The Canadian Journal of Neurological Sciences (2024), **51**, 323–324
doi:10.1017/cjn.2022.333

Canadian Journal of Neurological Sciences
Journal Canadien des Sciences Neurologiques

Letter to the Editor: New Observation

Enhancement of Subarachnoid Oculomotor Nerves in Bickerstaff Brainstem Encephalitis

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Keywords: CNS inflammation; Guillain Barre; Inflammatory diseases; Neuro-ophthamology

Bickerstaff brainstem encephalitis (BBE) is a central nervous system (CNS) variant of Miller Fisher syndrome (MFS) characterized by ophthalmoplegia, ataxia, and altered level of consciousness. MRI abnormalities in the form of non-enhancing T2-hyperintensities in the brainstem are present in up to 30% of patients with BBE.[1,2] We describe a case of BBE with bilateral, intense enhancement of cisternal third cranial nerves and demonstrate that MFS and BBE are likely part of the spectrum of the same condition that can preferentially affect either the peripheral or CNS, and sometimes both.

A 77-year-old man noticed acute onset of binocular oblique diplopia and right eyelid drooping. He had no recent fever or viral illness. Non-enhanced CT head in the emergency department was normal. MRI with time-of-flight angiography was performed to assess for aneurysmal compression of the right oculomotor nerve. Unexpectedly, it showed T2-hyperintensity in the right midbrain with no diffusion restriction (Figure 1A). Observation was recommended by a community neurologist, and follow-up MRI was arranged. Three weeks later, MRI demonstrated resolution of the previously seen right midbrain signal abnormality. However, a new area of diffusion restriction in the left thalamus was seen, consistent with acute infarction. During assessment at rapid-access stroke prevention clinic the following day, the patient was found to be confused and sleepy. He now had bilateral complete third nerve palsies. Contrast-enhanced MRI confirmed left thalamic infarction and showed a new right midbrain T2-hyperintensity without enhancement or diffusion restriction. A paired, avidly enhancing structure was seen passing through the interpeduncular cistern. This was first interpreted as a vascular anomaly but later identified as enhancing third cranial nerves (Figure 1B). Lumbar puncture showed mild lymphocytosis (nine white blood cells) and markedly elevated protein (3.2 g/L, normal <0.4). Serum and CSF serologies for multiple infectious agents were negative. MRI of the spine with contrast was normal and full contrast-enhanced body CT was unremarkable. Treatment with 5 days of oral prednisone commenced, and he was referred for neuro-ophthalmological consultation.

During neuro-ophthalmological assessment 2 months after the onset of symptoms, he remained drowsy and confused. Vision was 20/40 in each eye. Both pupils measured 8 mm in the dark without measurable response to light. There was bilateral complete ptosis with complete absence of adduction, supraduction, and infraduction. Deep tendon reflexes were normal, and there were no sensory or motor deficits. The patient had difficulty initiating gait, which appeared staggered. Repeat MRI brain showed decreased right midbrain T2-hyperintensity but persistent enhancement of both oculomotor nerves in their cisternal portion. Anti-Gq1b antibody titers were negative. He was treated with a 5-day course of intravenous immunoglobulin (IVIg) (1 g/kg) and over the following 3 months experienced gradual and near-complete resolution of systemic and ocular symptoms as well as all imaging abnormalities.

Though BBE is characterized as a central variant and MFS as a peripheral one of Guillain-Barre syndrome, both conditions belong to the spectrum of Gq1b-antibody-related disease, and this anatomic distinction is likely not clear-cut.[2] Ophthalmoplegia is a common feature of both conditions, though it is not known whether its mechanism is the same in both. Gq1b receptors are expressed on the extramedullary oculomotor nerves, which is the presumed location of pathology in MFS.

Our patient fit the clinical criteria for BBE and showed the characteristic radiologic finding of transient, non-enhancing brainstem T2/FLAIR hyperintensities on MRI. While post-contrast enhancement of the oculomotor nerves has been reported in MFS,[3] it is atypical and most cases of MFS demonstrate normal neuroimaging. Oculomotor nerve enhancement has not been previously reported in BBE, and its presence in this caselikely indicates that MFS and BBE represent the spectrum of the same condition. While inflammation of the subarachnoid portion of the third cranial nerves likely accounted for ophthalmoplegia, it could also have been due to pathological process affecting third nerve fascicles in the midbrain where T2-hyperintensities were seen on imaging. Though the transient nature of the midbrain lesions suggests that peripheral lesions were causative, it is difficult to draw conclusions due to the general lack of clinico-radiologic correlation in both MFS and BBE.[1,2]

We hypothesize that thalamic infarction in our patient was caused by inflammatory occlusion of perforating vessels in close

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Cite this article: Donaldson L, Jeeva-Patel T, Mandell D, and Margolin E. (2024) Enhancement of Subarachnoid Oculomotor Nerves in Bickerstaff Brainstem Encephalitis. *The Canadian Journal of Neurological Sciences* **51**: 323–324, https://doi.org/10.1017/cjn.2022.333

