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WOLFRAM SYNDROME: CASE REPORT

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SUMMARY

Wolfram syndrome is a rare neurodegenerative genetic disease, its prevalence is 1/700 000 cases. There are three known types. The first type is due to the mutation of WFS1 (4p16.1) gene. This results in the appearance in the first decade of life of diabetes mellitus type 1, diabetes insipidus, sensorineural hearing loss, bilateral optic atrophy and neurological damage signs. The second type is due to the mutation of CISD2 (4q24) gene. It differs from the first in the absence of diabetes insipidus. Types 1 and 2 are autosomal recessive. The third type or Wolfram-like syndrome is autosomal dominant, differs from the first two by the late onset of optic atrophy and diabetes mellitus type 1 (after adolescence) and hearing impairment is not always present. We report the first documented case of Wolfram syndrome at the University Hospital of Brazzaville in a nine year old girl.

INTRODUCTION

Wolfram syndrome Type 1 is due to a mutation of the WFS1 (4p16.1) gene. This gene encodes the Wolframine, a protein located in the endoplasmic reticulum and plays a role in calcium homeostasis. (1) This results in the appearance in the first decade of life of diabetes mellitus type 1, diabetes insipidus, sensorineural hearing loss, bilateral optic atrophy, sometimes neurological and psychiatric damage. (2) The sluggishness of the urinary tract, ataxia, peripheral neuropathy, psychiatric disorders and / or epilepsy are often reported. The disease progression is often fatal due to respiratory failure. (3) We report the first documented case of Wolfram syndrome type 1 at the University Hospital of Brazzaville.

CASE REPORT

A girl aged nine, deaf from birth, was seen for a major bilateral visual loss. She is also taking insulin for diabetes mellitus appeared when she was five years old. Her examination was as follows on both sides: visual acuity reduced to counting fingers at 50 cm, transparent lens, extreme papillary pallor (optic atrophy). No treatment was required, blindness having been attached to optic atrophy probably complicating hypo perfusion secondary to ischemia

related to diabetes. The patient had been revised a second time, in one month interval, for a re-assessment of the ophthalmology situation remained unchanged. Indeed despite insulin, polyuria (> 50 ml / kg per 24 hours nearly 1 liter per 24 hours for 15kg of weight) and polydipsia (from three to five liters per 24 hours) continued. The symptoms had even enriched by tonic-clonic seizures (from two to three attacks/day) sometimes accompanied by asthmatic respiratory distress (one crisis every two to three days). Examination of the cerebrospinal fluid and chest radiograph were normal. The persistence of this polyuria while the glycemic curve over two months was normal, had led us to realize the water restriction test with measurement of serum sodium and urine osmolality. These tested had confirmed the diagnosis of diabetes insipidus. The diagnosis of Wolfram syndrome type 1 was retained. Genetic evidence had not been made, the patient died in the hours following the diagnosis in an acute respiratory failure context.

DISCUSSION

The clinical criteria for the diagnosis of Wolfram syndrome type 1 are present during the first decade of life: diabetes mellitus type 1, bilateral optic atrophy and deafness. These clinical signs can sometimes

be reinforced by an epidemiological argument, the existence of family history of Wolfram syndrome. When conditions permit, biological confirmation of the diagnosis is made by detecting the mutation of WFS1 (4p16.1) gene. (3-5)

In addition to optic atrophy, some other ocular abnormalities could occur: abnormal pupillars reflexes, nystagmus, cataract, retinitis pigmentosa, diabetic retinopathy and glaucoma. (3, 5)

Abnormalities of other systems may be: abnormalities of the urinary tract (hydro ureter, urinary incontinence, recurrent infections ...), neurological manifestations (ataxia, myoclonus, epilepsy, cognitive impairment ...), psychiatric disorders (depression...), respiratory disorders (dyspnea, apnea ...), gastrointestinal disorders (intestinal ileus, encopresis...), and genital anomalies (hypogonadism ...). MRI revealed a widespread atrophy of the brain, particularly the cerebellum and the medulla oblongata. (1-6)

Differential diagnoses include mitochondrial diseases such as diabetes and deafness transmitted by the mother, Leber hereditary optic neuropathy, thiamine-dependent megaloblastic anemia, autosomal dominant optic atrophy and Mohr-Tranebjaerg syndrome. (1-3, 5, 7). In families where the causal mutation has been diagnosed, prenatal diagnosis can be performed. Transmission is autosomal recessive, genetic counseling can be offered to couples at risk. The management is symptomatic and includes among other: annual screening of diabetes mellitus type 1, an urodynamic assessment, an apparatus of hearing loss, low vision rehabilitation. The disease progression is often fatal to an early death from respiratory failure. (3-5)

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