A 21 years old female presented to us with progressive visual loss since 1 year. She was a known case of type I diabetes mellitus since 6 years of age and had hearing loss since the past 5 years. Her polyuria and polydipsia had been attributed to diabetes mellitus.

Imaging Findings:

She was advised MRI of brain and both orbits which revealed bilateral optic nerve atrophy along the entire length of optic nerves up-to the optic chiasma. Note was also made of absence of the pituitary bright spot. Mild hyper-intensity was seen in the region of pons and medulla alongwith brainstem and cerebellar atrophy. Based on the clinical and imaging findings, a diagnosis of Wolfram syndrome was made. Diabetes insipidus was later confirmed by decreased urine osmolality and water deprivation test.

Discussion:

Wolfram syndrome is an uncommon and complex genetic disease which presents with early onset of insulin dependent diabetes mellitus, progressive optic atrophy, diabetes insipidus and sensori-neural hearing loss. That is why it is also called as DIDMOAD syndrome (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, Deafness). It has two routes of genetic transmission – either autosomal recessive or mitochondrial. [1]

The earliest manifestation of Wolfram syndrome is usually type I diabetes mellitus, followed by optic atrophy, diabetes insipidus and sensori-neural deafness respectively.[2] A wide array of abnormalities of the central nervous system, urinary tract and endocrine glands may also be seen.[3] The time of onset of clinical symptoms may vary in different patients. Our patient showed late onset of visual loss and early onset of diabetes mellitus and insipidus, although, the diagnosis of diabetes insipidus was delayed.

The spectrum of radiological findings in Wolfram syndrome comprises of absence of the physiological high signal of the posterior lobe of the pituitary, atrophy of optic nerves, chiasma and tracts, atrophy of hypothalamus, brain stem, cerebellum, and cerebral cortex.[3] Pontine hyperintensity along-with marked atrophy of the brain stem, middle cerebellar peduncles, and cerebellum have also been described.[4]

Other hereditary causes affecting optic nerves are Septo-optic dysplasia and Leber’s hereditary optic neuropathy (LHON). MRI features of septo-optic dysplasia include hypoplastic optic nerves, optic chiasma and infundibulum, anterior pituitary hypoplasia, absent or ectopic posterior pituitary, partial or complete absence of septum pellucidum and corpus callosum with variable degrees of schizencephaly and hydrocephalus.[5] None of these findings were present in our case except for optic nerve atrophy and absent pituitary bright spot.

LHON shows bilateral symmetrical optic nerve atrophy with absence of any other imaging abnormality in brain and orbit.

A combination of optic nerve disease and periventricular and brainstem hyperintensity in a young female is
commonly seen in demyelinating diseases like Multiple Sclerosis. However, the clinical presentation as well as absence of MRI features like corpus callosum involvement and Dawson’s fingers helped to exclude this entity. [6] Neurodegenerative disorders like Multi System Atrophy and familial spinocerebellar degeneration also show brainstem and cerebellar atrophy with pontine hyperintensity.[4] However, none of them show pituitary – hypothalamic dysfunction and optic nerve atrophy.

We conclude that the diagnosis of Wolfram syndrome requires a high index of clinical suspicion along-with the rare combination of peculiar imaging findings.

Written informed patient consent for publication has been obtained.

**Differential Diagnosis List:** Wolfram syndrome, Septo-optic dysplasia, Multiple sclerosis, Leber’s hereditary optic neuropathy, Multi System Atrophy, Familial spinocerebellar degeneration

**Final Diagnosis:** Wolfram syndrome

**References:**


Description: Figure 1. Sagittal T1W image showing absent posterior pituitary bright spot. Origin: Department of Radiology, Teerthanker Mahaveer University, Moradabad, India.
Figure 2a. Axial T2W image showing atrophy of bilateral optic nerves.

Description: Figure 2a. Axial T2W image showing atrophy of bilateral optic nerves. Origin: Department of Radiology, Teerthanker Mahaveer University, Moradabad, India.
Description: Figure 2b. Coronal FLAIR images showing severe optic nerve atrophy (arrows)

Origin: Department of Radiology, Teerthanker Mahaveer University, Moradabad, India.
Description: Figure 4a. Axial T2W image showing atrophy of cerebellum and brainstem (at midbrain level) along-with brainstem hyperintensity. Origin: Department of Radiology, Teerthanker Mahaveer University, Moradabad, India.
Figure 4b. Axial T2W image showing atrophy of cerebellum and brainstem (at pons level) along-with brainstem hyperintensity. **Origin:** Department of Radiology, Teerthanker Mahaveer University, Moradabad, India.