Acquired Segmental Iris Dilator Muscle Synkinesis Due to Deglutition

Congenital ocular “misdirection dyskinesis” typically involves multiple cranial nerves. Acquired peripheral misdirection usually occurs in the same nerve; less frequently, more than one nerve are involved. We describe an unusual synkinesis of the iris dilator muscle due to deglutition, presumably caused by posttraumatic aberrant outgrowth of vagal nerve fibers to the cervical sympathetic chain.

Report of a Case. We describe an unusual synkinesis in a 10-year-old boy. On the sixth day of life a neuroblastoma was removed from the right side of his neck. A right-sided Horner syndrome and paralysis of the recurrent laryngeal nerve occurred postoperatively, as well as a flaccidity of the right soft palate, a deviation of the tongue to the right side, and an atony of the esophagus and the stomach that regressed within 2 weeks. When the child was 2 years old, the parents recognized that his right pupil became distorted when he was drinking and afterward regained its round shape within a few seconds. The iris appeared to tighten radially at the 7:30- and 1:30-o’clock positions. When we examined the patient at 10 years of age we confirmed these findings. A right-sided ptosis, facial vasodysregulation (flushed left side of the face, pale right side of the face after exercise), and anhidrosis (from forehead to larynx region; iodine starch reaction) were present, but not iris heterochromia. The right pupil dilated poorly on instillation of 4% cocaine hydrochloride and 5% pholedrine formate (equivalent to 1% hydroxyamphetamine hydrobromide; Figure 1).

Comment. The findings indicated a lesion of the postganglionic (third order) sympathetic neuron, either primary or by transsynaptic degeneration. Some axons of the postganglionic neuron must have been intact, because the synkinesis requires adrenergic innervation of the iris dilator muscle. There is a close topographic relationship among the sympathetic superior cervical ganglion, the inferior ganglion of the vagus nerve, the hypoglossal nerve, and the glossopharyngeal nerve.1 The esophagus and stomach atony and the recurrent laryngeal nerve paresis indicate an injury to vagal fibers. The swallowing disorder, the flaccidity of the soft palate, and the remaining deviation of the extended tongue indicate involvement of hypoglossal and glossopharyngeal fibers. We assume that the origin of the misinnervation was vagal, because the pupillary distortion could be elicited only by drinking, when permanent, significant esophageal peristalsis is required; but not by lower swallowing frequency (eating) and low volume load (saliva) at the same swallowing frequency as when the child was drinking. That is, the pupillary distortion was elicited mainly by the voluntary sequence of the swallowing act, which requires activity of the hypoglossal and glossopharyngeal nerves.

Descending vagal fibers in the neck are adjacent to the fibers of the ascending sympathetic chain (Figure 2). If these fibers are injured at the same time, aberrant vagal sprouts can grow into the cervical sympathetic path.2 Since the vagal sprouts are cholinergic, some of them may be lost owing to pharmacological incompatibility. But, if they reach sympathetic ganglion cells in the superior cervical ganglion, they may make a permanent—albeit inappropriate—cholinergic connection. If these sprouting fi-

Figure 1. Right-sided Horner syndrome, without swallowing (A), with pupillary distortion due to swallowing (B), 30 minutes after instilling 5% pholedrine formate in both eyes (an identical anisocoria was present after instilling 4% cocaine hydrochloride in both eyes) (C), and 15 minutes after instilling 5% phenylephrine hydrochloride in both eyes (D). Pupillary diameter expressed in millimeters for the right eye/left eye is as follows: (A) 4.5/5.2, (B) 7.3×7.4, (C) 4.5/7.4, and (D) 7.4/7.4.

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bers are to survive, they must still be connected to their original vagal ganglion cells.

