HEARING LOSS IN TURNER SYNDROME

Noriko Morimoto, MD, PhD, Toshiaki Tanaka, MD, PhD, Hidenobu Taiji, MD, PhD, Reiko Horikawa, MD, PhD, Yasuhiro Naiki, MD, PhD, Yuji Morimoto, MD, PhD, and Nobuko Kawashiro, MD, PhD

Objective To address the characteristics of hearing loss in patients with Turner syndrome (TS), we evaluated hearing levels of patients with TS and analyzed causative factors.

Study design Thirty-three patients with TS (8 to 40 years of age) were studied through the use of audiological measurements, and causative factors were explored.

Results Twenty cases (35 of 66 ears tested) showed high-frequency (8 kHz) sensory neural hearing loss (HFQ-SNHL). Fifteen cases (26 ears) and 15 cases (24 ears) of the impaired 20 cases were unresponsive to distortion-product otoacoustic emissions and transient-evoked otoacoustic emissions, respectively. HFQ-SNHL showed little relation to the history of middle ear infection and puberty, although middle ear infections were seen in 11 of the 20 cases. The hearing thresholds at high frequencies were correlated with age and body height ($P < .001$). The age-dependent increase in hearing thresholds in the high frequencies was more apparent in patients with TS with monosomic 45,X than in those with the mosaic type ($P < .05$).

Conclusions More than 60% of patients with TS had HFQ-SNHL. Because the increase in hearing threshold at high frequencies was shown to depend on karyotype and aging, regular otological examination is important for the determination of proper treatment. *(J Pediatr 2006;149:697-701)*

About 50% of patients with Turner syndrome (TS) have mild hearing loss: ~60% for sensory neural hearing loss (SNHL), ~25% for conductive hearing loss (CHL), and ~15% for mixed hearing loss, calculated from the previous studies shown in Table I (available at www.jpeds.com).[1,3-15] However, the causes of sensory neural hearing loss in patients with TS remain controversial. The reason for CHL in patients with TS is recurrent otitis media with effusion, chronic middle ear infection, and cholesteatoma in the middle ear, probably as the result of malfunction of the Eustachian tube associated with lymph edema[5] and anatomic shortening of the skull base. Apart from inflammation of the middle ear, recent research showed that hearing loss, middle ear infections, and malformations of the external ear in TS are related to the degree of deletion of the p-arm (short arm of the X chromosome)[1]; otological problems increase not only with an increase of deletion but also with decreases in body height and serum levels of Insulin-like Growth Factor-1.[2,9] In addition, the type of hearing loss is also likely to depend on the karyotype. Progressive SNHL is, for example, mostly found in patients with monosomic 45,X.[4] Another possible cause of SNHL is hormonal. Kim et al[16] elucidated the decreased incidence of SNHL with increased serum estradiol levels, which suggests an association between SNHL and estrogen in TS.

In addition to the underlying cause, the precise clinical features of hearing loss in TS also remain unclear. Some studies have shown that a profound dip in the 1 to 2 kHz region occurs in audiograms recorded from patients with TS with hearing loss.[4,6,8] On the other hand, Gungor et al[10] showed that SNHL in patients with TS is limited to the higher frequency region of 4 to 8 kHz rather than the middle frequency region of 1 to 2 kHz. Although women 40 years of age with TS have the same hearing capacity as women 60 years of age in the normal population,[4] it is not known if the mechanism behind this high-frequency hearing loss differs from that of presbycusis in general. Thus, further analysis is needed to clarify the precise clinical features and causative factors of hearing loss in TS.

The aim of this study was to determine the characteristics of hearing loss in TS.

CHL	Conductive hearing loss	SPL	Sound pressure level
DPOAE	Distortion-product otoacoustic emissions	TEOAE	Transient-evoked otoacoustic emissions
SNHL	Sensory neural hearing loss	TS	Turner syndrome

From the Departments of Otolaryngology and Endocrinology, National Center for Child Health and Development, Tokyo, Japan; and the Department of Medical Engineering, National Defense Medical College, Saitama, Japan.

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Reprint requests: Dr Noriko Morimoto, Department of Otolaryngology, National Center for Child Health and Development, 2-10-1, Okura, Setagaya, Tokyo 157-8535, Japan. E-mail: morimoto-n@ncchd.go.jp.

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Furthermore, to elucidate the causes of hearing loss, we also analyzed the relation between hearing loss and possible causative factors.

METHODS

Thirty-three female patients with TS, ages 8 to 40 years old, who were referred to the ENT clinic, participated in the study. All were diagnosed by chromosomal analysis, and all provided written informed consent before participating in the study, in accordance with the ethics committee of the National Center for Child Health and Development. Fifteen of the 33 patients (45%) had the classic monosomic 45,X, and the remaining 18 patients (55%) had the mosaic karyotype (Table II; available at www.jpeds.com). In addition to general medical history, information on otological states, including the onsets of previous and current ear problems and history of otological surgery, were taken. Each patient was also interviewed to determine their age at puberty onset and history of menstruation. Physical examinations to evaluate their hearing states were carried out as follows.

