ACQUIRED OCULAR MOTOR APRAXIA AFTER AORTIC SURGERY

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ABSTRACT

Purpose: To describe an unusual form of acquired ocular motor apraxia.

Methods: Case reports with electronic eye movement recordings.

Results: Three patients had surgery to repair aortic root or arch dissections or aneurysms. A few days after surgery, all had ophthalmoplegia. Neuro-ophthalmic examination found complete absence of horizontal and vertical volitional and reflex saccades in 1 patient and slow, hypometric saccades in 2 others. However, smooth pursuit, slow phases of optokinetic nystagmus, and the vestibulo-ocular response (VOR) were intact. Fast phases of the VOR were absent in 2 patients but were intact in the other. Video and electronic eye movement recordings documented the findings. Magnetic resonance imaging (MRI) in 1 patient showed small infarcts in a cerebellar hemisphere, pons, and cerebral hemispheres. The other patients' MRIs showed no significant lesions.

Conclusions: Acquired ocular motor apraxia with profoundly impaired volitional saccades after aortic surgery is a distinctive syndrome, but its pathophysiology is unclear. Studies of neurologic damage in animals and patients undergoing similar surgical procedures provide conflicting data. However, knowledge about the complex neural pathways generating saccades from animal and human studies, and detailed clinical observations, as in the patients described here, can help to determine the location of lesions. Based on the 3 cases reported here, we propose that this syndrome might be due to damage to excitatory burst and/or omnipause neurons in the brainstem or by damage to pathways from the frontal eye fields to the brainstem.

INTRODUCTION

Ocular motor apraxia is a form of supranuclear ophthalmoplegia, in which patients cannot make volitional saccades, but can make smooth pursuit, optokinetic, and vestibulo-ocular eye movements. It can be congenital or acquired. The congenital form can be idiopathic[1,2] or can be caused by prenatal injuries associated with cerebral palsy. Acquired ocular motor apraxia can be caused by a variety of neurologic disorders affecting the cerebral hemispheres, basal ganglia, and brainstem.[3] Although the ocular motor pathways involved in generating saccadic eye movements have been identified by studies in experimental animals and clinicopathologic studies in patients, the precise localization of lesions causing saccadic paralysis is not known in most forms of ocular motor apraxia.

An unusual form of acquired ocular motor apraxia with absent or slow horizontal and vertical saccades has been described in patients after cardiopulmonary surgery[4-10] or cardiac arrest.[11] We describe the case histories and neuro-ophthalmic findings in 3 patients who developed absent or slow saccades following aortic surgery. The eye movement findings were documented with video and electronic eye movement recordings in 2 patients. The results of neuroimaging are described, and we speculate about the locations of the lesions causing acquired ocular motor apraxia in these patients.

METHODS

The institutional review board approved the collection of data for this study. After informed consent was obtained from each patient, eye movements were recorded with video recording and DC electro-oculography. The bandwidth of the electro-oculography system was 0 to 100 Hz. The tracking target was a small laser spot that was projected onto the back of a screen facing the patients. Patients sat in a motorized, rotating chair. Optokinetic eye movements were induced by rotating a drum above the patients. The drum projected alternating black and white, vertical stripes onto a cloth screen that surrounded the patients.

RESULTS

CASE 1

A 52-year-old man suddenly experienced severe chest pain that radiated to his back. He was generally healthy, smoked 1 pack of cigarettes per day, and occasionally smoked marijuana and inhaled cocaine. Computed tomography (CT) showed an aortic dissection from the aortic root extending close to the iliac bifurcation and an aortic aneurysm extending from the ascending to the descending aorta. At surgery, tears of the intima of the ascending aorta were glued, the aortic arch was resected and reconstructed, and the aortic aneurysm was repaired. A cannula was placed from the aorta to the innominate artery to maintain blood flow during hypothermic cardiac arrest (HCA). The duration of cardiopulmonary bypass was 227 minutes, aortic cross-clamping 167 minutes, HCA and myocardial ischemia 139 minutes, and anterior cerebral perfusion 110 minutes.

Postoperatively, the patient had periods of agitation and was observed to have slurred speech and unsteady gait. A "gaze abnormality" was noted. Computed tomography showed small hypointensities in the right cerebellum and right precentral gyrus. A magnetic resonance imaging (MRI) scan showed small acute infarcts in the right cerebellar hemisphere and both sensory motor

cortices. There was a small, old infarction in the right pons. An MRI angiogram of the head and neck was normal. After discharge from the hospital, the patient veered to his left while walking. He had blurred vision when he stood up, when he moved his body or head, and while reading. Images on the television were clear. He complained, "My eyes don't move."

Neurologic examination showed mild dysarthria, hypophonia, and dystaxia on heel-knee-shin movements. Muscle stretch reflexes were slightly hypoactive, and his gait was broad-based and slightly ataxic.

