Optic Disc Edema in an Astronaut After Repeat Long-Duration Space Flight


Background: A number of ophthalmic findings including optic disc edema, globe flattening, and choroidal folds have been observed in several astronauts after long-duration space flights. The authors report the first astronaut with previously documented postflight ophthalmic abnormalities who developed new pathological changes after a repeat long-duration mission.

Methods: A case study of an astronaut with 2 long-duration (6 months) exposures to microgravity. Before and after his first long-duration space flight, he underwent complete eye examination, including fundus photography. Before and after his second flight, 9 years later, he underwent fundus photography, optical coherence tomography, ocular ultrasonography, and brain magnetic resonance imaging, as well as in-flight fundus photography and ultrasound.

Results: After his first long-duration mission, the astronaut was documented to have eye findings limited to unilateral choroidal folds and a single cotton wool spot. During a subsequent 6-month mission, he developed more widespread choroidal folds and new onset of optic disc edema in the same eye.

Conclusion: Microgravity-induced anatomical changes that occurred during the first mission may have set the stage for recurrent or additional changes when the astronaut was subjected to physiological stress of repeat space flight.

doi: 10.1097/WNO.0b013e31829b41a6
© 2013 by North American Neuro-Ophthalmology Society

In 2011, a report from the Space Medicine Division of the National Aeronautic and Space Administration (NASA) described 7 astronauts who developed a spectrum of ophthalmic findings, including optic disc edema, globe flattening, choroidal folds, and hyperopic shifts in refraction, after long-duration space flights to the International Space Station (ISS) (1). After a 161-day mission, one of these astronauts had ocular findings of choroidal folds inferior to the disc and a single cotton wool spot, both in the right eye. The purpose of this report was to document the recurrence of choroidal folds and the new onset of unilateral disc edema in the right eye of the same astronaut after a second long-duration (193 days) space mission 9 years after his first flight. Postflight ophthalmic abnormalities were captured with photographic and imaging documentation. Given this patient’s normal postmission lumbar puncture (LP) opening pressure, we hypothesize that local ocular vascular or orbital optic nerve sheath changes associated with microgravity fluid shifts may have played a leading role in the etiology of these anomalies.

CASE REPORT

A 57-year-old astronaut flew his first long-duration mission to the ISS in 2003 and his latest mission in 2011–2012. Due to the relative likelihood of attributability of these data, the subject has provided written informed consent.

Before the first mission, his fundus examination was normal. During this mission, a decrease in near visual acuity...
starting about 6 weeks into the flight was his only complaint. Examination on return to Earth revealed large choroidal folds inferior to the optic disc of the right eye without macular involvement and a single cotton wool spot along the inferotemporal vascular arcade (Fig. 1). Examination of the left eye was normal, and there was no evidence of optic disc edema in either eye. The cotton wool spot resolved within a month, and while the choroidal folds gradually diminished, they were still present in fundus photographs 3 years later. No other studies were undertaken, but subsequent recognition of these findings in other astronauts led to the implementation of in-flight ultrasound and retinal imagery in 2009. In 2011, 6 months before the second mission, the astronaut still had choroidal folds in the right eye that were detectable only on optical coherence tomography (OCT) (Fig. 2).

On OCT, preflight retinal nerve fiber layer (RNFL) thickness was normal in both eyes. Preflight magnetic resonance imaging (MRI) showed a normal appearance of the brain, bilateral optic nerve sheath distention, and optic nerve tortuosity with mild right globe flattening. These findings were confirmed using preflight ultrasound. One month into the mission, ultrasound demonstrated an increase in optic nerve sheath diameter (ONSD) that persisted throughout the mission. Toward the end of the mission, the degree of right globe flattening increased and globe flattening developed in the left eye. Approximately 3 months into the flight, retinal and optic nerve head images were captured by real-time remotely guided video funduscopy and downlinked to Mission Control Center in Houston, Texas. There was recurrence of subtle choroidal folds in the same location in the right eye, and 2 months later, the choroidal folds were now seen with mild right optic disc edema (Fig. 3). Orbital ultrasound and MRI results are shown in Table 1. The data compiled in Table 1 are based on newly developed testing methods that have not been fully analyzed for accuracy and reliability.