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Cyclosporine-Induced Resolution of Choroidal Neovascularization Associated With Sympathetic Ophthalmia

Choroidal neovascularization (CNV) is a sight-threatening complication of sympathetic ophthalmia, a classic example of endogenous posterior uveitis.1,2 Cyclosporine (cyclosporin A) has been shown to be effective in the treatment of sight-threatening disease associated with active intraocular inflammation in adults.3 We present a case report illustrating resolution of CNV in a child with active refractory sympathetic ophthalmia after starting cyclosporine therapy.

Report of a Case. A 3-year-old boy had a limbal rupture involving uveal prolapse of his right eye after he fell on his feeder cup. Primary repair was performed and postoperative visual acuity was 20/80 OD and 20/20 OS. When sympathetic ophthalmia developed 4 months later, his visual acuity deteriorated to finger counting in both eyes. Oral prednisone therapy at 1 mg/kg per day was started. His uveitis improved slowly; 1 year later he achieved a visual acuity of finger counting OD and 20/30 OS while receiving a maintenance dose of 1 mg/kg on alternate days. Funduscopy of the left eye revealed mild vitritis and a yellowish macular lesion, with a surrounding hyperpigmented ring and circinate hard exudates, which was clinically consistent with CNV (Figure 1). Despite systemic prednisone therapy, his visual acuity worsened to 20/200 OS 10 months later. Systemic cyclosporine therapy was added at 5 mg/kg per day. Three months later, visual acuity improved to 20/100 OD and 20/60 OS with resolution of left macular edema and hemorrhage (Figure 2).
Visual improvement continued, due to vitritis remission and complete CNV regression (Figure 3). Cyclosporine therapy was withdrawn 25 months after commencement. Then the patient’s visual acuity was 20/100 OD and 20/30 OS despite a residual atrophic left macular scar.

Comment. Sympathetic ophthal-mia–induced CNV has been reported twice,1,2 to our knowledge, both cases in children. Sympathetic ophthal-mia–induced CNV regression may have been spontaneous, but is not described when uveitis is active, as in our patient. Although it has proven effective in adult cases,3 cyclosporine therapy has rarely been used in pediatric refractory uveitis.1,2 When associated with active aggressive refractory uveitis, cyclosporine therapy suppresses the inflammatory response1 and contributes to resolution of inflammatory-induced CNV.

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Helicoid Peripapillary Chorioretinal Degeneration in Abetalipoproteinemia

Abetalipoproteinemia is a rare autosomal recessive disorder characterized by the absence of apolipoprotein B.1 It is caused by mutations of the microsomal triglyceride-transfer protein gene.2 Ocular manifestations include retinitis pigmentosa–like changes, nystagmus, ophthalmoplegia, ptopis, cataracts, anisocoria, and angioid streaks.1 Helicoid peripapillary chorioretinal degeneration (HPCD) is characterized by chorioretinal atrophy that radiates from the optic disc as winglike extensions.4 No systemic disease has been associated with HPCD. We report a case of HPCD associated with abetalipoproteinemia.

Report of a Case. A 24-year-old woman had been diagnosed with abetalipoproteinemia at age 2 years. The diagnosis was based on peripheral blood acanthocytosis, low serum cholesterol levels, absence of serum lipoprotein, and characteristic lipoid deposits in mucosal cells on small bowel biopsy. She was treated with vitamin E injection and oral vitamins A, D, and K. Results of initial ocular examinations were within normal limits.

At age 18 years, the patient voluntarily discontinued treatment with vitamin supplementation; afterward she reported worsening of night vision and progressive field changes. She was evaluated at the Ocular Genetics Clinic of The Hospital for Sick Children, Toronto, Ontario, at age 24 years. Best-corrected vision was 20/20 OU. Refraction was −0.75×0.50×165° OD and −1.00×1.00×175° OS. Ophthalmoscopy showed bilateral and symmetric helicoid peripapillary changes (Figure 1), equatorial retinal pigment epithelium (RPE) mottling, and attenuation of blood vessels but absence of true angioid streaks. There was no sign of inflammation. Fluorescein angiography showed a large peripapillary defect with no evidence of leakage or angioid streaks (Figure 2). A Goldmann visual field examination revealed bilateral constriction of the peripheral field and enlargement of the blind spot. Electroretinogram recordings were severely attenuated to all stimuli.

