Hearing loss in Takayasu's arteritis

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Abstract

Objective

Neurosensory hearing loss is well-documented in chronic autoimmune conditions such as systemic lupus erythematosus (SLE). However, the literature lacks data on the prevalence and characteristics of hearing impairment in Takayasu's arteritis (TAK). In this cross-sectional study, our principal objective was to systematically assess the auditory function of individuals diagnosed with TAK, against SLE patients and healthy controls (HC).

Method

Age and gender matched TAK and SLE patients followed up in a tertiary centre along with healthy controls were included in a two-phase study. In the first phase, a questionnaire on ENT symptoms was administered to the patient (TAK: n=104 and SLE: n= 151) and HC (n=174) groups. In the second phase, patients (TAK: n=53 and SLE: n=33) and HC (n=45) underwent audiometric tests.

Results

The questionnaire survey revealed that both TAK and SLE patients reported hearing loss (27.9%, 25.8%, 7.4%, p<0.001), tinnitus (49%, 35.8%, 13.8%, p<0.001) and vertigo (46.2%, 33.8%, 16.7%, p<0.001) at significantly higher rates than HC. Audiometry results indicated that both TAK (30.2%) and SLE patients (18.2%) had increased hearing loss compared to HC (8.9%), however, only TAK patients were found to have significantly increased risk in age adjusted logistic regression analysis (OR= 3.915, 95%CI: 1.179-12.998, p=0.026). Hearing loss was mainly neurosensory in all groups. TAK patients were affected at both low (<6000 Hz) and high (>6000 Hz) frequencies, whereas SLE patients were affected only at high frequencies. Hearing loss was significantly associated only with older age. No association was observed with the anatomical location of vascular involvement or history of stroke.

Conclusion

Our study reveals an increased prevalence of hearing loss in TAK. Further research is crucial to uncover the underlying causes.

Key words

Takayasu's arteritis, systemic lupus erythematosus, vasculitis, audiometric tests, hearing loss

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Introduction

Takayasu's arteritis (TAK) is a large vessel vasculitis characterised by granulomatous inflammation of the vessel wall. Its aetiology has not yet been fully clarified. The disease is frequently observed in young women aged 20–40 years (1, 2). Clinical course and prognosis may show geographical differences (3, 4). Although it is more frequent in Far Eastern countries, the annual incidence of TAK in Northern Europe and America has been reported to be 1–3 per million (5, 6). TAK primarily involves the arch and the major branches of the aorta (7). Partial or complete involvement of the thoracic and abdominal aorta is usually accompanied by the involvement of the proximal and middle subclavian arteries, carotids, brachiocephalic and vertebral arteries to varying degrees.

Vascular involvement may cause pain in the arms or legs and occasionally result in more severe manifestations like claudication. Patients with involved carotid and vertebral arteries may present with stroke, visual loss, or clinical manifestations associated with transient ischaemic stroke (TIA) such as syncope, dizziness or headache (8).

Increased frequency of hearing loss has been reported in autoimmune diseases including systemic lupus erythematosus (SLE), rheumatoid arthritis and various other inflammatory disorders including small vessel vasculitis (9-13). We had observed patients presenting with acute or chronic hearing loss, of specifically sensorineural type, among patients with TAK, however to the best of our knowledge there were no data in the literature supporting our observations. Therefore, we aimed to look formally at the frequency of hearing loss in TAK, compared with SLE and apparently healthy controls.

Materials and method

Patients and controls

The cross-sectional study was conducted between June 2017 and December 2019 at the Cerrahpaşa Medical Faculty, I.U.-C at Istanbul, Turkey. We studied age and gender matched patients with TAK and SLE who were seen consecutively at the department of rheumatology at the Cerrahpaşa Medical Faculty, I.U.-C at Istanbul, Turkey. TAK and SLE patients fulfilled the respective classification criteria for diagnosis (14, 15). Additionally, age and gender matched hospital staff who did not report any chronic inflammatory disease participated in the study as healthy controls (HC). Patients and healthy volunteers were all aged ≥18 years.

