Evaluation of the Vestibular System and Etiology in Children with Unilateral Sensorineural Hearing Loss

Leman Birdane, Armağan İncesulu, Erkan Özüdoğan, Cemal Cingi, Hamdi Caklı, Melek Kezban Gürbüz, Baki Adapınar

OBJECTIVE: The aim of this study was to evaluate the vestibular system of children with unilateral sensorineural hearing loss (USNHL), investigate the etiological factors of USNHL and analyze whether a genetic predisposition exists.

MATERIALS and METHODS: Thirty-three children aged less than 18 years with USNHL, who visited the ear, nose, and throat (ENT) department between January 2004 and December 2012, were included in this study. Cases with conductive hearing loss were excluded from the study. The patients were subjected to etiologic, genetic, and ophthalmologic evaluation; radiologic imaging; electronystagmography (ENG); and vestibular evoked myogenic potential (VEMP) tests. The control group, which included 25 healthy children (13 males and 12 females), had undergone audiological assessment and were subjected to ENG and VEMP tests.

RESULTS: All of the patients had severe-to-profound hearing loss. Mumps immunoglobulin G was positive in 22 (66.7%) of 33 patients. The 35delG mutation was not found in any of the patients. All of the patients underwent temporal computed tomography (CT) and magnetic resonance imaging (MRI). Inner ear anomaly was present in 51.5% of the patients. Overall, 21 of 31 ENG patients had canal paresis in the affected ear. The VEMP response was absent on the affected side in three patients. The n23 latency average of the patient group was longer than that of the control group.

CONCLUSION: Because USNHL causes irreversible problems in children, early diagnosis and auditory rehabilitation are very important. As USNHL is accompanied by inner ear anomaly, children with USNHL should undergo temporal bone CT and MRI. To evaluate the vestibular system, ENG and VEMP are non-invasive and diagnostic tests.

KEYWORDS: Children with unilateral hearing loss, electronystagmography, vestibular evoked myogenic potentials

INTRODUCTION

As the most common pathology among congenital neural pathologies, hearing loss may cause various problems in every stage of life [1]. Hearing loss affects 1–3 of every 1,000 infants and 11% of school-aged children [2]. Regarding unilateral sensorineural hearing loss (USNHL), the condition affects 3% of school-aged children [3]. As neonatal screening has become widespread, more realistic results pertaining to the incidence of hearing loss have been obtained. In a study conducted in Finland, the prevalence of USNHL was found to be 1.7 per 1,000 infants [4]. The incidence of bilateral hearing loss in infants was found to be 3.32% and that of unilateral hearing loss was found to be 1.40% in a study conducted at Eskişehir Turkey [5].

Bilateral hearing loss shows its signs in the early stages because of the impairment of language development; however, because the child continues to communicate through the intact ear, the diagnosis of USNHL may be delayed until the primary school period [6]. Children with USNHL do not have the advantage of binaural hearing and thus have a difficulty with auditory perception. Because the vestibular system may also be affected in cases with USNHL, imbalance and vertigo may also be present [1]. All of these negative effects may manifest in low academic performance, difficulties in social life, and lack of self-confidence [3, 7–11].

Although many examinations are conducted in cases of SNHL to determine the etiology, it is not always possible to obtain a definite result. Because inner ear anomalies and mass lesions are more common risk factors for USNHL than bilateral hearing loss, computed tomography (CT) and magnetic resonance imaging (MRI) investigations are necessary [12].

In unilateral hearing loss, the vestibular system is generally affected in addition to the cochlea. Clinical findings may vary, but the vestibular impairment may be asymptomatic because of central compensation. When the vertigo becomes symptomatic, the physical and emotional health of the child is adversely affected [13].
Our objective in this study was to evaluate the vestibular system in childhood USNHL and to determine the incidence of abnormalities on imaging studies, risk factors, and whether there is a genetic predisposition.

MATERIALS and METHODS
This study was conducted with 33 patients aged less than 18 years (14 males and 19 females; average age: 12.2±3.68 years) who visited our clinic with a complaint of unilateral hearing loss. The control group comprised 25 volunteer children (13 males and 12 females; average age: 12.4±4.21 years) with normal hearing. Patients with conductive hearing loss and chronic otitis media were excluded from the study.

