Hearing Loss Etiology in Patients Submitted to Cochlear Implant

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Abstract
Introduction: Hearing impairment is the most common sensorial disorder. Deafness has several etiologies. It is important to investigate them, not only because some may lead to lower performance with a cochlear implant, but also to define preventive strategies.
Objective: To determine deafness etiology among patients submitted to cochlear implantation.
Methods: Retrospective sampling of patients submitted to cochlear implantation between 2006 and 2017 in a Brazilian referral hearing impairment center. Patients were grouped into post-lingual or pre-lingual deafness and an etiological profile was outlined for each group.
Results: 159 patients were evaluated, 74 post-lingual and 85 pre-lingual. In post-lingual group, the most common cause of hearing impairment was meningitis (n = 16/21,62%). Other etiologies were: non-syndromic genetic hearing loss (n = 12/16,22%), otosclerosis (n = 7/9,46%), autoimmune (n = 5/6,76%), viral infections – mumps and measles (n = 3/4,05%), Alport syndrome (n = 2/2,7%), Meniиrers disease (n = 2/2,7%), ototoxicity (n = 2/2,7%), enlarged vestibular aqueduct (n = 2/2,7%), otitis media complications (n = 2/2,7%), trauma (n = 2/2,7%), lues (n = 1/1,35%), vestibular schwannoma (n = 1/1,35%), stroke (n = 1/1,35%), auditory neuropathy (n = 1/1,35%) and 15 patients (20,27%) had undefined etiology. In pre-lingual group, non-syndromic genetic hearing loss was the most prevalent cause (n = 22/25,88%), followed by perinatal complications (n = 20/23,53%), congenital infections – cytomegalovirus, rubella and mumps (n = 8/9,41%), genetic syndromes such as Waardenburg (n = 5/5,88%), meningitis (n = 5/5,88%), malformation – mostly incomplete partition type II (n = 3/3,53%), auditory neuropathy (n = 3/3,53%), ototoxicity (n = 2/2,35%) and 17 patients had undefined causes (20%).
Conclusion: In our population, the most frequent etiology for post-lingual deafness was meningitis and for pre-lingual deafness was non-syndromic genetic causes.

Key-words: Deafness, Etiology, Cochlear Implantation

Introduction

Hearing loss is the most common sensorial disorder in human population. Deafness or profound hearing loss is estimated to affect 1-3 in each 1000 newborns.[1] It is one of the most disabling diseases, for it compromises communication and interferes in emotional, social, psychological and intellectual aspects.[2–4]

Severe to profound hearing loss can be classified as pre-lingual or post-lingual, according to its establishment before or after language acquisition. [5]

Deafness may be attributed to innumerous etiologies, yet most patients are candidates to rehabilitation with cochlear implants (CI).[5] CI is a dispositive developed to replace the cochlear hair cellsr function, given that it stimulates the spiral ganglia cells directly.[6]

In many cases, deafness etiology can be determined after clinical investigation. Infections, ototoxicity, prematurity or other perinatal affections are risk factors that can be easily identified during anamnesis. Physical examination may detect certain ear diseases, as well as genetic syndromes. Imaging exams are useful to identify ear malformations.[7,8] Still, the cause of an important percentage of sensorineural hearing loss remains undefined. Genetic factors are found to be a common cause of hearing

impairment even when a strong familiar history is not identified. Genetic testing remains very expensive and not widely available for the general public in some world regions.[5]

Whilst most severe to profound hearing losses may be rehabilitated with CI, the performance after implantation may varies according to its etiologic. An isolated genetic hearing impairment, such as the mutation of connexin 26 gene, usually presents a better rehabilitation performance, possibly due to the absence of neurological anomalies or intellectual deficits. On the other hand, meningitis, congenital cytomegalovirus infection and auditory neuropathy spectrum disorder, associated with central nervous system impairment, seem to have poorer rehabilitation performance after cochlear implantation.[9]

Objective

This study aims to outline an etiological profile of patients submitted to CI in a Brazilian referral center.

Method

This retrospective observational study took place in the referral center for hearing loss of Universidade Federal de Sro Paulo (UNIFESP).

All patients submitted to cochlear implantation between 2006 and 2017 were enrolled. Brazilrs public healthcare system criteria for cochlear implantation consists in: severe to profound bilateral hearing loss confirmed by Audiometry, Otoacoustic Emissions and Brainstem Auditory Evoked Potential (BERA), poor results in speech recognition tests or low performance with hearing aids. All of them underwent temporal bone computed tomography (CT) imaging before cochlear implantation. Magnetic resonance imaging (MRI) was performed in all pre-lingual cases and in some selected post-lingual patients.

