Hearing threshold abnormalities in patients with alopecia areata

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Alopecia areata (AA) is a common disease of the hair follicle characterized by the appearance of patchy areas of hair loss leaving a smooth and nonscarred scalp. AA is a T-cell-mediated autoimmune disease with cytokines playing an important role. Follicular melanocytes is an important target in the autoimmune process of AA, and AA may have an effect on hearing function by affecting the melanocytes in the inner ear. Our study aimed at investigating autoimmune hearing loss in Egyptian patients with AA in comparison with controls. The study included 40 participants – 20 AA patients and 20 controls. All patients were subjected to a detailed history taking and examination to detect type, extent of AA in addition to complete clinical, otoscopic and audiological examination, including high frequencies for both ears of patients and age-matched controls. The study revealed a significant presence of sensorineural hearing loss in AA patients in comparison with controls. This hearing loss had a direct correlation with the disease severity, duration and the recurrence of attacks.

Keywords:
alopecia areata, autoimmune hearing loss, low and high frequencies hearing threshold

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Introduction

Alopecia areata (AA) is an immune-mediated disease presenting as hair loss that occurs in all ethnic groups, ages and both sexes. The estimated lifetime risk is 2% among the general population [1]. Circumstantial evidence in support of an autoimmune mechanism underlying AA comes from several sources. The association of AA with other autoimmune diseases has been reported. The presence of inflammatory lymphocytes around and within the affected hair follicles and the ability to promote hair regrowth with the use of immunosuppressive agents is consistent with an autoimmune hypothesis [2]. Moreover, previous studies suggested that follicular melanocytes may be an important target in the autoimmune process of AA [3].

AA may have an effect on hearing function by affecting the melanocytes in the inner ear. Therefore, there may be a relationship between sensorineural hearing loss and the autoimmune disease, AA [4].

The intrastrial fluid–blood barrier

Integrity of the intrastrial fluid–blood barrier is critical for solute homeostasis and prevention of the influx of toxic substances. The loss of intrastrial fluid–blood barrier integrity, with concomitant vascular permeability, results in cochlear edema in the stria vascularis. Cochlear edema is thought to be present in a number of hearing disorders, including autoimmune inner ear disease [5]. The intrastrial fluid–blood barrier is formed of cochlear microvascular endothelial cells connected to each other by tight junctions, an underlying basement membrane, and a second line of support consisting of cochlear pericytes and perivascular resident macrophage-type melanocytes (PVM/Ms) [6].

A large number of perivascular cells expressing both macrophage and melanocyte characteristics (named PVM/Ms), previously found in the intrastrial fluid–blood barrier, are also found in the blood–labyrinth barrier area of the vestibular system in normal adult cochlea, including in the three ampullae of the semicircular canals (posterior, superior and horizontal), utricle and saccule [7]. The PVM/Ms are positive for the macrophage and melanocyte marker proteins F4/80 and glutathione-*S*-transferase a-4. Glutathione-*S*-transferase a-4 is one of the glutathione-*S*-transferases, which participate in detoxification processes of many tissues. PVM/Ms have an important role in maintaining the integrity of the intrastrial fluid–blood barrier and hearing function [6].

The aim of this study is to investigate the audiological abnormalities, if any, in patients with AA in comparison with controls, in an attempt to estimate the association of autoimmune hearing loss with AA.

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Patients and methods

The present study included:

(1) Study group: 20 AA patients (14 males and six females).
(2) Control group: 20 age-matched and sex-matched healthy controls.They were recruited from the dermatology outpatient clinic of Ain Shams University Hospital from April 2014 to September 2014. An informed written consent was taken from patients before enrollment in the study.

Inclusion criteria

Both types of AA were included in the study: patchy and extensive (AT/AU).

Exclusion criteria

(1) Age above 55 years.
(2) History of otological disease.
(3) History of head trauma.
(4) History of chronic noise exposure.
(5) History of familial hearing loss.
(6) Middle ear disease (type B or C tympanogram, gap of at least 5 dB between the air and bone conduction thresholds in either ear).
(7) Systemic ototoxic drug – for example, gentamicin, furosemide and corticosteroid – intake.
(8) Systemic disease (diabetes or hypertension).
(9) Other autoimmune diseases – for example, autoimmune thyroid disorders, psoriasis, pernicious anemia and vitiligo.
(10) Other causes of patchy hair loss – for example, telogen effluvium, androgentic alopecia, trichotillomania and tinea capitis.