Study design

This study was designed to have two parts. We first tested our hypothesis with a questionnaire survey which collected information on demographic/sociocultural characteristics, comorbidities, history of hearing loss, hearing loss-related symptoms (tinnitus, etc.), accompanying symptoms/findings (episodic vertigo, acoustic trauma, otitis, ear discharge, surgical interventions, etc.) and currently used medications (Supplementary Table S1). The results of the survey confirmed our presumptions then we decided to proceed with audiometric tests which were offered similarly to age and gender matched patient and controls seen at the out-patient clinic. However, this time we examined a smaller number of patients and controls.

Otolaryngologic examination and audiometric tests

Patients and volunteers were then referred to an ear-nose and throat (ENT) specialist for otolaryngologic examination and those with intact tympanic membranes and no additional ear pathologies such as infection/inflammation underwent audiologic evaluation including tympanometry, acoustic reflex measurements, pure-tone audiometry, speech audiometry and high frequency audiometry.

Tympanometry and acoustic reflex assessments were done by using GSI Tympstar Middle Ear Analyzer V2 (Grason-Stadler Inc. Tiger/USA), tympanometry analysis of the study and the control groups were performed in the range of 100 daPa ±50 daPa with 226 Hz probe tone and 85 dB SPL stimulus. Acoustic reflex measurement was initiated in individuals with type A tympanograms for standardisation. Acoustic reflex measurement was performed at

frequencies of 5001000-2000-4000 Hz (ipsilateral and contralateral).

Pure tone and high frequency audiometry tests were performed in a soundproof booth (in accordance with ANSI S3.1-1991 standards) using a GSI AudioStar two-channel audiometer Pro (Grason-Stadler Inc. Tiger/USA). In pure tone audiometry, frequencies between 125 Hz and 8000 Hz were evaluated using Eartone Gold 3A (Etymotic Research, Inc. 61 Martin Lane Elk Grove Village, IL 60007) insert earphones for air hearing threshold assessment, and frequencies between 500 Hz and 4000 Hz were evaluated using Radioear B 71 (Audiometer Allé 1 5500 Middelfart Denmark) bone vibrator for bone conduction hearing threshold assessment. High frequency hearing thresholds were measured with Sennheiser HDA-200 (Sennheiser Audio Labs GmbH Klettgaustr. 21 79761 Waldshut-Tiengen Germany) headphones at frequencies between 9 and 16 kHz.

GSI AudioStar Pro (Grason-Stadler Inc. Tiger/USA) two-channel audiometer was used for the speech audiometry and the tests were performed in a soundproof booth (in accordance with ANSI S3.1-1991 standards). Following the pure tone audiometry analysis, the pure tone threshold mean values (arithmetic mean of frequencies between 500 Hz-2000 Hz) were calculated and speech audiometry tests were performed. First, the Speech Recognition Threshold (SRT-Speech Recognition Threshold) was determined with the Turkish Phonetically Balanced Three Syllable Word List. Then, the Speech Discrimination Score (SDS-Speech Discrimination Score) was calculated using the Turkish Phonetically Balanced One-Syllable Word List at the sound level that the individuals were comfortable with.

Statistical analysis

Normally distributed continuous values were expressed as mean ± SD and non-normally distributed continuous values were expressed as median [IQR]. Chi-square or Fisher exact test was used for comparison of categorical values. For normally distributed continuous values, one-way ANOVA (for comparisons of more than two groups) or Student's t-test (for pairwise group comparisons) was used. Post-hoc Tukey test was used in the calculation of one-way ANOVA. Mann-Whitney U-test (pairwise comparison) and Kruskal-Wallis test (multiple comparison) (Bonferroni correction) were used for the comparison of continuous values that did not show normal distribution. The odds ratios and 95% confidence intervals (CIs) for hearing loss were calculated by binary logistic regression models. Healthy controls were accepted as the reference group. Logistic regression analysis was done first with no adjustment, then repeated after adjustment for age which was the only significantly associated variable with hearing loss besides being diagnosed with TAK. A p-value of <0.05 was accepted as statistically significant. Statistical analysis was done using SPSS 18.0 (SPSS inc, USA).