Age, sex, hearing loss etiology data and exams were obtained from the institutionrs medical records. Non-syndromic genetic hearing loss diagnosis was based on familiar history of premature deafness or parental consanguinity, once genomic tests are not accessible for the majority of our patients.

Patients were grouped as pre-lingual or post-lingual based on language acquisition prior or posterior to deafness. Microsoft Excel software and R statistics were used to perform descriptive statistics and charts.

According to Resolution 466/12 from the National Health Council for Human Research this study was submitted to the institutional review board and approved (CAAE 97621718.7.0000.5505).

Results

Our sample is composed of 159 patients submitted to cochlear implantation between 2006 and 2017. There are 74 post-lingual cases and 85 pre-lingual cases.

Post-lingual deafness onset age ranged from 3 to 72 years, with median in 22,5 years, lower quartile in 7,75 years and upper quartile in 41 years.

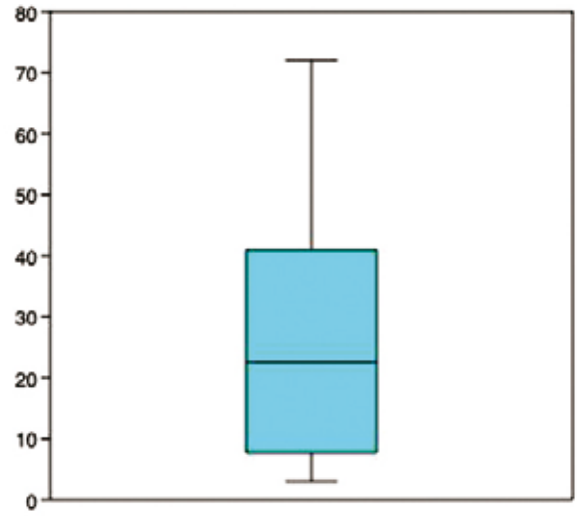

Chart 1. Boxplot: post-lingual deafness onset age distribution (in years).

Over half of the pre-lingual deafness cases were congenital, with its onset ranging from 3 days of life to 2 years old.

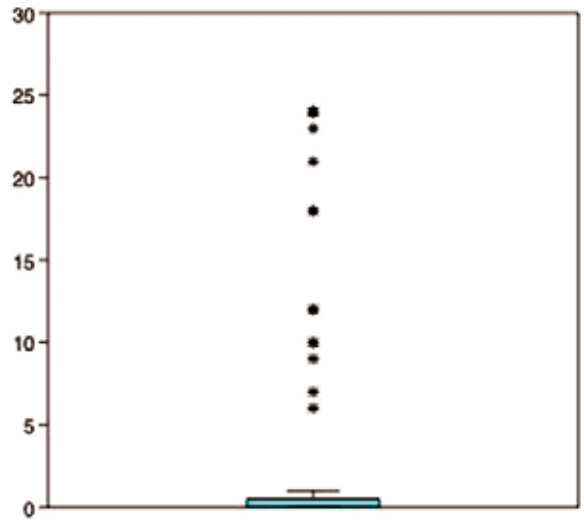

Chart 2. Boxplot: prelingual deafness onset age distribution (in months).

Sex distribution in each group can be observed in table 1.

Table 1. Sex distribution in post-lingual and pre-lingual groups.

		Post-lingual		Pre-lingual	
		n	%	n	%
Sex	Female	40	54	40	47
	Male	34	46	45	53

In the post-lingual deafness group, the main etiology was meningitis, with 16 patients (21,62%). Non-syndromic genetic hearing loss was attributed to 12 patients (16,22%); otospongiosis to 7 (9,46%); autoimmune disease to 5 (6,76%); viral infections to 3 (4,05%) – 2 mumps and 1 measles; genetic syndromes to 2 (2,7%) – both of them diagnosed as Alport syndrome; Ménière's disease to 2 (2,7%); ototoxicity to 2 (2,7%); malformation to 2 (2,7%) – both with enlarged vestibular aqueduct syndrome; trauma to 2 (2,7%); otitis media complication to 2 (2,7%); lues to 1(1,35%); vestibular schwannoma to 1 (1,35%) – unilateral tumor with a contralateral sudden deaf episode some years before; stroke to 1 (1,35%) and auditory neuropathy to 1 (1,35%).

Hearing loss etiology could not be identified in 15 patients (20,72%).

