Mutations in exon 13 of *USH2A* gene in 63 patients with Usher syndrome: clinical data in the aim of exon skipping therapy

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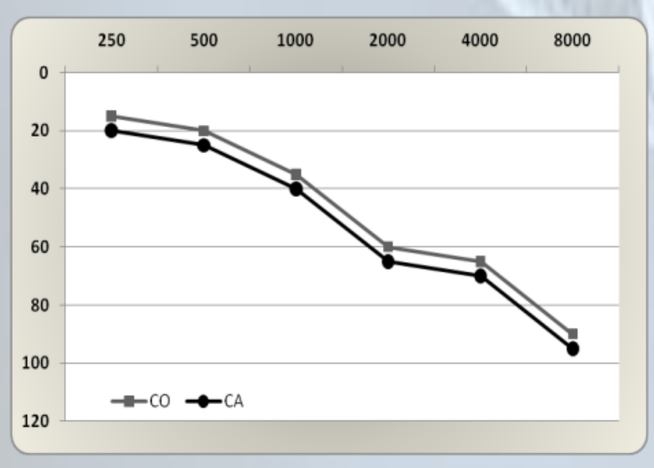
INTRODUCTION

Biallelic *USH2A* mutations are a known cause of Usher syndrome type 2, an autosomal recessive syndrome with congenital deafness and later onset retinitis pigmentosa.

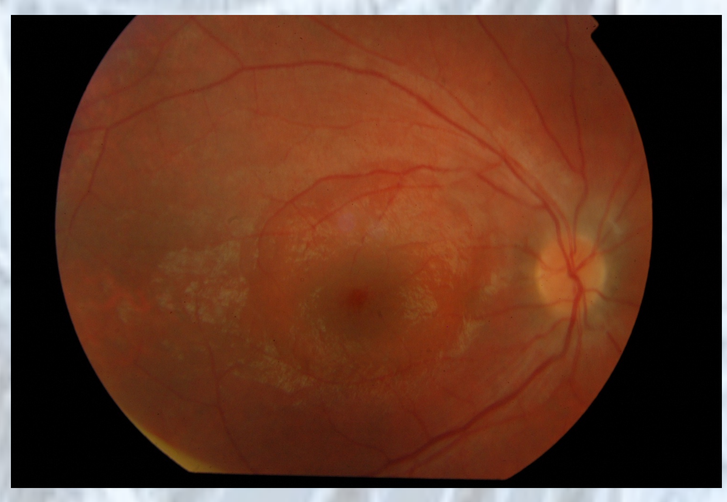
Here, we focus on a subgroup of patients with a mutation identified in exon 13 of *USH2A*. In this subgroup, skipping of exon 13 could be considered as a therapeutic approach following proof of concept in the zebrafish model.

METHODS

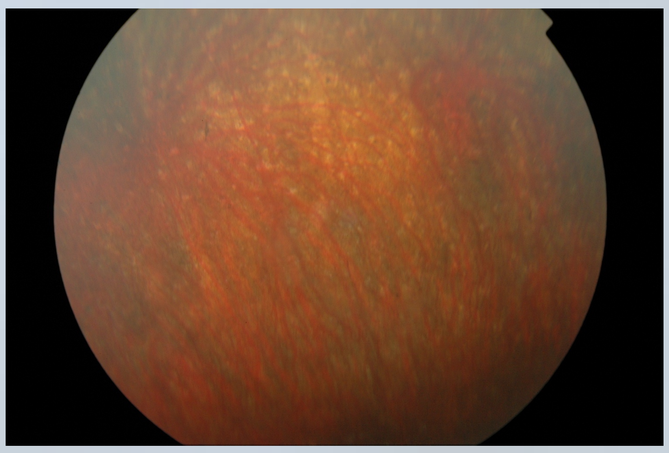
Patients with hearing loss and retinitis pigmentosa were subsequently screened for exonic and splice site variants in *USH2A* applying a targeted next generation sequencing approach. The database of a National centre in rare inherited retinal dystrophies (France) was screened for patients with biallelic mutations in USH2A, one identified in exon 13. Clinical, color, autofluorescence and spectral domain optical coherence tomography SD-OCT) data of these patients were reviewed. Ganzfeld full-field ERG was performed according to the guidelines of the International Society for Clinical Electrophysiology of Vision.



