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Usher Syndrome: Clinical Presentation

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Abstract **Case Report**

Usher syndrome is a genetic disorder that causes a dual sensory deprivation resulting in deaf-blindness world widely. We report the case of two brothers from a non-consanguineous marriage presenting with pigmentary retinopathy and congenital hearing loss, suggesting usher syndrome. This syndrome is divided into three subtypes that are clinically and genetically different. While many promising treatments are under investigation, no treatment is approved to this date. Audiological rehabilitation, as well as psychological follow up, are essential to improve patients' life quality.

Keywords: Pigmentary retinopathy, ciliopathy, deaf-blindness, hearing loss.

INTRODUCTION

Usher syndrome is the most common cause of deaf-blindness worldwide with a prevalence ranging between 3 and 6 in 100 000 [1].

It is a group of recessively inherited disorders resulting in dual sensory impairment of the audiovestibular and visual systems. It has been divided into three main clinical types: 1, 2, and 3, which are caused by mutations in different genes that are still not completely identified until this day.

This article aims to present the case of two siblings with usher syndrome and an update on this entity.

MATERIAL

We report the case of two brothers from a non-consanguineous marriage who presented with usher syndrome.

OBSERVATION

A 20-year-old patient, with a history of severe congenital deafness, which prevented him from acquiring language, was admitted to our hospital for a progressive bilateral degradation of visual acuity and nyctalopia in both eyes. Best-corrected vision was 8/10 in both eyes (OSD) and P2. Anterior segment showed no abnormality, fundus examination revealed a diffuse arteriolar narrowing, a pale papilla and, above all, the presence of dark intra-retinal pigmented migrations distributed over the peripheral retina suggesting a retinitis pigmentosa (figure 1).

Optical coherence tomography (SD-OCT) revealed a loss of the outer retinal structure, while the electroretinogram (ERG) measurement showed reduction and delay of amplitudes in scotopic and photopic tests (figure2).

Static perimetry detected mid-peripheral visual field loss.

The Otorhinolaryngology examination, was normal, however, the patient presented an evident hearing impairment, with a mean hearing loss of 55dB in both ears (figure 3).

The rest of the family was examined, parents had normal fundus and vestibular function, whereas the older brother had a best corrected visual acuity of 2/10 right eye, and 8/10 for the left, slit lamp examination showed a polar cataract OD, funduscopy revealed a bilateral retinitis pigmentosa, and a profound hearing loss in the high frequencies (figure 4).

The patient benefited from a phacoemulsification for his cataract, and visual acuity 1 month post operatively was 4/10.

Both patient were addressed for genetic testing and psychiatric counselling, but were lost to follow up.

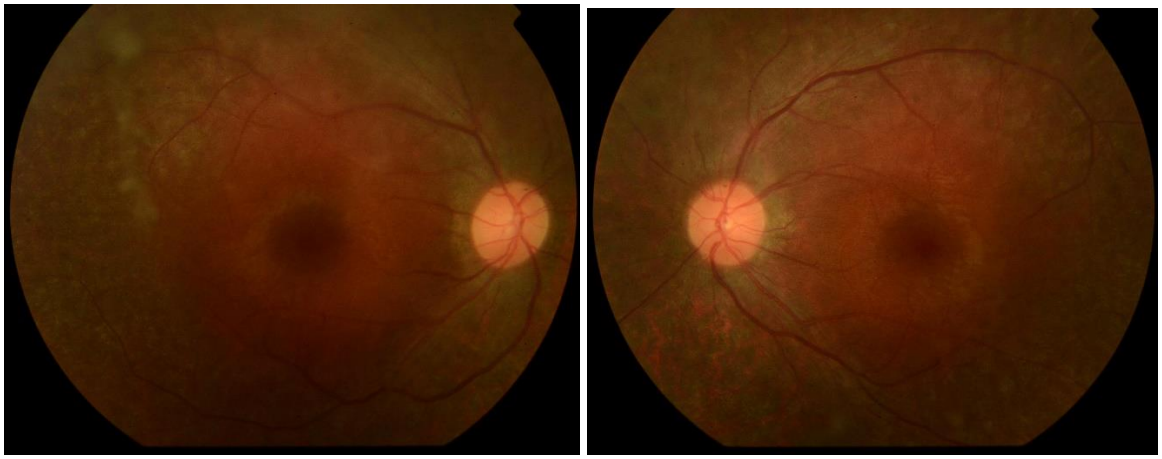

Figure1: Retino-photography showing an aspect of pigmentary retinopathy in both eyes

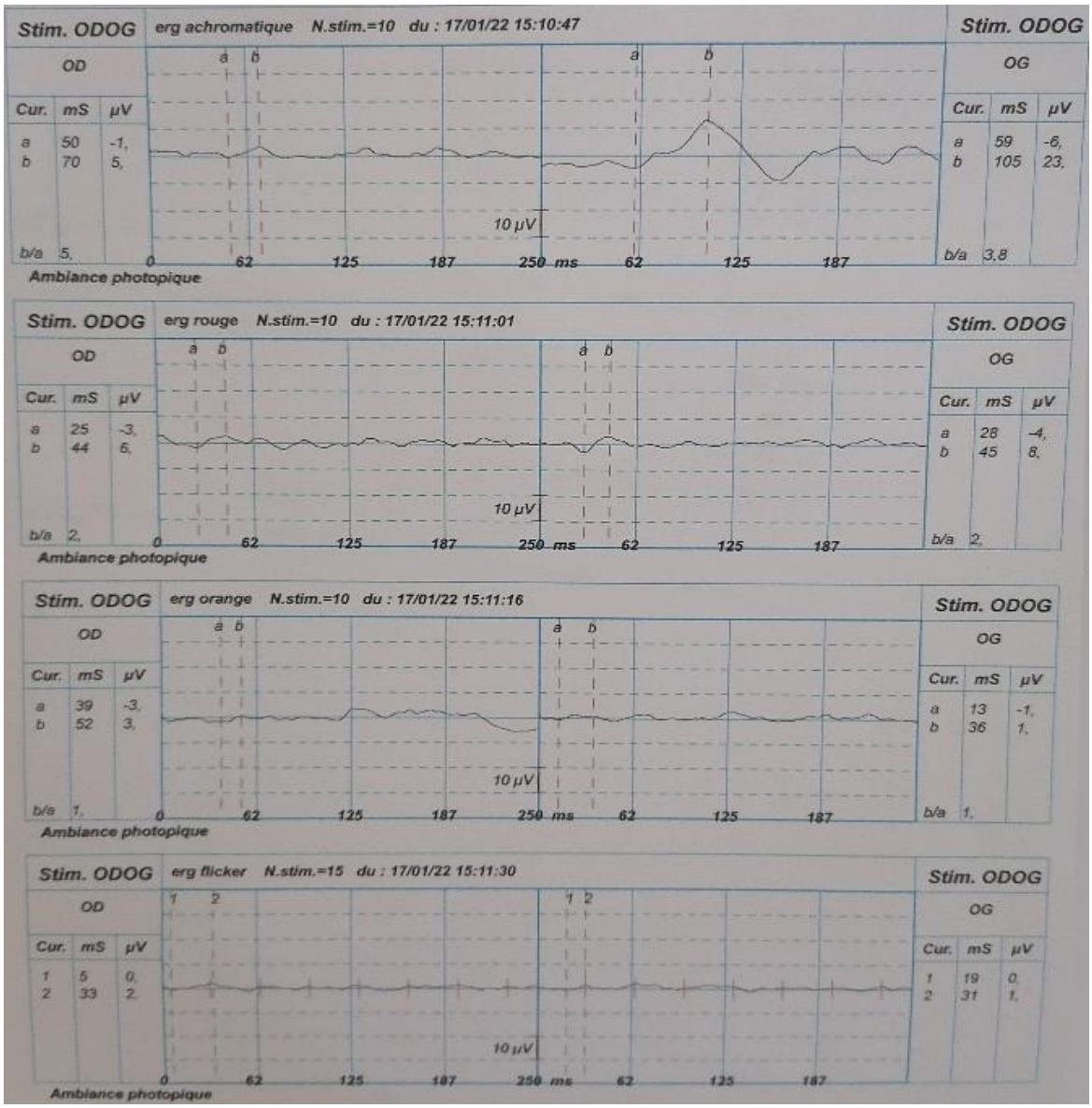

Figure 2: Altered responses to different stimulation in the electroretinogram

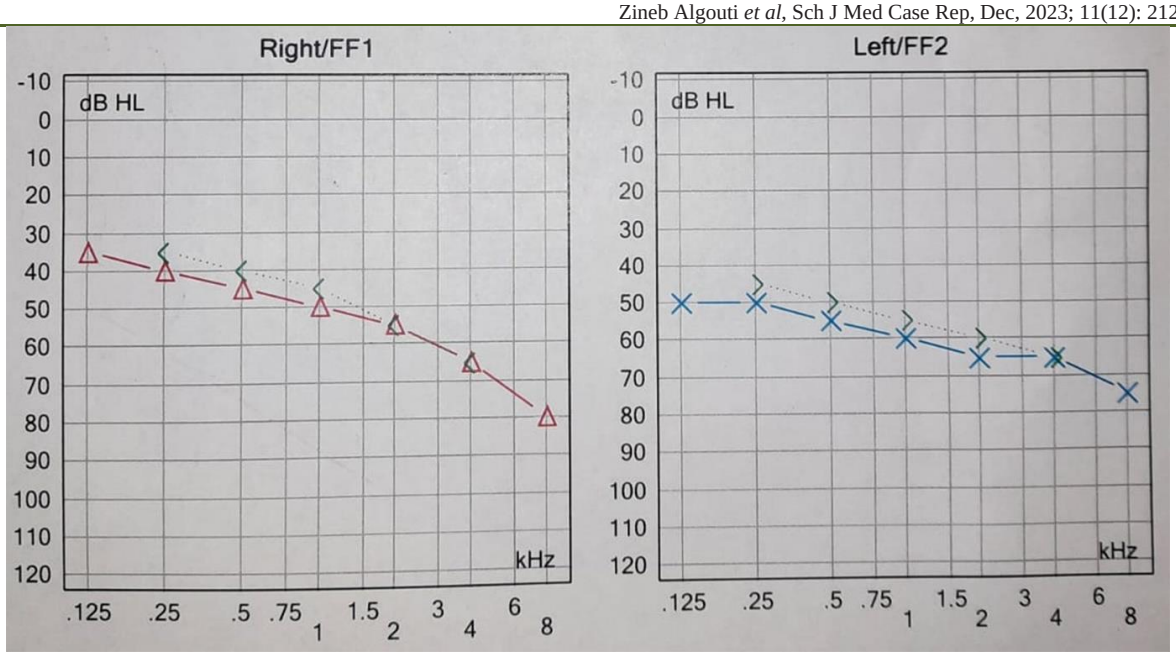

Figure 3: High frequency sloping audiogram in both ears

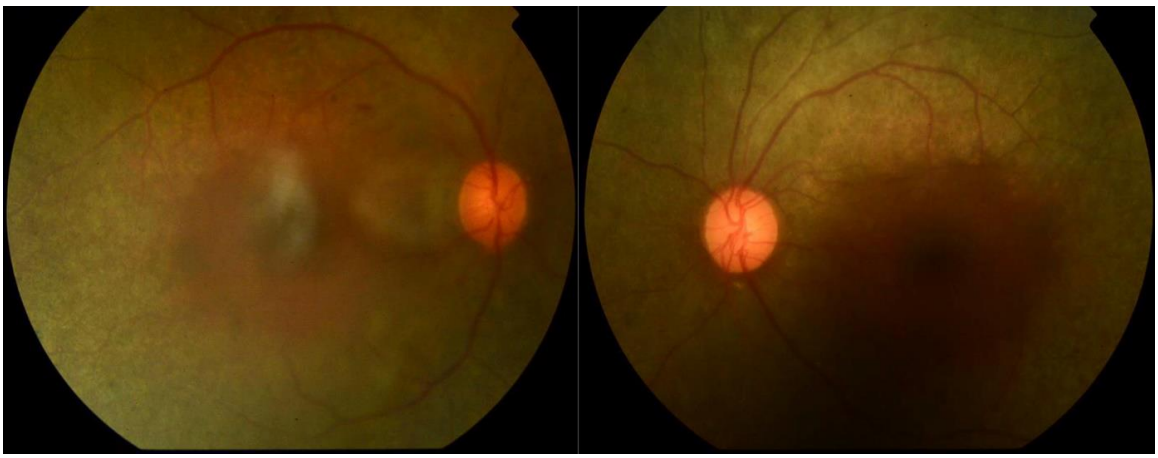

Figure 4: Retinitis pigmentosa in the second patient

DISCUSSION

Ciliopathies are a group of disorders caused by a defect in ciliogenesis. Almost every cell in our body contains cilia, including the photoreceptors, therefore a deficiency in ciliary proteins typically affect multiple organ systems [2].

Usher syndrome is a recessively inherited ciliopathy characterized by dual sensory impairment of the audiovestibular and visual systems [3].

USH is both clinically and genetically heterogeneous, and is divided into three distinct clinical subtypes associated with a number of genetic loci.

The subtypes are distinguished by the severity and progression of hearing loss and the presence or absence of vestibular dysfunction, with visual loss due to retinitis pigmentosa being common to all three subtypes.

USH1 is the most severe with congenital profound hearing loss, absent vestibular function, and an early onset of the RP.

