Published in final edited form as:

Auris Nasus Larynx. 2016 December ; 43(6): 614–619. doi:10.1016/j.anl.2016.01.001.

Stria Vascularis and Cochlear Hair Cell Changes in Syphilis: A Human Temporal Bone Study

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Abstract

Objective—To observe any changes in stria vascularis and cochlear hair cells in patients with syphilis

Materials and Methods—We examined 13 human temporal bone samples from 8 patients with syphilis (our syphilis group), as well as 12 histopathologically normal samples from 9 age-matched patients without syphilis (our control group). We compared, between the 2 groups, the mean area of the stria vascularis (measured with conventional light microscopy connected to a personal computer) and the mean percentage of cochlear hair cell loss (obtained from cytocochleograms).

Results—In our syphilis group, only 1 (7.7%) of the 13 samples had precipitate in the endolymphatic or perilymphatic spaces; 8 (61.5%) of the samples revealed the presence of endolymphatic hydrops (4 cochlear, 4 saccular). The mean area of the stria vascularis area *did not* significantly differ, in any turn of the cochlea, between the 2 groups ($P > 0.1$). However, we *did* find significant differences between the 2 groups in the mean percentage of outer hair cells in the apical turn ($P < 0.026$) and in the mean percentage of inner hair cells in the basal ($P = 0.001$), middle ($P = 0.004$), and apical ($P = 0.018$) turns. In 7 samples in our syphilis group, we observed either complete loss of the organ of Corti or a flattened organ of Corti without any cells in addition to the absence of both outer and inner hair cells.

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Conflict of Interest: The authors declare that they have no conflict of interest.

Conclusion—In this study, syphilis led either to complete loss of the organ of Corti or to significant loss of cochlear hair cells, in addition to cochleosaccular hydrops. But the area of the stria vascularis did not change.

Keywords

syphilis; cochlea; hair cell; temporal bone; histopathology

INTRODUCTION

Syphilis, caused by the spirochete *Treponema pallidum*, can cause cochlear and vestibular dysfunction. Both congenital and acquired syphilis can be associated with sensorineural hearing loss [1]. Ootosyphilis should be considered in patients with syphilis and a history of vestibular symptoms, tinnitus, and fluctuating sensorineural hearing loss [2]. Endolymphatic hydrops can be seen during a routine pathologic evaluation of an ear specimen from patients with a history of ootosyphilis [3, 4]. However, any association of endolymphatic hydrops with other pathologic findings and symptoms remains unclear, as does its causative mechanism. In this study, using human temporal bone samples from patients with syphilis, we investigated the area of the stria vascularis, the organ of Corti, and cochlear hair cells.

MATERIALS AND METHODS

Samples

We examined a total of 25 human temporal bone samples from 17 deceased patients: 13 samples from 8 patients with syphilis (our syphilis group), as well as 12 histopathologically normal samples from 9 age-matched patients without syphilis (our control group). In our syphilis group, the mean age of the 8 patients (5 male, 3 female) was 70 ± 7 years (range, 58 to 78). In our control group, the mean age of the 9 patients (6 male, 3 female) was 67 ± 7 years (range, 60 to 77).

Excluded from our study were temporal bone samples from patients known to have had the following conditions that might affect the cochlea: head trauma, systemic autoimmune disorders, ototoxic drug use, and any defined otologic diseases (e.g., active otitis media, labyrinthitis, and internal auditory canal tumor).

We obtained samples from the archived human temporal bone collection of the University of Minnesota. All temporal bones had previously been removed at autopsy, fixed in 10% formalin solution, decalcified, and embedded in celloidin. Each temporal bone was serially sectioned in the horizontal plane at a thickness of 20 μ m from superior to inferior. Every 10th section was stained with hematoxylin and eosin. The institutional review board of the University of Minnesota (0206M26181) approved this study.

