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An unusual case of bilateral tractional detachment

One of the most common etiologies of tractional retinal detachment (TRD) is proliferative diabetic retinopathy. The pathogenesis consists of chronic ischemia leading to elevated vascular endothelial growth factor (VEGF) which stimulates neovascularization and subsequent fibrovascular complexes that place tractional and shearing forces on the neurosensory retina[1]. We present a case of bilateral TRD in a young patient with multiple comorbidities that could contribute to chronic vasoconstriction, especially unilateral Moyamoya disease and chronic methamphetamine abuse.

A 38 year-old male without ocular history presented to clinic with subacute bilateral painless decreased vision. Medical history revealed type 2 diabetes mellitus, hypertension, obesity, alcohol and tobacco dependence on Metformin, Lexapro, and Chantix. Visual acuities were 3/200 OD, 20/150 OS; IOP 17 OD, 19 OS; pupils and slit lamp exams were normal except for mild cataracts. Fundus examination and optical coherence tomography (Figure 1), however, revealed bilateral macula-off tractional retinal detachments, extensive neovascularization overlying nerves, vitreous hemorrhage, and macular edema consistent with proliferative diabetic retinopathy. He underwent bilateral intravitreal Eylea injections, an uncomplicated surgery in left eye, with post-op week one vision remaining 20/150 with resolution of detachment (Figure 2).

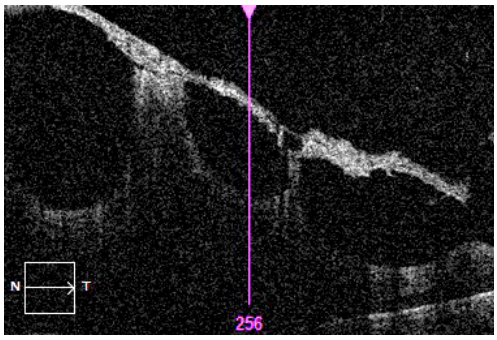

Figure 1: Optical Coherence Tomography of left macula revealing detachment with subfoveal traction. This patient had bilateral tractional retinal detachments

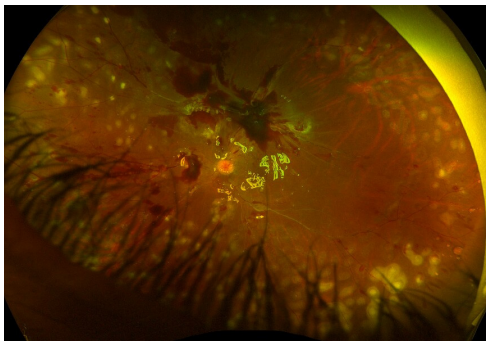

Figure 2: Post-operative week one, left eye. Unfortunately no pre-operative fundus photo of the left eye is available.

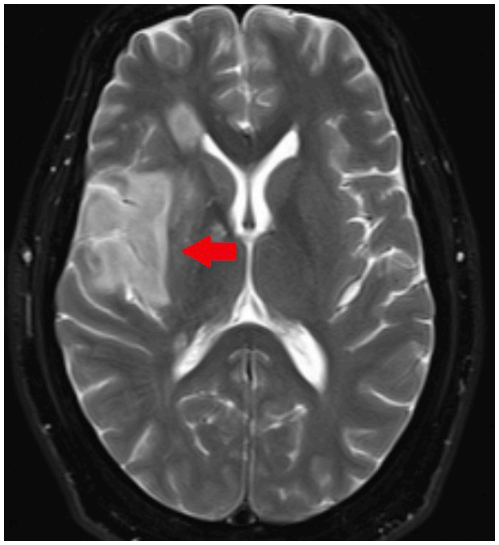

Figure 3A: Axial section of MRI brain revealing acute right middle cerebral artery infarct.

