are required to better understand the risks, benefits, and limits of this therapeutic modality.

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Real-time Ophthalmoscopic Findings of Intraophthalmic Artery Chemotherapy in Retinoblastoma

Superselective intraophthalmic artery chemotherapy (SSIOAC) has become increasingly popular as a treatment for retinoblastoma. We describe the real-time ophthalmic findings of SSIOAC in a 5-month-old baby treated for bilateral disease.

Methods. After obtaining informed consent, SSIOAC was performed under general anesthesia. The right femoral artery was accessed using a Cathlon 24-gauge needle. A 0.018-inch access guidewire was passed through the needle and the needle was removed. A 4F access sheath was installed and attached to a heparin saline flush system. Heparin (100 IU/kg) was administered. A coaxial system was used. The guide catheter was a 4F glidcath (Terumo Europe NV). A straight Marathon microcatheter (0.51 mm; 1.5F at the distal tip; ev3 Neurovascular) was advanced through the guiding catheter right to the ostium of the ophthalmic artery. Selective angiography of the ophthalmic artery was performed. Every 5 minutes, the position of the catheter was checked under fluoroscopy. The infusion consisted of 2.5 mg of melphalan diluted in 30 mL of saline at a rate of 1 mL/min for 30 minutes.

A Retcam 1300 pediatric lens (Clarity Medical Systems) was used to take serial fundus photographs and videos every 4 minutes. The frequency of the imaging was adjusted according to the findings.

Results. Left Eye. During the infusion, there was visible intermittent pallor of the optic nerve and narrowing and blanching of the retinal vessels were noticed 24 minutes into the infusion. Immediate reperfusion was noticed when the injection was stopped, allowing for completion of the treatment.

Figure 1. Real-time ophthalmoscopic evaluation of the left eye. A, Pretreatment photograph. B, Visible pallor of the optic nerve and narrowing and blanching of the retinal vessels were noticed 24 minutes into the infusion. C, Immediate reperfusion was noticed when the injection was stopped, allowing for completion of the treatment.
No areas of choroidal ischemia or retinal precipitates were noted.

**Right Eye.** Sixteen minutes into the infusion, whitening of the nasal choroidal vasculature was noticed (**Figure 2B**). These changes were followed by severe generalized vasoconstriction of the retinal arteries and veins that progressed to total obscuration of the retinal arteries with no visible blood flow. The retinal arteries then completely whitened, consistent with intravascular retinal precipitates (**Figure 2C**). The infusion was stopped 1 minute later. The retinal and choroidal circulation remained compromised for an additional 3.5 minutes. The procedure was aborted after injecting 1.3 mg of melphalan in 15 mL of saline. Findings on fluorescein angiography performed 1 day later were unremarkable.

Signs of tumor regression were noticed in both eyes 1 week later. There were no systemic complications.

**Comment.** Transient acute chorioretinal ischemia can be detected during SSIOAC with melphalan. Isolated diffuse retinal vasculature blanching was immediately reversed, allowing for completion of treatment in the left eye. Vascular changes affecting both the retina and choroid in the right eye required additional time to recover and caused us to abort our treatment. We do not yet know the clinical significance of these ischemic episodes. Vasodilators such as nitroglycerin may prove useful. Also, the addition of real-time ophthalmoscopic observation into the current treatment protocol may alert the physician to tailor treatment to prevent acute toxic effects. We observed a favorable outcome of the tumor in the right eye despite a lower dose of chemotherapy. We can speculate that this effect may be either a direct response to melphalan or an indirect response to transient ischemia.

Our results are similar to those that Wilson et al1 found in a nonhuman primate model. We too had pulsatile optic nerve and choroidal blanching, retinal artery narrowing, and retinal artery precipitates. Other reported vascular complications from SSIOAC include avascular retinopathy,2 microemboli to retina and choroid, vitreous hemorrhage,3 ophthalmic artery stenosis,4 concomitant central or branch retinal artery occlusion, and choroidal atrophy.4

To our knowledge, we are the first to describe transient chorioretinal ischemia during SSIOAC with melphalan in real time. Direct visualization of the fundus dur-
ing the infusion may help to recognize this adverse effect and adjust the treatment accordingly. The early and long-term adverse effects of SSIOAC on the retinal and choroidal vasculature should be investigated.

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**ARMS2 A69S Polymorphism and the Risk for Age-Related Maculopathy: The ALIENOR Study**

Since the first evidence of an association of age-related maculopathy (ARM) with a locus on chromosome 10q26 (first named LOC387715, then renamed age-related maculopathy susceptibility 2 [ARMS2]) was reported,1,2 many case-control studies have confirmed this finding. However, few data are available from population-based studies, which are less subject to selection bias, and few studies have assessed the association of this polymorphism with early ARM.

In this study, we assessed the associations of ARMS2 A69S genotypes with early and late ARM in the framework of a population-based study of French elderly subjects.

**Methods.** The ALIENOR (Antioxydants, Lipides Essentiels, Nutrition et Maladies Oculaires) Study is a population-based epidemiological study on nutrition- and age-related eye diseases.3 It also aims to assess the association of eye diseases with genetic, vascular, and metabolic factors. Between October 2, 2006, and May 23, 2008, 963 residents of Bordeaux, France, aged 73 years or older were recruited among participants of an ongoing cohort study on vascular risk factors for dementia, the 3C Study.

We classified ARM from nonmydriatic 45° color retinal photographs taken using a nonmydriatic retinograph (TRC NW6S; Topcon). Photographs were interpreted according to the international classification4 in double by 2 trained technicians (Delphine Castanet and Helène Thebault) and adjudicated by a specialist (C.D.) when inconsistent. All cases of late ARM were confirmed by a retina specialist (J.-F.K., M.-B.R., and M.-N.D.). We classified ARM in 5 exclusive stages: none; early ARM1 (large soft distinct drusen without pigment abnormalities or pigment abnormalities without large soft drusen); early ARM2 (large [>125 µm] soft indistinct drusen and/or reticular drusen and/or large distinct drusen with pigment abnormalities); late atrophic ARM (pure geographic atrophy); and late neovascular ARM (serous or hemorrhagic detachment of the retinal pigment epithelium or sensory retina, subretinal or sub–retinal pigment epithelial hemorrhages, and fibrous scar tissue).

The ARMS2 A69S polymorphism (rs10490924) was determined from blood collected between April 15, 1999, and July 7, 2001, in the framework of a genome-wide association study performed in the 3C Study.5 Samples were genotyped with Illumina Human 610-Quad BeadChip (allowing the determination of 537 029 single-nucleotide polymorphisms) and subjected to standard quality control procedures.

Associations were estimated using logistic generalized estimating equations models, subjects without ARM

Table. Associations of the Different Types of Age-Related Maculopathy With ARMS2 A69S Genotypes, Adjusted for Age, Sex, CFHY402H Genotypes, and Smoking

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Early ARM1 (n = 144)</th>
<th>Early ARM2 (n = 110)</th>
<th>Late Atrophic ARM (n = 34)</th>
<th>Late Neovascular ARM (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GT</td>
<td>1.52 (1.03-2.23)</td>
<td>1.45 (0.85-2.49)</td>
<td>1.78 (0.70-4.50)</td>
<td>2.47 (0.98-6.23)</td>
</tr>
<tr>
<td>TT</td>
<td>4.60 (1.54-13.73)</td>
<td>13.77 (5.18-36.66)</td>
<td>23.63 (5.28-105.67)</td>
<td>16.15 (3.32-78.59)</td>
</tr>
</tbody>
</table>

Abbreviation: ARM, age-related maculopathy.

*Values are statistically significant at P < .05.