

Wolfram (DIDMOAD) syndrome with ventral central pontine hyperintensity without brainstem atrophy

Sir,

A 27-year-old male, diagnosed to be having a juvenile-onset diabetes mellitus and bilateral sensory neural hearing loss, presented with an 8-year history of gradually progressive visual loss. The history was suggestive of the typical Wolfram (DIDMOAD, Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness) syndrome. He had features of hypogonadism, and no other neurological symptoms or signs were noted. His best corrected visual acuity was 3/60 N36 in the right eye and 6/60 N18 in the left eye. Fundus examination showed temporal disc pallor with moderate non-proliferative diabetic retinopathic changes in both eyes. Visual evoked potential (VEP) was not elicitable in both the eyes. His visual field charting revealed severe visual field defects with macular sparing [Figure 1]. He underwent a magnetic resonance imaging (MRI), which showed T2/fluid-attenuated inversion recovery (FLAIR) hyperintensity in the anterior half of lower pons [Figures 2a-c]. High signal intensity was seen in the ventral and central pons, with subtle hyperintensity in the ventral paramedian position [Figures 2b and c]. No atrophy of the pons,

cerebellum, or cerebellar peduncles was seen. Although subtle FLAIR hyperintensity was seen in the optic radiation, it was not entirely convincing [Figure 2d]. The posterior pituitary T1 hyperintense bright spot was seen, albeit small in size [Figure 2e]. Bilateral optic nerves were small with prominence of perioptic cerebrospinal fluid spaces [Figures 2f-h]. Mild T1 hyperintensity was seen in both the globus pallidi.

Wolfram syndrome 1 (WFS1) is a rare autosomal recessive genetic disorder, in which optic atrophy, diabetes mellitus, and hearing loss are associated with diabetes insipidus, commonly due to the mutation of the WFS1 gene on chromosome 4p16.1. Wolfram syndrome 2, in which optic atrophy, diabetes mellitus, and hearing loss are seen, but not diabetes insipidus, is caused by *CISD2* gene mutation.^[1] Juvenile-onset diabetes mellitus and optic atrophy are minimal requirements for the diagnosis of both the varieties of WS, whereas sensorineural hearing loss, ataxia, and urinary tract problems are the other major symptoms,^[2] with or without diabetes insipidus. Juvenile diabetes mellitus is probably the first clinical manifestation

of the syndrome, whereas visual deterioration and hearing loss present during the second or third decade of life. Ataxia or imbalance is one of the common neurological problems seen in up to 60% of patients;^[2] psychiatric symptoms^[3,4] and cognitive impairment are the other less common neurological presentations.

MRI findings previously described in this syndrome are brainstem atrophy,^[5] optic tract atrophy, absent posterior pituitary T1 bright spot, cerebellar atrophy, and third ventricular atrophy.^[6] Although optic tract atrophy was reported in 100% of cases in larger series,^[6] in our case, there was no evidence of optic tract atrophy; however, the visual evoked potential (VEP) was inelicitable. This was attributed to sparing of some proportion of optic tract fibres sufficient enough to preserve his macular vision and give a normal MRI appearance but inadequate to give a positive response on VEP testing. Mild T1 hyperintensities in bilateral globus pallidi were probably suggestive of a more widespread degenerative process even in the absence of gross cerebral parenchymal atrophy. This finding is in accordance with a previous study, in which multimodal imaging demonstrated brain abnormalities even in the early stage of the syndrome.^[7] Previously reported cases showed either normal or absent posterior pituitary signal intensity on T1 weighted images; however, in our case, the posterior pituitary T1 bright spot was small but discernable. Due to progressive degeneration of supraoptic and paraventricular nuclei, posterior pituitary atrophy may occur. This may lead to the absence of the posterior pituitary bright spot in the late stages, as well as its presence in the early stages of the disease. Probably, our case is representative of an intermediate stage of degeneration in the spectrum. Moderate atrophy of

