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WOLFRAM SYNDROME: A RARE DIFFUSE NEURODEGENERATIVE DISORDER

Radiology

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ABSTRACT

Wolfram syndrome (DIDMOAD – Diabetes insipidus, Diabetes mellitus, Optic atrophy, Dementia and Deafness) is very rare diffuse neurodegenerative disorder. There are two types of it : 1. Familial 2. Sporadic. A few MRI examinations that have been reported show absent physiological high signal intensity of the neurohypophysis, shrinkage of the optic nerves, optic chiasma and tracts and atrophy of the hypothalamus, brain stem, cerebellum and cerebrum. We report a 37 years old female with features of wolfram syndrome.

KEYWORDS

DIDMOAD, Diabetes insipidus, Diabetes mellitus, Optic atrophy.

INTRODUCTION

Wolfram and Wagener described a family in 1938 in which siblings had bilateral optic atrophy, diabetes mellitus, deafness, incontinence and ataxia. All the cases led to acronym DIDMOAD, indicating four cardinal features: Diabetes insipidus, Diabetes mellitus, Optic atrophy and Deafness.[1] It is considered as autosomal recessive disorder and a nuclear encoded gene has been mapped on the short arm of chromosome 4p specifically D4S431.[2] Since optic atrophy, ataxia, deafness and diabetes mellitus are often associated with mitochondrial disorder, a mitochondrial inheritance has been suggested.[3]

CASE REPORT

A woman now 37 years old, came to the attention of another institution when she was 6 years old because of measles viral infection. After that patient developed diabetes insipidus. At the age of 8, she developed epileptic fit with blurring of the vision and went for MRI Brain scan. She was diagnosed with bilateral optic atrophy and cerebellar atrophy. Her all symptoms are gradually increased till now with near vision reduced upto 4 feet only. Since last 4 years, she stopped all the activities and facing sluggishness in every activity.

MRI revealed mild cerebral atrophy (Fig-1.a), moderate to severe diffuse cerebellar atrophy (Fig-1.b) and moderate atrophy of pons (Fig-1.b). MRI was also suggestive of moderate bilateral optic nerve atrophy (Fig-1.c) and mild diffuse abnormal hyperintense signal in bilateral periventricular and subcortical white matter and bilateral peri trigonal region extending along optic tracts (Fig-2.a). There is evidence of blurring of the posterior margin of substantia nigra, corresponding to 'probably abnormal' category in the spectrum of "swallow tail" appearances in movement disorder (Fig-2.b). Other Parkinson plus related MRI parameters are within normal limit. MR Spectroscopy findings reveal mild reduction in NAA in the gray matter, suggestive of neuronal loss (Fig-2.c). MR Volumetry studies reveals mild decrease in the whole brain and bilateral hippocampal volumes (Fig-2.d).

DISCUSSION

Previous studies on wolfram syndrome reflected a diffuse neurodegenerative process in the central nervous system. It is also a primary neurodegenerative disease with urological and endocrine abnormalities, gonadal and thermoregulation abnormalities.[4] Diabetes mellitus could result from loss of B islet cells of pancreas and hypothalamic degeneration. Optic atrophy could result from atrophy, severe axonal loss and demyelination of the optic nerves, chiasm, tracts and optic radiations, which can lead to degeneration of the superior colliculi and lateral geniculate bodies. Diabetes insipidus is associated with atrophy and degeneration of the hypothalamus, with loss of vasopressin secreting neurons in the supraoptic and paraventricular nuclei and degeneration of posterior lobe of the pituitary. In this syndrome, deafness is mostly sensorineural in nature with retro cochlear defect due to degenerative process and atrophy of the vestibulocochlear nuclei and inferior colliculi.[5,6]

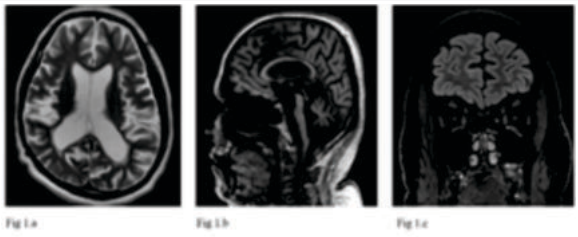

Fig 1.a : Widened sulci with prominent gyri suggests age inappropriate cerebral atrophy.
Fig 1.b : Widened cerebellar folia suggests severe cerebellar atrophy. Atrophy of the pons is also noted in same image. Fig 1.c : Both optic nerves are thinned out suggest bilateral optic nerve atrophy.

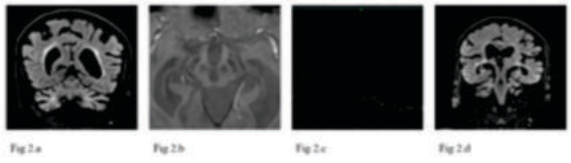

Fig 2.a : Mild diffuse abnormal hyperintense signal in bilateral periventricular and subcortical white matter and bilateral peri trigonal region extending along optic tracts.
Fig 2.b : Blurring of the posterior margin of substantia nigra, corresponding to 'probably abnormal' category in the spectrum of "swallow tail" appearances in movement disorder.
Fig 2.c : MRS shows mild reduction in NAA in the gray matter suggests neuronal loss.
Fig 2.d : MR Volumetry studies reveals decrease in the whole brain and bilateral hippocampal volumes

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