WriteClick: Editor's Choice

Editors' Note: Dr. Sundal discusses hereditary diffuse leukoencephalopathy with spheroids. Dr. Antezana et al. report a case of glatiramer acetate (GA)–induced hepatotoxicity and question whether liver function should be monitored in all patients initiated on GA. In reference to "Teaching Neuro*Images:* Microvascular decompression of the optic nerve," Dr. Ghuman and authors Woodall and Alleyne discuss the diagnosis of idiopathic intracranial hypertension in monocular vision loss.

—Megan Alcauskas, MD, and Robert C. Griggs, MD

MICROGLIA: MULTIPLE ROLES IN SURVEILLANCE, CIRCUIT SHAPING, AND RESPONSE TO INJURY

Christina Sundal, Gothenburg, Sweden: Dr. Benarroch[1] provided an excellent overview of the role of microglia. Microglia are implicated in many neurodegenerative disorders and we noted that the newly identified colony stimulating factor 1 receptor (*CSF1R*) gene mutation is causative for hereditary diffuse leukoencephalopathy with spheroids (HDLS).[2] HDLS is an inherited progressive disorder of axons and myelin with a variable phenotype, mimicking other disorders such as primary progressive multiple sclerosis, frontotemporal dementia, other dementias and atypical parkinsonian disorders.[2,3] The *CSF1R* gene encodes a tyrosine kinase transmembrane receptor for the cytokine CSF1, which is trophic for phagocytic cells of the myeloid lineage including microglia, and for interleukin 34 (IL-34).[4] It has been established that lipid-laden microglia are a consistent microscopic finding in HDLS pathology. The *CSF1R* gene mutation thus establishes HDLS as a microgliopathy.[2] However, the exact mechanism is unclear. It may be related to an abnormal innate immune response predisposing to neurodegeneration. Discovering the role of *CSF1R* signaling in HDLS might offer novel insights into microglial physiology and the involvement of this cell type in neurodegeneration.

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GLATIRAMER ACETATE–INDUCED ACUTE HEPATOTOXICITY IN AN ADOLESCENT WITH MS

Ariel Antezana, Joseph Herbert, James Park, Ilya Kister, New York: Similar to Makhani et al.,[1] we saw a case of glatiramer acetate (GA)–induced hepatotoxicity with no history of interferon exposure. A 28-year-old woman with multiple sclerosis developed jaundice, choluria, acholia, elevated aspartate aminotransferase/alanine aminotransferase (905/1,103 U/L) and direct and total bilirubin (4.3/8 mg/dL) after 6 months of GA therapy. Viral and autoimmune hepatitis serologies were negative. Liver biopsy revealed hepatocellular necrosis of zone 3 with portal bridging and portal lymphocytic inflammation consistent with medication-induced hepatocellular injury. Thirty days after GA was discontinued, liver function normalized. Natalizumab was initiated and tolerated without complications for more than a year.

The US Food and Drug Administration Adverse Event Reporting System database contains 95 reports of liver injury suspected to be a result of GA, including 51 cases in which GA was the only medication administered.[2] The mechanism of hepatotoxicity is unclear as GA is not known to be metabolized in the liver.

Although GA was not found to cause hepatotoxicity in clinical trials, these cases[1,3–5] raise the question of whether liver function should be monitored in patients who are initiated on GA. It seems prudent to inform patients about symptoms of hepatotoxicity and advise them to seek immediate attention if these symptoms develop.

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TEACHING NEUROIMAGES: MICROVASCULAR DECOMPRESSION OF THE OPTIC NERVE

Mandeep S. Ghuman, Chandigarh, India: We were interested to read the Neuro*Image* by Woodall et al.[1] In addition to ectatic internal cerebral artery abutting the optic nerve, we also noted the tortuous course of intraorbital optic nerves with dilated perineural subarachnoid space, features consistent with idiopathic intracranial hypertension (IIH). IIH also results in vision diminution and even though the cause-and-effect relationship of vascular loop compression is unclear, it is important to rule out other causes and provide conservative management before resorting to surgery.

Compression over cranial nerves by redundant vessels and the correlation between compression and neurologic symptoms have not been shown. Vascular loop compression of the 5th cranial nerve resulting in trigeminal neuralgia was first suggested by Dandy[2] in 1934. The same concept was expanded to explain various cranial nerve disorders including hemifacial spasms, glossopharyngeal neuralgia, and geniculate neuralgia. Janetta[3] was the first to perform microvascular decompression and proposed that the redundant arterial loops compress the 8th cranial nerve at the cerebellopontine angle leading to symptoms of vertigo, tinnitus, and auditory loss.

The pathophysiology of vascular compression syndromes is controversial. A redundant vascular loop abutting, indenting, or even compressing any nerve is frequently seen on imaging in asymptomatic subjects, and demonstration of vascular compression should not be the sole diagnostic criterion when considering surgical decompression.[4–6]

Author Response: M. Neil Woodall, Cargill H. Alleyne, Jr., Augusta, GA: We appreciate Dr. Ghuman's comments regarding our article.[1] Dr. Ghuman correctly argued that vascular compression of the optic nerve is not the sole diagnostic consideration in the workup of monocular visual loss. Based on MRI findings, he argued that our patient should have been diagnosed with, and treated for, IIH rather than taken to surgery. Our patient presented with painless, progressive, monocular visual loss. He specifically denied any history of headaches and had no other signs or symptoms of increased intracranial pressure. On formal funduscopic examination, no papilledema was appreciated to support a diagnosis of IIH.[7] The diagnosis of IIH is clinical.[8] While neuroimaging features such as posterior globe flattening, optic nerve sheath distension, nerve tortuosity, and an empty sella are associated with IIH, only posterior globe flattening reliably predicts a diagnosis of IIH.[9] Our diagnosis is further supported by the patient's improvement in vision following microvascular decompression. While vascular compression of the optic nerve is not the only diagnostic consideration in cases of visual loss, it is vital when another explanation is not apparent, not only for our patient but for other reported patients.[10]

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Author disclosures are available upon request (journal@neurology.org).

Glatiramer acetate–induced acute hepatotoxicity in an adolescent with MS

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