The serum level of vitamin A was 0.20 µmol/L (normal range, 1.05-3.14 µmol/L), whereas for vitamin E, it was 7.0 µmol/L (normal range, 12.0-46.0 µmol/L). Vitamin therapy was restarted, and 6 months into treatment there was no progression of symptoms.

Comment. Helicoid peripapillary chorioretinal atrophy is a rare disorder characterized by winglike chorioretinal atrophy emanating from the optic disc. A dominant form was recently mapped to chromosome 11p15.4 The differential diagnosis of HPCD includes serpiginous chorioiditis, angioid streaks, malignant myopia, paravenous retinocoroidal atrophy, and radial lattice reti-
nal degeneration.\textsuperscript{3} The absence of inflammatory signs, the symmetry of the fundus lesions, the characteristic wing-shaped atrophy, and the absence of leakage on fluorescein angiography in our patient support the diagnosis of HPCD.\textsuperscript{5}

Brazitikos and Safran\textsuperscript{6} suggested that HPCD is caused by dysplastic abnormalities of the peripapillary RPE, which predispose it to damages from mechanical stretching of the globe during growth, progressive tearing of the RPE, and subsequent chorioretinal atrophy. The pathogenesis of HPCD, and its possible relationship to angiod streaks remains to be clarified.

Vitamin E deficiency has been implicated as a cause of retinal changes in abetalipoproteinemia.\textsuperscript{7} Vitamin E acts as a free radical scavenger and prevents oxidative injury to membrane lipids.\textsuperscript{1} Deficiency of vitamin E may decrease its protective effect on the RPE, predisposing the RPE to the tearing mechanism proposed by Brazitikos and Safran.\textsuperscript{6}

To our knowledge, this case represents the first association of HPCD with abetalipoproteinemia. Whether HPCD represents a true distinct manifestation of abetalipoproteinemia or a variant of angiod streaks remains to be clarified.

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Long-term Persistence of Antirecoverin Antibodies in Endometrial Cancer-Associated Retinopathy

Autoantibodies to recoverin are found in the serum of patients with cancer-associated retinopathy syndrome (CAR), in which retinal degeneration occurs in the presence of systemic tumor growth without metastasis to the eye. The presence of antirecoverin antibodies has, so far, been associated with small cell carcinoma of the lung. We describe a patient with an endometrial carcinoma who possesses T cells and antibodies that react with recoverin. The demonstration of autoantibodies in a patient’s serum is important to the diagnosis of CAR and cancer and monitoring treatment of diseases. Although several studies have reported the presence of antibodies specific to CAR antigens even before the diagnosis of cancer, to date, no long-term follow-up studies have examined the prevalence of antirecoverin antibodies in those patients’ recoverin.

