Retinal Vascular Precipitates During Administration of Melphalan Into the Ophthalmic Artery

We describe the real-time ophthalmic findings during 3 consecutive bilateral superselective intraophthalmic artery chemotherapy treatments in a 5-month-old baby with retinoblastoma.

Methods | After obtaining informed consent, 3 bilateral superselective intraophthalmic artery chemotherapy treatments were performed 1 month apart, following a previously described protocol.1 Each infusion consisted of 2.5 mg of melphalan in 30 mL of saline at a rate of 1 mL/min for 30 minutes per eye. A RetCam 1300 lens (Clarity Medical Systems) was used to take serial fundus photographs and videos. The frequency of the imaging was adjusted according to the findings. Care was taken to avoid applying pressure to the eye.

Results | First Treatment. Results of the first treatment were reported in detail elsewhere.1 In the right eye, signs of widespread chorioretinal ischemia including pulsatile pallor of the optic nerve, sectoral choroidal blanching, retinal arterial thinning, and intra-arterial retinal precipitates (IARPs) were noticed 16 minutes into the infusion. The infusion was immediately aborted and the IARPs persisted for 4.5 minutes. In the left eye, pulsatile pallor of the optic nerve, sectoral choroidal blanching, and marked retinal arterial thinning followed by loss of the blood column along the arterial and venous tree were intermittently recorded during the infusion. Immediate revascularization was noticed following temporary interruption of the infusion. No IARPs were detected. Treatment was completed.

Second Treatment. In the right eye, IARPs were noticed 8.5 minutes into the treatment. The infusion was immediately withheld. The IARPs persisted for 9.5 minutes. When clinical chorioretinal reperfusion was detected, the treatment was re-instituted and completed uneventfully (Figure 1). In the left eye, findings were similar to those of the first treatment.

Third Treatment. In the right eye, IARPs were noticed 28 minutes into the treatment. The treatment was aborted. The IARPs persisted for 11 minutes. In the left eye, the first episode of IARPs was recorded 20 minutes into the infusion and lasted 9 minutes. When complete chorioretinal reperfusion was clinically noticed, the infusion was continued (Figure 2, Video 1, and Video 2). A second ischemic episode with IARPs was recorded immediately after reinstitution of treatment, lasting 7 minutes. Treatment was aborted.

Figure 1. Serial Fundus Photographs Taken During the Second Intra-arterial Treatment of the Right Eye

A, Intra-arterial retinal precipitates were noticed 8.5 minutes into the treatment, affecting all 4 quadrants. B, Following abortion of treatment, reperfusion proceeded centrifugally in a pulsatile manner. C, The posterior pole was reperfused within the first 90 seconds. D, Full reperfusion of the posterior pole and peripheral retina was noticed clinically 9.5 minutes later.

[Video at jamaophthalmology.com]
Two months following completion of the treatments, the retinal and choroidal circulation appeared clinically normal. Bilateral electroretinograms were recorded as normal. The tumors were controlled.

**Discussion** | Vaso-occlusive disease has been described following superselective intraophthalmic artery chemotherapy as a potentially sight-threatening complication.2,4 The earliest reported changes consist of ophthalmic and retinal artery occlusions at 1 month following treatment.2 Choroidal vascular atrophy was reported several months later.2 We hypothesize that our intra-procedural vaso-occlusive findings are the cause of vaso-occlusive disease reported by others as late findings. Real-time observation combined with titration of chemotherapy administration may prevent some of these late vaso-occlusive complications.

We hypothesize that these ischemic events would have increased in duration had the infusion been allowed to continue. The IARPs persisted in the right eye and increased in duration with each successive treatment despite immediate withholding of treatment, administration of nitroglycerine, and/or removal of the catheter from the ostium of the ophthalmic artery (Table). In the left eye, the pattern of ischemia changed, from transient ischemic episodes to the presence of IARPs.

Despite our titrated treatment, we had late finding of mild retinal pigment epithelial clumping with normal retinal vasculature and a normal electroretinogram at 2 months’ follow-up (Figure 2). Further studies are needed to elucidate the maximal ischemia that the choroid can tolerate and the role of electroretinography in monitoring these patients.

Until more information becomes available, we are proposing real-time examinations during the infusion with the goal of decreasing the duration of an acute ischemic event.

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Prenatal Presentation of Fronto-orbital Congenital Infantile Fibrosarcoma: A Clinicopathologic Report

Congenital infantile fibrosarcoma (CIFS) is a mesenchymal tumor that occurs in the first year of life and rarely involves the orbit. We describe a patient with a prenatal presentation of orbital and forehead CIFS.

Report of a Case | A prenatal ultrasonographic scan at 37 weeks’ gestation showed a large right frontal mass with orbital involvement (Figure 1A), prompting early cesarean delivery. At birth, the mass was 9 × 7 × 4 cm, firm, nonpulsatile, and opaque, with dark and vascular discoloration inferiorly (Figure 1B). Postnatal ultrasonography, computed tomography, and magnetic resonance imaging showed a variegated soft-tissue mass at the glabella extending into the right superomedial orbit and displacing the right globe downward (Figure 1C and D). The anterior tables of both frontal bones were thinned, including a 5-mm-diameter bony defect with associated periosteal thickening. On day 8, the lesion was surgically excised, with preservation of pseudocapsule integrity except in the deep orbit, where the tumor tail was excised piecemeal. The frontal defect was reconstructed with local flaps.

Morphological, immunohistochemical, and molecular features were consistent with a diagnosis of CIFS. Fluorescence in situ hybridization confirmed translocation involving ETV6.

Figure 1. Ultrasonographic, Clinical, Computed Tomographic, and Magnetic Resonance Images

A, The 4.5 × 4.2 × 3.0-cm mass on a prenatal ultrasonographic scan at 37 weeks’ gestation. B, Clinical image from day 1 of life. C, Sagittal computed tomographic image showing globe displacement and compression by the mass. D, Postnatal sagittal magnetic resonance image showing a large variegated lesion with patchy intralesional hyperattenuations consistent with hemorrhage.