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The ENT Manifestation of Wolfram Syndrome (DIDMOAD): A Case Report

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Case Report

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Abstract

Objective: Describe the clinical and therapeutic aspects of WOLFRAM syndrome (DIDMOAD) presenting with deafness.

Materials and Methods: We report the case of a 21-year-old man who presented with a WOLFRAM syndrome associated with a tympanic perforation.

Clinical Case: This is a 21-year-old R.Y from a consanguineous marriage (first cousin 1st degree) Due to the association of symptoms (type 1 diabetes, urinary and ophthalmologic signs), genetic counseling was sought to confirm WOLFRAM syndrome.

Conclusion: Since sensorineural hearing loss can be the first symptom of SW, audiologists, and otolaryngologists should be vigilant in referring patients with hearing loss for an ophthalmic examination.

Keywords: WOLFRAM Syndrome; Sensorineural Hearing Loss; Tympanic Perforation; Tympanoplasty

Abbreviations: SW: Wolfram Syndrome.

Introduction

In 1938, Wolfram first observed, then described with Wagener, a clinical feature characterized by diabetes mellitus, optic atrophy, and deafness [1]. These abnormalities appeared in four brothers at different times during the first and second decades of life. An atypical form of ataxia occurred in one of these patients and there was a neurogenic bladder in another later. In the following years, other abnormalities, diabetes insipidus, neuropsychic and endocrine disorders, were added, thus increasing the original symptomatic feature. For this reason, the same Wolfram syndrome (SW) is defined with the term Wolfram syndrome DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, and deafness) in the literature [2-7]. It is a recessive inherited disease, the pathogenesis of which is still poorly understood [8-10].

Clinical Observation

This is a 21-year-old R.Y from a consanguineous marriage (first cousin 1st degree) of a sibling of 3, followed since an early age for type I diabetes under insulin therapy. The course is marked by the appearance of repeated urinary

tract infections; the diagnosis of a neurogenic bladder was made and then operated on at the age of 16. Due to the association of symptoms, genetic counseling was sought to confirm WOLFRAM syndrome. Routine ophthalmologic examination showed a decrease in visual acuity of one-tenth on both sides, associated with severe bilateral optic atrophy (Figure 1), with a significant reduction in visual fields. The neurological examination was normal (Figure 2).

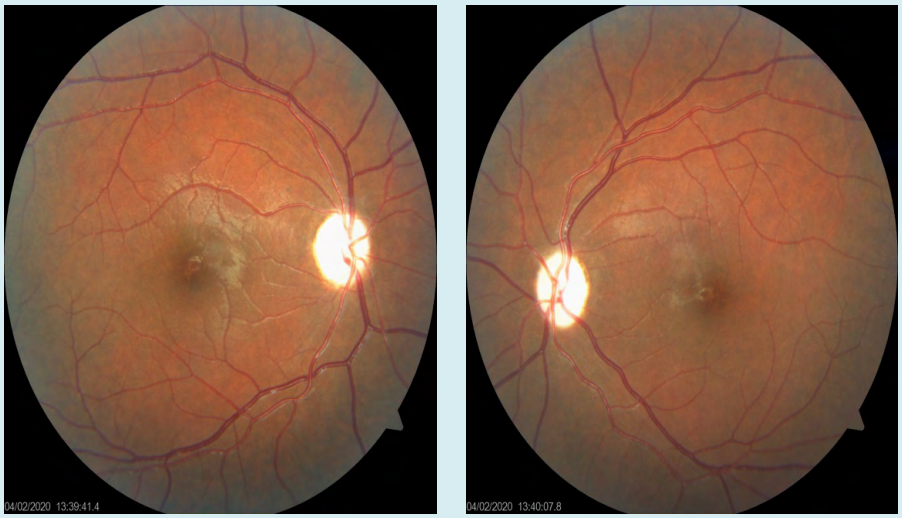

Figure 1: Funduscopic examination showed a bilateral optic atrophy.