Report of a Case. A 61-year-old white woman had endometrial cancer in 1991 and had had a hysterectomy for undifferentiated carcinoma with neuroendocrine features in September 1991. In July 1992, metastatic disease of the lumbar spine was detected. The tumor was surgically removed; she was treated with a
combination of radiation and 5-fluorouracil. In October 1992, she noticed floaters, “dark” vision with a loss of color vision in the left eye, and “blurring vision” in the right eye. Visual acuity was 20/70 OD and counting fingers OS. A fundus examination showed vitreous cells (possible vitreitis) and optic nerve pallor. In December 1992, her vision worsened. Her blood serum tested positive for the presence of antirecoverin antibodies, which led to the diagnosis of CAR. She was given methylprednisolone (Medrol), and her vision improved to 20/25+ with full color vision and full fields in the right eye, and 20/400 with poor, but improved, color vision and damaged fields in the left eye with eccentric gaze. She had osteoporosis and posterior subcapsular cataracts; treatment with steroids was tapered. Her vision decreased again, and she tested positive for recoverin antibodies in March 1993. Her dose of methylprednisolone was increased, which led to improvement in her visual acuity to 20/25 OD and 20/400 OS, but by May 1993, her vision deteriorated again. She received no positive effect from increasing her dose of methylprednisolone even to very high doses; therefore, treatment with methylprednisolone was stopped. Results of multiple metastatic workups, including magnetic resonance imaging, computed tomographic scans, bone scans, blood tests, x-ray films, and clinical examinations, were negative. Cancer-associated retinopathy antigens tested negative. The patient was given a combination of megestrol acetate (Megace) and 714X (an experimental drug to prevent cancer recurrence). In December 1993, her electroretinogram showed no cone response, despite computer averaging, and a highly abnormal rod response, about 1% of normal. Dark adaptation was elevated. In February 1994, she underwent left hip replacement for a hip fracture that was due to the heavy steroid treatment. In January and April 1994, plasmapheresis was performed and her color vision improved immediately; however, in May, her vision worsened again. Her electroretinogram showed a barely detected response, about half of the response 6 months previously. In August 1994, the antibody titer started to gradually increase and reached a very high level (1:12 800). There were no signs of metastasis. She was prescribed Tolpa Torf Preparation, a natural immunomodulator drug. The antirecoverin antibody level dropped dramatically and reached almost normal levels in July 1995; at this point her visual acuity stabilized at hand motions OU.

**Antirecoverin activities of serum antibodies and lymphocytes were measured over 3 years (Figure 1).** The specificity of antibodies was confirmed by immunostaining of purified recoverin (Figure 2). Iso-typing showed that antirecoverin antibodies were mostly IgG1. Because we recently have demonstrated that recoverin was expressed in lung carcinoma of a patient with CAR,1 we tested the patient’s tumor for recoverin expression. A reverse transcription–polymerase chain reaction yielded the predicted size of products corresponding to the recoverin sequence from the endometrial carcinoma and a normal donor retina used as a control source of recoverin, Figure 2.

**Comment.** Although there have been 3 previous case reports of CAR syndrome associated with endometrial cancer,2,4 to our knowledge this is the first such case where antirecoverin antibodies and T-cell responses have been documented. Un-
Antirecoverin antibodies have only been demonstrated in patients with small cell carcinoma of the lung. This case is unique in two respects. First, to our knowledge this is the first time that an endometrial cancer in a patient with CAR has been shown to express messenger RNA for recoverin, suggesting that the aberrant expression of this protein, normally expressed only in the eye, might have triggered the abnormal immune response. Also novel is the documentation of persistent elevated level of antirecoverin antibodies in the serum after the presumed source of autoantigen (recoverin in endometrial cells) had been removed.

Our recent studies have shown that antirecoverin autoantibodies could penetrate living cells and trigger retinal cell death that occurs through an apoptotic mechanism.1 If antibodies play a causative role in the syndrome, the prolonged presence of serum antibodies in the circulation is detrimental and should be controlled. Steroid treatment, plasmapheresis, and immunomodulation with Tolpa Peat Preparation were effective in lowering those antibodies in the serum, vision was stabilized, and occasionally improved. In contrast, T-cell activities were moderate to low, and increases were not accompanied by overt disease, probably suggesting a lesser role in the pathogenicity.

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Figure 1. Fundus photograph of the left eye demonstrating morning glory disc anomaly and macular hole (arrow). Macular hole appears closer to the disc than normal due to the enlargement of the optic disc rim.

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The studies were performed in accordance with our institution’s guidelines. Legacy-Institutional Review Board has approved the protocols and informed consent has been obtained.