Methods

At the first visit all patients were subjected to:

History

A full history taking was conducted with special emphasis on essential data that were collected according to the guidelines of National Alopecia Areata Foundation as follows [8]:

(1) *Personal history*: Name, age, sex, occupation, marital status and special habits of medical importance and residency.
(2) *History of the present illness*: Onset, course, duration of disease and of the last episode, number of episodes of AA, pattern of hair loss, number of AA patches and other symptoms (scalp burning or itching).
(3) *Medical history*: History of other skin diseases or other systemic diseases (vitiligo, psoriasis, thyroid disorders, pernicious anaemia).
(4) *Drug history and past history*: History of drug intake for any medical problem or AA; history of surgical operations.
(5) Family history of AA.

General and dermatological examinations

(1) General examination was done to exclude associated systemic diseases.
(2) Dermatological examination was done:
    (a) To diagnose AA lesions with a special emphasis on number and symmetry.
    (b) To exclude any scalp or hair disorders (erythema, scales, inflammation, tinea capitis or seborrhea).
    (c) To exclude any skin diseases such as psoriasis, vitiligo, systemic lupus erythematosus (SLE) and seborrheic dermatitis.

Clinical assessment of the severity of alopecia areata

Our study used a global severity score called the 'severity of alopecia tool' or SALT score. It is useful to find out the quantitative assessment of scalp hair loss [8].

Otologic and audiometric examination by an audiologist

(1) Clinical examination for both ears was conducted to detect any discharge, abnormality or deformity.
(2) Bilateral otoscopic examination was conducted.
(3) Immittancemetry was performed to exclude middle ear pathologies in both patients and controls.
(4) Audiometric examinations were performed on both ears for patients and controls using a pure tone audiometer in a silent cabin. Pure tone thresholds were determined for each ear at frequencies of 250–12 000 Hz for air conduction.

Statistical analysis

Data was analysed using Statistical Program for Social Science (SPSS) version 18.0, USA. Quantitative data were expressed as mean ± SD. Qualitative data were expressed as frequency and percentage. The following tests were done:

(1) Independent samples *t*-test of significance when comparing between two means.
(2) χ^2-Test of significance to compare proportions between two qualitative parameters.
(3) Pearson's correlation coefficient (*r*) test for correlating data.

Odds ratio

An odds ratio is a measure of association between an exposure and an outcome.

Probability (P-value)

P-value less than 0.05 was considered significant.

P-value of 0.01 was considered as highly significant.

P-value greater than 0.05 was considered insignificant.

Results

The aim of this study was to detect possible audiological abnormalities in AA patients. This case–control study was conducted on 20 patients with AA (group I) and 20 normal individuals serving as controls (group II).

Age

In group I, the patient group, age ranged from 10 to 48 years with a mean of 26 ± 10.2. In group II, the control group, age ranged from 10 to 42 years with a mean of 23.7 ± 9.

Sex

In group I, patients with AA were 14 males (70%) and six females (30%). In group II, the normal controls were 15 males (75%) and five females (25%).

Family history of alopecia areata

In five patients (25%) there was a family history of AA, affecting their first degree relatives.

The pattern of alopecia

Fifteen patients (75%) had patchy AA while two patients (10%) had alopecia totalis and three patients (15%) had alopecia universalis.

The severity of alopecia areata according to SALT score [8]

Thirteen patients (65%) were S1 with less than 25% hair loss, two patients (10%) were S2 with 25–49% hair loss, and five patients (25%) were S4 with 75–99% hair loss.

Duration of the last episode of alopecia areata

The disease duration ranged between 2 weeks and 12 months with a mean of 4.2 ± 3.6 months.

Recurrence

Seven patients (35%) had previous attacks. These patients were further classified according to the number of previous episodes. One patient had one previous episode, two patients had two previous episodes, three patients had three previous episodes and one patient had seven previous episodes.

Our study measured the hearing thresholds by air conduction insert earphones for both right and left ears of both groups (patients and control) at 250, 500, 1000, 2000, 4000, 8000 and 12 000 Hz, and drew a comparison between hearing thresholds of the right and left ears of the patients (Table 1).

Comparison between hearing thresholds of the right and left ears of the control group

The previous two tables showed no statistically significant difference between Rt and Lt ears of both groups – using paired sample – so they were summed up to 40 ears (Table 2).