Two days after the space mission, the right fundus showed Frisen grade 1 optic disc edema with choroidal folds above and below the disc (Fig. 4). The left fundus was normal. There was prominent RNFL thickening.

FIG. 1. After first space mission, right fundus shows choroidal folds (black arrows) inferior to the optic disc and a cotton wool spot (white arrow).

FIG. 2. Top: Before the second mission, the fundi appear normal. Bottom: Spectral domain optical coherence tomography demonstrates mild choroidal folds (arrows) in the right eye.
in the right eye, with normal thickness in the left eye (Fig. 5).

At this time, axial length (IOL Master, Jena, Germany) decreased by 0.14 mm in the right eye and 0.13 mm in the left eye, compared to preflight measurements. MRI performed 6 days postflight confirmed the presence of bilateral globe flattening and a partial empty sella. Both MRI (Fig. 6) and ultrasound (Fig. 7) demonstrated a moderate increase in the ONSD compared to preflight, paradoxically, left eye > right eye (Table 1). An opening pressure of 18 cm of water was measured on LP 8 days after landing. Intraocular pressure averaged 12 mm Hg in each eye during the mission, compared to preflight and postflight measurements of 10 mm Hg. The astronaut noted no change in visual acuity during his second flight and in-flight distance, and near visual acuity testing was consistent with preflight. No complaints of headache, pulsatile tinnitus, or diplopia were noted during either flight. Cycloplegic refraction did not change after the second flight, and his vision remained correctable to 20/20 in each eye.

Fundus photographs taken 52 days postmission documented a normal optic disc in both eyes. RNFL thickness measured 52 days postflight returned to near normal (Fig. 5). It should be added that this astronaut had a short duration (16 days) Space Shuttle flight in 2008 between his 2 ISS missions and had thus spent a total of 370 days in space during a 9-year period.

**DISCUSSION**

During the past 7 years, the space agencies participating in the ISS program have intensified the medical surveillance of crew members. Ophthalmic procedures now include high-resolution

<table>
<thead>
<tr>
<th>TABLE 1. Measurements obtained with orbital ultrasound and magnetic resonance imaging during 193-day space mission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Right eye</td>
</tr>
<tr>
<td>Ultrasound axial length</td>
</tr>
<tr>
<td>Optic nerve sheath diameter</td>
</tr>
<tr>
<td>Optic nerve diameter</td>
</tr>
<tr>
<td>Sheath/nerve ratio</td>
</tr>
<tr>
<td>Globe flattening grade</td>
</tr>
<tr>
<td>Disk protrusion grade</td>
</tr>
<tr>
<td>Sheath hypoechogenicity grade</td>
</tr>
<tr>
<td>Sheath inhomogeneity grade</td>
</tr>
<tr>
<td>Nerve tortuosity grade</td>
</tr>
<tr>
<td>Left eye</td>
</tr>
<tr>
<td>Ultrasound axial length</td>
</tr>
<tr>
<td>Optic nerve sheath diameter</td>
</tr>
<tr>
<td>Optic nerve diameter</td>
</tr>
<tr>
<td>Sheath/nerve ratio</td>
</tr>
<tr>
<td>Globe flattening grade</td>
</tr>
<tr>
<td>Disk protrusion grade</td>
</tr>
<tr>
<td>Sheath hypoechogenicity grade</td>
</tr>
<tr>
<td>Sheath inhomogeneity grade</td>
</tr>
<tr>
<td>Nerve tortuosity grade</td>
</tr>
</tbody>
</table>

All measurements in centimeters. All grades determined as: 0 = none; 1 = mild; 2 = moderate; 3 = severe. Ultrasound axial length measurements are underestimated due to use of nonophthalmic scanner without adjustment for propagation speed.

MRI, magnetic resonance imaging; US, ultrasound.
fundus photography, cycloplegic refraction, ocular and optic nerve ultrasound, MRI of the brain and orbits, and retinal and optic nerve OCT. Using these tests, after approximately 6 months of continuous space flight, 7 astronauts were shown to have varying degrees of optic disc edema, globe flattening, choroidal folds, and hyperopic shifts in refraction (1). All changes were seen in men and were observed more frequently in the right eye. From the inception of the US Space Program through July 2012, a total of 47 American astronauts have completed long-duration (>30 days) space missions, and

**FIG. 4.** Right fundus findings 2 days after space mission. **A.** Mild optic disc edema is present with inferior choroidal folds (arrow). **B.** Scanning laser ophthalmoscope image demonstrates superior and inferior choroidal folds (arrows). **C.** Choroidal folds are shown with spectral domain optical coherence tomography on vertical scan obtained just nasal to the optic disc.

**FIG. 5.** Retinal nerve fiber layer (RNFL) thickness measured by optical coherence tomography: (A) preflight; (B) 2 days postflight; (C) 52 days postflight. OD, right eye; OS, left eye.
5 were repeat long-duration flyers. Since the implementation of ocular surveillance program of NASA in 2006, 27 US astronauts have flown long-duration missions. Of this group, 12 were found to have one or more of the ocular abnormalities observed in our case. Asymptomatic disc edema was also documented in 8 of 16 long-duration cosmonauts studied during the Russian Mir Space Station program (2).

Three possible mechanisms have been proposed to explain the ophthalmic findings. These are not mutually exclusive and may be multifactorial. The first possibility is that the ocular changes resulted from increased intracranial pressure (ICP). It is thought that venous stasis in the head and neck, produced by cephalad fluid shifts in microgravity, may cause impairment of cerebrospinal fluid (CSF) outflow and cerebral venous congestion, both of which could lead to a rise in ICP (1,3). Support for this hypothesis includes borderline high opening pressures in 2 of the astronauts described previously (1), an elevated ICP of 28.5 mm H$_2$O in one (1) and MRI evidence of moderate concavity of the pituitary gland in 3 astronauts (4). Also, it has been proposed that pre-existing chemical differences in some individuals, possibly associated with defects in the folate and vitamin B$_{12}$-dependent 1-carbon transfer pathway, which have little or no demonstrable effect under Earth-gravity conditions, may set the stage for pathological changes leading to an increase in ICP in prolonged microgravity exposure (5).

A rise in ICP could cause distension of the optic nerve sheaths, stasis of axoplasmic flow, axonal swelling, and optic disc edema. The magnitude of the difference between CSF pressure within the optic nerve sheath and intraocular pressure (IOP) across the lamina cribrosa (translaminar pressure difference) may also play a role (6). In some astronauts, this pressure difference may lead to increased nerve sheath volume and exert an anterior force that indents the posterior sclera, resulting in posterior globe flattening, decreased axial length, and choroidal folds. Although the LP opening pressure was normal in our patient 8 days after landing, no LP was performed preflight or during the mission, so the role of CSF pressure is problematic. Elevated ICP as the sole etiology is not proven since: 1) not all of the measured postflight opening pressure on LP have been elevated, and most of those that were elevated were in the borderline range; 2) common symptoms seen in patients with idiopathic intracranial hypertension (IIH), such as headache, pulse-synchronous tinnitus, transient visual obscurations, and diplopia, have not been reported in astronauts; 3) choroidal folds, while a known finding in IIH, seem to be a more prominent finding in our patient cohort; and 4)
the presence of cotton wool spots cannot be explained based on elevated ICP alone.