Ethical statement

The study was approved by local ethical committee for clinical studies at Cerrahpaşa Medical Faculty, Istanbul University-Cerrahpaşa (258886/2017). Oral informed consent was obtained from each enrolled participant before the otolaryngologic examination and audiometric tests. All study procedures were carried out in accordance with the ethical standards of the Helsinki Declaration.

Table I. Demographics and clinical characteristics of patients and controls included in the questionnaire survey.

	TAK (n=104)	SLE (n=151)	HC (n=174)	*p*
Female /Male, n	97/7	147/4	159/15	0.075
Age, years (mean ± SD)	43.8 ± 11.2	44.6 ± 11.9	42.2 ± 9.0	0.119
Disease duration, years (mean ± SD)	11.3 ± 8.0	12.9 ± 8.0	-	0.127
Co-morbidities				
Hypertension, n (%)	68 (65.4)	70 (46.4)	15 (8.6)	<0.001*¶§
Diabetes mellitus, n (%)	14 (13.5)	12 (7.9)	12 (6.9)	0.156
Immunosuppressive treatment				
Non-biologics, n (%)	59 (56.7)	67 (44.4)	-	0.057
Biologics, n (%)	48 (46.2)	12 (7.9)	-	<0.001
Corticosteroids, n (%)	59 (56.7)	88 (58.3)	-	
Hydroxychloroquine, n (%)	0	120 (79.5)	-	NA
Hearing loss, n (%)	29 (27.9)	40 (26.5)	13 (7.4)	<0.001*¶
Tinnitus, n (%)	51 (49.0)	54 (35.8)	24 (13.8)	<0.001*¶§
Vertigo, n (%)	48 (46.2)	51 (33.8)	29 (16.7)	<0.001*¶§
Trauma or surgical intervention, n (%)	5 (4.8)	3 (2.0)	0	0.028 **§

*TAK *vs*. HC $p<0.001$; **TAK *vs*. HC $p<0.05$; ¶SLE *vs*. HC $p<0.001$; §TAK *vs*. SLE $p < 0.05$.
NA: not applicable.

Results

Questionnaire survey

A total of 104 (97F/7M) patients with TAK, 151 (147F/4M) patients with SLE and 174 (159F/15M) healthy volunteers were included in the questionnaire survey.

Subclavian arteries (n=89, 85.6%), common carotid arteries (n=78, 75%) and aorta (total: n=57, 54.8%; thoracic aorta: n=33, 31.7%, abdominal aorta: n=45, 43.3%) were the most frequent sites of vascular involvement in 104 TAK patients. Among the 151 SLE patients 42 (27.8%) had renal involvement and 14 (9.3%) had antiphospholipid syndrome. Demographic and clinical characteristics of the patients and controls are shown in Table I.

Study and control groups were comparable in terms of age and gender distribution (Table I). The disease duration for TAK and SLE patients was similar. Compared to healthy controls, the prevalence of hypertension was significantly higher in the TAK and SLE groups, while the prevalence of diabetes mellitus was similar. TAK patients used significantly more frequently immunosuppressive therapy (both biologic and non-biologic agents) than SLE patients. Corticosteroid use was similar in both groups.

Both TAK and SLE patients reported having hearing loss, tinnitus or vertigo at significantly higher rates than healthy

subjects. Percentage of subjects reporting hearing loss was similar in both disease groups, whereas cases reporting tinnitus and vertigo were more common in TAK group. Similarly, patients with a history of ENT-related surgery or perforation of the tympanic membrane were more prevalent in the TAK group.

In the study and control groups it was noteworthy that those who reported having hearing loss, tinnitus or vertigo were older than those who did not. However, there was no correlation between hearing associated findings and the duration of disease. Furthermore, neither comorbidities nor being on immunosuppressive treatment has been found to be associated with hearing loss, tinnitus or vertigo.

Audiometric tests

A total of 139 subjects underwent audiometric tests. Three patients with TAK, two with SLE and three HC were excluded from the analysis due to a history of acoustic trauma, ear infection or absence of acoustic reflex following the ENT evaluation done prior to the audiometry. Thus, audiometric tests were analysed in 53 (45F/8M) patients with TAK, 33 (30F/3M) patients with SLE and 45 (35F/10M) healthy controls. Table II shows the demographic data and audiometry results of the patients and controls studied in the second part.