A detailed history was obtained from the patients and their families, including with respect to consanguineous marriage, hearing loss, and family history of the syndrome. Antenatal or perinatal infections, premature birth, ototoxic drug use, noise exposure, and trauma were assessed. After otological examination, all of the patients underwent vestibular evaluation tests. In addition to undergoing the Romberg test, Unterberger stepping test, head shake test, and head impulse test, they were examined by a pediatric neurologist and ophthalmologist. The patient and control groups were also subjected to pure tone threshold and suprathreshold audiometry using the AC-40 audiometry device (Interacoustics; Assens, Denmark). The middle ear pressure and stapedius reflex were measured using the AZ-7 device (Interacoustics). The complete blood count, antinuclear antibody (ANA) level, antinuclear cytoplasmic antibody level, human leukocyte antigen (HLA) type, sedimentation rate, thyroid hormone level, and urea and creatinine levels with respect to renal function were evaluated in all of the patients. Mumps immunoglobulin (Ig) M and IgG levels were measured in all of the patients, and they all underwent electrocardiography (ECG). The ECG results were evaluated by a cardiologist; particularly, QT intervals were measured. All of the patients underwent high-resolution CT (HRCT) and MRI for radiological monitoring, and the images were evaluated by a neuroradiologist at our university hospital. The inner ear anomaly, diameter and size of the semicircular canals, and width of the vestibular aqueduct and internal auditory canal were particularly evaluated by CT scans. The mass lesions and presence of the eighth nerve were evaluated by MRI. The patient and control groups were both subjected to the electronicystagmography (ENG) test using the Chart Medical ENG device (ICS Co. Ltd.; Iwate, Japan). The ENG test battery was composed of a saccadic test, a gaze (fixation) test, an optokinetic test, a tracking (smooth pursuit) test, a caloric test, and positional tests. The water used in the bithermal caloric test was maintained at 30°C and 44°C. When the difference between the sums of the nystagmus durations of the horizontal canals generated with hot and cold water was more than 20%, it was accepted as canal paresis.

The vestibular evoked myogenic potential (VEMP) records were taken with the Medelec Synergy version 10 (VIASYS Health Care UK; Surrey, UK) device that is used in our ENT department. First, the skin of the patient was cleaned with alcohol to prevent artefacts. The active electrode was replaced at the middle-third of the sternocleidomastoid muscle (SCM), the reference electrode was replaced at the sternal notch, and the earth electrode was replaced at the middle of the forehead. It was demanded from the patient that he/she turn his/her head to the opposite side to that of the stimulus (during the “click” stimulus). In the meantime, the muscle action potential from the SCM was recorded. The test was repeated twice for both sides. The first positive wave was detected as p13, and the first negative wave was detected as n23. The latencies of p13 and n23 and the amplitude values between the two waves (p13–n23) were measured. The normative data from the control group were compared with the latency and amplitude values of the patient group. The waves, in which p13 and n23 latencies were longer than the average latency of the control group and the peak-to-peak amplitude value was lower than that of the control group, were determined as impaired.

Genetic examination of the patients was performed at Ankara University School of Medicine, Department of Medical Genetics. The connexin 26 gene of the samples was examined for the presence of the 35delG mutation. DNA isolation was performed using the classic phenol/chloroform method. Blood samples (9 mL) were collected from the patients into polyethylene tubes (Sigma-Aldrich; St. Louis, MO, USA) containing 1 mL of 0.5 M ethylenediaminetetraacetic acid (EDTA). After the blood samples had been obtained, the PCR products were evaluated in 2% agarose gels, and enzyme cuts of the c.35delG mutation were evaluated in 3% agarose gels. The 35delG mutation was examined via the polymerase chain reaction-restriction fragment length polymorphism (PCR/RFLP) method.

Statistical evaluation was performed using the Statistical Package for the Social Sciences (SPSS) for Windows software (SPSS Inc.; version 15.0, Chicago, IL, USA). The data were compared by t-test and Fisher’s exact test. A p value less than 0.05 was deemed to indicate statistical significance.

The study was approved (date: 19.11.2009; number: 23) by the Medical Ethics Committee of our school. Informed consent was obtained from the parents of all of the patients and volunteers.

RESULTS
In total, 33 patients (14 males and 19 females) and 25 healthy children (13 males and 12 females) were included in this study. The average age of the patients was 12.2±3.68 years (range: 5–18 years) and that of the control group was 12.4±4.21 years (range: 4–18 years). There was no statistically significant difference in the average age between the groups. The main complaint of the patients was unilateral hearing loss.

The average age at which hearing loss was first diagnosed was 9.06 years. None of the patients visited the clinic with a complaint of sudden hearing loss. There were 20 patients with right-sided hearing loss and 13 with left-sided hearing loss. All of the patients had stable, unilateral, severe-to-profound sensorineural hearing loss.

