CASE REPORT

Psychotic Manifestation in a Patient with Wolfram Syndrome (DIDMOAD)

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**Abstract**

Wolfram syndrome (WFS) is a rare neurodegenerative disorder which is characterized by presentation of diabetes insipidus, juvenile diabetes mellitus, optic atrophy and deafness. We describe a case of WFS with presentation of psychosis. A 17-year-old female presented with psychiatric manifestations, namely inappropriate behaviour and second person auditory hallucination since the age of 16 years. The patient was diagnosed with type 1 diabetes mellitus at the age of 10 years old and subsequently progressive hearing and visual loss a year later. Her ophthalmic evaluation revealed total blindness due to optic atrophy. However she did not have renal dysfunction and diabetes insipidus which are also features of the syndrome. There is scarce literature to describe on psychiatric presentation in WFS. In the past, the psychiatric manifestation which was reported most of times was mood and suicidal behaviour. Hardly any article reported about psychosis (hallucination). We believe, her psychiatric manifestations were related to sensory deprivation due to blindness and deafness caused by the progression of WFS.

**Keywords:** Wolfram Syndrome, Diabetes Mellitus, Optic Atrophy, Psychiatric Manifestation

**Introduction**

The Wolfram syndrome is a rare, complex, hereditary, progressive neurodegenerative genetic disorder which was first described by Wolfram and Wagener in 1983.¹ It is characterized by non-inflammatory atrophic changes in the brain and in pancreatic islets resulting in diabetes insipidus, diabetes mellitus, optic atrophy and deafness. The syndrome is denoted by the acronym of
DIDMOAD which elaborates its medical presentations.\(^2^3\)

The underlying pathogenesis of the syndrome is not well known, however genetic inheritance through autosomal recessive is identified as a strong etiological explanation. The prevalence of WFS in general population is rare with the estimation of 1 per 770,000 population.\(^4\) Generally there is equal gender distribution between males and females. Parental consanguinity has been noted to be common among WFS cases and it is estimated happened 1 in 350 people carrying the genes of Wolfram Syndrome.\(^4\)

In literature, patients with Wolfram Syndrome have been reported with psychiatric presentations but mainly mood symptoms and depression not psychosis. This paper describes the presentation of psychotic symptoms by a patient with Wolfram Syndrome.

**Case Report**

A 17-year-old female was referred to the Department of Psychiatry and Mental Health, Hospital Tunku Ampuan Afzan Kuantan for psychiatric evaluation. She presented with abnormal behaviour and having auditory hallucination since the age of 16. She was diagnosed to have diabetes mellitus at the age of 10 years old and currently on regular insulin injection. She developed progressive hearing and visual loss and bilateral optic atrophy at the age of 12 years.

The abnormal behaviour consisted of laughing and crying for no apparent reasons. She repeatedly complained of being disturbed by someone’s voices near her though she was alone at that time. She would respond back by saying ‘please do not disturb me’ according to her mother. Though the communication was difficult it was clearly presence of second person auditory hallucinations through hearing aid.

The parents described her to be irritable and tended to shout inappropriately. She was socially withdrawn and most of the time she would isolate herself in a room. She neglected her personal hygiene and her speech was irrelevant at times.

She was born of consanguineous marriage. Her parents are first degree cousins. Two out of her siblings were also diagnosed to have WFS. The elder was diagnosed at the age of 10 years and another sister at the age of 13 years. Otherwise, there was no family history of psychiatric illness.

Mental state examination revealed poor rapport and labile mood. She kept on knocking her hands on a table. She was making incomprehensible sounds and kept on saying “go away”. Sometimes she smiled inappropriately and there was loosening of association in her speech. When she was asked about perceptual disturbance, she admitted of having visual and auditory hallucination since a few months back. She required a hearing aid device to help to enhance her hearing.

Bilateral papillary atrophy was found in optic fundoscopic examination. Her audiometric examination revealed of unilateral neurosensory deafness. She was diagnosed to have psychotic symptoms due to underlying Wolfram clinical manifestation. She was started on tablet Risperidone 0.5 mg daily and she responded well. Her behavioural abnormalities and psychosis resolved immediately within few weeks. As for 9 months from her referral to psychiatrist, she was well behaved without any abnormal behaviour and noted to be
fairly manageable. MRI of the patient showed no obvious abnormal findings.

Discussion

We present here a classical case of Wolfram syndrome with psychotic symptoms. She has consanguineous parents with two other siblings were also diagnosed with Wolfram syndrome. This patient was presented with diabetes mellitus associated with optic atrophy in the first decade; sensorineural deafness and blindness in the second decade. However renal tract abnormalities and multiple neurological abnormalities such as cerebellar ataxia, myoclonus, and psychiatric illness which commonly reported in their fourth decade are not present in this patient. In this case the psychosis presentation is rather slight early unlike what was been reported in literature.

In our literature search, there are not many literatures mentioning about psychiatric presentation in WFS except very few case reports which tried to identify the cause of psychotic symptoms and the psychiatric symptoms were mainly reported as mood fluctuations. It has been reported that patients with Wolfram syndrome were more likely to have mood disorders such depression, mood swings and also suicidal tendency. Mood swings in Wolfram syndrome is said may also be caused by hypoglycaemia syndrome. Further search specifically on the aspect of psychosis or hallucination is even scarce. Although there are not many literatures to elaborate on the etiological cause of psychiatric presentations in Wolfram syndrome, it has been reported minimally in a few case reports. In this case we regard her auditory hallucination was resulted from sensorial deprivation. In literature not related to WFS, perceptual disturbances such as auditory and visual hallucinations could be influenced by environmental conditions such as sensorial deprivation or exposure to noise or other forms of ambiguous stimulation. In this case, the patient developed auditory and visual hallucinations after having hearing and visual losses.

Severe psychiatric symptoms of depression, psychosis and organic brain syndrome are reported in up to 25% of patients. Despite family studies indicate autosomal recessive inheritance, there is no convincing evidence of an increased risk of psychiatric illness in the first degree relatives who may be carriers.

With regards to medical presentations, diabetes mellitus was the presenting symptom in 78% of cases. The presenting age ranges from 3 weeks to 16 years with median age of 6 years. It is non-autoimmune, insulin deficient, and non-HLA linked. Microvascular complications are rare and seem to develop slower than in type 1 diabetes. Partial cranial diabetes insipidus occurs in about three quarters of patients at a median age of 14 years (ranges from 3 months to 40 years) and respond to vasopressin treatment. The magnetic resonance imaging showed loss of signal on hypothalamus and posterior pituitary clearly proved the cranial nature of insipidus.

The presence of optic atrophy in a patient with type 1 diabetes of short duration has alerted the clinician to the possibility of Wolfram syndrome. The optic atrophy is progressive and eventually leads to blindness irrespective of the level of diabetic control. The presenting age ranges from 6 weeks to 19 years with median age of 11 years.

A neurosensory deafness in this patient had been ascertained by the audiometric assessment. The audiometric abnormalities
have been reported in 60 percent of patients with high tone nerve deafness as the characteristic feature. Symptomatic sensori-neural deafness develops in two thirds of patients at a median age of 16 years (ranges: 5-39 years); and a quarter of these requires hearing aids for high frequency loss. Dilated renal outflow tracts presents in two thirds of patients at median age of 20 years (ranges from 10-44 years); with urinary frequency, incontinence and recurrent infections.

References


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