Comparison between the two studied groups as regards

Age

Our study compared the patient group and the control group as regards their age using independent

Table 1 Comparison between Rt and Lt ears of the patients group

Sound frequencies	Patients (*n* = 20)	Difference	*t*-Test	
	Mean ± SD	Mean	*t*	*P*-value
Rt 250 Hz	17.3 ± 7.2	−0.25	−0.134	0.895
Lt 250 Hz	17.5 ± 6.2			
Rt 500 Hz	16.5 ± 5.9	0.25	0.175	0.863
Lt 500 Hz	16.3 ± 3.9			
Rt 1000 Hz	16.3 ± 5.6	2.00	1.361	0.189
Lt 1000 Hz	14.3 ± 4.9			
Rt 2000 Hz	14.3 ± 8.3	−0.25	−0.123	0.904
Lt 2000 Hz	14.5 ± 4.8			
Rt 4000 Hz	17.0 ± 11.5	−0.50	−0.309	0.761
Lt 4000 Hz	17.5 ± 9.8			
Rt 8000 Hz	24.3 ± 11.4	0.75	0.358	0.724
Lt 8000 Hz	23.5 ± 11.1			
Rt 12 000 Hz	31.8 ± 13.8	−2.00	−0.748	0.464
Lt 12 000 Hz	33.8 ± 18.8			

Table 2 Comparison between Rt and Lt ears of the control group

Sound frequencies	Control (*n* = 20)	Difference	*t*-Test	
	Mean ± SD	Mean	*t*	*P*-value
Rt 250 Hz	18.3 ± 3.7	0.50	0.357	0.725
Lt 250 Hz	17.8 ± 5.0			
Rt 500 Hz	13.0 ± 5.0	−0.75	−0.616	0.545
Lt 500 Hz	13.8 ± 6.0			
Rt 1000 Hz	13.0 ± 5.2	−0.75	−0.547	0.591
Lt 1000 Hz	13.8 ± 5.6			
Rt 2000 Hz	13.8 ± 5.1	1.00	1.000	0.330
Lt 2000 Hz	12.8 ± 4.1			
Rt 4000 Hz	15.0 ± 6.3	0.00	0.000	1.000
Lt 4000 Hz	15.0 ± 6.3			
Rt 8000 Hz	18.5 ± 5.9	0.00	0.000	1.000
Lt 8000 Hz	18.5 ± 6.9			
Rt 12 000 Hz	23.5 ± 7.5	1.25	0.773	0.449
Lt 12 000 Hz	22.3 ± 6.2			

t-test. There was no statistically significant difference (P = 0.370) – that is, patients and controls were age matched.

Sex

Our study compared the patients group and control group as regards their sex using χ^2-test (odds ratio); no statistically significant difference was found (P = 0.723) – that is, patients and controls were sex matched.

Sensorineural hearing loss in relation to other variables

Sex

Regarding the sex in our study, there was no difference between males and females as regards sensorineural hearing loss (SNHL). This corresponds to a study that concluded that AA had no sex predilection [1] (Tables 3 and 4).

Alopecia areata severity

Table 4.

Correlation study between the hearing threshold and alopecia areata severity in patients

Recurrence

There was a positive and significant correlation between AA severity and SNHL at 8000 and 12000 Hz. Also, between recurrence and SNHL at 12000 Hz.

Duration of disease

There was a direct correlation between SNHL at 8000 and 12000 Hz and duration of AA.

Discussion

Several studies of AA suggest that melanogenesis-associated peptides expressed by melanin-producing anagen high frequency (HFs) are the key autoantigens targeted by autoreactive cytotoxic T cells [9,10]. Possible involvement of melanogenesis-associated autoantigens in AA was suggested by the following observations: sparing of white/greying HFs in AA, regrowing hair shafts are usually white followed by repigmentation, association with vitiligo, and the sudden onset of fulminant AA affecting mostly pigmented HFs.

Audiological abnormalities with AA were not investigated much before. The only previous study to our knowledge was done by Ucak *et al.* [4] who studied the audiological abnormalities in patients with AA, and they stated that they were the first to do this investigation. A total of 51 patients with AA and 51 healthy controls similar in terms of age and sex were enrolled in their study.

