Case Report

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A Rare Case of Wolfram Syndrome

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A 15-year-old boy was referred because of bilateral hydroureteronephrosis. He had poorly controlled diabetes mellitus since he was 4 years old. He had polyuria and polydipsia. On water deprivation test, he developed hypernatremia along with increased levels of BUN and creatinine. He also had hypertension that was effectively managed with losartan. Bilateral optic atrophy was detected on ophthalmoscopic examination. It seems that this boy is a rare case of Wolfram syndrome.

Keywords: Diabetes Insipidus; Diabetes Mellitus; Wolfram Syndrome; DIDMOAD; Deafness; Optic Atrophy.

Running Title: A Rare Case of Wolfram Syndrome

Introduction

Clinical feature of Wolfram Syndrome (WS) (also known as DIDMOAD syndrome) include four most common features 1) Diabetes insipidus (DI), 2) Diabetes Mellitus (DM), 3) Optic atrophy and 4) Deafness. It is a rare hereditary disorder which results in vasopressin deficiency, as well [1]. The association of DM and progressive optic atrophy are the cardinal features of this syndrome. Other features include DI (70 – 75 %) and auditory nerve hearing loss (65%) [2]. Basically WS is due to mutations in the WFS1 gene positioned on chromosome 4 (4p16.1) resulting in deficiency of antidiuretic hormone (ADH) release [1, 2]. It is a progressive neurodegenerative disorder presenting with non autoimmune and non-HLA linked DM along with optic atrophy in the first decade, DI and sensorineural deafness in the second decade, and renal tract abnormalities early in the third decade of life.

Multiple neurological abnormalities, like myoclonus, cerebellar ataxia, and psychiatric illnesses appear during early years of the fourth decade [3]. About 60 percent of the patients with WS develop neurologic or psychiatric disorders. Most common of these abnormalities are physical imbalance and poor coordination problems such as ataxia that typically begin in early adulthood. Patients with WS also referred for irregular breathing caused by the brain's inability to control breathing, peripheral neuropathy, and intellectual impairment. Psychiatric disorders associated with WS include psychosis, severe depression, and impulsive and aggressive behavior [4]. Wolfram patients usually die from central respiratory failure as a result of brain stem atrophy in the third or fourth decade of life [5]. There are two types of WS with many overlapping features. The two types are differentiated by their genetic cause.

In addition to the usual features of WS, individuals with WS type 2 have stomach or intestinal ulcers and excessive bleeding after an injury. The tendency to bleed combined with the ulcers typically leads to abnormal bleeding in the gastrointestinal system. People with WS type 2 do not develop DI [4]. In this report, we present a boy with long term insulin dependent diabetes mellitus (IDDM) who was referred to the nephrology clinic for evaluation of severe hydroureteronephrosis. Consent was taken from patient and his parents to report the case.

Case Report

A 15-year-old boy was referred for evaluation bilateral hydroureteronephrosis. Two female siblings of him did not have any problems. He had poorly controlled DM since 4 years of age and ophthalmic problems without a definitive diagnosis. He was referred to nephrology clinic for incidental kidney and urinary tract sonography that revealed severe hydroureteronephrosis and bladder enlargement with a high volume of post voiding residue. He had moderate hypertension adequately controlled with oral losartan. He also had enuresis polyuria and polydipsia, and day time incontinence.

The thyroid function tests, liver function tests, serum calcium and phosphor were in the normal range. Renal function was decreased as the serum creatinine level was 1.2 mg/dl and GFR was 64mL/min/1.73m^2. The urine was very dilute with a very low specify gravity (SG=1002). His urine output was 13 -15 lit/24 h. HbA1C was 9% and the level of 25(OH) vitamin D was insufficient that was managed carefully. Water deprivation challenge test led to hypernatremia and elevation of BUN and serum creatinine levels. After desmopressin usage, the specific gravity of the urine increased, urine output decreased, and hypernatremia improved.

On ophthalmology evaluation, bilateral optic atrophy was reported with minimal changes of diabetic retinopathy and decreases visual acuity. He had a normal audiometric test. He also had depression and psychiatric consultation was requested. Following the administration of desmopressin, enuresis and day time incontinency improved, urine specific gravity increased, and blood sugar controlled with the same dose of insulin. Follow up renal sonography 2 months after desmopressin therapy reviled decreasing of urinary tract dilatation. The BUN and serum creatinine levels also decreased effectively.

Discussion

Wolfram Syndrome is a rare diffuse neurodegenerative disorder characterized by DI, DM, optic atrophy, deafness, and a wide variety of central nervous system abnormalities. Insulin-dependent diabetes mellitus with optic nerve atrophy is essential criteria for diagnosis of this disorder [6]. Endocrine disorders that have been described in this condition include hypogonadotropic hypogonadism, growth failure, and hypothyroidism.

Another common finding is depression pre-existing the diagnosis of WS [7]. The patient had DM, DI, optic atrophy, depression, but had no deafness and endocrine dysfunction. He had urinary tract abnormality due to long term polyuria. One cause of severe bilateral hydroureteronephrosis is atonic bladder in the associated background neuropathy.

Urodynamic study showed high pressure voiding, so we prescribed oxybutinine and baclofen. After starting desmopressin, his day-time incontinence improved and enuresis became better. It seems that the cause of hypertension in this patient is renal ischemia and decreased perfusion and activation of rennin angiotensin system due to severe hydronephrosis. Finally, blood sugar and HbA1C were controlled better in our patient. Bilateral hydroureteronephrosis has many different causes, one of which is DI. WS has multi organ features. The patients need close follow-up by an endocrinologist, an ophthalmologist, a nephrologist, an audiologist, a urologist and a psychiatrist at the same time along with the attention of the family throughout the life.

Conflict of Interest

None declared

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