Nine of the patients had a history of mumps parotitis, of whom six had hearing loss in the first week after recovering from mumps. One of the patients had a diagnosis of bilateral horseshoe kidney. Two patients had neuromotor retardation up to 2 years of age, and six had stayed in an incubator for a period of 1.5 months. One of the patients had a history of tricyclic antidepressant drug abuse at 3 years of age. Five of the patients had a history of febrile convulsion; however, their pediatric neurology consultation was normal, and there was no abnormality on electroencephalography (EEG). No risk factors were identified in any of the histories of any of the other nine patients. The
family history of hearing loss in all patients was negative (Table 1). The middle ear pressure of all of the patients was normal, and the acoustic stapedius reflex was absent on the affected side. The bilateral hearing level and results of immittance testing were normal in the control group.

In total, 17 (51.5%) of the patients had inner ear anomaly, of whom 11 had lateral semicircular canal hypoplasia; 2 patients had semicircular canal aplasia. There was cranial nerve 8 aplasia in one patient. One patient had a common cavity. A bilateral, enlarged vestibular aqueduct (EVA) was found in two cases. In five patients, there was contrast enhancement in the cochlea and vestibule, and it was thought that this may have occurred secondary to an infection (Figure 1).

In total, 24 (72.7%) of 33 patients had vestibular symptoms. There were 16 patients with complaints of vertigo, 7 with vertigo accompanied by migraine, 4 with stomach ache and vomiting attacks, and 5 with aural fullness and tinnitus. Eight patients showed imbalance (Table 2).

The results of the Romberg test, Unterberger stepping test, and head thrust and head shake tests were normal. None of the patients had spontaneous nystagmus. The vestibular examination of the control group was completely normal. The ENG test could not be applied in 2 of 33 patients because of strabismus. In total, 21 (67.7%) of 31 ENG tests showed canal paresis on the affected side. Seven patients had abnormal optokinetic test results, two had abnormal saccadic and tracking test results, and one had bilateral hypoactivity on caloric tests. Two patients in the control group had abnormal optokinetic test results. The control group had normal caloric test results. The rate of canal paresis in the study group was statistically significantly higher than that in the control group (p<0.001). There was no significant difference between the two groups with respect to the results on the optokinetic test (p>0.05) or the saccadic and tracking tests (p>0.05) or in terms of bilateral hypoactivity (p>0.05) (Table 3).

The patient and control groups both underwent the VEMP test. In three patients, there was no VEMP response in the affected ear. The average p13 and n23 latencies of the affected ears in the patient group were 13.11±0.95 ms and 22.32±1.17 ms, respectively, and the average amplitude was 191.68±102.32 μv. The average p13 and n23 latencies of the unaffected ear in the study group were 12.97±0.89 ms and 21.61±1.50 ms, respectively, and the average amplitude was 203.48±95.31 μv. The average p13 and n23 latencies of the left ear were 13.4 ms and 21.08 ms, respectively, and the average amplitude was 214.68 μv. The n23 latency average of the patient group was longer than that of the control group.

Because cardiac syndromes are accompanied by hearing loss, all of the patients were consulted by a cardiologist, ECG examinations were performed, and QT intervals were measured. The ECG results and QT intervals of all of the patients were normal as were their detailed biochemical analysis results, blood count, thyroid function, ANA, anti-neutrophil cytoplasmic antibody (ANCA), and HLA typing test results. Mumps IgG was positive in 22 (66.7%) of 33 patients. The 35delG mutation was not found in any of the patients.

Table 1. Risk factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>n</th>
<th>Risk factor</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of parotitis</td>
<td>9</td>
<td>Drug abuse</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral horseshoe kidney</td>
<td>1</td>
<td>Febrile convulsion</td>
<td>5</td>
</tr>
<tr>
<td>Neuromotor retardation</td>
<td>2</td>
<td>Family history</td>
<td>-</td>
</tr>
<tr>
<td>History of staying in an incubator</td>
<td>6</td>
<td>No risk factor</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 2. Comparison of symptoms accompanying vertigo

<table>
<thead>
<tr>
<th>Accompanying symptom</th>
<th>Patient (n)</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertigo+migraine</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>Vertigo+aural fullness+tinnitus</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>Vertigo+stomach ache+nausea</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Imbalance</td>
<td>8</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3. Comparison of ENG findings between the study group and control group

<table>
<thead>
<tr>
<th>ENG findings</th>
<th>Study group (n=31)</th>
<th>Control group (n=25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canal paresis</td>
<td>21</td>
<td>-</td>
<td>p=0</td>
</tr>
<tr>
<td>Optokinetic asymmetry</td>
<td>7</td>
<td>2</td>
<td>p=0.116</td>
</tr>
<tr>
<td>Abnormal findings in central tests</td>
<td>2</td>
<td>-</td>
<td>p=1</td>
</tr>
<tr>
<td>Bilateral hypoactivity</td>
<td>1</td>
<td>-</td>
<td>p=0.497</td>
</tr>
</tbody>
</table>

