Value of systematic aetiological investigation in children with sensorineural hearing loss

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Summary Sensorineural hearing loss is the most common form of sensory impairment in children. As a precise aetiological diagnosis has major prognostic and management implications, it is useful to evaluate the contents of the aetiological investigation of sensorineural hearing loss in France. This article presents a retrospective review of professional practices by comparing the aetiological investigation of hearing loss in children with a cochlear implant and children without a cochlear implant.

Patients and methods: One hundred and seven children under the age of 18 years with unilateral or bilateral sensorineural hearing loss attending the paediatric ENT department for the first time between January 2007 and January 2009 were included in the study. Data from the clinical interview and all complementary investigations were analysed.

Results: The various aetiologies of hearing loss were classified as genetic, acquired, or unknown in each of the two populations. Hearing loss was of unknown origin in 52% of the 87 non-implanted children and 15% of the 20 children with a cochlear implant.

Conclusion: This study demonstrates the heterogeneous practices in terms of aetiological investigation of sensorineural hearing loss as a function of the target population. A more systematic aetiological investigation was performed in children fitted with a cochlear implant, requiring multidisciplinary management. This study indicates the need to define a standard aetiological investigation for all children with sensorineural hearing loss.

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Introduction

Moderate to profound sensorineural hearing loss is the most common form of sensory impairment in children, affecting one in every 800 newborn infants [1]. Early management of sensorineural hearing loss is designed to prevent impaired language development, which can interfere with the child’s cognitive performances and socio-emotional development [2].

One of the first steps of management of sensorineural hearing loss is to establish an aetiological diagnosis, which has major implications for prognosis and treatment. For example, discovery of a radiological abnormality of the inner ear, such as enlarged vestibular aqueduct, indicates a risk of deteriorating and/or fluctuating hearing loss, requiring prevention of head injury, bacterial meningitis vaccination, and screening for gene mutations. Children with profound

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hearing loss must be investigated for long QT syndrome because of the risk of sudden death (Jervell and Lange-Nielsen syndrome). Another example concerns congenital cytomegalovirus infection, for which treatment protocols are currently under evaluation [3]. These few examples justify systematic aetiological investigation according to a clearly defined protocol. Clinical practice guidelines for the aetiological investigation of severe to profound bilateral hearing loss were published in the United Kingdom in 2002 [4]. However, despite the existence of these guidelines, this aetiological investigation is not systematically performed. The results of an audit conducted by Yoong and Spencer in Bradford, United Kingdom, concerning application of official recommendations showed partial compliance with these guidelines, partly due to parental choices and financial aspects [5]. This situation appears to be even more complex in the case of investigations for mild to moderate unilateral and bilateral hearing loss, as published studies show that the cause of unilateral hearing loss remains unknown in 35% to 60% of cases despite progress in medicine and genetics [6,7].

No official guidelines have been published in France, but this type of aetiological investigation is currently being developed. This investigation comprises a rigorous clinical interview, family audiology, CT scan of petrous temporal bones, ophthalmological consultation, CMV serology, and proposal of a genetic consultation [8–12] and is completed by urine dipstick tests in the case of progressive hearing loss, electroretinogram (ERG) in the case of delayed motor development, such as delayed walking, and electrocardiogram (ECG) in children with profound bilateral hearing loss.

It therefore appeared important to assess clinical practice in relation to the aetiological investigation of hearing loss in children according to the characteristics of the hearing impairment, as Fortnum, in 2006, showed that the aetiological investigation of hearing-impaired children fitted with a cochlear implant was more exhaustive than in non-implanted hearing-impaired children [13].

The objective of this study was to compare the aetiological investigation of sensorineural hearing loss performed in a group of non-implanted hearing-impaired children and a group of implanted hearing-impaired children in order to demonstrate differences in the distribution of aetiologies between the two groups and to analyse the reasons for these differences.

Patients and methods

This study included children under the age of 18 years with unilateral or bilateral sensorineural hearing loss of at least 25 dB on the better of the two ears, attending the paediatric ENT department for the first time between January 2007 and January 2009. The study population was divided into two groups. The first group (G1) comprised hearing-impaired children with or without a conventional hearing aid and the second group (G2) comprised cochlear-implanted children.