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Morning Glory Disc Anomaly and Moyamoya Vessels

The morning glory disc anomaly comprises a congenital excavation of the peripapillary fundus, enlargement of the optic disc, anomalous peripapillary glial tissue, and a complex pattern of retinovascular anomalies.1 Unlike other optic disc anomalies, the morning glory disc anomaly is consistently associated with a profound retinal vascular dysgenesis. We describe a patient who had signs of middle cerebral artery occlusion and moyamoya vessels ipsilateral to a morning glory disc anomaly.

Report of a Case. A 5-year-old Asian boy was evaluated for decreased vision in the left eye of unknown duration. His birth, developmental, and medical histories were unremarkable. Visual acuity was 20/25 OD and 20/100 OS. A left relative afferent pupillary defect was present. Funduscopic examination in the left eye (Figure 1) revealed a morning glory disc anomaly, a persistent hyaloid artery, and a chronic macular hole accompanied by rhegmatogenous retinal detachment limited to the posterior pole.

A magnetic resonance imaging scan and magnetic resonance angiogram of the brain disclosed narrowing of the left intracranial carotid artery and its bifurcation into middle and anterior cerebral arteries. The lenticulostrate arteries were increased in size, consistent with moyamoya vessels (Figure 2).

Comment. Moyamoya disease is a rare cerebrovascular disorder of unknown etiology characterized by progressive bilateral stenosis or occlusion of the distal internal carotid arteries.2 The stenosis can progress to involve the proximal an-
terior and middle cerebral arteries. Progressive brain ischemia triggers formation of a collateral vascular network in the basal ganglia region referred to as moyamoya vessels. The disorder is more common in Asians, and the name moyamoya derives from the Japanese term for “puff of smoke,” which describes the angiographic appearance of the abnormal vessels. The most common clinical features are transient ischemic attacks and stroke in children but intracranial hemorrhage in adults. The natural history of unilateral moyamoya vessels is unknown, and the prognosis depends on the condition of the circle of Willis and its ability to provide blood from the unaffected side.

Moyamoya is usually an idiopathic disorder, or is sometimes acquired in the setting of cranial irradiation or atherosclerosis. However, moyamoya vessels can be associated with underlying congenital conditions such as neurofibromatosis, tuberous sclerosis, sickle cell anemia, Down syndrome, saccular aneurysms, and arteriovenous malformation. Our patient had none of these disorders.

Anomalous retinal vasculature is one of several features that distinguish the morning glory disc anomaly from other excavated optic disc anomalies such as optic disc coloboma and peripapillary staphyloma. With rare exceptions, the central retinal vasculature is ophthalmoscopically absent in the morning glory disc anomaly. The major retinal vessels curve abruptly as they emerge from the periphery of the optic disc, then run an abnormally straight course over the peripapillary retina. The vessels appear to be increased in number, and it may be difficult to distinguish arterioles from venules. Arteriovenous communications frequently interconnect the major retinal vessels, producing a rosette or arcade appearance on fluorescein angiography. The anatomical basis of this anomalous retinovascular system is speculative, since all histopathological descriptions have lacked clinical confirmation.

The association of morning glory disc anomaly with intracranial vascular anomalies is probably underrecognized, since carotid angiography is rarely performed in these individuals. Hanson et al described a 9-year-old girl with a morning glory disc anomaly in whom carotid angiography disclosed multiple branch occlusions of the ipsilateral middle cerebral arteries associated with moyamoya vessels in the region of the basal ganglia. A second patient with a morning glory disc anomaly had a history of multiple facial hemangiomas. Carotid angiography disclosed occlusion of the ipsilateral internal carotid artery at its origin with reconstitution intracranially via an enlarged branch of the right internal maxillary artery.

Our patient confirms the association of moyamoya vessels with the morning glory disc anomaly and strengthens the argument that an intracranial vascular dysgenesis may underlie at least some cases of the morning glory disc anomaly. Magnetic resonance angiography is a noninvasive screening technique that is widely available. We advocate its use in conjunction with routine magnetic resonance imaging to identify and further define the prevalence of intracranial vascular anomalies of the carotid system in patients with anomalous optic discs of the morning glory variety.

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