

Sensorineural Hearing Loss in Children

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Abstract

The objective of the study was to examine the aetiology of sensorineural hearing loss (SNHL) in a paediatric population presenting to the National Centre of Medical Genetics. A retrospective chart review from 1998 to 2006. One hundred and twenty nine children were investigated for SNHL. The average age of diagnosis of hearing loss was 36 months. The degree of hearing loss was mild in 8 children, moderate in 33 children, severe in 31 children and profound in 57 children. Eighty-five children (66%) were diagnosed with a hereditary hearing loss, 11 (8%) children had an acquired hearing loss and no cause found in 33 (26%) children. This is the first report of the causes of hearing loss in Irish children. The mean age of diagnosis in our cohort is high and emphasises the need for a neonatal screening programme. There remains a number of children for whom the cause of hearing loss remains unknown.

Introduction

The incidence of hearing loss in European children is approximately 1.4 to 2.1:1000 live births. Bilateral SNHL in children leads to poor development of language and speech skills, a decrease in intellectual ability and a poorer quality of life. The identification of the aetiological cause of deafness is vitally important for prognosis, management, genetic counseling, prevention and effective rehabilitation. The aetiology of hearing loss is traditionally classified as acquired, hereditary and unknown and it has been estimated that up to 50% of all congenital moderate to profound SNHL cases are genetic in etiology. Hereditary deafness is further classified as syndromic or non-syndromic and each of these is sub-categorised, depending upon the inheritance pattern; autosomal dominant (AD), autosomal recessive (AR), X-linked or mitochondrial. The majority appear to be transmitted in an AR manner although the relative preponderance of the different aetiologies varies across different populations and cohorts. Although a number of guidelines exist for the investigation of children with hearing loss the aetiological diagnosis of SNHL can be difficult to achieve and the incidence of SNHL of unknown cause remains relatively high. Furthermore, for some patients congenital hearing loss may not manifest itself until later in childhood. The aim of this study was to examine the aetiology of SNHL in a paediatric population presenting to the National Centre of Medical Genetics of Ireland.

Methods

This was a retrospective review of all children with SNHL who attended for the NCMG between 1998 and 2006. This tertiary referral centre serves as the principal department investigating the genetic causes of SNHL in children for the Republic of Ireland. Data was recorded for the source of referral, patient demographics, clinical, genetic and family history, findings from clinical examinations, results of radiological and haematological investigations and audiological findings. In principle, the British Association of Community Doctors in Audiology (BACDA) guidelines for the medical investigation of hearing loss in childhood serves as the template for investigating children attending the NCMG. The results of audiological investigations were obtained from the referral source; investigations used included tympanometry, brainstem evoked response audiometry (BSER), pure tone audiometry (PTA) or visual reinforcement audiometry (VRA) depending upon the age and capabilities of the patient. The PTA results were classified according to the average threshold in the frequencies 0.5, 1.2 and 4 kHz. The average hearing loss was classified as mild (15-30dB), moderate (31-60), severe (61-90) or profound (>91dB) and was reported for the better hearing ear. The methods used to identify a pattern of inheritance for hearing loss with specific mutation unknown, was based upon clinical and genetic history.

Results

One hundred and twenty nine children with SNHL were seen for genetic screening at the NCMG between 1996 and 2006. These children were from 104 unrelated families. This group included 68 males and 61 females. There were no children from consanguineous relationships.

Source of Referral

Sixty four (49.6%) children were referred from the national cochlear implant unit at Beaumont Hospital, 15 (11.6%) from other otolaryngology departments from around the country, 27 (20.9%) from paediatricians, 14 (10.8%) from area medical officers or community audiologists, 5 (3.8%) from general practitioners and 4 (3.1%) from neurologists.

Hearing Tests

Forty-two children underwent BSER and 20 children a VRA. The remaining 67 children underwent PTA.

Hearing Loss

The average age of diagnosis of SNHL was 36 months (range 1-196 months, median 24). The chronological age at diagnosis of hearing loss is detailed in Table 1. There was a correlation between a greater degree of hearing loss and an earlier diagnosis; detailed in Table 2. The degree of hearing loss (in the better hearing ear) was mild in 8 children, moderate in 33 children, severe in 31 children and profound in 57 children.

Aetiology of Hearing Impairment (Table 3)

Eighty-six (66%) of 129 children were diagnosed with a hereditary hearing loss (16 syndromic and 70 non-syndromic). 10 (8%) patients had a suspected acquired hearing loss; 2 had Rubella and one child developed measles. Seven children were thought to have developed SNHL secondary to prematurity. In 33 (26%) children no cause of hearing loss was identified. The details of each of these groups are shown in Table 4.

Laboratory Testing

Connexin 26 testing was performed in 70 patients and was abnormal in 18 (26%) of those tested. Screening for Pendredâ s syndrome, was abnormal in 6 out of 20 (30%) patients tested; all 20 patients were tested based upon the detection of radiological abnormalities of the cochlear or temporal bone or thyroid abnormalities. One patient tested positive for MELAS syndrome. TORCH screening was only performed in two patients and was normal for both. Chromosomal Analysis was carried out in 42 patients and in only one of these was an abnormality detected (22q11 deletion).

Radiological Investigations

Computed Topography (CT) scanning was performed on 61 children. An abnormality was found in 14 (23%) scans. The details of these abnormalities are detailed in table 5. Five children underwent Magnetic Resonance Imaging (MRI). This demonstrated cerebellar atrophy in 2 children. Two children had renal ultrasound performed and in one child it demonstrated renal failure.