In the present study, hearing thresholds at low (<8000 Hz) and high (≥8000 Hz) frequency sounds were assessed in the control group and were considered as the normal standard in comparison with the hearing thresholds of the patients. However, this work found a statistically significant difference in hearing thresholds at high frequencies for both right and left ears of the patients group – that is, bilateral sensorineural hearing loss at 8000 and 12 000 Hz in AA patients (Table 5).

Table 3 Comparison between males and females as regards sensorineural hearing loss

Sound frequencies (Hz)	Mean ± SD		*t*-Test	
	Male (*n* = 28)	Female (*n*=12)	*t*	*P*-value
250	18.0 ± 6.6	15.8 ± 6.7	0.966	0.340
500	17.3 ± 5.0	14.2 ± 4.2	1.916	0.063
1000	15.7 ± 5.6	14.2 ± 4.7	0.842	0.405
2000	15.7 ± 6.9	11.3 ± 5.3	1.999	0.053
4000	18.0 ± 10.7	15.4 ± 10.5	0.714	0.479
8000	25.9 ± 12.0	19.2 ± 7.0	1.803	0.079
12 000	33.8 ± 18.4	30.4 ± 10.3	0.587	0.561

Table 4 Comparison between alopecia areata severity as regards sensorineural hearing loss

Sound frequencies (Hz)	AA Severity	Mean ± SD	*t*-Test	
			t	*P*-value
250	Mild	16.7 ± 6.3	−0.84	0.407
	Moderate and severe	18.6 ± 7.2		
500	Mild	16.2 ± 5.5	−0.38	0.705
	Moderate and severe	16.8 ± 3.7		
1000	Mild	15.2 ± 4.8	−0.09	0.927
	Moderate and severe	15.4 ± 6.3		
2000	Mild	13.8 ± 7.1	−0.67	0.504
	Moderate and severe	15.4 ± 6.0		
4000	Mild	15.4 ± 8.2	−1.55	0.129
	Moderate and severe	20.7 ± 13.6		
8000	Mild	20.6 ± 7.0	−2.76	0.009 (S)
	Moderate and severe	30.0 ± 14.7		
12 000	Mild	27.3 ± 13.5	−3.19	0.003 (S)
	Moderate and severe	42.9 ± 16.7		

Significant effect of the AA degree at 8000 and 12000 Hz

Table 5 Comparison between patients and controls as regards hearing thresholds

Sound frequencies (Hz)	*X* ± SD		*t*-Test	
	Patients (*n* = 40)	Control (*n* = 40)	*t*	*P*-value
250	17.4 ± 6.6	18.0 ± 4.4	0.50	0.619
500	16.4 ± 4.9	13.4 ± 5.5	1.57	0.052
1000	15.3 ± 5.3	13.4 ± 5.4	1.57	0.120
2000	14.4 ± 6.7	13.3 ± 4.6	0.87	0.385
4000	17.3 ± 10.6	15.0 ± 6.2	1.16	0.249
8000	23.9 ± 11.1	18.5 ± 6.3	2.65	0.010 (S)
12 000	32.8 ± 16.3	22.9 ± 6.8	3.53	0.002 (S)

Significant difference between controls and patients at 8000 and12000 Hz

Table 6 Correlation study between sensorineural hearing loss and alopecia areata severity in patients group using Pearson correlation coefficient test

Sound frequencies (Hz)	AA severity
250	
r	0.147
P-value	0.365
500	
r	0.012
P-value	0.942
1000	
r	−0.117
P-value	0.474
2000	
r	0.066
P-value	0.687
4000	
r	0.212
P-value	0.189
8000	
r	0.349
P-value	0.027 (S)
AA 12 000	
r	0.449
P-value	0.004 (S)

AA, alopecia areata; *r*, Pearson correlation coefficient; $P < 0.001$ (HS); $P < 0.05$ (S); $P > 0.05$ (NS); Significant correlation between sensorineural hearing loss and alopecia areata severity at 8000 and 12000 Hz.

