Letters

COMMENT & RESPONSE

Why Space Flight–Associated Neuro-ocular Syndrome May Differ From Idiopathic Intracranial Hypertension

To the Editor We very much appreciate the paper recently published in *JAMA Ophthalmology* by Lee et al.[1] In line with the idea that increased intracranial pressure (ICP) may not be the sole, or even the primary, cause of optic disc swelling in astronauts, the authors discuss important differences between space flight-associated neuro-ocular syndrome (SANS) and (terrestrial) idiopathic intracranial hypertension (IIH) and emphasize that postmission lumbar puncture opening pressures measured thus far were only mildly elevated. Based on the latest evidence from research, we believe there may be a plausible explanation for why SANS may differ from IIH.

While papilledema in IIH may result primarily from raised ICP, increased ICP and changes in cerebrospinal fluid (CSF) outflow routes in and around the optic nerve in the setting of SANS may work together to cause optic disc edema. Anatomically, the subarachnoid space (SAS) of the optic nerve becomes a cul de sac at the back of the eye.[2] Given the microgravity-induced redistribution of CSF volume in the cranial direction, it is unlikely that CSF, once in the orbital CSF space, can change its direction of flow from the SAS of the optic nerve toward the intracranial SAS. Furthermore, the orbital optic nerve lymphatic drainage systems may be affected by microgravity-induced cephalad fluid shifts, which could lead to lymph stasis.[3] Both factors may impede CSF outflow from the SAS of the optic nerve, and, as an alternative CSF outflow pathway, CSF may be pushed from the SAS of the optic nerve to the paravascular glymphatic pathway within the optic nerve. Evidence of a glymphatic pathway in the optic nerve in which CSF enters the optic nerve through spaces immediately surrounding blood vessels has very recently been reported.[4] In astronauts, reduction or reversal of the normal posteriorly directed trans-lamina cribrosa pressure difference (calculated by subtracting ICP from intraocular pressure) that arises because of increased ICP may further facilitate paravascular CSF influx into the eye while impeding the posterior paravascular fluid outflow from the eye.[5]

We believe that optic disc edema in astronauts may occur at least in part as a result of the imbalance between ocular glymphatic inflow and outflow. Furthermore, in coexistence with the described microgravity-induced changes in CSF outflow, even mildly elevated ICP could be sufficient to contribute to the observed optic disc swelling in astronauts. To our knowledge, this may explain why astronauts with SANS did not report the typical and classic symptoms of IIH as it is experienced on Earth.

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