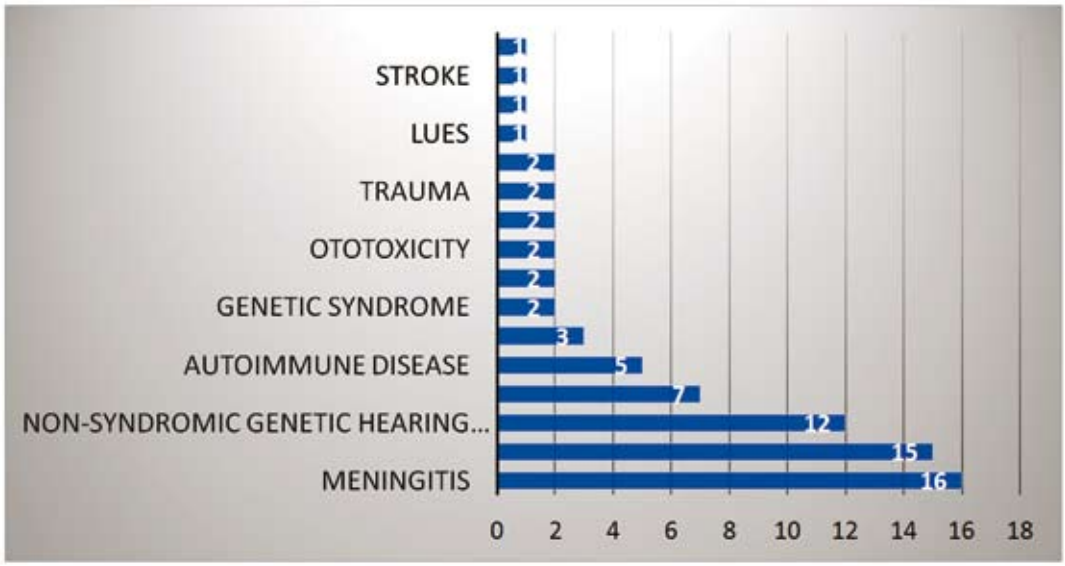

Chart 3. Pre-lingual deafness etiology in patients submitted to cochlear implants.

In pre-lingual deafness group, non-syndromic genetic hearing loss was the main cause, identified in 22 patients (25,88%), followed by perinatal complications (neonatal asphyxia, prematurity, intensive care unit admission, jaundice) in 20 patients (23,53%), congenital infections (cytomegalovirus, rubella and mumps) in 8 (9,41%), genetic syndromes (Waardenburg, hypotonic syndrome) in 5 (5,88%), meningitis in 5 (5,88%), malformation (incomplete partition type II, vestibule and lateral semicircular canal dilatation) in 3 (3,53%), auditory neuropathy in 3 (3,53%) and ototoxicity in 2 (2,53%). Deafness etiology could not be determined in 17 patients (20%).

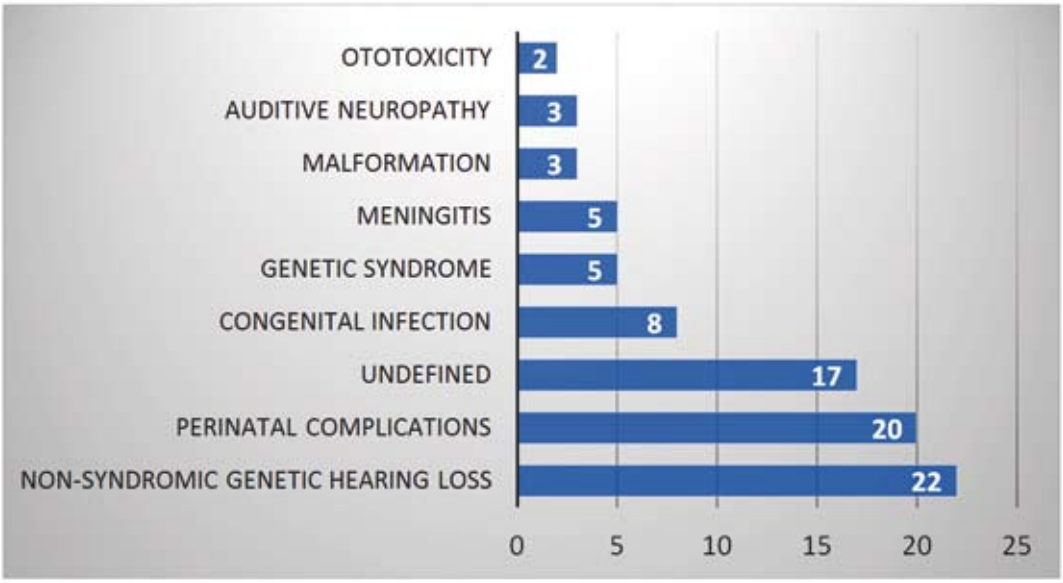

Chart 4. Post-lingual deafness etiology in patients submitted to cochlear implantation.