Two and one-half months after his surgery, neuro-ophthalmic examination showed absence of spontaneous or volitional, horizontal or vertical saccades. Smooth pursuit produced normal ranges of eye movements horizontally and vertically. Optokinetic stimulation produced smooth eye movements in the direction of stripe movement horizontally and vertically, but no fast phases. Fixation of a stationary target and rotation of the head (doll's-head maneuver) produced normal ranges of horizontal and vertical, vestibulo-ocular responses (VORs). Bell's phenomenon was normal in both eyes.

Eye movements were recorded with video and electro-oculography. The recordings confirmed the absence of volitional and reflex saccades. Figure 1 shows horizontal smooth pursuit while the patient tracked a small laser target moving sinusoidally at 0.2 Hz and 23 degrees/second peak velocity. Figure 2 shows horizontal VOR while he was seated in a chair rotating sinusoidally in the dark at 0.05 Hz and 60 degrees/second peak velocities. Fast components of the VOR were absent during rotation in the dark and during synergistic visual-vestibular interactions when he was rotated within a stationary optokinetic drum. When the patient was seated within the optokinetic drum rotating sinusoidally at 0.05 Hz and 60 degrees/second peak velocity, horizontal optokinetic nystagmus (OKN) had no fast phases. Two months later, the patient could make slow horizontal saccades of 5 degrees to the right and left and downward saccades of 10 degrees. He was instructed to use head thrusts to re-fixate targets.
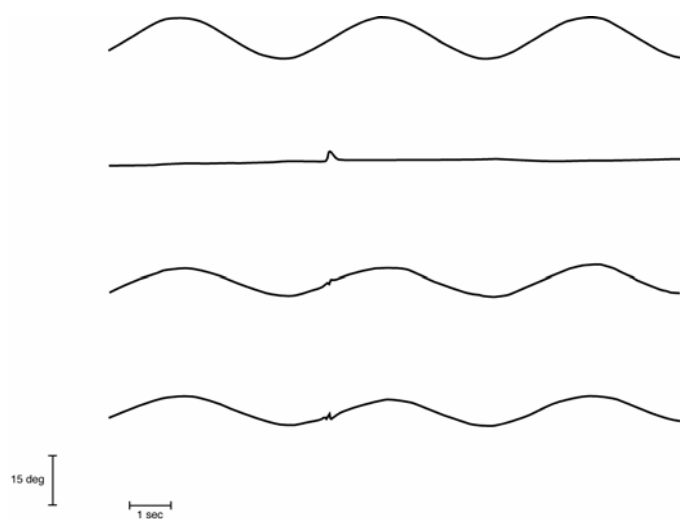
FIGURE 1

Case 1. Horizontal smooth pursuit. Top line, Target is moving sinusoidally at 0.2 Hz and 23 deg/sec peak velocity (up = right, down = left). 2nd line, Right eye vertical (up = up; down = down). 3rd line, Right eye horizontal. 4th line, Left eye horizontal. Note vertical and horizontal artifacts from eyelid blinking and intact pursuit movements.
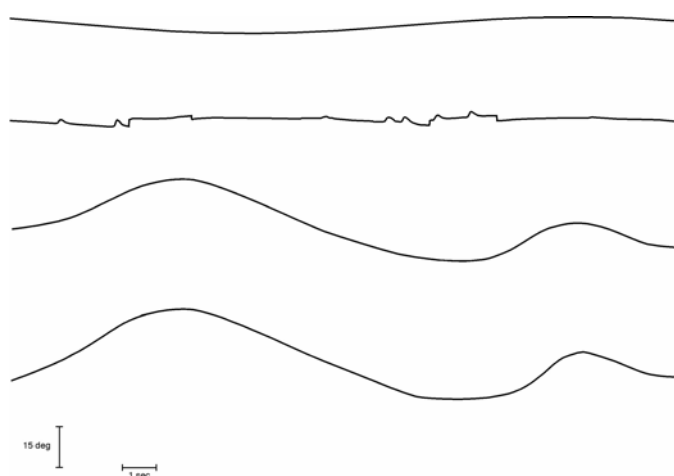
FIGURE 2

Case 1. Horizontal vestibulo-ocular response. Top line (chair velocity), Chair is rotating sinusoidally in the dark at 0.05 Hz and 60 deg/sec peak velocity (up = right, down = left). 2nd line, Right eye vertical (up = up, down = down). 3rd line, Right eye horizontal. 4th line, Left eye horizontal. Note absence of fast phases and intact slow phases.

CASE 2

A 37-year-old man had chest discomfort. Computed tomography of the chest showed an aneurysm of the ascending aorta. He had a past medical history of hypertension, hypercholesterolemia, and type 2 diabetes mellitus. He smoked 2 to 3 packs of cigarettes each day. The aneurysm enlarged over 1 year. At surgery, he was found to have an aneurysm of the ascending aorta, a bicuspid aortic valve, and aortic regurgitation. He underwent aortic root repair and an aortic valve replacement with cardiopulmonary bypass and hypothermia.