A second possible explanation of our findings is that the optic disc edema and other abnormalities are the result of localized events occurring at the level of the intracanalicular and intraorbital optic nerve that are independent of CSF pressure (1). In a 1-gravity (1 G) environment, it is assumed that there is homogeneity of both pressure and biochemical constituents of CSF throughout the subarachnoid space (SAS). However, the unique cul de sac–like anatomical connection between the intracranial SAS and the SAS of the optic nerve may create a fragile flow equilibrium that could be impacted by long-standing microgravity fluid shifts and optic nerve sheath compliance (7,8). The fluid shifts may cause alterations in CSF flow dynamics in the intraorbital portion of the SAS, such that CSF enters the SAS but outflow may be impeded (9,10). Perhaps, under prolonged microgravity conditions, CSF in the SAS of the optic nerve may gradually become partially or completely sequestered, producing a type of optic nerve compartment syndrome. The fact that our astronaut had a normal LP opening pressure in conjunction with severe bilateral enlargement of the ONSD lends support to this theory. Perhaps, slight anatomical differences between the intraorbital optic nerves and sheaths, which may be inconsequential at 1 G, become the salient features during extended microgravity and may account for the optic disc edema and disc edema asymmetry noted in previous astronauts, as well as the unilateral disc edema in this astronaut. In addition, microgravity-related changes in CSF flow within the intraorbital portion of the optic nerve may lead to biochemical changes in CSF that prove toxic to the optic nerve causing the cotton wool spot noted during our astronaut’s first mission (1).

Previous research conducted on the anatomy and CSF dynamics of the optic nerve sheath have some bearing on our findings. Hayreh (11) demonstrated that the capacity of the optic nerve sheath to expand during a rise in ICP varied along its length. The retrobulbar area expanded the most while the intracanalicular portion expanded the least. He also noted that elevated SAS pressure resulted in increased ONSD, even before papilledema appeared. Hansen and Helmke (12) showed that the optic nerve sheath expands rapidly in vivo after small pressure changes during intrathecal infusion tests. In isolated human optic nerves, changes from baseline sheath diameter occurred with as little as a 5 mm Hg increase in SAS fluid pressure (13). They demonstrated that even if SAS pressure is later reduced, a new baseline ONSD may persist. Our data suggest that, regardless of the specific mechanism of increased intrasheath pressure, a similar resetting of ONSD may have occurred during this astronaut’s first mission. The sheath may have remained enlarged after his return to the Earth after his first flight, and the distension process may have resumed during the second flight from an already expanded baseline.

A third possible etiology for the optic disc edema observed is ocular hypotony. Although no long-term studies of IOP in microgravity have been performed, some head-down bed rest (14,15) and postflight studies (16) suggest

FIG. 7. Ultrasound images taken 3 days postflight. A. Axial section of the right eye shows elevation of the disc area, nasal flattening of the posterior globe, and a tortuous optic nerve. The white line represents axial length. B. Oblique sagittal view of the same eye shows localized flattening of the posterior globe. C. Oblique axial section through the left eye. The bulbar segment of the sheath is markedly dilated (white line) and measured 0.79 cm (13 MHz linear array probe, depth of view 4 cm).
that a lowering of the IOP may occur during prolonged microgravity exposure (17). Ocular hypotony is known to cause disc edema, posterior globe flattening, choroidal folds, and a hyperopic shift in refraction (18,19). However, since this astronaut’s IOP during the mission remained near pre-flight values, this mechanism seems unlikely.

Regardless of the specific etiology, our documentation of more widespread choroidal folds and the new onset of optic disc edema after a second long-duration flight, 9 years after the first, suggest that for this astronaut the ocular effects of repeat space travel may have been cumulative. We speculate that the microgravity-induced anatomical changes that occurred during the first mission could have predisposed our astronaut to recurrent and additional changes when subjected to the physiological stress of repeat space flight. Continued preflight, in-flight, and postflight ophthalmic evaluation of astronauts will help determine the long-term clinical significance of these findings and whether the results seen in this astronaut are found in other repeat long-duration flyers.

REFERENCES