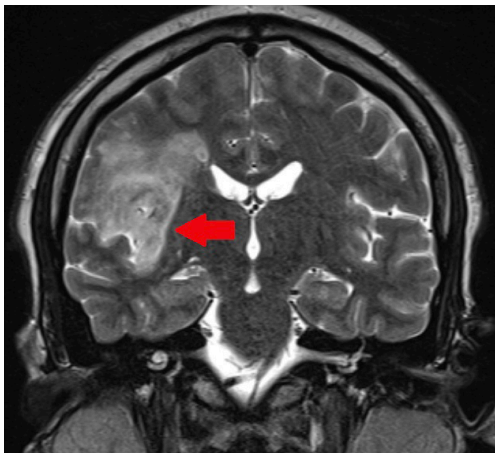

Figure 3B: Coronal section demonstrating corresponding middle cerebral distribution.

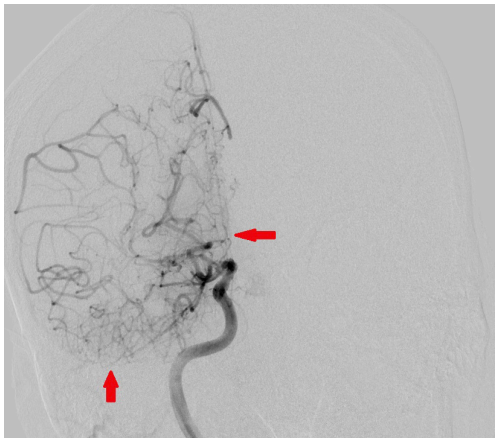

Figure 4A: Cerebral angiography of right intracranial vasculature. Diagnosis of Moyamoya disease based on complete right internal carotid artery terminus occlusion with collaterals suggestive of chronicity.

On postoperative day ten, the patient was admitted to the hospital again and found to have multiple acute cerebrovascular events outside the window for tPA. Lab workup and echocardiogram with bubble study were unrevealing. Head and neck CTA revealed occlusion of the right middle cerebral artery with narrowing of the right anterior cerebral artery, with corresponding MRI of the brain demonstrating acute infarcts along the right middle cerebral artery territory (Figure 3). Cerebral angiography findings were consistent with complete occlusion of right internal carotid artery (Figure 4). Such were demonstrative of Moyamoya syndrome.

Interestingly, hemoglobin A1c was 6.3 and urine drug test was positive for methamphetamines. This patient was optimized on cardiovascular medications and underwent uncomplicated right sided encephaloduroarteriosynangiosis with neurosurgery several months later. This procedure involves the transposition of a portion of a scalp artery onto the surface of the brain. This procedure is meant to improve collateral blood flow to the brain. The patient was lost to follow-up.

Moyamoya disease is an idiopathic vasoconstrictive and occlusive syndrome with peak prevalence in the second decade of life in males or third decade in females[2], caused by progressive stenosis of the branches of the Circle of Willis. This syndrome was named by researchers who noted unique “puff of smoke” collaterals on cerebral angiography[3], the primary mode of diagnosis. Patients present with stroke symptoms due to recurrent cerebral ischemia and hemorrhages. Reported ocular manifestations include amaurosis fugax, central retinal artery occlusion, ocular ischemic syndrome, and morning glory disc anomaly[3].

Though initially presumed to be proliferative diabetic retinopathy, our case was not straightforward as his hemoglobin A1c of 6.3 was insufficient to explain such severe ischemic diabetic retinopathy. Unilateral Moyamoya disease and possibility of ocular ischemic syndrome do not fully explain bilateral retinopathy either.

One possibility for bilateral ischemic retinopathy is concomitant use of methamphetamine, a synthetic amine that can be ingested, inhaled, or injected, that induces both acute and chronic effects on the central and peripheral nervous systems by way of raising levels of monoamine neurotransmitters. Methamphetamine has been reported to induce cerebral vasculitis leading to ischemic or hemorrhagic cerebral infarctions through repeated vasospasms, arterial narrowing, and intracranial arterial beading[4]. Although Moyamoya was diagnosed in this patient, this case is likely multifactorial with chronic cerebrovascular changes can lower the threshold for acute stroke with use of sympathetic substances such as cocaine[5] and in our case, methamphetamines.