Each child’s medical charts were reviewed for the following variables of the clinical interview: family history of hearing loss, consanguinity, disease during pregnancy and delivery, birth weight less than 1500 g, significant personal history (administration of ototoxic medications, infectious diseases, etc.) and walking age. Data of complementary investigations analysed in this study corresponded to those recommended by the genetic hearing loss reference centers expert group [9,12]: family audiology, CT of petrous temporal bones, ophthalmological consultation, Cytomegalovirus (CMV) serology and proposal of a genetic consultation.

The various aetiologies of hearing loss were classified as genetic, acquired, or unknown in each of these two populations. A child was considered to present genetic hearing loss in the presence of a perfectly documented family history of sensorineural hearing loss affecting a first-degree relative, parental consanguinity, a gene mutation demonstrated by molecular biology diagnosis, an inner ear malformation demonstrated by imaging or a more complex syndrome comprising hearing loss.

Results

One hundred and seven children (54% females (n = 47) and 46% males (n = 40)) were included in this study.

The group of non-implanted children (G1) comprised 87 children (81.3%), 64 (73.6%) of whom were fitted with a hearing aid and 23 (26.4%) without a hearing aid. Children not fitted with a hearing aid presented either unilateral or bilateral hearing loss. The median age at the time of the first visit to the department was 7 years (range: 1 to 7 years). Eighteen (20.7%) children presented unilateral hearing loss and 69 (79.3%) children presented bilateral hearing loss. Mild hearing loss was detected in 24.1% of children (n = 21), and moderate to profound hearing loss was detected in 75.9% (n = 66). The results of clinical interview were as follows: a family history of hearing loss was investigated in 48.3% of cases (n = 42) and was present in 28 families. The presence of parental consanguinity was investigated in 14% (n = 12) of cases and was present in two families (2/12). The course of pregnancy was recorded in 38% of cases (n = 33), revealing ten pathological pregnancies (two cases of hypertension of pregnancy, one CMV seroconversion, two cases of intrauterine growth retardation (IUGR), three cases of use of medications not recognised as being potentially ototoxic, one motor vehicle accident, one case of maternal alloimmunisation). The modalities of delivery were recorded in 38% of cases (n = 33) with nine pathological births (four neonates required admission to the intensive care unit, three cases of neonatal jaundice, two cases of acute fetal distress). The birth weight was recorded in 19.5% of cases (n = 17): four infants had a birth weight less than 1,500 g (23.5%). The child’s personal history (use of ototoxic medications, infections, etc.) was recorded in 70% of cases (n = 61): four children had a history of meningitis (three cases of pneumococcal meningitis, one case of staphylococcal meningitis) and one child had received an ototoxic drug treatment. The walking age was recorded in 33.3% of cases (n = 29): five children presented delayed walking greater than 18 months.

The results of complementary investigations were as follows (Table 1): family audiology was performed in 17% of cases (n = 15), CT scan of petrous temporal bones was performed in 48% of cases (n = 42), ophthalmological consultation was performed in 16% of cases (n = 14), but CMV
serology was not performed. A genetic consultation was proposed in 29% of cases (n = 25).

The second group (G2) comprised 20 implanted children (18.7%) with a median age of 4 years at the time of the first visit to the department (range: 1 to 7 years). All implanted children presented severe to profound bilateral hearing loss. The results of clinical interview were as follows: a family history of hearing loss was investigated in 70% of cases (n = 14) and was present in five families. The presence of parental consanguinity was investigated in 35% of cases (n = 7) and was present in two families. The course of pregnancy was reported in 60% of cases (n = 12) and revealed 5 pathological pregnancies (one case of eclampsia, two infections, including one case of rubella, one case of use of a potentially ototoxic medication and one case of IUGR). The modalities of delivery were recorded in 70% of cases (n = 14), revealing five pathological births (two cases of prematurity, one HELP syndrome, one case of respiratory distress and one case of prematurity associated with respiratory distress). The birth weight was recorded in 75% of cases (n = 15); one neonate had a birth weight less than 1,500 g. The child’s personal history (use of ototoxic medications, infections, etc.) was recorded in 80% of cases (n = 16): two children had a history of meningitis (one case of pneumococcal meningitis, one case of meningococcal meningitis) and 1 child had received treatment with an ototoxic medication. The walking age was recorded in 75% of cases (n = 15): three children presented delayed walking greater than 18 months.

