Case Report with Review of Literature

A young diabetic with suicidal risk: Rare disease with a rarer presentation

Rajeev Philip, P. Prem Patidar, Pankaj Agarwal, K. K. Gupta

Department of Endocrinology, LLRM Medical College Campus, Meerut, Uttar Pradesh, India

ABSTRACT

Rare genetic or inherited forms of diabetes can mimic immune mediated type 1 diabetes. Early age of onset and associated features help to differentiate these diseases from type 1 diabetes. Wolfram syndrome, an inherited neuro degenerative disorder, presents as insulin dependent diabetes mellitus, diabetes insipidus, optic atrophy and deafness. But less well described features like psychiatric manifestations can be the presentation of this disease. We present such a case. Wolfram syndrome should be considered as a differential diagnosis in insulin dependent diabetic children who present with neuropsychiatric problems.

Key words: Diabetes in young, neuropsychiatric manifestations, wolfram syndrome

Introduction

Rare genetic or sporadic forms of diabetes can present as insulin dependent diabetes in children and can mimic type 1 diabetes. Very early onset of symptoms and associated features help in differentiating these forms of diabetes from type 1 diabetes.[1] One of the rare forms of diabetes is Wolfram syndrome, which is an inherited or sporadic neuro degenerative disorder, presenting as, diabetes insipidus, diabetes mellitus, optic atrophy and deafness (DIDMOAD). But there are less well known manifestations of this syndrome, which include neuropsychiatric manifestations, reproductive abnormalities, limited joint mobility, cardiovascular and gastrointestinal autonomic neuropathy, any of which can be the presenting feature.[2-4] We report a case of Wolfram syndrome, whose presentation was of severe depression with suicidal risk. Truly, a rare disease with a rarer presentation.

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Case Report

A 15 year diabetic boy was admitted in our hospital for evaluation of behavioural problems. He was diagnosed to have diabetes at the age of 4 years, and was on thrice daily pre mix insulin. His current problem was severe depressive symptoms for the past 5 years. He also had history of temper tantrums, with frequent fights with his classmates over minor issues. Off late, he had become very aloof, with decreasing peer interactions and strained relations with his parents. His scholastic performance had also declined significantly. He also had history of decreased vision for the past 4 years, and decreased hearing for the past 2 years. His glycemic control was good till six months back, but recently had widely fluctuating blood glucose, with the last two/HbA1c levels above target.

Examination revealed that he had significant loss of vision, with 6/24 vision in both eyes. Fundoscopy was suggestive of optic atrophy [Figure 1]. An audiometry revealed significant sensory neural hearing loss, especially at the higher frequencies. A 24 hour urine output was measured after control of blood sugars, which was 4.1 litres, indicating polyuria. The serum osmolality was high-305 mOsm/kg (corresponding blood glucose 147 mg/dl) and urine osmolality was low (168 mOsm/kg), and serum sodium was 146 meq/l, suggestive of diabetes insipidus. MRI of the brain was done, which showed altered signal intensity at the optic nerve, absent

Corresponding Author: Dr. Rajeev Philip, G10, PG Hostel, LLRM Medical College Campus, Garh Road, Meerut, Uttar Pradesh - 250 004, India. E-mail: endollrm@yahoo.com

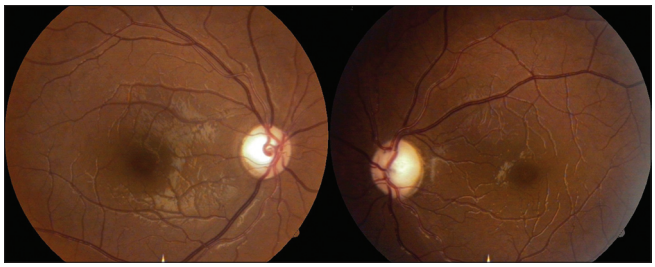

Figure 1: Fundus photograph showing optic atrophy

posterior pituitary bright spot in T1 (suggestive of central diabetes insipidus), with atrophy of the brainstem [Figure 2]. Based on these findings-DIDMOAD and psychiatric manifestations, the final diagnosis of Wolfram syndrome was made.

Discussion

Wolfram syndrome is a rare neuro degenerative disorder which may be autosomal recessively inherited or may be sporadic. First described in 1938 by Wolfram and Wagener, Wolfram syndrome manifests as a combination of young onset non-immune insulin dependent diabetes mellitus and progressive optic atrophy in all patients with added diabetes insipidus and sensory neural deafness in 70% of the patients and hence referred as DIDMOAD syndrome.[5]

The syndrome is due to the defective synthesis of wolframin, (a 100-kd transmembrane protein encoded by WFS1, a gene located at 4p16.1.116) found in the endoplasmic reticulum and in the neuronal and neuroendocrine tissues. Wolframin induces ion channel activity with a resultant increase in intracellular calcium and may play an important role in intracellular calcium homeostasis.[6]

Due to variable expression of the protein, the phenotype of the disease varies, with diabetes mellitus manifesting early followed by optic atrophy in all the patients. Other manifestations like diabetes insipidus, deafness, neurologic manifestations, other hormonal deficiencies like ACTH deficiency and growth hormone deficiency, thiamine responsive sideroblastic anaemia, have variable penetrance.[7]

Psychiatric manifestations of Wolfram syndrome occur less commonly and are less well documented. Upto 22% of patients can have psychiatric problems, based on different series. The major manifestations include severe depression, suicidal risk, poor scholastic performance, temper tantrums and adjustment disorder.[7,8] Moreover, heterozygous carriers of the gene for Wolfram syndrome, who constitute about 1% of the general population are at a higher risk of developing psychiatric illness and have a 26 fold more chance of having a psychiatric hospitalisation.[9]

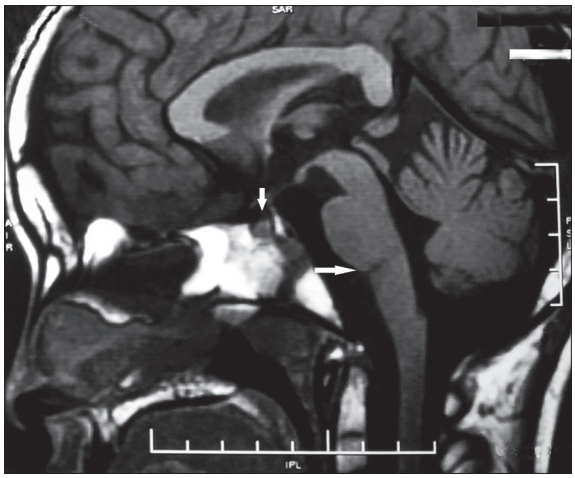

Figure 2: MRI brain (T1) showing absent bright spot of posterior pituitary (small arrow) and brainstem atrophy (big arrow)

Our case is unique in the aspect that the psychiatric manifestations were the presenting feature, which lead to the diagnosis of the disease. This also brings to light the less talked about neuropsychiatric problems associated with Wolfram syndrome, and gives the message that Wolfram syndrome should be considered as a differential diagnosis in insulin dependent diabetic children who present with neuropsychiatric problems.

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