Two days after surgery, his wife noticed that he was making unusual head movements and could not look eccentrically. He complained of blurred vision in both eyes and had dysphagia, drooling, bruxism, imbalance, and difficulty with short-term memory. An MRI scan performed 5 days after surgery showed no lesions of the cerebral hemispheres, basal ganglia, or brainstem.

Two months after surgery, neuro-ophthalmic examination showed that he made slow, small amplitude, horizontal volitional saccades with great effort. He made no spontaneous saccades. Vertical volitional saccades were absent. Horizontal and vertical, smooth pursuit was also markedly limited in range. However, horizontal and vertical VOR during the doll's-head maneuvers had normal velocities and amplitudes. The Bell's phenomenon was normal. Two months later, the patient reported being better able to

compensate for his ophthalmoplegia by thrusting his head. His horizontal saccades were still markedly slowed and limited in amplitude. He could not make volitional, vertical saccades. Horizontal smooth pursuit had normal range, but he could not make vertical smooth pursuit movements.

CASE 3

A 70-year-old woman had a long history of coronary artery disease, which required several stenting procedures. Her past medical history included chronic obstructive pulmonary disease, cigarette smoking, hypercholesterolemia, and peripheral vascular insufficiency. She had moderately severe aortic insufficiency. Computed tomography showed an aneurysm of the ascending aorta. She underwent replacement of the aortic valve, resection of the aneurysm of the ascending aorta and aortic arch, replacement of the aortic arch, and coronary artery revascularization using an internal mammary artery. During surgery, she was placed on cardiopulmonary bypass, and she was cooled to 15°C.

Postoperatively, she had confusion and agitation. After discharge from the hospital, she complained of blurring at distance and near, difficulty reading, and trouble tracking visual objects. Eight months after her surgery, neuro-ophthalmic examination showed that she made only small, slow, horizontal volitional saccades with great effort. She could not make vertical saccades. However, the ranges of horizontal and vertical smooth pursuit were normal. Doll's-head maneuver produced full range of horizontal and vertical VOR. When asked to make horizontal or vertical re-fixations, she thrust her head in the direction of the intended target, obtained fixation of the target, and then moved her head back to face the target. An MRI scan showed no significant lesions of the cerebral hemispheres or brainstem.

Eye movement recordings by video and electro-oculography showed markedly slow, hypometric volitional saccades in both eyes. Smooth pursuit and the VOR were intact. Figure 3 shows pursuit eye movements while the patient was tracking a target moving sinusoidally at 0.4 Hz and 45 degrees/second peak velocity. However, unlike in case 1, fast phases of the VOR and OKN were intact. Figure 4 shows the VOR during sinusoidal rotation in the dark at 0.2 Hz and 23 degrees/second peak velocity.
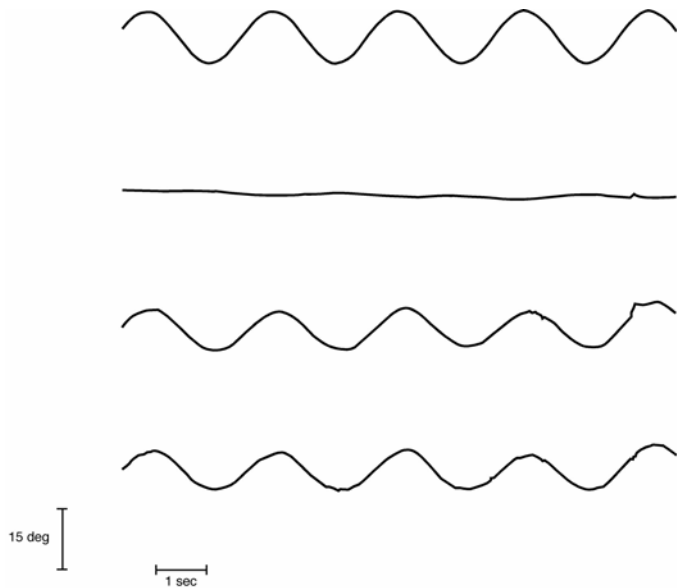
FIGURE 3