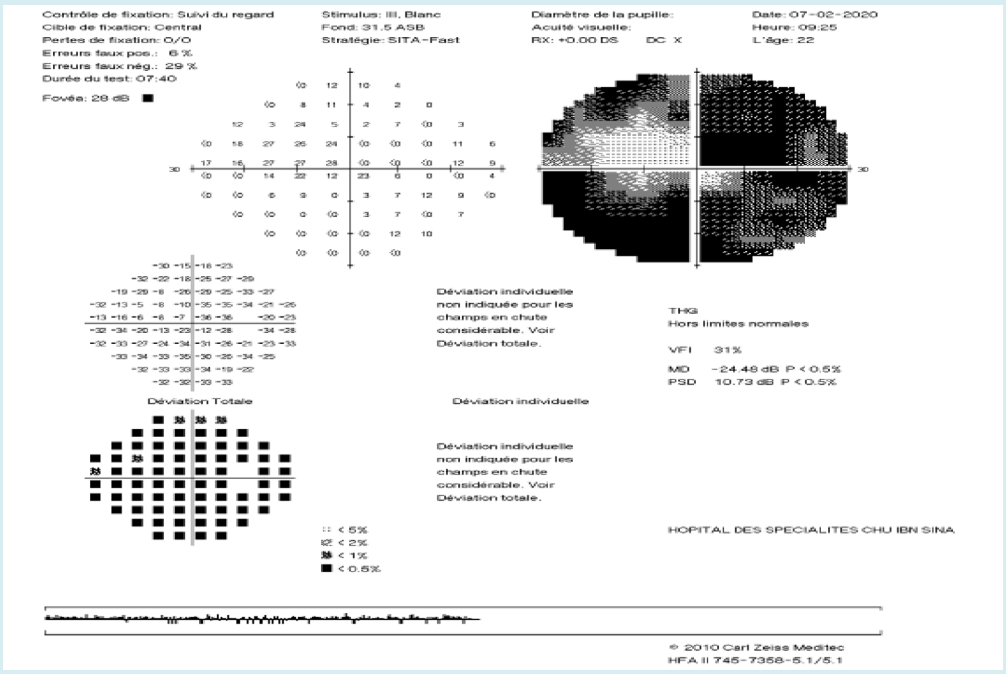

Figure 2: Measurement of visual fields showing a significant reduction in the capacity of both eyes.

On the other hand, the patient reported a notion of repeated left otitis externa for 2 years with a notion of homolateral hypoacusis without any notion of tinnitus or vertigo. The initial otoscopic examination revealed subtotal non-marginal tympanic perforation, with a dry fundus, and a positive Valsalva maneuver, and on acumetry left conductive hearing loss. The contralateral ear exam, as well as the rest of the ENT exam, were normal. The tone audiogram showed conductive hearing loss at 30 dB in the left ear, as well as a drop in treble in the right ear (Figure 3).

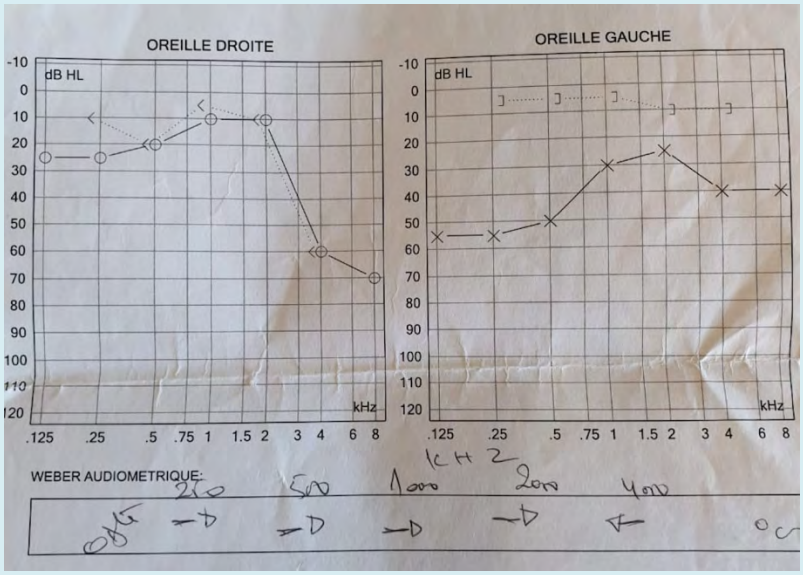

Figure 3: Pre-operative tonal audiogram showing a conductive hearing loss in the right ear and a drop in the treble on the left ear.

The patient underwent type I tympanoplasty with placement of autologous concha cartilage. The immediate postoperative follow-up was normal. Eight months after the surgery, the tonal control audiogram shows a clear improvement in hearing, but still with a decrease in the high frequencies (Figure 4).

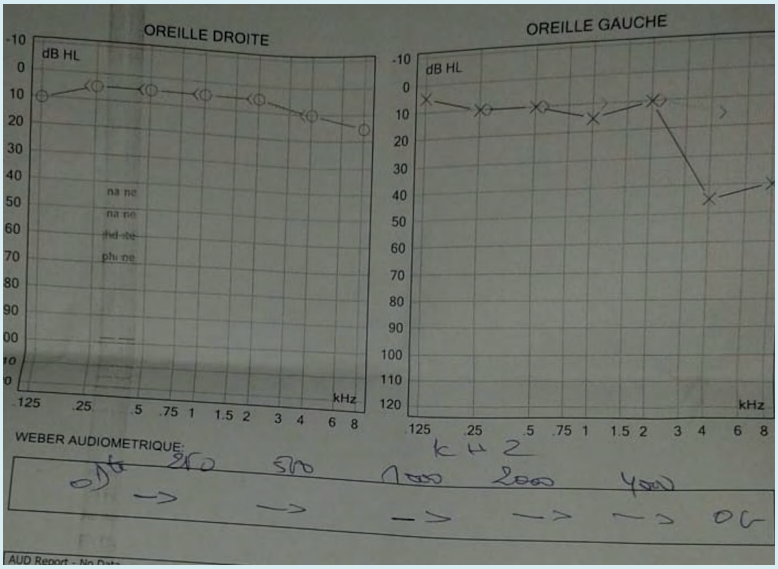

Figure 4: Post-operative tonal audiogram showing une hearing improvement, but always with a drop in the high frequencies.

