Wolfram syndrome presenting with upbeat nystagmus

H.Y. Rhee[1], Y.Y. Shin[1], S.S. Yoon[2]
[1]*Department of Neurology, Kyung Hee University Hospital at Gangdong, South Korea*
[2]*Department of Neurology, Kyung Hee University Hospital, South Korea*

Wolfram syndrome (WFS) is a rare autosomal recessive genetic disorder characterized by diabetes insipidus, diabetes mellitus, optic atrophy and deafness. Imaging studies revealed atrophy of brainstem and cerebellum in WFS but its clinical significance remained unclear. A 18-year-old woman visited to our hospital for anosmia which had developed two years before the admission. She had been diagnosed with diabetes mellitus at the age of 3 and bilateral optic atrophies at the age of 11. On admission, the patient was totally blind and video nystagmography revealed upbeat nystagmus in central gaze both with or without fixation. MRI of the brain demonstrated diffuse atrophy of brainstem and cerebellum. Diagnostic exome sequencing test revealed two distinct variants (c.1232_1233delCT; p.Ser411Cysfs*131 and c.2168TC; p.Leu723Pro). WFS is associated with smaller intracranial volume with specific abnormalities in the brainstem and cerebellum even at the earliest stage of clinical symptoms but there is a variable degree of mismatching between clinical and radiologic findings in brainstem and cerebellum of WFS patients. Pendular nystagmus and gaze-evoked nystagmus have been described as the corresponding neurological deficit. Upbeat nystagmus is commonly localized to the caudal medulla, more rostral brainstem lesions with interruption of the ventral tegemental tract, or brachium conjunctivum in the rostral pons and medulla. Although the specific neural substrate for the abnormality is not clear, it is possible that brainstem and cerebellar abnormality in WFS present with upbeat nystagmus in this case.