Case 3. Horizontal smooth pursuit. Top line, Target is moving sinusoidally at 0.4 Hz and 45 deg/sec peak velocity (up = right). 2nd line, Right eye vertical (up = up, down = down). 3rd line, Right eye horizontal. 4th line, Left eye horizontal. Note intact pursuit movements.
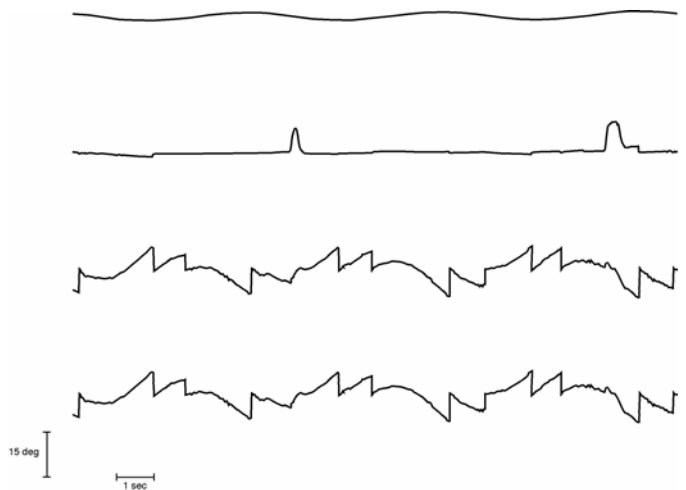
FIGURE 4

Case 3. Horizontal vestibulo-ocular response. Top line (chair velocity), Chair is rotating sinusoidally in the dark at 0.2 Hz and 23 deg/sec peak velocity (up = right, down = left.; 2nd line, Right eye vertical (up = up; down = down). 3rd line, Right eye horizontal. 4th line, Left eye horizontal. Note fast phases and slow phases are present.

DISCUSSION

TERMINOLOGY

The 3 patients discussed here, as well as several other patients described in previously published reports,[4-10] had complete or nearly complete loss of volitional saccades but preservation of VOR following cardiac and/or aortic surgery. The preferred terminology for this unusual disorder remains controversial. Several of these previous reports referred to the disorder as *acquired ocular motor apraxia*. However, Devere and colleagues[4] preferred the term *acquired supranuclear ocular motor palsy* to differentiate this acquired type of ophthalmoplegia from congenital ocular motor apraxia (COMA), as described by Cogan and Adams,[1,2] and from acquired ocular motor apraxia caused by bilateral frontoparietal lobe lesions.[12]

Classification might be based on the presence or absence of pursuit movements as well as saccades. In children with COMA, volitional, horizontal saccades are initially absent, but smooth pursuit, slow phases of OKN, and slow phases of the VOR are present. Spontaneous and volitional vertical saccades are intact. As the children age, horizontal volitional saccades return, although evidence of impaired initiation of saccades with head thrusts and blinking may persist. Reflex horizontal saccades, including spontaneous, re-fixation saccades and fast phases of OKN and the VOR return. Among previously reported patients with loss of saccades after cardiac and/or aortic arch surgery, smooth pursuit was described in 17. Pursuit was impaired in 12 and intact in 5. Two of our patients had preservation of smooth pursuit at their first neuro-ophthalmic examinations, and the other patient had recovered smooth pursuit at his second examination.

Alternatively, terminology could be based on dissociation between volitional and reflex fast eye movements. Sharpe and Johnston[13] suggested that *ocular motor apraxia* be used when volitional saccades are absent but reflex saccades are spared. Volitional saccades include saccades made to an examiner's verbal commands and saccades made to predictable target movements. Reflex saccades include saccades to unpredictable target movements and fast phases of OKN and vestibular nystagmus. They suggested that *ocular motor paresis* was more appropriate for the patient described by Pierrot-Deseilligny and colleagues.[14] In this patient, volitional and reflex saccades were severely impaired when the head was immobilized but were present when the head was free.

We think that the term acquired *ocular motor apraxia* is acceptable to describe the syndrome of ophthalmoplegia following cardiac and/or aortic arch surgery, because other investigators have used this term in their reports. Furthermore, in these patients smooth pursuit can be intact, impaired, or absent, and reflex saccades can be absent or intact.

LOCALIZATION OF LESIONS

Pathways that generate saccades in the cerebral hemispheres, basal ganglia, thalamus, brainstem, and cerebellum are complex. Leigh and Zee in their textbook[3] and Ramat and colleagues in their review article[15] summarized these pathways. They also described the effects of experimental lesions in animals and lesions in humans at various locations in the pathways.

The frontal eye fields (FEFs), supplementary eye fields, and lateral parietal cortex participate in identifying and selecting targets for volitional saccades. These cortical areas project to the superior colliculus (SC) directly or indirectly via the basal ganglia. These areas also project to the pontine nuclei. Neurons in the intermediate and deep layers of the SC also help to select targets for re-fixation saccades or smooth pursuit in retinotopic coordinates and help initiate the movements. Superior colliculus cells project to the raphe interpositus nucleus and the brainstem reticular formation.