Ocular manifestations of methamphetamine use include episcleritis, scleritis, corneal ulceration via neurotoxicity, and retinal vasculitis resembling polyarteritis nodosa[6]. Few individual case reports have been reported bilateral ischemic retinopathy in the presence of methamphetamine use, with possible mechanism being production of oxidative stress that in turn causes vasoconstriction and vasospasms, leading to ischemia and neovascularization. The pathophysiology remains unclear, but Wallace et al report an OCTA of a patient using intranasal methamphetamine for seven years demonstrating dropout of both superficial and deep capillary plexuses within the neurosensory

retina[7]. An in vivo study measuring inflammatory markers and retinal proteins in mice after administration of methamphetamine showed vascular loss of platelet endothelial cell adhesion molecule-1 (PECAM-1) and glycocalyx in the central retinal artery and an increase of several matrix metalloproteinases in vessel walls. They postulated that methamphetamine is involved in retinal degeneration by way of vascular endothelial wall dysfunction[8]. Other reported retinal manifestations include central retinal artery or vein occlusions, intraretinal hemorrhages, and retinal vasculitis, all of which are attributed to vascular spasms[9].

Treatment specific to retinopathy resulting from methamphetamine use has not been reported, however one can treat based on the pathophysiology of neovascularization and tractional retinal detachments. This includes anti-VEGF intravitreal injections to control neovascularization followed by release of traction via vitrectomy, peeling fibrous membranes, and re-opposing the retina with a tamponading agent such as silicone oil. This approach seemed to have worked well for our patient (with limited follow-up). Additionally, involving addiction medicine to help with substance abuse and a primary care team to optimize vascular comorbidities is recommended.

In summary, this is likely a multifactorial case of methamphetamine-induced ischemia to bilateral eyes in the presence of unilateral Moyamoya disease that led to bilateral tractional retinal detachments in an otherwise well-controlled diabetic patient.

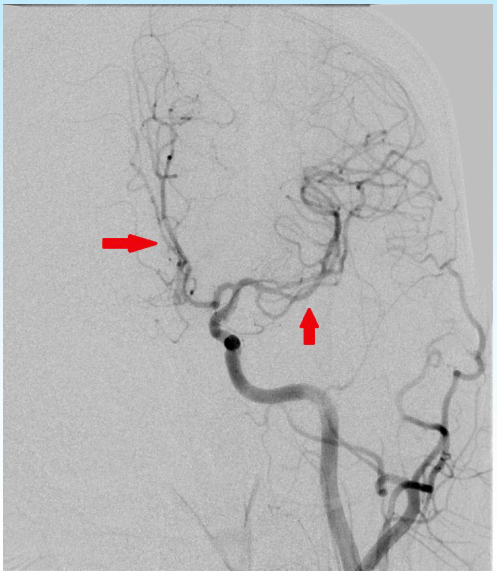

Figure 4B: Left internal carotid and branches appear patent.

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Enrolling Studies:

Dry AMD

Teaneck and Toms River

Gallego: A Phase II, Multicenter, Randomized, Single-masked, Sham-controlled Study to Assess Safety, Tolerability, and Efficacy of Intravitreal Injections of FHTR2163 in Patients with Geographic Atrophy Secondary to Age-related Macular Degeneration (Gallego)

Diabetic Retinopathy

Teaneck

Altitude: A Phase 2, Randomized, Dose-escalation, Observation-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of RGX-314 Gene Therapy Delivered Via One or Two Suprachoroidal Space (SCS) Injections in Participants with Diabetic Retinopathy (DR) without Center Involved-diabetic Macular Edema (CI-DME) (ALTITUDE)

Wet AMD

Edison

Opthea Coast: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Aflibercept, Compared with Aflibercept Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Toms River

Opthea Shore: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Ranibizumab, Compared with Ranibizumab Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Teaneck

Daylight: :A Two-arm, Phase 3 Study to Evaluate the Efficacy and Safety of Intravitreal KSI-301 Compared with Intravitreal Aflibercept in Participants with Neovascular (Wet) Age-related Macular Degeneration.

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