Table 7 Correlation between recurrence and sensorineural hearing loss

Sound frequencies (Hz)	Mean ± SD		*t*-Test	
	Positive ($n = 14$)	Negative ($n = 26$)	*t*	*P*-value
250	17.5 ± 8.3	17.3 ± 5.7	0.087	0.931
500	15.4 ± 4.1	16.9 ± 5.3	−0.956	0.345
1000	13.6 ± 5.0	16.2 ± 5.3	−1.491	0.144
2000	13.6 ± 6.9	14.8 ± 6.7	−0.550	0.585
4000	20.0 ± 14.1	15.8 ± 8.0	1.216	0.231
8000	26.4 ± 14.7	22.5 ± 8.6	1.067	0.293
12 000	41.8 ± 17.3	27.9 ± 13.8	2.781	0.008 (S)

Significant correlation between sensorineural hearing loss and recurrence of alopecia areata at 12000 Hz

In this study, a significant difference was found as regards SNHL in patients who had recurrent attacks. This suggested the autoimmune aetiological nature of SNHL as an audiological abnormality with AA patients and that recurrent cases have a more aggressive autoimmune pathology. There was also a positive and significant correlation between AA severity and SNHL at 8000 and 12 000 Hz, and a direct correlation between SNHL and duration of the last episode of AA (Tables 6–8). These results agree with Ucak *et al.* [4] as there was a high rate of hearing loss in the patients with high disease duration – hearing loss was detected in 54.5% of patients with a disease duration of more than 12 months. This suggests that a severe form and longer duration of illness may increase the risk of hearing loss.

Table 8 Correlation study between sensorineural hearing loss and duration of current episode of alopecia in patients group using Pearson correlation coefficient test

Sound frequencies	Duration of alopecia (months)
AA 250 Hz	
r	0.179
P-value	0.269
AA 500 Hz	
r	0.151
P-value	0.353
AA 1000 Hz	
r	0.032
P-value	0.846
AA 2000 Hz	
r	0.162
P-value	0.318
AA 4000 Hz	
r	0.383
P-value	0.015 (S)
AA 8000 Hz	
r	0.379
P-value	0.016 (S)
AA 12 000 Hz	
r	0.627

AA, alopecia areata.

In addition, Ucak and his colleagues mentioned that hearing loss was more frequent in patients with a family history of AA and nail involvement. The present study could not determine this relation, probably due to our smaller sample size.

Conclusion

(1) SNHL correlates with severity and duration of AA with higher hearing thresholds in more severe diseases.
(2) Follicular melanocytes may be an important target in the autoimmune process of AA, and AA may have an effect on hearing function by affecting the melanocytes in the inner ear.

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Conflicts of interest
There are no conflicts of interest.

References

1 Finner AM. Alopecia areata: clinical presentation, diagnosis, and unusual cases. Dermatol Ther 2011; 24:348–354.
2 McElwee KJ, Spiers EM, Oliver RF. Partial restoration of hair growth in the DEBR model for alopecia areata after in vivo depletion of CD41 T cells. Br J Dermatol 1999; 140:432–437.
3 Tobin DJ, Fenton DA, Kendall MD. Ultrastructural observations on the hair bulb melanocytes and melanosomes in acute alopecia areata. J Invest Dermatol 1990; 94:803–807.
4 Ucak H, Soylu E, Ozturk S, Demir B, Cicek D, Erden I, Akyigit A. Audiological abnormalities in patients with alopecia areata. J Eur Acad Dermatol Venereol 2014; 28:1045–1048.

5 Shi X. Cochlear pericyte responses to acoustic trauma and the involvement of hypoxia-inducible factor-1alpha and vascular endothelial growth factor. Am J Pathol 2009; 174:1692–1704.

6 Neng L, Zhang F, Kachelmeier A, Shi X. Endothelial cell, pericyte, and perivascular resident macrophage-type melanocyte interactions regulate cochlear intrastrial fluid-blood barrier permeability. J Assoc Res Otolaryngol 2013; 14:175–185.

7 Zhang F, Zhang J, Neng L, Shi X. Characterization and inflammatory response of perivascular-resident macrophage-like melanocytes in the vestibular system. J Assoc Res Otolaryngol 2013; 14:635–643.

8 Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, *et al*. National Alopecia Areata Foundation. Alopecia areata investigational assessment guidelines. Part II. National Alopecia Areata Foundatin. J Am Acad Dermatol 2004; 51:440–447.

9 Paus R, Slominski A, Czarnetzki BM. Is alopecia areata an autoimmune-response against melanogenesis-related proteins, exposed by abnormal MHC class I expression in the anagen hair bulb? Yale J Biol Med 1993; 66:541–554.

10 Gilhar A, Landau M, Assy B, Shalaginov R, Serafimovich S, Kalish RS. Melanocyte-associated T cell epitopes can function as autoantigens for transfer of alopecia areata to human scalp explants on SCID mice. J Invest Dermatol 2001; 117:1357–1362.