In animals, chronic, bilateral lesions of the FEF or SC alone do not abolish saccades.[16] However, simultaneous, bilateral lesions of the frontal and parietal eye fields impair volitional saccades.[17] In humans, acute bilateral lesions of the frontal lobes or frontal and parietal lobes can cause permanent loss of volitional saccades and smooth pursuit.[12,14,18] However, the VOR and its fast phases (reflex saccades) are preserved. These lesions are typically large infarcts, which are unlikely to be missed by MRI. For example, Dehaene and Lammens[11] described the clinicopathologic findings in a woman who was resuscitated from a cardiac arrest but died 30 days later. She had no horizontal or vertical saccades, smooth pursuit, or OKN. The VOR in the doll's-head maneuver and response to cold caloric irrigation were intact. At autopsy, a 7-mm-long area of necrosis of the left middle frontal gyrus and a 15-mm-long area of necrosis along the upper and lower banks of the left intraparietal sulcus were found. Microinfarctions of the cortex in the same areas were found on the right side. The investigators thought that the lesions were compatible with watershed infarcts after systemic hypotension. Although MRI was not performed in this patient, these lesions would have been found with MRI, as in the patient described by Pierrot-Deseilligny and colleagues.[14] Genc and colleagues[18] described a man who had Takayasu arteritis and a dissecting aneurysm from the aortic arch to the descending aorta. He had spontaneous saccades in all directions but could not perform saccades to command nor execute smooth pursuit or optokinetic eye movements. Doll's-head eye movements were intact. Computed tomography and MRI showed large, bilateral infarcts of the FEF and parietal eye field. The supplemental eye fields were spared. Based on the MRI findings in our patients, we do not think that FEF infarction was the cause of our patients' eye movement disorder.

Before considering brainstem structures as the possible localization of the damage in this disorder, it is useful to review the anatomy and physiology of normal eye movements. Excitatory burst neurons (EBNs) in the brainstem are essential to generate the high peak velocities of saccades. Their sudden increase in firing rate, called the saccadic pulse, is required to produce forceful contractions of the extraocular muscles. These contractions are needed to overcome the viscous forces within the orbit that tend to keep the eyes in their original positions, accelerate the eyes, and rotate them to new positions in the orbit

EBNs excite the motor neurons and interneurons in the ipsilateral abducens nucleus and the motor neurons in the oculomotor and

trochlear nuclei. EBNs for horizontal saccades are in the ipsilateral pontine paramedian reticular formation (PPRF) below and rostral to the abducens nucleus. EBNs for vertical and torsional saccades are in the nucleus of the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) in the midbrain. Inhibitory burst neurons (IBNs) have the same firing patterns during saccades as EBNs, but predominately project to the contralateral EBNs, IBNs, and abducens nucleus. Firing of horizontal IBNs inhibits activity in the contralateral, antagonistic extraocular muscles (Sherrington's law of reciprocal innervation). Horizontal IBNs are located below and caudal to the abducens nucleus in the medullary reticular formation. IBNs for vertical and torsional saccades are located in the riMLF and interstitial nucleus of Cajal. They have similar functions as horizontal IBNs.

EBNs for horizontal, vertical, and torsional saccades are tonically inhibited by omnipause neurons (OPNs) in the raphe interpositus nucleus in the midline pons. Omnipause neurons project bilaterally to the pons and midbrain. They stop firing just prior to the pulse, allowing increased discharge of EBNs that produces the pulse. Just before the end of the pulse, OPNs resume firing and inhibit the EBNs. Omnipause neurons might have functions other than disinhibiting and inhibiting EBNs during saccades.

Long-lead burst neurons provide the trigger to activate the neurons described above by inhibiting the OPNs. Long-lead burst neurons are located in the central mesencephalic reticular formation, nucleus reticularis tegmenti pontis, and throughout the brainstem reticular formation. They receive input from the SC, FEF, supplementary eye field, lateral intraparietal eye field, and fastigial nucleus of the cerebellum. They begin a slow buildup of activity hundreds of milliseconds before a saccade, and discharge 40 msec or longer before the pulse. In contrast, OPNs decrease their discharge, and EBNs and IBNs increase their discharge 10 to 20 msec before a saccade. Long-lead burst neurons seem to sum signals from the SC and cerebral cortical areas to prepare for a saccade. SC neurons also project directly to the raphe interpositus nuleus. They might also provide the trigger to inhibit OPNs.

Discrete damage to specific brainstem structures causes distinctive patterns of eye movement abnormality. Bilateral lesions of the PPRF in animals and in humans produce loss of horizontal saccades with preservation of the VOR. Smooth pursuit and slow phases of OKN are intact, if axons of passage in the PPRF are spared. However, fast phases of the VOR and OKN are absent. Vertical saccades may be slowed but are still present. These findings can be explained by damage to EBNs in the PPRF. Bilateral lesions of the riMLF produce loss of downward saccades or loss of all vertical saccades. Vertical pursuit and VOR can be intact. These findings are explained by damage to EBNs in the riMLF. Vertical pursuit and VOR are also impaired if nearby structures, such as the medial longitudinal fasciculus and interstitial nucleus of Cajal, are damaged. In humans, bilateral lesions are usually caused by occlusion of the posterior thalamosubthalamic paramedian artery.