The results of complementary investigations were as follows (Table 1): family audiometry was performed in 10% of cases (n = 2); CT scan of petrous temporal bones was performed in 100% of cases, leading to the diagnosis of inner ear malformations in 6/20 cases (Mondini malformation (n = 2), enlarged vestibular aqueduct (n = 2), early ossification (n = 2, including 1 child with an abnormal cochlea)); ophthalmological consultation was performed in 25% of cases (n = 5); CMV serology was never performed. A genetic consultation was proposed in 30% of cases (n = 6).

In the first group (G1), a genetic origin was suspected in 23% of cases (n = 20), an acquired origin was suspected in 25% of cases (n = 22) and the origin remained unknown in 52% of cases (n = 45) (Table 2).

In the second group (G2), a genetic origin was suspected in 45% of cases (n = 9), an acquired origin was suspected in 40% of cases (n = 8) and the origin remained unknown in 15% of cases (n = 3) (Table 2).

In the overall population (G1 + G2), a genetic origin was suspected in 26.6% of cases (n = 28), an acquired origin was suspected in 27.6% of cases (n = 30) and the origin remained unknown in 45.8% of cases (n = 49) (Table 2).

Discussion

This study was part of a real retrospective review of our professional practices. This study demonstrated heterogeneous clinical practice in relation to the aetiological investigation of sensorineural hearing loss as a function of the target population. A more systematic aetiological investigation was performed in cochlear-implanted children than in non-implanted children, indicating the need for a systematic aetiological investigation protocol. For example, application of the British aetiological investigation guidelines in 47 newly diagnosed hearing-impaired children in the Bradford district in the United Kingdom between March 2002 and 2004 allowed recording of clinical characteristics such as the presence of consanguinity, the family history, the presence of antenatal or neonatal risk factors, and the absence of risk factors, in 100% of cases [5]. This study confirmed the value of a standard aetiological questionnaire for identification of clinical characteristics. The age difference between the two groups of the present study (mean age of 7 years for G1 and 4 years for G2) reflected the delayed diagnosis and demand for aetiological investigation in the group of non-implanted children. However, in children presenting at a later age, the parents may forget various aspects of the clinical history, which could compromise the aetiological investigation. The study by Tharpe in 2008 evaluating the aetiologies of mild unilateral and bilateral sensorineural hearing loss reported delayed diagnosis due to the absence of systematic screening and the frequent lack of clinical information [14]. Availability of clinical data therefore appears to be positively correlated with the severity of the hearing loss and the presence of a cochlear implant.

The major distinguishing feature between the two groups in terms of complementary investigations was the systematic use of CT of the petrous temporal bones in implanted children, which can be explained by the fact that this examination is systematically required before surgery in addition to its role in the aetiological investigation. According to Wilson [15], petrous temporal bone imaging is one of the most useful investigations to establish an aetiological diagnosis of hearing loss. However, these examinations are performed in some hospitals, including our own, under general anaesthesia for children under the age of 4 years. Although general anaesthesia is not the standard procedure,
it is justified to rigorously ensure the child’s immobility in order to obtain good quality CT examination of the petrous temporal bone avoiding unnecessary repetition of this irradiating examination. In our group of non-implanted children, CT was generally performed after the age of 4 years either because of the parents’ refusal of general anaesthesia before this age, or because of the clinician’s refusal or omission to propose this examination. Delayed CT of the petrous temporal bone could also have an impact on proposal of a genetic consultation, as screening for gene mutations is partly based on the presence of malformations of the inner ear. For example, the presence of an enlarged vestibular aqueduct indicates the need to screen for an SCL26A4 gene mutation. When CT examination is normal, genetic screening primarily concerns connexin 26 and 30 gene mutations. A genetic consultation was not proposed in children presenting known risk factors for hearing loss or acquired causes, such as a history of meningitis. Our study highlights the need to systematically propose a genetic consultation in order to identify additional genetic causes of hearing loss, establish a more comprehensive DNA bank, identify multifactorial causes of hearing loss and obtain more comprehensive data of the clinical interview and other examinations. However, this approach is somewhat hypothetical, as, in reality, samples for connexin 26 and 30 gene mutation screening can also be taken, after written consent from the parents, during anaesthesia for other indications and a genetic consultation is then only proposed in the case of positive results.