Subclavian arteries (n=35, 66.0%), common carotid arteries (n=28, 52.8%) and aorta (n=21, 39.6%) were the most frequent sites of vascular involvement in 53 TAK patients included in the second part of study, followed by axillary (n=9, 17.0%), vertebral (n=8, 15.1%), renal (n=8, 15.1%) and internal carotid arteries (n=7, 13.2%). Coronary, pulmonary and mesenteric, and lower extremity arteries were other less frequently involved sites. A total of 5 (9.4%) patients (all female) had a history of stroke (n=4) or TIA (n=1). Among the 33 patients with SLE, 23 (69.7%) had arthritis, and 4 (12.1%) had antiphospholipid syndrome. Haematological, renal and cardiac involvement were seen in 10 (30.3%), 8 (24.2%) and 5 (15.2%) patients, respectively. None of the patients with SLE had a history of stroke. Other demographic and clinical characteristics of the subjects are demonstrated in Table II.

Table II. Demographics and clinical characteristics of patients and controls evaluated with audiometric tests.

	TAK (n=53)	SLE (n=33)	HC (n=45)	*p*
Female /Male, n	45/8	30/3	35/10	0.287
Age, years (mean ± SD)	41.6 ± 10.0	42.5 ± 10.2	38.5 ± 9.5	0.159
Disease duration, years (mean ± SD)	10.9 ± 7.9	9.5 ± 5.6	-	0.358
Co-morbidities				
Hypertension, n (%)	26 (49.1%)	13 (39.4)	3 (6.7)	<0.00*¶
Diabetes mellitus, n (%)	3 (5.7)	3 (9.1)	2 (4.4)	0.688
Immunosuppressive treatment				
Non-biologics, n (%)	41 (77.4)	17 (51.5)	-	0.012
Biologics, n (%)	25 (47.2)	5 (15.2)	-	0.002
Corticosteroids, n (%)	32 (60.4)	19 (57.6)	-	0.797
Hydroxychloroquine, n (%)	0	25 (75.8)	-	NA
Hearing loss, n (%)	16 (30.2)	6 (18.2)	4 (8.9)	0.030*¶§
Sensorineural type, n (%)	11 (68.8)	4 (66.6)	2 (50.0)	0.087
Mixed type, n (%)	0	1 (16.7)	0	
Conduction type, n (%)	5 (31.2)	1 (16.7)	2 (50).0	

*TAK *vs*. HC: $p<0.001$; ¶: SLE *vs*. HC: $p<0.001$; §TAK *vs*. SLE: $p<0.05$.
NA: not applicable.

Table III. Results of the pure tone audiometry (means of 500-1000-2000 Hz).

	TAK (n=53)	SLE (n=33)	HC (n=45)	*p*
Bone conduction - right ear (dB)	9.13 ± 12.7	7.5 ± 16.3	4.7 ± 4.3	0.182*
Bone conduction - left ear (dB)	10.1 ± 13.6	6.3 ± 7.7	5.0 ± 4.3	0.030§*
Air conduction - right ear (dB)	15.8 ± 16.7	12.4 ± 23.3	8.9 ± 6.6	0.114*
Air conduction - left ear (dB)	17.4 ± 18.2	9.5 ± 8.2	8.4 ± 6.5	0.001*

*TAK *vs*. HC: $p<0.05$; §TAK *vs*. SLE: $p<0.05$; ¶SLE *vs*. HC: $p<0.05$.
Hz: Hertz.

Both TAK (30.2%) and SLE patients (18.2%) showed higher rates for hearing loss compared to healthy subjects (8.9%) ($p=0.030$) (Table II). TAK patients had the highest frequency and when compared to HC, only TAK patients were found to be associated with an increased risk for hearing loss in age adjusted logistic regression analysis (OR=3.915, 95%CI: 1.179–12.998, $p=0.026$).

Results of the audiometric analysis are summarised in Tables III and IV. Pure tone audiometry showed that patients with TAK significantly required higher decibel levels than healthy controls, consistent with bilateral hearing loss (Table III). No significant difference was found between SLE patients and healthy controls in pure tone analysis.