Ramat and colleagues[15] and Miura and Optican[19] described a model of saccade generation that offers another explanation for slowing of horizontal and vertical, volitional saccades in some disorders. Omnipause neurons might also increase the sensitivity of EBNs so that they are easily stimulated during saccades, but also reduce their sensitivity at other times to prevent unstable activity of EBNs that might produce unwanted saccadic oscillations. In their model, damage to OPNs in the raphe interpositus nucleus can produce slowing of horizontal and vertical saccades without lesions of the EBNs in the PPRF and riMLF. Hanson and colleagues[10] described a case that would support this theory regarding pathophysiology. Their patient had repair of an ascending aorta aneurysm and aortic valve, which was complicated by severe bleeding and hypotension. He lost horizontal and vertical, volitional and fast phases of caloric vestibular nystagmus and OKN but had intact smooth pursuit and VOR. Computed tomography with thin sections through the brainstem was normal. An autopsy 2 months after surgery showed loss of neurons and gliosis in areas of the pons in which EBNs and OPNs are normally found. The riMLF and FEF were normal.

Of the 26 patients who developed ocular motor apraxia after cardiac and/or aortic surgery described in previously published reports, 25 had absent or slow horizontal and vertical volitional saccades. One had no vertical saccades but intact horizontal saccades. We believe that in 2 of the patients described here (case 1 and case 2), lesions of the PPRF and riMLF damaged the EBNs needed to generate volitional and reflex saccades. Consistent with this mechanism, both volitional and fast phases of OKN and VOR were absent in these cases. The fast phases of the VOR were specifically described in only 3 of the 26 previously reported patients. They were absent in all 3 patients, suggesting similar locations of lesions in these cases.

The other patient (case3) had impaired volitional horizontal and vertical saccades, but OKN and VOR fast phases were intact. This pattern could be explained by bilateral lesions of the FEF, since cortical areas are not needed to generate reflex saccades. The patient's MRI, however, did not show any significant lesions in the cerebral hemispheres. We believe that this patient most likely had lesions in the brainstem affecting projections from the FEF. It is more likely that neuroimaging missed small brainstem lesions below the threshold of detection on MRI, than lesions in the FEF of sizes similar to those of the patients reported by Pierrot-Deseilligny and colleagues[14] and Genc and colleagues.[18] Similarly, MRI in patients with internuclear ophthalmoplegia often does not show small (<1 mm) lesions of the MLF. No brainstem lesions were evident on MRI in our 3 patients. Twenty-four of the 26 previously reported patients had MRI or CT, and none of these studies showed cerebral hemisphere or brainstem lesions that could account for the ophthalmoplegia. We believe that lesions in the cerebral cortex from infarction, demyelination, or hemorrhage, which are large enough to cause acquired ocular motor ophthalmoplegia, would not be missed by MRI, but that small lesions in the brainstem from these causes might be missed.

Other investigators described 2 patients with ophthalmoplegia similar to case 3. However, the patients had large cerebral hemisphere lesions, which would have been or were evident on neuroimaging. The patient described by Dehaene and Lammens[11] lost volitional horizontal and vertical saccades but had preserved fast phases of caloric, vestibular nystagmus. She had large lesions of the frontal and parietal lobes, which would not have been missed by MRI or CT. Leigh and Zee[3] described a patient with multiple sclerosis, who had difficulty initiating small-amplitude, volitional, horizontal and vertical saccades. Fast phases of OKN and VOR were preserved. Large bilateral lesions of the centrum semiovale, frontal lobes, and parietal lobes were shown by CT.

A similar syndrome has been reported in children after cardiac surgery for congenital heart defects.[5,6] The eye movement disorder in these cases was associated with chorea and seemed to develop after a latent period of days to weeks in some patients. These cases exhibited loss or slowing of volitional horizontal and vertical saccades with intact VOR. Partial or complete resolution of chorea and ophthalmoplegia occurred over weeks to months. In contrast, our adult patients and other previously reported adult patients have shown little or no recovery of volitional saccades. We do not have information about neuroimaging in these children.

MECHANISM OF DAMAGE

The mechanism of neurologic damage in our patients and in patients with similar ocular motor apraxia after aortic arch or cardiac surgery is not known. Embolism, hypoxia, hypotension, hyperviscosity, hypothermia, and lack of perfusion during circulatory arrest have been suggested as possible causes. However, in most cases, there was no description of significant complications during surgery or in the postoperative period. We suspect that damage, either from ischemia or hypothermia, to brainstem areas in the territories of the medial perforating arteries of the basilar artery (median and paramedian pons) and the posterior thalamosubthalamic paramedian artery of the basilar artery produced the ocular motor apraxia in 2 of the patients (cases 1 and 2). We think that similar damage to projections from the FEF in the brainstem might have occurred in the other patient (case 3).

Hypothermic cardiac arrest has become a well-established procedure in complex cardiac and aortic arch surgery in children and adults, as a means of reducing postoperative neurologic damage. Spielvogel and colleagues[20] recently reviewed their techniques for such surgery in adults and the development of HCA in animals and humans. Therapeutic hypothermia is designated as moderate with core temperatures of 27°C to 11°C and profound with temperatures of 10°C to 6°C. Most published series of patients used moderate to profound levels of hypothermia. Nineteen percent of 200 patients in Spielvogel's series[20] had transient neurologic dysfunction, including obtundation, confusion, agitation, and transient parkinsonism. These symptoms correlated with the duration of HCA and increasing patient age.

The mechanisms of brain damage in HCA are unknown. Edmunds and colleagues[21] induced profound HCA in dogs. Histologic examination of the brains in animals that had survived showed multiple infarctions of varying size in the gray matter and white matter. They were mostly in the cerebral hemispheres, rhinencephalon, basal ganglia, and cerebellum. Interestingly, they were not found in the brainstem. Many of the lesions were small (2 mm or less in surface area). The investigators thought that the infarctions were caused by occlusions of arterioles and capillaries due to sludging of blood from intravascular aggregation of red blood cells induced by hypothermia. Dogs whose carotid arteries were perfused with low-molecular-weight dextran before cardiac arrest had fewer and smaller lesions. The investigators did not believe that hypothermia or cardiac arrest was the main cause of brain damage.

In contrast, DeLeon and colleagues[22] concluded that hypothermia was a major cause of brain damage in dogs undergoing cardiopulmonary bypass without circulatory arrest. A temperature of 15°C caused significantly more loss and degeneration of neurons (2 to 8 cells per 1000 cells) than a temperature of 32°C (none per 1000 cells). Lesions were found in the basal ganglia, cerebral cortex, and cerebellar cortex. Neuronal loss was most marked around capillaries. The investigators did not find infarctions and did not describe histologic sections of the brainstem. Neuroimaging was not performed in these 2 animal studies.[21,22]

There are few reports describing the pathologic changes in humans following surgical hypothermia. Egerton and colleagues[23] described a series of 16 adult patients who had aortic valve surgery with profound hypothermia. Ten had severe or moderate brain damage. The investigators attributed focal neurologic signs in patients with moderate damage to brainstem injury. They described lower motor neuron, facial nerve palsies and unspecified "supra nuclear palsies affecting eye movements and accommodation." Focal and generalized neurologic signs (memory loss and hypotonia) improved and generally resolved in 2 to 4 months. They believed that neurologic damage was correlated with duration of profound hypothermia. One patient had postmortem examination of the brain. There were petechiae in the white matter, especially in the brainstem, and generalized neuronal degeneration and acute hemorrhages near small blood vessels. The investigators reported no signs of brain damage in a subsequent series of 24 patients for whom they used hypothermia of 24°C to 30°C and local cooling of the heart to 10°C to 14°C. The results of neuroimaging were not reported in this study.

Advances in surgical technique and anesthesia, including HCA, have made surgical repair of complex cardiac and aortic disorders more effective and safer than in the past. However, transient or permanent neurologic damage is a significant risk. Patients who develop damage usually have multiple, preexisting, systemic and cardiovascular risk factors for cerebrovascular ischemia. In these patients, precautions to avoid brain damage were not effective. Although acquired ocular motor apraxia following cardiac and/or aortic arch surgery is uncommon, it is a distinct syndrome. It causes significant visual impairment and should be considered as a possible cause of blurring of vision, difficulty reading, or trouble tracking objects after surgery. Lesions of the cerebral hemispheres or brainstem might not be found by MRI, but careful, neuro-ophthalmologic examination can help to localize the lesions.

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PEER DISCUSSION

Dr Brian R. Younge: I would like to thank the authors, my neuro-ophthalmology colleagues, Drs Yee and Purvin, for their paper, and to the AOS for the opportunity to discuss it.

My neurologic colleagues at Mayo have discussed this phenomenon with me, and some of our cases are similar. Of interest in this peculiar phenomenon is the biphasic onset in our patients and the close parallel of the patients presented here to one of my recent patients.

