Adverse Drug Reaction Probability Scale (Naranjo algorithm), which consists of 10 questions to standardize assessment of causality for all adverse drug reactions, serous retinal detachment in our patient was a probable side effect of isotretinoin.[7] Isotretinoin might have caused RPE dysfunction by interfering with vitamin A metabolism and could have accelerated the detachment of the neurosensory retina in our case.

Our patient also had a coexistent ocular pathology, keratoconus, which was stable after collagen cross-linking, and his visual acuities were very good with eye-glass correction. Keratoconus is known to be associated with some other ocular pathologies. Could keratoconus have led to serous macular detachment in our case? There is only one report suggesting the coexistence with CSCR in 3 patients with keratoconus.[8] In that report, it was suggested that epithelium and basement membrane dysfunctions might be the common mechanism in the pathogenesis of those 2 entities. However, currently, the data in the literature are insufficient to conclude that serous macular detachment is associated with keratoconus in our patient.

The reason why this side effect was not encountered previously may be a latent defect in RPE metabolism, possibly related to keratoconus in our patient, which was manifested by isotretinoin.

Isotretinoin use probably caused serous macular detachment in our patient, but to support our suggestion, further case–control or cohort studies are required.

Nesrin Buyuktortop, Zafer Onaran, Fatma Özkal, Erhan Yumusak, Ayşe Anil Karabulut
Kirikkale University, Kirikkale, Turkey.

Correspondence to:
Nesrin Buyuktortop, MD: tortopn@kku.edu.tr

References

1. Fraunfelder FT, Fraunfelder FW, Edwards R. Ocular side effects possibly associated with isotretinoin usage. *Am J Ophthalmol.* 2001;132:299-305.
2. Liegl R, Ulbig MW. Central serous chorioretinopathy. *Ophthalmologica.* 2014;232:65-76.
3. Wang M, Munch IC, Hasler PW, Prünte C, Larsen M. Central serous chorioretinopathy. *Acta Ophthalmol.* 2008;86:126-45.
4. Nicholson B, Noble J, Forooghian F, Meyerle C. Central serous chorioretinopathy: update on pathophysiology and treatment. *Surv Ophthalmol.* 2013;58:103-26.
5. Liew G, Quin G, Gillies M, Fraser-Bell S. Central serous chorioretinopathy: a review of epidemiology and pathophysiology. *Clin Exp Ophthalmol.* 2013;41:201-14.
6. Turno-Kręcicka A, Grzybowski A, Misiuk-Hojło M, Patryn E, Czajor K, Nita M. Ocular changes induced by drugs commonly used in dermatology. *Clin Dermatol.* 2016;34:129-37.

7. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30:239-45.
8. Eandi CM, Del Priore LV, Bertelli E, Ober MD, Yannuzzi LA. Central serous chorioretinopathy in patients with keratoconus. *Retina*. 2008;28:94-6.

Can J Ophthalmol 2018;53:e162–e165
0008-4182/18/$-see front matter © 2017 Canadian Ophthalmological Society.
Published by Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.jcjo.2017.10.032