Discussion

There are several hearing loss determinants identified in Brazilian public health system users. A considerable number of patients submitted to cochlear implantation does not have a precise cause for deafness once they do not present common risk factors recognized through anamnesis. It is believed that the majority of those patients carries genetic mutations linked to hearing genes. As genetic research is still scarce in our public system, IC surgery is not delayed or conditioned to genetic mapping.

It is estimated that nearly 50% of pre-lingual deafness cases have a genetic connection.[1,10] In 70% of those cases, it is related to a non-syndromic mutation, 80% being of recessive inheritance, 15% of dominant inheritance and 1% linked to the X cromossome.[7] The most common mutation occurs in the GJB2 gene, responsible for coding the connexin 26.[1,10] The prevalence of genetic deafness suffers regional variations and the influence of consanguineal marriages, frequent in some cultures.[5] In this study, only 22 pre-lingual deafness patients (25,88%) and 12 post-lingual patients (16,22%) were considered to be under a strong genetic influence, half of the percentage usually found in medical literature. This may be explained due to the lack of resources to carry out a genomic investigation.

Cytomegalovirus is the most prevailing non-genetic congenital deafness etiology, being responsible for 10 – 21% of cases. Other pre-natal infections related to deafness are: rubella, toxoplasmosis, herpes simplex and syphilis.[7] In our sample, 8 cases of pre-lingual deafness (9,41%) were attributed to pre-natal infections such as rubella, mumps and cytomegalovirus, while only 3 cases of post-lingual deafness (4,05%) were related to mumps and measles. A reduction of these indexes is expected due to large coverage vaccination against measles, mumps, *haemophilus influenzae* type B and pneumococcus.[5]

Meningitis is an important cause for profound hearing disability around the world.[6] In this study, it was responsible for most of post-lingual deafness (21,62%), being also responsible for 5,88% of the pre-lingual cases. Pneumococcus is the main agent related to hearing sequela, followed by haemophilus and meningococcus.[6]

Inner ear malformations were diagnosed in 2 post-lingual patients (2,7%) and in 3 pre-lingual patients (3,53%). Both cases of post-lingual deafness where related to the enlarged vestibular aqueduct syndrome, a frequent inner ear malformation, found to be associated with non-syndromic hereditary disorders (DFNB4) as well as syndromic disorders such as Pendred, Brachio-oto-renal syndrome and Waardenburg, which can be related to SLC26A gene mutation.[11] Two of the pre-lingual cases were correlated with incomplete partition type II (Mondini's).[12]

Waardenburg syndrome, an inherited disturb characterized for sensorineural hearing loss, dystopia

canthorum, a forelock of white hair, heterochromia, broad nasal root, synophrys and skin hypopigmentation was the most prevalent genetic disorder detected in pre-lingual group. The IC surgery in those eligible patients is likely to be a challenge due to a high incidence of inner ear anomalies not found in our cases.[13]

Ototoxicity was linked to 2 pre-lingual and 2 post-lingual cases. A clear association with previous use of medications such as aminoglycosides, macrolides, loop diuretics, platinum-based chemotherapics, non-steroidal inflammatory drugs and anti-malarial medications is observed.[14]

Otosclerosis was an important etiology in post-lingual group (9,46%). Most cases were classified as far advanced forms presenting severe sensorineural hearing loss without benefit with hearing aids.[15]

Meniиrers disease was attributed to 2 post lingual cases. This condition is closely related to endolymphatic hydrops and is defined by the presence of two or more spontaneous episodes of vertigo, each lasting 20 minutes to 12 hours; audiometrically documented low- to medium-frequency sensorineural hearing loss in the affected ear on at least 1 occasion before, during, or after one of the episodes of vertigo and fluctuating aural symptoms (hearing, tinnitus, or fullness) in the affected ear. Some patients might develop profound hearing loss but their response to the IC is still debatable.[16]

Auditory neuropathy is characterized by moderate hearing loss in tonal threshold audiometry, poor speech discrimination, present otoacoustic emissions and/or cochlear microphonics in combination with absent or abnormal auditory brainstem response. In newborns, this condition is defined by the presence of otoacustic emissions and the absence or abnormal auditory brainstem response (only I and II waves). In children, it can either develop to normal hearing or to complete deafness. Several factors are involved in its physiopathology such as OTOF or OPA1 gene mutation.[17] In our study 1 post-lingual and 3 pre-lingual cases were linked to auditory neuropathy.

Conclusion

Meningitis was found to be the most common cause for deafness in post-lingual group. Non-syndromic genetic mutations were responsible for most of the pre-lingual cases. A important percentage remained undefined in both groups.

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