Discussion

Genetically, the wolframine gene (WFS1) was identified in 2001 as responsible for syndromic deafness, Wolfram syndrome, in which deafness is associated with diabetes mellitus and insipidus and neurological and ophthalmological symptoms. Two teams have shown that WFS1 was also involved in an autosomal dominant non-syndromic form, DFNA38, characterized by progressive deafness, beginning between 5 and 15 years of age and preferentially reaching

the severe frequencies. 75,76 Deafness then reaches all frequencies and becomes moderate/severe around 40 years old. The DFNA6, DFNA14, and DFNA38 loci overlap and all three correspond to the WFS1 gene. Young et al. demonstrated mutations in two families from the United States and two Dutch families whose deafness was linked to DFNA38, but also in the two families tested without prior localization, with dominant deafness affecting the low frequencies. Bespalova studied five families with progressive deafness on severe frequencies in Belgium, Holland, and the United States: in all five families, the deafness was due to a mutation in WFS1. WFS1 is therefore probably a frequent gene in these forms with an ascending audio-metric curve.

We do not yet know the prevalence of WFS1 in the different populations and its possible implication in dominant deafness with non-ascending audiometric curves. The molecular diagnosis of WFS1 can be proposed in families of autosomal dominant deafness predominant or having started on severe frequencies.

Hearing loss is observed in 62% to 72% of patients with SW Higashi [11], Kumar [12]. The most frequently reported presentation of hearing loss in WS is high-frequency sensorineural hearing loss which is typically diagnosed in the second or third decade of life. However, with notable exceptions Pennings, et al. [13], Plantinga, et al. [14], Hilson, et al. [15], the majority of published studies do not provide sufficient detail on the audiological measures used to specify the severity or progression of hearing loss. in SW. Since there are very few reports of vestibular function in patients with SW, and even fewer in which both auditory function and vestibular function are measured, the relationship between balance and hearing function remains unclear.

According to previous studies, hearing loss is underreported if it is based on patient or parent reports rather than audiometric measurements Barrett and Bundey [16], Simsek, et al. [17], Lombardo, et al. [18], Kumar [12]. Since hearing loss in SW usually affects high frequencies first and usually progresses slowly, age at diagnosis may be several months or years later than the age of onset. Regarding treatment Hilson, et al. [15] reported that the use of hearing aids has failed, but the study by Roanne, et al. suggests otherwise. The four patients in their cohort use bilateral amplification devices (3 patients with hearing aids and one with a cochlear implant). Although hearing benefit has not been formally assessed, their routine use of the devices is a subjective indicator of benefit.

Regarding the vestibular assessment, rotary chair testing in the study by Roanne, et al. indicated a profound vestibular loss in one of the oldest patients in the study (23.8 years), although the Vestibular function was normal in a patient who was approximately the same age (Figure 5).

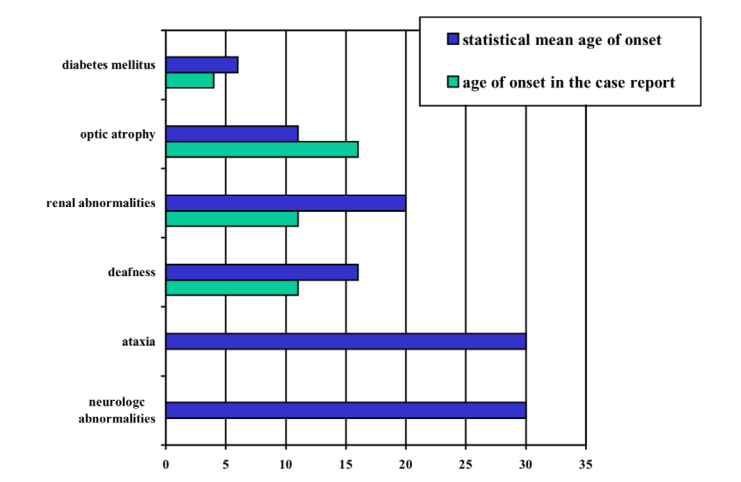

Figure 5: Age of symptom onset in our case compared to the chronology of symptom onset described in the literature.

Conclusion

Hearing loss can occur sooner than expected, and comprehensive testing, including speech-in-noise testing, may reveal deficits not apparent with a pure-tone test. Particular configurations of hearing loss may indicate the need for a full vestibular assessment. Since sensorineural hearing loss can be the first symptom of SW, audiologists, and otolaryngologists should be vigilant in referring patients with hearing loss for an ophthalmic examination.

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