Pure-Tone Audiometry

Hearing thresholds for air and bone conduction were determined by a standard measurement technique in a sound-proof room. The test frequencies were 0.125, 0.25, 0.5, 1, 2, 4, and 8 kHz for air conduction and 0.25, 0.5, 1, 2, and 4 kHz for bone conduction. Hearing loss was assessed according to the criteria of the Genetic Deafness (GENDEAF) study group.[17]

Tympanometry

The compliance of the tympanic membrane was bilaterally measured by an electroacoustic impedance method. The tympanometric curve was classified into Jerger's classification system of A, As, Ad, B, and C types. Two ears with a history of tympanoplasty and one ear with a ventilation tube were excluded from this examination.

Otoacoustic Emission Test

Distortion-product otoacoustic emissions (DPOAEs) and transient-evoked otoacoustic emissions (TEOAEs) were measured by using an OAE instrument (ILO292, Otodynamic System, Herts, United Kingdom) in a sound-proof room. DPOAEs were measured with a setting of 70/70 dB sound pressure level (SPL) L1/L2 at 9 discrete frequencies that were randomly selected from 1 to 6 kHz. Each f2/f1 ratio at 9 discrete frequencies was adjusted at 1.22. A response with amplitude of ≥3 dB above the noise level at all the frequencies of 2, 3, and 4 kHz was defined as a present DPOAE.[18] TEOAEs were obtained from an average of 260 responses using nonlinear click stimulation with an intensity of 77 dB SPL. Otoacoustic emissions with an intensity of more than 5 dB SPL and with reproducibility of better than 50% were considered to represent a TEOAE response.[18]

Statistical Analysis

Examination of the relation between subjects' scores on two categorical variables (eg, SNHL and history of middle ear infection) was determined by the cross-tab procedure with the χ^2 test. Multiple linear regression was used to assess the influence of age, karyotype, and body height on the hearing threshold.[1] These statistical analyses were performed with the use of SPSS-11.5 software (SPSS Japan, Tokyo, Japan) on data per ear unless otherwise specified. A level of $P < .05$ was considered to indicate statistical significance.

RESULTS

Pure-tone audiometry revealed that mild hearing loss with a decrease of 21 to 40 dB in the mean hearing level (the average of the four hearing thresholds at 0.5, 1, 2, and 4 kHz) occurred in 17 of 33 cases (29 ears). Moderate (41 to 70 dB) and severe (71 to 95 dB) hearing loss occurred in 3 of 33 cases (4 ears) and 1 of 33 cases (1 ear), respectively (Figure 1, A). In the 21 cases (34 ears) of hearing loss, 17 cases (26 ears) were diagnosed as SNHL and 7 cases (8 ears) were diagnosed as CHL, which was defined as an average air-bone gap of ≥15 dB in the mean hearing level at frequencies of 0.5, 1, 2, and 4 kHz. In the 7 cases (8 ears) of CHL, one case (1 ear) had moderate hearing loss. Focusing on the hearing level at a high frequency of 8 kHz, 8 cases (15 ears), 11 cases (19 ears), and 1 case (1 ear) showed mild, moderate, and severe hearing loss, respectively, indicating that a total of 20 cases (35 ears) were considered high-frequency SNHL (Figure 1b). When a hearing dip was defined as being at least 15 dB greater in a frequency (or serial frequencies) than in both the lower and higher frequencies,[19,20] 1 case (2 ears) showed the hearing dip in the mid frequency region of 1 to 2 kHz.

Tympanic function analysis by electroacoustic impedance examination revealed that 30, 7, 2, and 2 cases (49, 10, 2, and 2 ears) were classified as type A (normal middle ear compliance), As (abnormally stiff with middle ear static compliance less than 0.28 cc of equivalent volume), Ad (excessive flaccid with static compliance more than 2.5 cc of equivalent volume), and C (near-normal compliance, usually reflects poor Eustachian tube function), respectively. No ear showed type B. In the 7 cases with As type, 2, 2, and 1 case showed low-frequency SNHL, horizon-type SNHL, and high-frequency SNHL, respectively, whereas the 2 cases with Ad type included CHL (1 case) and low-frequency SNHL (1 case).

Otoacoustic Emission Test

TEOAEs and DPOAEs were absent in 16 (28 ears) and 20 cases (31 ears), respectively. Fifteen of the 20 cases with SNHL at the frequency of 8 kHz and all 7 cases with CHL did not show DPOAEs (26 of 35 ears with high-frequency SNHL and 8 of 8 ears with CHL). Fifteen of the 20 cases with SNHL at the frequency of 8 kHz and 5 of the 7 cases with CHL did not show TEOAEs (24 of 35 ears with high-frequency SNHL and 6 of 8 ears with CHL).

Table III (available at www.jpeds.com) summarizes the history of middle ear–related problems of the participants.