TAK patients had considerable hearing loss at both low (<6000 Hz) and high (>6000 Hz) frequencies compared to healthy controls, while this was true only for high frequencies (>6000 Hz) in SLE patients (Table IV).

Bone conduction hearing thresholds in pure tone audiometry are shown in Table IV. Patients with TAK significantly differed from healthy controls in terms of bone conduction hearing, especially more pronounced at increased frequencies in both ears. In this regard, no difference was observed between SLE patients and healthy subjects. In TAK patients 68.8% of hearing loss was neurosensory, while the rest was conductive. In SLE similarly, sensorineural type hearing loss was the most common type (66.6%), while the rest was mixed (16.7%) and conductive (16.7%). Among HC, of the 4 individuals with hearing loss, 2 had sensorineural type and the remaining had conduction type.

Associated factors with hearing loss in TAK

Among TAK patients, those who were identified with hearing deficit were significantly older than those who were

Table IV. Hearing threshold levels (dB) at various frequencies.

	Takayasu arteritis (n=53)	Systemic lupus erythematosus (n=33)	Healthy volunteers (n=45)	*p*
		(Air conduction, left ear)		
125 Hz	16.7 ± 12.0	16.1 ± 13.0	11.4 ± 8.0	0.046*¶
250 Hz	15.8 ± 13.6	14.4 ± 13.2	11.7 ± 8.1	0.234
500 Hz	16.1 ± 17.5	11.1 ± 11.2	9.8 ± 7.5	0.049*
1000 Hz	16.9 ± 19.8	9.2 ± 10.3	8.4 ± 6.9	0.007§*
2000 Hz	16. 9 ± 14.6	9.9 ± 8.1	7.2 ± 7.2	<0.001§*
4000 Hz	18.2 ± 16.6	10.5 ± 9.6	9.1 ± 7.8	0.001§*
6000 Hz	24.5 ± 18.2	20.8 ± 10.1	13.6 ± 9.6	0.001*¶
8000 Hz	20.5 ± 20.5	15.6 ± 17.0	10.9 ± 11.2	0.024*
9000 Hz	26.3 ± 22.3	28.0 ± 17.4	13.9 ± 13.6	0.001*¶
10 kHz	26.6 ± 22.9	30.5 ± 19.0	17.8 ± 17.6	0.019*¶
11.2 kHz	31.9 ± 23.9	39.1 ± 23.2	20.5 ± 18.2	0.001*¶
12.5 kHz	37.3 ± 26.2	41.0 ± 23.8	24.7 ± 19.7	0.006*¶
14 kHz	35.0 ± 23.6	42.6 ± 19.6	25.9 ± 22.6	0.008¶
16 kHz	34.3 ± 18.9	44.6 ± 13.6	27.4 ± 21.4	0.002§¶
		(Air conduction, right ear)		
125 Hz	17.0 ± 8.9	13.8 ± 10.7	14.7 ± 10.0	0.269
250 Hz	15.8 ± 10.1	13.0 ± 11.0	13.0 ± 8.8	0.292
500 Hz	14.4 ± 14.8	9.6 ± 12.7	10.8 ± 8.6	0.166
1000 Hz	16.7 ± 17.7	9.6 ± 14.9	9.2 ± 7.8	0.016§*
2000 Hz	16.6 ± 19.5	8.9 ± 15.2	7.4 ± 6.3	0.006§*
4000 Hz	19.4 ± 19.5	8.0 ± 12.1	9.9 ± 8.3	0.001§*
6000 Hz	25.3 ± 22.5	17.6 ± 11.6	13.0 ± 8.8	0.001*¶
8000 Hz	21.9 ± 24.4	12.1 ± 14.4	11.5 ± 12.5	0.011§*
9000 Hz	25.4 ± 18.8	23.6 ± 15.0	14.6 ± 13.2	0.004*¶
10 kHz	29.8 ± 21.1	27.7 ± 16.3	15.8 ± 14.1	<0.001*¶
11.2 kHz	34.9 ± 23.9	37.6 ± 23.1	19.0 ± 15.5	<0.001*¶
12.5 kHz	42.0 ± 28.2	40.6 ± 24.8	20.7 ± 18.2	<0.001*¶
14 kHz	38.7 ± 24.6	37.0 ± 20.1	22.3 ± 21.4	0.002*¶
16 kHz	39.4 ± 16.7	44.8 ± 11.8	26.5 ± 23.1	<0.001*¶
		(Bone conduction)		
500 Hz (Left ear)	9.0 ± 10.6	5.9 ± 7.5	6.6 ± 5.9	0.181
1 kHz (Left ear)	8.5 ± 12.2	5.9 ± 8.6	4.6 ± 4.9	0.108*
2 kHz (Left ear)	12.2 ± 15.4	5.2 ± 7.6	4.6 ± 5.5	0.001§*
4 kHz (Left ear)	11.3 ± 12.4	7.6 ± 9.0	5.8 ± 6.1	0.021*
500 Hz (Right ear)	8.6 ± 9.5	6.2 ± 11.5	7.1 ± 7.8	0.490
1 kHz (Right ear)	8.2 ± 12.3	5.9 ± 12.6	4.8 ± 4.9	0.274
2 kHz (Right ear)	11.1 ± 15.4	5.8 ± 13.1	4.1 ± 4.6	0.014*
4 kHz (Right ear)	11.0 ± 12.5	6.1 ± 11.2	5.5 ± 5.9	0.020*