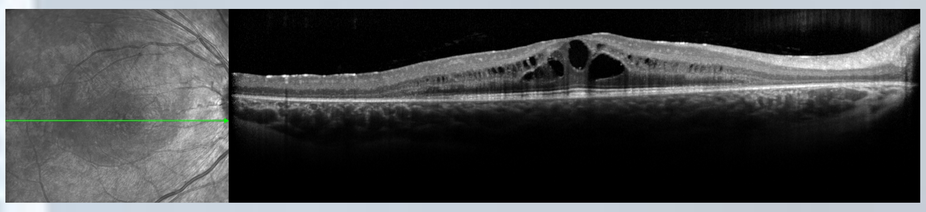
Hearing loss



Retinitis pigmentosa



Most frequently withish lesions

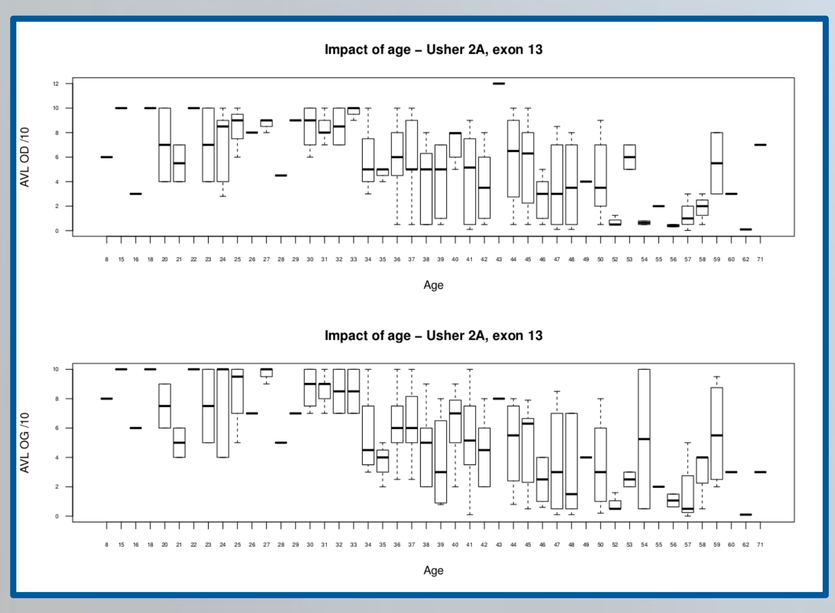


Macular edema

RESULTS

Among 173 patients with genetically proven USH2A syndrome, 53 patients had one of the two mutations localized in the exon 13. There were 24 men and 29 women. The mean age at first consultation was 38 year-old (14 to 71 years). Mean visual acuity was 20/40 (20/200 to 20/20). Visual acuity was ≤ to 20/40 in at least one eye in 24 out of 53 patients (45.3%) and both eyes in 23 patients (43.4%).

A history of macular oedema or a macular oedema was noted in 8/53 cases (15%). A tubular visual field (<20°) was noted in 29 patients (mean age: 39 years). The single base-pair deletion in exon 13 (c.2299delG, p.Glu767Serfs*21) was identified in 45 of the 53 patients. Other exon 13 mutations were c.2276G>T (ex 13) → p.Cys759Phe and c.2168-1G>C, lVS12-1G.



CONCLUSION

Our study significantly contributes to the clinical spectrum of patients with one major single base-pair deletion in exon 13 in the aim of an exon skipping therapy

(i) this therapy could be proposed in one out of three patients,

(ii) even during adulthood (mean age 38 with a mean VA of 20/40).