Table 4. Comparison of VEMP findings between the study group and control group

<table>
<thead>
<tr>
<th>VEMP value</th>
<th>Study group affected ear</th>
<th>Control group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>p13</td>
<td>13.11±0.95</td>
<td>13.4±1.57</td>
<td>0.293</td>
</tr>
<tr>
<td>n23</td>
<td>22.32±1.17</td>
<td>21.08±1.42</td>
<td>0.001</td>
</tr>
<tr>
<td>Amplitude</td>
<td>191.68±102.32</td>
<td>214.68±73.99</td>
<td>0.355</td>
</tr>
</tbody>
</table>

Figure 1. Distribution of CT and MRI findings

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>n</th>
<th>Risk factor</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of parotitis</td>
<td>9</td>
<td>Drug abuse</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral horseshoe kidney</td>
<td>1</td>
<td>Febrile convulsion</td>
<td>5</td>
</tr>
<tr>
<td>Neuromotor retardation</td>
<td>2</td>
<td>Family history</td>
<td>-</td>
</tr>
<tr>
<td>History of staying in an incubator</td>
<td>6</td>
<td>No risk factor</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 1. Risk factors

Figure 1. Distribution of CT and MRI findings

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>n</th>
<th>Risk factor</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of parotitis</td>
<td>9</td>
<td>Drug abuse</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral horseshoe kidney</td>
<td>1</td>
<td>Febrile convulsion</td>
<td>5</td>
</tr>
<tr>
<td>Neuromotor retardation</td>
<td>2</td>
<td>Family history</td>
<td>-</td>
</tr>
<tr>
<td>History of staying in an incubator</td>
<td>6</td>
<td>No risk factor</td>
<td>9</td>
</tr>
</tbody>
</table>
DISCUSSION

Because unilateral hearing in early childhood cannot be verbally expressed by children, such that their families are unaware of any impairment, early treatment is not possible. Patients typically realize they have hearing loss in primary school with the help of their teacher, or while talking on the phone or listening to music using earphones. Besides having low academic performance in school, affected children may also show difficulties in understanding conversations in a noisy environment [7, 9].

Unilateral sensorineural hearing loss is often dismissed as an environmental entity, and the etiological basis has not been explored deeply. As the etiology of sensorineural hearing loss varies widely, we performed most of the recommended laboratory tests. To define autoimmune-mediated inner ear disease, HLA typing, ANA levels, and anti DNA levels were investigated [14]. However, we obtained no positive result. The most common cause of viral neuritis and co-chleitis in childhood is mumps. Hearing loss is seen in approximately 0.005%–0.3% of all post-mumps cases and is generally unilateral and profound [15-17]. Mumps vaccination has been made mandatory since 2007 in Turkey; however, it remains a common cause of hearing loss. In our study, 22 of 33 patients had a positive mumps IgG value, and none of these patients had been vaccinated against mumps.

The most common genetic cause of congenital hearing loss in Turkey is the mutation of 35delG. In one of the most recent studies, it was reported that there may be a mutation in the GJB3, TECTA, and COCH genes in USNHL [18]. None of the patients had a mutation in the 35delG gene.

Many studies have shown that USNHL might be accompanied by inner ear anomaly. Compared with bilateral cases, inner ear anomaly and mass lesions are more frequently seen in unilateral hearing loss. In the study by Laury et al. [19], 8 of 11 patients had cochlear nerve aplasia, and 2 patients had a mass lesion. In another study, the rate of inner ear anomaly was found to be 66.7% [18]. In our study, 17 (51.5%) of 33 patients had inner ear anomaly in the vestibular or cochlear region. Eleven patients had lateral semicircular canal hypoplasia, two had bilateral EVAs, two had bilateral semicircular aplasia, one had no cranial nerve 8, and one had vestibulocochlear anomaly (Figure 1). It should be noted that both the child and parents were informed that it was necessary to avoid contact sports and be careful to avoid head trauma to preserve the unaffected ear. The gold standard methods for detecting inner ear anomalies and mass lesions are CT and MRI [20-23]. It is necessary to perform imaging procedures on children who have USNHL to relieve the anxiety of their families and to eliminate the possibility of unknown pathologies that could affect the healthy ear.