An ophthalmological consultation must be systematically performed, as a higher prevalence of refractive disorders has been demonstrated in the severe and profound hearing-impaired population (50%), who consequently require optical rehabilitation to avoid a double sensory disability, and specific disorders of the ocular fundus may also be observed, such as retinitis pigmentosa, or congenital cataract suggesting the presence of a more complex syndrome comprising hearing loss [15].

CMV serology was never ordered in this study due to the limited value of this serological test after the first six months of life. After the age of six months, only negative CMV serology is useful to exclude this aetiology. PCR of Guthrie card DNA can be used to detect this aetiology after the age of 6 months, but this test is not yet part of routine clinical practice. In every case, the aetiological investigation can be optimised by ensuring the early diagnosis of prelingual deafness and immediately screening for congenital CMV infection.

ECG and screening for microscopic haematuria and/or proteinuria were not systematically performed. ECG, looking for a repolarisation disorder with a risk of sudden death, should be performed in all cases of severe and profound hearing loss because of the risk of Revel and Lange-Nielsen syndrome. Glomerulonephritis in children with Alport syndrome can be detected by urine dipstick tests. Alport syndrome predominantly affects boys and is usually responsible for progressive hearing loss. This simple and inexpensive test should therefore be performed systematically in all cases of progressive sensorineural hearing loss.

The results of the aetiological investigation differed between the two groups, as the cause of the hearing loss remained unknown in only 15% of cases in group G2 versus 52% of cases in group G1. This difference can be explained by the multidisciplinary management of implanted children. A systematic and complete clinical interview combined with CT scan of the petrous temporal bones constitute the cornerstone of this aetiological investigation. However, the aetiologies of unilateral and mild hearing loss also differ from those of severe and profound hearing loss. In the overall study population (groups G1 + G2), a genetic aetiology was suspected in 26.6% of cases, an acquired aetiology was suspected in 27.6% of cases and no aetiology was identified in 45.8% of cases. The percentage of unknown causes was similar to that reported in a Finnish study [16], in which the authors recorded the aetiologies of 92 Finnish children with mild to profound hearing loss born between 1988 and 2002. Acquired, unknown and genetic aetiologies represented 14%, 40% and 46% of cases, respectively. According to the authors, congenital infections were underestimated, as were genetic causes due to genes that have not yet been identified or that are not systematically tested. Unknown causes can be mainly considered to be cases of autosomal recessive genetic hearing loss.

The results of this study cannot be analysed from an epidemiological point of view due to the absence of a comprehensive aetiological investigation, but they illustrate and clearly justify the need to perform a standardised aetiological work-up. On the basis of this study, a standardised clinical interview, an ophthalmological consultation, petrous temporal bone imaging and CMV serology should be systematically performed in all cases of hearing loss. A genetic consultation with family audiometry must be systematically proposed. The other complementary investigations (ECG, urine dipsticks, etc.) should be performed subsequently as a function of the characteristics of each child’s hearing impairment. British guidelines distinguish the aetiological investigation for mild to moderate bilateral hearing loss and for severe to profound hearing loss. The first-line investigations are similar for the two types of hearing loss and comprise systematic clinical interview and clinical examination, family audiometry, ophthalmological examination, screening for microscopic haematuria, screening for connexin 26 gene mutation, petrous temporal bone imaging and CMV serology [4,17]. It is recommended to systematically perform ECG in children with severe or profound hearing loss [4]. Our current recommendations strongly resemble these British guidelines. This aetiological investigation needs to be adapted to the severity of the hearing loss, as recommended in the British guidelines.

Conclusion

The aetiological investigation conducted to establish the diagnosis of sensorineural hearing loss in children varies from one population of children to another. Systematic and meticulous clinical interview and imaging of the petrous temporal bones must constitute the basis of any aetiological assessment. This assessment must be completed by ophthalmological examination and genetic counselling must be proposed both to help the child’s family and also to more clearly determine the distribution of the causes of hearing loss.
In the future, this aetiological investigation should be a mandatory part of clinical practice, as is already the case in the United Kingdom. Nevertheless, prospective studies with systematic application of the standardised aetiological investigation proposed in this article should be realized to improve the feasibility and the optimal management.

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Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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