Whereas, USH2 accounts for over half of all USH cases and is characterized by congenital moderate-to-severe hearing impairment, generally more severe in the higher frequencies, with normal vestibular function, but late onset, usually young adults RP.

In USH3, the hearing loss is progressive and the vestibular function variable, RP's onset essentially during early adulthood. USH3 is rare in most populations apart from Finland, and among Ashkenazi Jews where it may be responsible for over 40% of USH cases [4].

Clinical findings in our patients were in favor of usher syndrome type 2 due to the presence of the retinitis pigmentosa, the profound sensorineural hearing loss, and the normal vestibular function.

Patients are often registered severely sight impaired but there can be significant intra- and interfamilial phenotypic variability. A significant proportion of Usher patients may also develop cataracts such as our second patient and/or cystoid macular oedema [5].

At present, 10 causative genes have been identified for Usher syndrome, with MYO7A accounting for >50% of type 1 and USH2A contributing to approximately 80% of type 2 Usher syndrome [6].

While many promising treatments are under investigation, such as gene therapy, subretinal implantation of capsules containing human cells that release ciliary neurotrophic factor, viral delivery of rod-derived cone viability factor, there is no approved treatment for this disease to date [7, 8].

Audiological rehabilitation for all forms of Usher syndrome begins immediately after diagnosis with the fitting of bilateral hearing aids.

Children with Usher syndrome have been reported to develop mental and behavioural disorders, including autism, conduct disorder, psychosis and learning difficulty. This could be multifactorial, but the main theories are stress due to sensory deprivation, and genetic predisposition induced by mutations in genes causing both USH and schizophrenia for example.

Therefore, communication and language rehabilitation, as long as clinical support during early childhood for both children and their parents, are found to be important in preventing mental and behavioral disorders and psychosocial difficulties [9].

CONCLUSION

Usher syndrome is one of the most common autosomal recessive syndromes with a vast clinical and genetic heterogeneity. Despite the advances that were made, more research is needed to improve our understanding of this entity, in order to provide the best treatment for those patients.

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