*TAK *vs*. healthy controls: $p<0.05$; §TAK *vs*. SLE: $p<0.05$; ¶SLE *vs*. healthy controls: $p<0.05$.
Hz: Hertz; kHz: kilohertz.

not (mean age: 47.4±8.2 *vs*. 39.2±10.2 years, respectively, $p=0.006$). On the other hand, disease duration was not found to be different (12.6±9.3 *vs*. 10.6±7.4 years, respectively, $p=0.402$). No correlation was observed between hearing loss and anatomical localisation of vascular involvement or history of stroke or TIA.

Discussion

This study is the first to investigate the association of hearing loss/impairment in TAK. Our results indicate that hearing loss is significantly prevalent in patients with TAK in comparison to age and gender matched healthy subjects when surveyed via a questionnaire and after audiometric testing (27.9% and 30.2%, respectively). Similar rates were also found in patients with SLE (25.8% and 18.2%, respectively). However, audiometric tests indicated that only TAK patients were found to have significantly higher risk when compared to HC. Patients with hearing loss in both disease groups were older than those who had no hearing problems. No correlation could be demonstrated between hearing loss and the duration of the disease. Results of the audiometric analysis revealed that patients with TAK and SLE are differently affected. Hearing in TAK patients was impaired both in pure tone analysis and at high frequencies, while in SLE patients it was affected only at high frequencies. Interestingly, in patients with TAK we could not identify any association of impaired hearing with the anatomical location of vascular involvement.

The majority of data concerning hearing loss in rheumatological disorders are derived from studies conducted in individuals with SLE. In SLE patients, the prevalence of symptomatic and/or laboratory-detected hearing-related findings varies widely, ranging from 8 to 70% at different levels (16-20). The fact that the frequency of hearing loss has been reported in such a wide range suggests the presence of multiple underlying mechanisms. SLE may also involve the inner ear (16-21). Autoantibody-mediated attack against antigenic structures in the inner ear, cellular cytotoxicity against cochlear and vestibular hair cells, and microvascular immune complex deposition have all been suggested to underlie the pathophysiology of impaired hearing in SLE (9).

In a meta-analysis, Di Stadio and Ralli reported polymorphous cell infiltration (31%), vasculitis (27%), fibro-osseous reaction (21%), new bone formation (17%) and granulation tissue (4%) in temporal bone samples of 52 lupus patients. In the same study, most common pathological findings observed in cochlear structures were hair cell death, stria vascularis atrophy and spiral ganglion degeneration, while hair cell loss was the most prevalent feature in vestibular structures (9). Vasculitis associated immune-complex (IC) deposition in temporal bone and IC induced apoptosis have been accused of underlying the death of cochlear/vestibular hair cells and spiral ganglion cells in lupus patients.

