

WOLFRAM SYNDROME: A CASE REPORT**Bouziane Soukaina*, Hassimi Ouail, Bennis Ahmed, Chraibi Fouad, Abdellaoui Meriem and Benatiya Andaloussi Idriss**

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SUMMARY

Wolfram syndrome is a rare autosomal recessive neurodegenerative disorder characterized by the onset of insulin-dependent diabetes mellitus in childhood associated with bilateral optic atrophy that often results in blindness. Diabetes insipidus, deafness, psychiatric disorders, anosmia, urinary tract abnormalities, nystagmus, ataxia, and myoclonus are less common. We report a case of Wolfram syndrome, diagnosed in a 12-year-old boy with a history of insulin-dependent diabetes. The work-up was motivated by the occurrence of a bilateral and progressive visual acuity decrease related to optic atrophy and peripheral visual field constriction.

KEYWORDS: Wolfram syndrome, optic atrophy, diabetes mellitus.**INTRODUCTION**

Wolfram syndrome is an autosomal recessive neurodegenerative disorder. Juvenile diabetes mellitus and bilateral optic atrophy are its major manifestations and are sufficient to establish the diagnosis. Urinary manifestations should be considered as an integral part of the syndrome as they are present in almost 62% of cases and constitute one of the major causes of morbidity.^[1,2]

Although Wolfram's syndrome has been described for a long time, it still raises questions. Its very definition is subject to discussion. Indeed, this disorder was named DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, deafness) by Anglo-Saxon authors to underline the existence of a cardinal syndrome grouping together diabetes insipidus, diabetes mellitus, optic atrophy and sensorineural deafness. This name was later criticized because it puts on an equal footing elements of very unequal frequency; on the one hand, diabetes mellitus and optic atrophy present in 99% and 98% of cases respectively, and on the other hand, sensorineural deafness and diabetes insipidus, which are much less common (about 50% of cases).^[1,2,3]

OBSERVATION

This is a young patient, 12 years old, with consanguineous parents (first cousins) and an older brother (17 years old), free of any clinical or biological signs that could suggest Wolfram syndrome.

His clinical history goes back to the age of 6 years with the discovery of an insulin-dependent diabetes put on insulin, 4 years later a sensorineural hearing loss was diagnosed in him in front of his school inflection (figure 1).

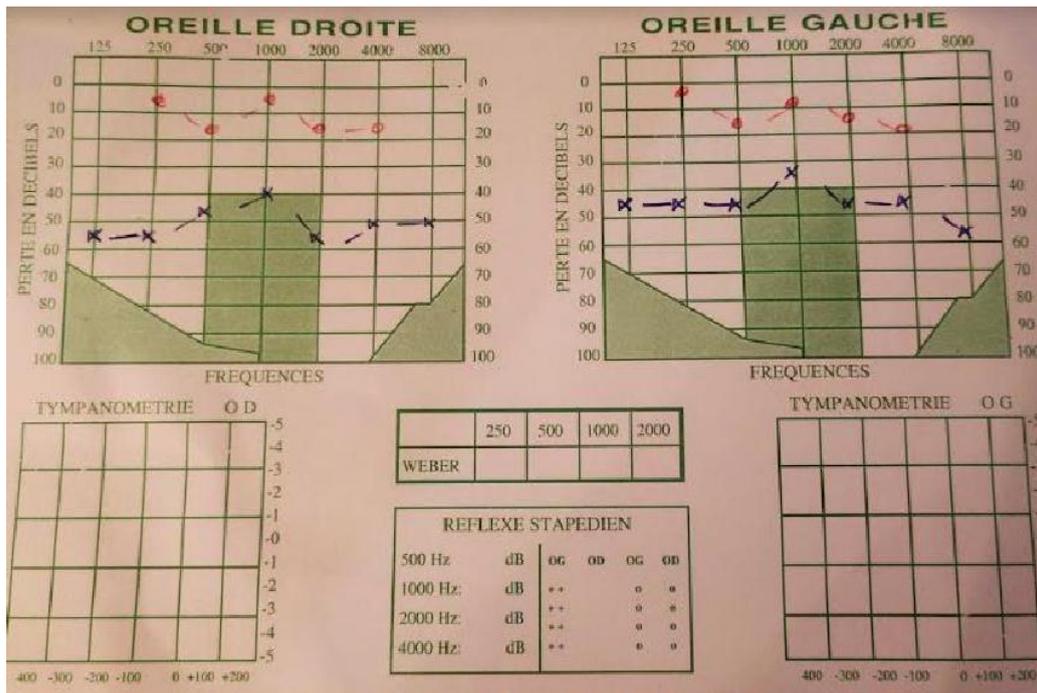


Figure 1: Audiometry showing moderate sensorineural hearing loss.