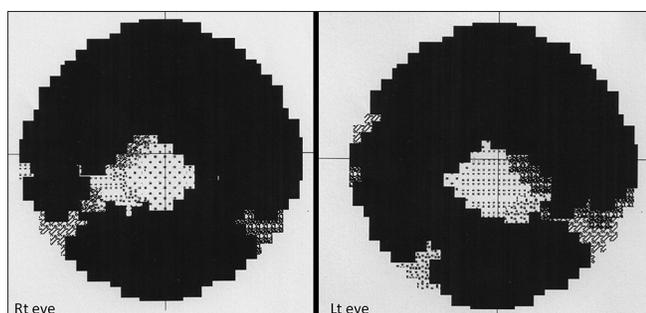


Figure 1: Visual field chart showing macular sparing visual field defect in both eyes

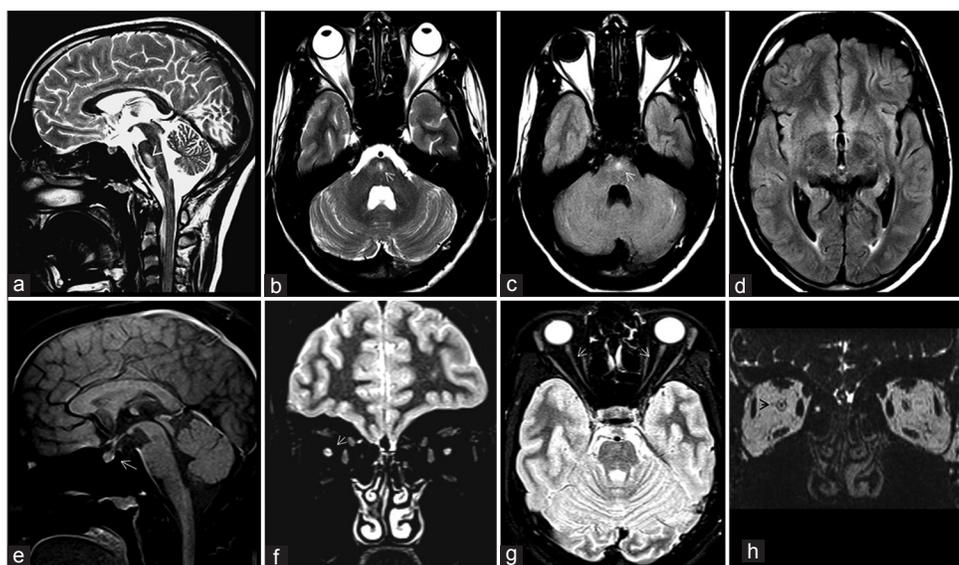


Figure 2: (a) Midsagittal T2-weighted, (b) axial T2, (c) axial FLAIR MR images showing ventral lower pontine hyperintensity without volume loss, with normal cerebellum. (d) Axial FLAIR image showing normal optic radiation. (e) Midsagittal T1-weighted image showing small posterior pituitary bright spot. (f-h) Coronal and axial T2-weighted images showing bilateral optic nerve atrophy

the brainstem and cerebellum was described as the first sign even in patients without clinical evidence of neurological problems;^[3] however, the first sign in our case was T2/FLAIR hyperintensity in the central and ventral pons without atrophy. The possible etiology of this hyperintensity is the degeneration of the ventral nucleus of trapezoid body, that represents the major decussation of the central auditory pathway. As the patient had residual hearing for low frequencies, he did not have the advanced stage of the disease. Probably, only patients in an advanced stage produce the typical central and bilateral paramedian T2/FLAIR hyperintensities of ventral lower pons with associated atrophy.^[8]

In conclusion, we report a case of WS with T2/FLAIR hyperintensity in the ventral midline pons in the absence of brain atrophy. The presence of T2/FLAIR hyperintensity in anterior central pons could be one of the initial MRI abnormalities of the brain. In addition, our case describes the additional MRI findings associated with the syndrome, that is, bilateral globus pallidi T1 hyperintensities, and a small posterior pituitary T1 bright spot.

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Conflicts of interest

There are no conflicts of interest.

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