The sudden hearing loss reported in patients with lupus is thought to be caused by a vasculitis associated sudden decrease in blood flow to the inner ear. Indirect evidence for this is the complete or near-complete reversal of hearing loss with regressing vasculitis after treatment. Recurrent vasculitis at-

tacks might lead to chronic impaired oxygenation, and consequently, to fibrosis in the related tissues resulting in permanent hearing loss (10, 22, 23). Some studies suggested increased atherosclerosis as the underlying cause of the hearing loss in SLE (24-26).

Consistent with the findings in the literature most of the SLE patients in our study suffered from sensorineural hearing loss (SNHL). Furthermore, our results with SLE patients were in support of the data which suggests that SNHL was not associated with either disease activity, or the duration of the disease (21, 27).

Audiovestibular dysfunction has been reported in patients with giant cell arteritis (GCA), a primary systemic vasculitis, similar to TAK, involves medium- and large-sized arteries. Almost 90% of patients with GCA were found to have vestibular dysfunction, which was usually reversible and resolved after several days of glucocorticoid treatment. Patients with persistent vestibular dysfunction were reported more likely to exhibit persistent head-shaking nystagmus (28). Recent case reports, studies based on patient reported surveys and retrospective data analysis suggest that 25–35% of patients with GCA have concurrent hearing loss (29-32)

Furthermore, patients with GCA presented more frequently with benign paroxysmal positional vertigo than did the controls. Ischaemic complications associated with the vasculitis have been accused (33). In our TAK study cohort vertigo was reported by almost half of the patients. Neurosensory hearing loss usually improves following steroid administration. Post-steroid recovery of hearing loss has been reported to occur in 56% of patients, however, improvement of vertiginous symptoms was not as striking as it was with hearing loss (29). Early administration of glucocorticoids is an important component of the treatment outcome. Delayed institution of glucocorticoid treatment has been associated with persistent neurosensory hearing loss (31).

The existing literature lacks solid information on the pathophysiology of hearing loss in patients with TAK. In contrast to SLE, TAK could not be considered as an autoimmune disorder, thus mechanism of disease leading to impaired hearing is expected to be different in TAK. Several theories have been postulated regarding the mechanism of deafness in GCA, including vascular occlusion, immune-mediated damage and viral infections, all of which leading to inflammation and damage of the posterior or terminal cochleovestibular circulation (34). In an earlier report, however, anti-endothelial cell antibodies could not be identified in biopsy-proven giant cell arteritis patients (35)

We speculate that the increased rates of hearing loss observed in patients with TAK should largely be associated with ischaemia induced pathologies in a vasculitis setting. The arterial circulation of the inner ear is supplied by the arteria labyrinth which originates from the vertebral arteries. Vertebral arteries, in turn, branch off from the proximal part of the subclavian arteries. It is well recognised that in almost 80% of patients with TAK the subclavian arteries are involved at varying degrees ranging from mild stenosis to total occlusion. In this setting, it is essential to consider that TAK is strongly linked to premature atherosclerosis, which may impact the arterial supply to the inner ear, alongside the effects of vasculitis. This intricate relationship suggests that both vasculitis and atherosclerosis may play a role in the observed hearing loss among TAK patients (36-38). This is also supported by the fact that older age is associated with hearing loss.

The limitations of our study, conducted in a tertiary centre and based on voluntary participation, should be acknowledged. Firstly, the results may not be fully generalisable to a broader population. The possibility of selection bias, resulting in the potential exclusion of less severe cases could not be ruled out. Unfortunately, radiological studies were not reassessed at the study entry. Conversely, current radiological images may not accurately depict the initial disease burden, as treatment might have ameliorated vascular involvement without necessarily affecting inner ear structures leading to permanent hearing defects. This may explain the discordance in our results showing no correlation between the vascular involvement and impaired hearing. Finally, the small number of patients and controls included in the second part of the study might be another limitation.

Conclusions

This is the first study showing an increased rate of impaired hearing in patients with TAK. The pathophysiologic mechanisms of this finding are yet to be clarified. Inflammatory involvement with or without associated atherosclerosis of the vertebral and/or subclavian arteries could potentially contribute to ischaemia, resulting in hearing loss through either permanent or temporary damage to inner ear structures. This speculation needs to be confirmed by longitudinal studies with sequential imaging of the related vasculature.

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