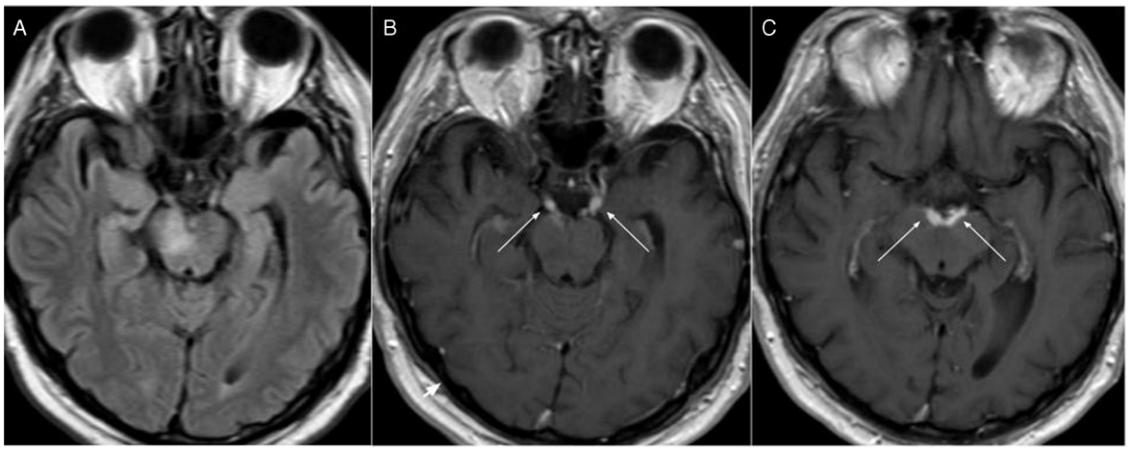

Figure 1: MRI findings in Bickerstaff brainstem encephalitis. (A) Axial T2-weighted FLAIR image showing hyperintensity within the right aspect of the midbrain. (B, C) T1-weighted, contrast-enhanced axial images shows intense enhancement of the cisternal segments of the third nerves bilaterally (white arrows).

proximity to the midbrain lesions as the thalamic stroke coincided with their appearance. Stroke has been reported in MFS after administration of IVIg and presumed to be secondary to ischemia developing due to underlying hyperviscosity syndrome. However, in our case, thalamic infarction occurred prior to treatment.

Our patient was seronegative for anti-Gq1b antibodies despite having clinical and radiologic findings typical of BBE. The monophasic nature of his symptoms and their complete resolution after IVIg treatment also supported the diagnosis of BBE. While most patients with MFS and BBE have measurable anti-Gq1b antibodies, around 10% of all cases described in the literature are seronegative.[4,5] One case series reported that seronegative cases are less likely to have history of antecedent infection or sensory disturbance and more likely to have lesions on MRI,[5] all of which were true of our patient. Antibodies to other gangliosides, ganglioside complexes and lipo-oligosaccarides, may be detected in some seronegative cases; however, few laboratories offer this testing.[4]

In summary, we describe the first case of BBE with bilateral enhancement of the cisternal portions of the third cranial nerves. This illustrates that peripheral nerve involvement may also be a prominent feature in BBE, and it is likely that MFS and BBE represent a spectrum of the same condition.

Funding. There are no funding sources to disclose.

Conflict of Interest. The authors have no conflict of interest.

Statement of Authorship. All authors contributed equally to data gathering, manuscript preparation, writing, editing, and final approval.

References

1. Odaka M, Yuki N, Yamada M, et al. Bickerstaff's brainstem encephalitis: clinical features of 62 cases and a subgroup associated with Guillain-Barré syndrome. Brain. 2003;126:2279–90. DOI 10.1093/brain/awg233.
2. Ito M, Kuwabara S, Odaka M, et al. Bickerstaff's brainstem encephalitis and Fisher syndrome form a continuous spectrum: clinical analysis of 581 cases. J Neurol. 2008;255:674–82. DOI 10.1007/s00415-008-0775-0.
3. Nagaoka U, Kato T, Kurita K, et al. Cranial nerve enhancement on three-dimensional MRI in Miller Fisher syndrome. Neurology. 1996;47:1601–2. DOI 10.1212/WNL.47.6.1601.
4. Koga M, Gilbert M, Takahashi M, et al. GQ1b-seronegative Fisher syndrome: clinical features and new serological markers. J Neurol. 2012;259:1366–74. DOI 10.1007/s00415-011-6360-y.
5. Yoshikawa K, Kuwahara M, Morikawa M, Kusunoki S. Bickerstaff brainstem encephalitis with or without anti-GQ1b antibody. Neurol Neuroimmunol Neuroinflamm. 2020;7:1–8. DOI 10.1212/NXI.0000000000000889.

https://doi.org/10.1017/cjn.2022.333 Published online by Cambridge University Press