No Investigations

20 (16%) children did not undergo any investigations during the course of genetic screening. 9 of these children were diagnosed with SNHL of unknown cause and 11 with hereditary loss (6 AR and 5 AD inheritance pattern).

Discussion

The early intervention and management of hearing loss is critical to the childâ s development. The diagnosis of the cause is also helpful for families to understand what is happening and to provide genetic counselling. The BACDA guidelines have served as the basis for the investigation of SNHL in children seen in the NCMG, since they were introduced in 2002. Although the guidelines have been targeted towards children with severe to profound hearing impairments, they have been utilized also for all children, regardless of the degree of hearing loss. The mean age of diagnosis of SNHL in our group of patients was 36 months and there was a correlation

between a greater degree of hearing loss and an earlier diagnosis. Thirty-six months represents a delay in diagnosis and consequently management. This figure may be skewed by some patients having milder hearing deficits, which results in a later pick up, or reflect the fact that some hereditary hearing losses do not manifest until later in life. However, if it does reflect an actual delay in diagnosis it highlights the need for a nationwide neonatal screening programme in Ireland.

In 96 (74%) children assessed, a cause for the SNHL was identified. The remaining 33 (26%) had no identifiable cause for their deafness. Niehaus et al found the percentage of unknown to be 12.8 to 67% in their review from 1953 to 1995¹⁰ and Morzaria et al found a mean incidence of 38% of unknown cause in their systematic review of the literature from 1990 to 2002. However, it is neither clear what guidelines were used to evaluate the aetiology of SNHL. Our results would, therefore, appear to compare well with other studies. Thirty-six patients (28%) were diagnosed with AR SNHL. The diagnosis of AR SNHL is presumptive upon genetic history and clinical findings there is potential overlap with patients who have been simply diagnosed as aetiology unknown. It is likely that patients with hearing loss classified as unknown represent various cases of AR hearing loss and vice versa.

Hearing loss of unknown cause may also represent a number of other conditions, such as sub-clinical infections including cytomegalovirus, rubella or toxoplasmosis, which have not been detected; serological testing becomes unreliable after the first six months of life and therefore was not performed in our cohort¹⁷. The discovery that mutations in GJB2, the gene that encodes for connexin 26 has had huge implications for genetic testing. Connexin 26 forms gap junctions between cells and is thought to help recirculate ions in the cochlear endolymph. The relatively small size of the connexin 26 gene and the existence of common mutations make it suitable for genetic testing. As twenty-four (34%) children from the above groups (aetiology unknown and AR SNHL) did not undergo any form of genetic testing it is likely that hearing loss caused by a connexin 26 mutation occurs more frequently than the rate of 13% we have seen. Testing for connexin 26 mutations has increased over the last few years, in line with recommended protocols, and this is reflected in this diagnosis now being discovered more frequently.

Prematurity as a cause for hearing loss was seen in seven patients. The cause of the SNHL in this group cannot be identified with certainty as they were all exposed to a number of risk factors for SNHL: 6 developed hyperbilirubinaemia, 4 developed sepsis, 4 received ototoxic medication and 3 required admission to the special care baby unit.

The incidence of acquired hearing loss in our cohort was 8%. This figure is low compared to previously published reports. We attribute this to selection and referral bias. Typically, patients are referred to the NCMG when the aetiology of SNHL remains unknown. Meningitis is frequently cited as one of the most common causes of acquired hearing loss and yet was not seen in any of the children that we saw is assumed, therefore, that some children will not have been referred where an obvious cause for hearing loss has already been elucidated. Also, the national cochlear implant unit provides the bulk of referrals (approximately 50%) to the NCMG and generally these children will have a greater degree of hearing loss and may not accurately represent the deaf population as a whole.¹³ It

There are just over 60,000 live births per annum in Ireland and of these approximately 80 children each year are born with a significant SNHL. Between 1998 and 2006 the NCMG saw nearly 14 new patients per annum which would suggest that approximately only one-fifth of children with SNHL are referred to the NCMG for investigation. Reasons for non-referral are not clear but presumably most patients are not referred when a diagnosis has already been identified. Deafness is also reported to occur in the Traveller community of Ireland, where consanguineous marriages occasionally occur. No children with deafness from consanguineous marriages were seen at the NCMG during the 10 year period and this is noted by the authors. We have found that the tests with the highest yield for positive results are CT scanning and genetic testing for Connexin 26 mutations and Pendreda's syndrome mutations. Strike rates for CT scanning as high as 40% have been previously reported and our study (abnormalities found in 23%) would correlate with these figures, emphasizing the clinical usefulness of this as an investigative tool^{14,15}. A high yield (30%) was seen when for testing for Pendreda's, but this might be expected in the presence of clinical or radiological findings. The importance of testing for mutations in the GJB2 gene has been elucidated to already. Hutchin et al suggest in their review of genetic testing for hearing loss that screening the GJB2 and SLC26A4 genes should form the basis of any genetic testing programme for childhood deafness and our findings would support this also. In contrast, the yield from other tests including blood tests, urinalysis and electrocardiogram was generally low and this has also been observed previously^{14,15,17}.

In summary, we present the first report from Ireland examining the causes of SNHL in children. We have found that hereditary deafness accounts for 66% of cases of SNHL, acquired 8% and 26% cases have unknown etiology. The mean age of diagnosis, particularly with respect to the developing and maturing brain, is still high and the majority of children with SNHL are not referred for investigation; this emphasises the need for neonatal screening as well as a system for reporting and storing information nationally.

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Comments:
