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Sensorineural Hearing Loss in Selective Immunglobulin A Deficiency

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Original Investigation

Abstract

Objective: To assess hearing functions in pediatric patients with selective immunoglobulin A (IgA) deficiency (SIGAD).

Methods: Pure-tone audiometry, acoustic impedance, otoacoustic emission, and brainstem audiometric measurements were taken during a non-infectious period in 28 patients with SIGAD and 28 healthy children with normal otoscopic examination. The results of the hearing tests were compared between the two groups.

Results: Two male patients and one female patient in the SIGAD group were found to have sensorineural hearing loss (SNHL). However, a comparison of the average pure tone cut-off values at 0.5, 1, 2, and 4 kHz did not reveal any statistically significant difference between the groups ($p>0.05$).

Conclusion: Pediatric patients with SIGAD may exhibit SNHL at certain frequencies and require follow-up for the potential development of hearing loss.

Keywords: Sensorineural hearing loss, primary immunodeficiency, pediatric, selective IgA deficiency

Introduction

Selective immunoglobulin A (IgA) deficiency (SIGAD) is defined as a serum IgA level of less than 7 mg/dl in children over 4 years of age with normal immune system. SIGAD may be partial or complete and may represent the most common form of primary immune deficiencies, with an average prevalence between 1/143 to 1/18500 per population (1). Patients with SIGAD generally have an increased risk of sinopulmonary infections, allergy, and auto-immune conditions. Arnold et al. (2), using immunohistochemical methods, confirmed the presence of IgA and IgG in the epithelial cells of the inner ear and in the lumen of the endolymphatic sac of healthy individuals. Moreover, inflammatory conditions have been found to be associated with increased IgA levels in the endolymphatic sac (3).

Several immune disorders have been shown to occur in adults with autoimmune sensorineural hearing loss (4, 5). Furthermore, patients with X-linked agammaglobulinemia (XLA) and common variable immune deficiency (CVID) have been shown to suffer from sensorineural hearing loss (SNHL) (6, 7).

Patients with SIGAD are more susceptible to recurrent infections, especially acute otitis media. Hearing loss caused by recurrent infections may frequently occur in these patients. However, there are very few studies examining the frequency of SNHL in patients with SIGAD. In this study, our objective was to assess the functions of the inner ear in patients with SIGAD.

Methods

This study was performed at Başkent University, with the support of the Research Council of the School of Medicine at Başkent University and with the approval of the local ethics committee (Project No: KA 17/02). Patients with a diagnosis of SIGAD followed up at the Immunology department were included in this study based on the following inclusion criteria:
1- Serum IgA <7 mg/dL

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2- Normal serum IgG and IgM
3- Absence of Ig prophylaxis
4- Absence of acute or chronic ear conditions
5- Normal screening test results during the newborn period
6- Absence of a family history of SNHL

Patients with a history of premature birth, low birth weight, hyperbilirubinemia, systemic conditions, ototoxic medications, or acoustic trauma were excluded. Informed consent was obtained from the parents of the patients.

Otoscopy results were found to be normal in all patients. The following tests were performed during a non-infectious period: pure-tone audiometry, acoustic impedance, otoacoustic emission, and brainstem audiometry. A bone threshold level greater than 20 dB at any frequency was considered to indicate the presence of SNHL. Cochlear and retrocochlear SNHL were differentiated, and those with retrocochlear hearing loss were excluded from the study. Alterations in hearing functions in these cases were recorded and compared with those in the healthy pediatric control group. Data analysis was performed using Statistical Package for the Social Sciences 17.0 software pack (SPSS Inc.; Chicago, IL, USA). Audiometry results were compared using the chi-square test, and all tests were performed at a significance level of 0.05.

Results

A total of 28 children with SIGAD and 28 healthy controls were included in this study. The demographic characteristics of the patients are summarized in Table 1. The groups were compared in terms of age and gender distribution.

The pure-tone audiometric examination revealed the presence of unilateral SNHL in two male patients and bilateral SNHL in one female patient (Table 2).

A comparison between the groups with regard to the average pure-tone thresholds did not reveal any significant difference at 0.5, 1, 2, and 4 kHz (Table 3).