He was hospitalized 6 months ago for a bilateral ureterohydronephrosis with a severe urinary infection with good evolution after drainage and antibiotic therapy, then a urodynamic assessment is planned at home. During his hospitalization, the patient was referred to our clinic for a possible ophthalmological opinion due to a progressive decrease in visual acuity.

His bilateral ophthalmological examination revealed: a

visual acuity limited to the fingers at 3 meters, an examination of the appendages and the anterior segment without any particularities, a correct ocular tone, at the back of the eye: a pale papilla, without any signs of retinopathy or diabetic maculopathy (figure 2). A cerebro-orbital MRI was performed and showed hypotrophy of both optic nerves without any abnormalities at the cerebral level. The visual field and color vision were difficult to evaluate in him.

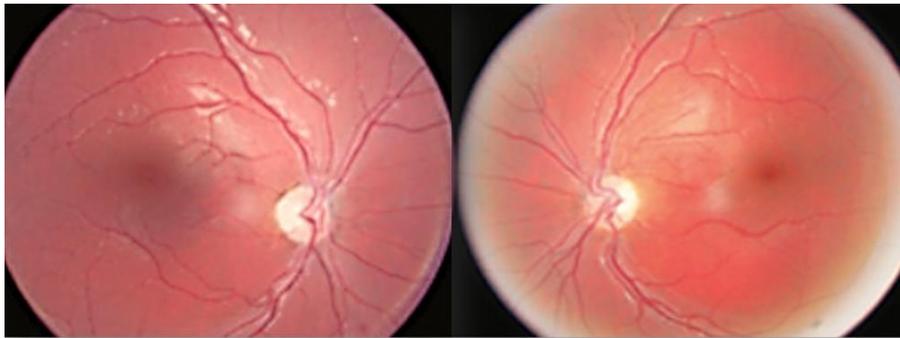


Figure 2: Fundus image showing bilateral papillary pallor.

The diagnosis of Wolfram syndrome was made in view of the tetrad: diabetes, optic atrophy, deafness and urinary signs.

DISCUSSION

Currently, if the authors agree to give back its importance to the classic tetrad of DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, deafness) found in 53% of the cases, it is admitted that the association of diabetes mellitus and bilateral optic atrophy having started in childhood or during adolescence is sufficient to make the diagnosis of

Wolfram syndrome.^[1,2] This syndrome can be familial or sporadic.^[1]

Neurological disorders are not uncommon, especially central apnea and upper airway collapse leading to respiratory distress and death. It is currently agreed that Wolfram syndrome has a neurodegenerative origin.^[1,2,4] Magnetic resonance imaging (MRI) reveals images of cerebral atrophy, in particular pontine and mesencephalic.^[1,3]

The urinary involvement, given its frequency, must be considered as one of the major elements of Wolfram

syndrome.^[4,5] Its etiopathogeny is not yet elucidated but the primary alteration of ureteral and bladder innervation seems to be incriminated.^[4] It most often takes the form of a retentionist bladder, with frequently a more or less important dilatation of the upper apparatus.^[5] It is important to look for associated urinary malformations, which can significantly worsen the symptomatology and the evolution.^[4]

The most common causes of mortality and morbidity are due to neuropsychiatric manifestations and urological complications of the syndrome (infections, renal failure).^[1]

Ophthalmologic manifestations are dominated by optic atrophy, which is found in 98 to 100% of cases. Ocular damage is due to progressive atrophy of the entire visual system, i.e. optic nerve, chiasma and optic bands, the origin of which is poorly defined. The fundus will eventually lead to the diagnosis of bilateral optic atrophy at an advanced stage of the evolution. This is the case of our patient who was diagnosed at a late stage with bilateral optic atrophy. Pigmentary anomalies of the peripheral retina are rare in this syndrome.^[6,7]

The visual field study at an early stage of the disease will show a central scotoma or a peripheral visual field constriction. Visual evoked potentials show abnormalities, which are consistent with optic nerve damage in all patients, the electroretinogram is normal in the majority of cases. Magnetic resonance imaging (MRI), performed at an early stage, will show hyposignal and bilateral atrophy of the optic nerves, chiasma and optic bands.^[6]

Other ophthalmological disorders have been described: damage to the extrinsic muscles with strabismus and ptosis, nystagmus, damage to the intrinsic muscles with a lazy photomotor reflex which is absent at the stage of constituted optic atrophy, anomalies of the anterior segment with posterior embryotoxon.^[6,7]

CONCLUSION

Wolfram syndrome is a serious disease with a poor prognosis and a life expectancy of no more than 30 years. In all diabetic children, the fundus, visual field and color vision should be monitored. At the slightest abnormality of these complementary examinations, wolfram disease should be suspected and an MRI should be systematically indicated in order to make an early diagnosis and effective management and thus prolong the life expectancy of the patients and certainly improve the quality of this survival.

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