Discovery Of The C2299G Deletion Of The USH2A Gene In An Algerian Family

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In An Algerian Family

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Introduction:

Deafness is the most common sensory deficit in children. Its social consequences depend on the moment of appearance and its severity. It presents a genetic heterogeneity.

This genetic deafness is isolated in most cases (70%) but is associated with damage to other organs in 30% of cases.

Usher syndrome is one of those syndromic deafness that associates congenital neurosensory deafness, retinitis pigmentosa and sometimes signs of vestibular involvement. It is the most common cause of hereditary deafness (C.Bonnet and all).

The aim of this work is to investigate the genetic causes of this deficit in the Algerian population.

Materials and methods

Some fifty Algerian families with at least one case of neurosensory hearing loss are recruited at the central laboratory of Blida University Hospital.
Deafness is the reason for consulting families. It is a severe to profound hearing loss confirmed by complementary examinations and which required the installation of cochlear implant in most cases.

Clinical history was taken for each patient. The patients underwent audiograms, ocular fundus autofluorescence imaging, and electroretinogram.

Among these families, most had isolated deafness but ten had the Usher syndrome phenotype, that is to say, profound deafness confirmed by the audiogram, clinical signs favoring a retinitis pigmentosa such as a decrease night vision and signs of vestibular damage.

A 28-year-old patient (SA4) had the clinical signs of Usher syndrome type 2, his deafness was not profound and he had no vestibular disturbances but his retinitis pigmentosa was very advanced since he almost lost his sight.

Electroretionogram (ERG) confirmed the presence of retinitis pigmentosa.

All the members of the families were taken on EDTA tube and the DNA is extracted by the « salting out » method in the laboratory of genetic biochemistry of CHU Babeloued.

The molecular study was conducted at the Paris Vision Institute using targeted exome sequencing and bioinformatic analysis(( C.Bonnet et all 2011).

Results and Discussion:

Several mutations have been found, including this ancestral deletion (C.2299delG) in the exon 13 of the gene USH2A which was diagnosed in the homozygous state in a patient with the Usher syndrome type2 phenotype.

This patient is from of an inbred family.

This deletion of a guanine at position 2299 of the nucleotide sequence caused the substitution of glycine at position 767 of the peptide sequence in serine
which caused the appearance of a stop codon after 21 amino acid of position 767.

The segregation of the mutation identified in the SA4 patient was studied by sanger sequencing DNA fragments in the parents and other family members.

The C.2299G is considered the most common mutation in USH2A (E. Lennassi and al 2014). To date, this ancestral mutation in exon 13 of the USH2A gene has not yet been described in North Africa. We report here for the first time its presence in Algeria.

The 2299delG is distinguished by its high frequency through several studies [Beneyto et al 2000, Dreyer et al 2000, Liu et al 1997, Weston et al 2004]. It seems to have an origin European ancestry [E. Aller et al 2010], this explains its presence in populations of different origins, reported by an old Spanish study [B. Dreyer 2008]. According to this study, the 2299delG is widespread in Europe and in America.

It has been described in 43 American families of European origin (United States, Canada) and 70 European families (United Kingdom, Denmark, Norway, Netherlands, Sweden, Belgium, France and Spain).
This geographical distribution can be linked to the migration of European populations to the new world.

The history of Algeria, which is a melting pot of populations, could explain the presence of this deletion in the SA4 family of our cohort.

**Conclusion:**

The genetic diagnosis of congenital deafness is essential for early management of sensory deficit and other deficits in the case of syndromic deafness. It also allows genetic counseling and avoids consanguineous marriages for members carrying heterozygous mutations.

**References:**


- **E. Lennassi and al 2014**: Lenassi Eva, MD, PhD, Zubin Saihan, MD, PhD, Valentina Cipriani, PhD, Polona Le Quesne Stabej, PhD, Anthony T. Moore, MD, FRCoPhth, Linda M. Luxon, MD, CBE, FRCoPhth, Maria Bitner-Glindzicz, MD, PhD, Andrew R. Webster, MD, FRCoPhth. Natural History and Retinal Structure in Patients with Usher Syndrome Type 1 Owing to MYO7A Mutation: Ophthalmology, Volume 121, Issue 2, February 2014, Pages 580-587.