A recent case example is as follows: A 70-year-old right-handed man, in November 2005, underwent reportedly uncomplicated aortic valve replacement, surgery for bicuspid aortic valve, and an aneurysm of ascending aorta. Five days following surgery a pacemaker was implanted under general anesthesia. Immediately after the implant surgery, the patient had difficulty opening his eyes. Speech was slurred, balance was poor, and he had difficulty swallowing. These manifestations gradually increased over the upcoming 2 months, stabilized, and began to show some improvement. A significant dysarthria has remained essentially unchanged. Based on a diagnosis of myasthenia gravis, he received 5 sessions of plasma exchange, mestinon, and prednisone, with little effect. He had difficulty with vision, and in particular with reading, as he could not seem to move his eyes across the page. At the time of his eye exam at Mayo, his acuity was fairly normal, but he had complete paralysis of voluntary horizontal saccades. He could move his eyes vertically and pursue a slowly moving target in all directions. He had learned to close his eyes and thrust his head to change from one object of fixation to another, the apraxia of an acquired type. MRI shows only a small unrelated infarct near the temporal horn of the R lateral ventricle. Neither contrast nor fat suppression showed any brainstem abnormality.

Our previous experience with this condition is similar, but the mix is usually more of a vertical gaze saccadic palsy, similar to progressive supranuclear palsy.[1] Again the MRI studies often fail to reveal any significant brainstem or supranuclear lesions. There are other acquired causes of saccadic palsy, particularly vertical, associated with the syndrome of sea-blue histiocytosis, later found to be Niemann-Pick disease, type C. This also produces a similar neurodegenerative syndrome to progressive supranuclear palsy, or PSP, in which the saccadic palsy is more specific to the vertical gaze, with some involvement of horizontal. Smooth pursuit is often very normal. Another cause is the paraneoplastic syndrome, as exemplified by a recently seen 46-year-old with renal cell carcinoma, but a negative MRI. She has horizontal saccadic palsy, somewhat asymmetric, with normal vertical voluntary saccades.

The discussion as to localization is intriguing, particularly since there have been only a few pathologic specimens, as mentioned in this paper, to help with localization. The authors point out that often in lesions of the medial longitudinal fasciculus, producing internuclear ophthalmoplegia, there are minimal or no abnormal MRI findings. I think the discussion of the excitatory burst neurons, the long-lead burst neurons, the rostral interstitial nucleus of the medial longitudinal fasciculus, the pontine paramedian reticular formation, and so on, along with their locations, elucidates the complexity of this area, in terms of both localizing lesions and understanding the physiology. Too bad I can't understand it all. Something is happening in the region that we are just not quite able to see with the resolution of existing scanners.

The authors are to be congratulated for pointing out the salient clinical features of this unfortunate complication, along with the first steps in determining the causes. Maybe this will lead to prevention in the future.

ACKNOWLEDGMENTS

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DR. JOHN T. FLYNN: No financial interest. Bob, just like your patients, I have a child who developed choreoathetosis, hemibalismus, and a Parkinson-like syndrome after the type of surgery you described with associated hypothermia. As those signs lessened, the dyslexia associated with the ocular motor apraxia became more apparent when he went to school. This proved to be the most persistent and functionally incapacitating aspect of the syndrome for him. To better understand the pathogenesis of the condition; would a functional MRI or a positron emission tomographic (PET) scan performed while reading help to elucidate the affected pathways? This patient did not recover whatsoever, and as he progressed in school it became more difficult for him to stay up with his schoolwork.

DR. ROBERT D. YEE: Thank you for those comments and questions. Dr. Younge mentioned head thrusting that occurs in Cogan oculomotor apraxia to compensate for the lack of ability to voluntarily re-fixate is one of the striking clinical features. I observed that finding in some of my patients during the first several days after surgery, so patients often learn this compensatory activity. Regarding the issue of rehabilitation, one report describes the attempts in three patients. The most effective, but not very effective, maneuver was the training of children or adults to perform head thrusts if they had not spontaneously learned to do so. In children the time course of the clinical problem is a somewhat different than in adults. Often there is a delay of weeks after surgery before the signs of basal ganglion dysfunction and oculomotor apraxia occur. In one report, many of the signs improved or lessened with time. This suggests that the initial injury may not be related to an acute event, such as occurs with an infarct or hemorrhage, but perhaps occurs as a result of a diffuse degeneration that may take some time to develop. This raises a question of why MRI and CT cannot image these lesions. Magnetic Resonance Imaging and CT studies can demonstrate demyelination, hemorrhage, and infarction; however, they have limited spatial resolution. Often lesions less than 1 mm. in the medial longitudinal fasciculus (MLF) that are associated with intranuclear ophthalmoplegia cannot be visualized with these techniques. We need better imaging systems and I am not certain if these other types of functional imaging studies will demonstrate the lesions. Magnetic Resonance Imaging studies do not demonstrate the lesions in other types of oculomotor apraxia that occur in patients with progressive supranuclear palsy, ataxia telangiectasia, and in hereditary cerebellar ataxias. I suspect that the pathophysiology is of a diffuse nature and that the degeneration is related to hypothermia, which may trigger a set of metabolic changes.