Brain stem lesion in mitochondrial DNA G11778A mutation of Leber’s hereditary optic neuropathy

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Leber’s hereditary optic neuropathy (LHON) is one of the most common optic neuropathies. Although magnetic resonance imaging (MRI) is an important auxiliary tool for the diagnosis of optic neuropathies, it often fails to reveal parenchymal brain lesions in patients with LHON. Here, we report a case of LHON with MRI-revealed brain stem involvement.

Our patient was a 27-year-old Taiwanese male who had a history of recurrent pancreatitis, alcoholic hepatitis, and diabetes mellitus. Recently, he noticed a blue shadow occluding his central vision of the right eye, causing severe blurred vision. The same symptoms occurred in his left eye later, and he came to our hospital for evaluation. In our clinic, ophthalmologic examinations showed central scotoma and remarkable vision decrease in both eyes with a visual acuity of 20/2000. Ocular motility was normal and no nystagmus, diplopia, dysphagia, or unstable gait was detected. An ophthalmoscopic examination revealed mild hyperemic optic discs with minimal swelling. With the suspicion of LHON, an analysis of mitochondrial DNA (mtDNA) was performed, the results of which confirmed G11778A mutation.

Brain MRI was performed 1 month later, which revealed an unusual signal change presenting symmetric hyperintensities on the T2-weighted image and fluid attenuation inversion recovery over bilateral sides of the substantia nigra. These symmetric lesions were not enhanced and no other signal abnormalities were found on the brain MRI (Fig. 1).

The MRI changes in patients with LHON are not common, and the most commonly reported findings are hyperintensity of the T2-weighted image of the optic nerve, chiasm, tract, and gadolinium enhancement of the optic nerve or chiasm. Real brain involvements in patients with LHON are rare, and most of these patients also have other complications such as dystonia, cerebellar ataxia, ophthalmoplegia, Parkinsonian syndrome, Leigh’s disease, epilepsy, corticospinal tract dysfunction, and Ondine’s curse. We reviewed previous articles and concluded four patterns of brain involvements,
namely, diffuse intracranial lesions with cerebellar atrophy, striatal lesions, brainstem and hypothalamic lesions, and periventricular lesions. The involved areas of G11778A mutation are not specified and can occur in any location. The lesions of G14459A particularly occur in the striatum, brainstem, and thalami. In addition, the lesions of G3460A, T14484C, and G11778A are also reported in the brainstem, hypothalamus, and periventricular regions.

Neuromyelitis optica (NMO) and multiple sclerosis (MS) might also cause brain stem lesions. However, the brain stem lesions in patients with NMO are typically located in the dorsal part of brain stem with unsymmetrical poorly defined margins; and patients with MS have brain stem lesions in both the ventral and dorsal parts with unsymmetrical defined margins. In our patient, however, the brain stem lesion was symmetrical; therefore, dorsal parts with defined margin may be one of characteristics that differentiate the MS or NMO diseases from LHON.

In conclusion, the LHON disorder should be screened in hot spot of mtDNA mutation by a molecular method if a family history of visual disorder and the brain stem lesion are disclosed. Brain stem lesion in an MRI study may provide an evidence to support and narrow down the differential diagnosis of optic neuropathy.

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References