Table 1. Demographic data of the study groups

	SIGAD	Controls
Number of subjects	28	28
Gender (M/F)	15/13	16/12
Age	5-15 (mean 7.6)	4-16 (mean, 8.1)

SIGAD: selective IgA deficiency; M: male; F: female

Table 2. Results of hearing tests among patients with selective IgA deficiency

	Bilateral SNHL	Unilateral SNHL
Number of patients with SNHL	1 (3, 57%)	2 (7, 14%)
SNHL frequency	500-1000 Hz	2000-4000 Hz 250-500 Hz
SNHL level	25 dB	25 and 30 dB

SNHL: sensorineural hearing loss; Hz: Hertz; dB: decibel

Table 3. Average hearing thresholds for the study subjects

	0,5 kHz	1 kHz	2 kHz	4 kHz
SIGAD	18 dB	21 dB	20 dB	22 dB
Controls	15 dB	19 dB	18 dB	17 dB
p>0.05				

SIGAD: selective IgA deficiency; Hz: Hertz; dB: decibel

Discussion

The increased frequency of recurrent upper respiratory tract infections as well as ear infections in patients with SIGAD has been clearly documented previously (8). Moreover, the increased levels of IgA in the epithelial cells of the inner ear and in the endolymphatic sac has been demonstrated, with inflammatory conditions. Obviously, these represent a component of the immune response. Thus, patients with SIGAD are more likely to experience weakened immune responses in the inner ear with a subsequent increase in the risk of hearing loss. In the present study, audiometric examinations were performed in patients with SIGAD. One female patient had bilateral SNHL of 25 dB at 500 and 1000 Hz, whereas one male patient had unilateral SNHL of 25 dB at 2000-4000 Hz and another male patient had unilateral SNHL of 30 dB at 250-500 Hz.

In the study by Berlucchi et al. (6) that examined a total of 25 patients with XLA using audiometry, seven patients (28%) were found to have SNHL. However, all patients with XLA included in that study had Bruton Tyrosine Kinase gene mutations, as well as a past history of meningoencephalitis in two patients, Arnold-Chiari malformation in one, and polio-myelitis in one patient. In a study by Midilli et al. (7) that involved a total of 13 patients with CVID, SNHL was found to be present at higher frequencies (>8 kHz), although they concluded that further comparative studies in larger sample populations are warranted for better elucidation of their results. In a previous study comparing patients with autoimmune SNHL and healthy adult controls, significant reductions in IgG1 and IgG3 serum levels were found. In that study, however, serum IgA levels were also compared and no significant differences were observed (4).

In adult patients with SNHL, autoimmune processes have been implicated in the etiology of this condition. However, autoimmune processes are extremely complex, with no clear-cut results from efforts to develop reasonable models (9). IgA plays a role in the integration of systemic and mucosal immune responses, and its deficiency is associated with an increased frequency of several autoimmunological conditions, including hemolytic anemia, thrombocytopenic purpura, and juvenile rheumatoid arthritis (8). Moreover, weakened IgA responses may represent a part of the immune reactions that occur during the process leading to the development of hearing loss. A majority of pediatric SNHL cases are congenital, which

may be readily detected using screening methods during the newborn period (10). In our study, patients with congenital SNHL were excluded based on the results of otoacoustic emission tests performed during the newborn period. Other causes of SNHL include the use of ototoxic medications and acoustic trauma, which lead to SNHL at higher frequencies (>4 kHz) (11). No patients in our study were found to have hearing loss above the frequency of 4 kHz as confirmed using otoacoustic emission and brainstem audiometric tests.

Selective IgA deficiency is associated with recurrent boots of upper respiratory tract and ear infections. Repetitive courses of upper respiratory tract infections due to viruses and ear infections may result in the development of hearing loss. In the present study, three patients were found to have SNHL at limited frequencies. A major limitation of our study, similar to other conditions of the inner ear, was our inability to perform a comparison between our findings and histopathological characteristics of the inner ear, with a consequent absence of information on the histopathological aspects of the condition. Several electrophysiological measurements were taken to compensate for this lack of histopathological findings. Other limitations include the small sample size and the cross-sectional nature of the study. Such factors might have decreased the statistical significance of our results. Further studies involving larger patient populations and longer follow-up periods may better delineate the effect of SIGAD on inner ear functions.

Conclusion

Pediatric patients with SIGAD may experience SNHL at certain frequencies. An association between these two conditions may be better defined with the involvement of higher number of patients with recurrent middle-ear infections followed up for longer durations. Moreover, examination of the development of autoimmune SNHL in pediatric patients with SIGAD may shed further light on the pathogenesis of this condition.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Başkent University (Project No: KA 17/02).

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