Most patients with inner ear anomalies also show vestibular symptoms [24]. Grimmer et al. [25] reviewed 21 pediatric patients with EVAs and found that the incidence of vestibular symptoms was 48.0%; 6 patients (28.6%) had episodic vertigo, whereas 1 patient showed imbalance. In our study, 24 (72.7%) of 33 patients had vestibular symptoms, of whom 16 had episodic vertigo attacks. Vertigo attacks in seven of these patients were accompanied by migraine. Four children had vertigo accompanied by stomach ache, nausea, and vomiting. Vertigo attacks in five patients were accompanied by aural fullness, tinnitus, and nausea. Eight patients had complaints of dizziness. After detailed vestibular testing, all of the patients underwent ENG, which can record and evaluate the nystagmic response and allow central and peripheral vertigo to be distinguished. The pediatric patients could tolerate ENG easily [20]. Canal paresis was found in 21 patients after ENG. One patient had a bilateral hypoactive caloric test. The abnormal ENG results and vestibular complaint rates were similar. In our study, cooperation during ENG, even with a 4-year-old patient, was acceptable, and there were no problems after the test.

Another test that has been frequently used in recent years for the differential diagnosis of patients with vertigo is VEMP. This test can be performed in two different ways: ocular or cervical. Our patients were subjected to the cervical VEMP test, which provides information about the saccular and inferior vestibular nerve using the sacculococil reflex arc. The VEMP test is easy to implement and tolerable by children [27, 28]. Our objective in using the VEMP test was to determine its effectiveness in measuring the vestibular function in children and to ascertain whether the factor that causes hearing loss also damages inner ear dynamics. Regarding the pathologies relevant to the vestibular system in children, besides medical history, physical examination, audiography, and hematological evaluation, the ENG and VEMP tests also provide important information to clinicians for the differential diagnosis [29]. In the study by Yulian et al. [30] on athletes with congenital hearing loss, 75% of the patients had normal VEMP waves. In contrast, Kegel et al. [31] found a high incidence of VEMP response absence among hearing-impaired children. In our study, the VEMP response was absent unilaterally in three patients (9.09%). VEMP responses were in the normal range in the control group. The n23 latency of the affected ear in the study group was longer than that in the control group, and the difference was statistically significant. It was assumed that the vestibular anomaly or etiological factors of hearing loss caused the absence of the VEMP wave. These findings are valuable for the future evaluation of young children with vestibular symptoms.

Children with vertigo should undergo ophthalmological examinations. In the study by Haffey et al. [6] one-third of patients with unilateral hearing loss had a refractive defect. All of the patients in the study group underwent an ophthalmological examination in our study and one patient had uveitis. Four patients had a refraction defect; but this impairment was not related to vertigo (as assessed in the Department of Ophthalmology).

Although it is commonly accepted that unilateral hearing loss causes only auditory perception problems, Bess et al. [3] suggested that children with USNHL greater than 45 dB since early childhood may show retarded language development and behavioral disorders. They also remarked that 35% of the children in their study had failed at least once during their school careers, 13% needed private tutoring at their home, and 20% had behavioral disorders [19]. It is well known that such children have problems and difficulties in their academic life. Language development depends on healthy binaural hearing. Even children with asymmetric or mild hearing loss have difficulties in learning at school; therefore, their cognitive abilities are poor. Children with USNHL also have problems in sound localization, and the IQs of children with unilateral hearing loss since early childhood have been found to be lower than those of children with binaural hearing; therefore, the former group needs additional academic support [7, 9].
The school performance of 14 of the patients in our study was poor; six of these children had failed at least once during their school careers. Twelve patients remarked that their school performance was moderate, and seven children indicated they were successful at school. It is of utmost importance that these children should receive auditory rehabilitation to ensure psychosocial development and academic success. For these children, hearing aids such as contralateral routing of signals (CROS) or bone-anchored hearing aid (BAHA) can be used, or cochlear implantation can be performed.

Because sensorineural hearing loss is an irremediable pathology, early diagnosis is vital. Screening of newborns for hearing ability allows diagnosis in the early period of life. Radiological imaging, ENG, and VEMP should be a part of the routine evaluation of USNHL. Auditory and vestibular rehabilitation is the main objective of treatment to improve the social functioning and communication of affected children.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Eskişehir Osmangazi University (No: 23/19.11.2009).

**Informed Consent:** Written informed consent was obtained from patients’ parents who participated in this study.

**Peer-review:** Externally peer-reviewed.


**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**REFERENCES**

15. Tsubota M, Shojaku H, Ishimaru H, Fujisaka M, Watanabe Y. Mumps virus may damage the vestibular nerve as well as the inner ear. Acta Otolaryngol 2008; 128: 644-7. [CrossRef]