Qualitative Histopathologic Assessment

We used light microscopy to examine all 25 human temporal bone samples (13 in our syphilis group and 12 in our control group). We assessed each labyrinth for the presence or absence of precipitate within the endolymphatic and perilymphatic spaces. We defined

hydrops by any distention of the membranous walls of the saccule and utricle or any distention of Reissner's membrane of the cochlea. In our syphilis group, we excluded at this point 1 sample from a patient with a history of otitis media, except for purposes of evaluating endolymphatic hydrops, so our final syphilis group comprised 12 samples for statistical analysis.

Area of Stria Vascularis

We measured the area of the stria vascularis in the lower basal turn, the upper basal turn, the lower middle turn, the upper middle turn, and the apical turn of the cochlea in the midmodiolar section and in the 2 adjacent sections above and below. We then determined the mean area of those 3 sections in the 12 remaining samples in our syphilis group and in the 12 samples in our control group. To examine the sections, we used conventional light microscopy with a digital camera connected to a personal computer, whose monitor displayed the sections. We determined the area of the stria vascularis using commercially available image analysis software (SPOT Advanced software, SPOT Imaging Solutions, Sterling Heights, MI, USA). We included only the cellular part of the stria vascularis, excluding all observed cystic-like structures and concretions.

Spiral Ganglion Cells

To evaluate total number of spiral ganglion cells, we used the method defined by Otte et al. previously [5]. We divided Rosenthal's canal into 4 segments as described previously: segment I (from base to 6 mm); II (6 to 15 mm); III (15 to 22 mm) and IV (22 mm to apex). All nuclei were counted in each section. The number of ganglion cells was determined for each segment and for the cochlea as a whole by multiplying their summed counts by 10 to account for the un-mounted sections and by a factor of 0.9 to account for cells that would be counted because of their location at the interface between sections. The percentages of spiral ganglion cell loss was calculated using the age matched normative data determined previously [6].

Loss of Cochlear Hair Cells

To reconstruct cochleae, we used standard cytochleograms, per the methods previously determined by Schuknecht and Gacek [7]. We performed cytochleograms for the 12 samples in our syphilis group and for the 12 samples in our control group. In each section, we counted the number of present and missing cochlear hair cells. In 3 turns (basal, middle, and apical) of the cochlea, we calculated the percentage of loss of hair cells by dividing the number of missing hair cells by the total number of hair cells possible in that turn. We considered both outer and inner hair cells as missing in samples that revealed either complete loss of the organ of Corti or a flattened organ of Corti without any cells (Fig. 1).

Statistical Analysis

Results are presented as the mean $\pm$ SD (standard deviation). To assess the normality of distribution of the groups, we used the Kolmogorov-Smirnov normality test. To compare the mean areas of the stria vascularis between the 2 groups, we used the parametric Student *t* test. To compare the mean percentages of cochlear hair cell loss between the 2 groups, we

used the nonparametric Mann-Whitney *U* test. For all analyses, we used SPSS 23.0 software for Windows (SPSS, Inc., Chicago, IL). A *P* value less than 0.05 was considered statistically significant.

RESULTS

In our syphilis group, all 8 patients had a clinical and laboratory diagnosis of the disease: 4 patients had positive reactive *Venereal Disease Research Laboratory* (VDRL) test results, and 4 patients had positive reactive fluorescent treponemal antibody-absorption (FTA-ABS) test results, 1 of whom also had a positive *Treponema pallidum* immobilization (TPI) test result. We were not able to see detailed diagnostic laboratory information for all 8 patients, but a certain diagnosis of syphilis was recorded in their medical records. Although their otologic histories were not comprehensive, we know from their medical records that 4 patients had sensorineural hearing loss, 2 had tinnitus, and 2 had a history of vertigo and/or dizziness.

Table 1 summarizes the clinical and histopathologic findings, the areas of the stria vascularis, and the percentages of cochlear hair cell loss percentages for all 8 patients with syphilis. We did not observe any significant temporal osteitis or microgumma in any sample. Only 1 (7.7%) of the 13 temporal bone samples in our initial syphilis group had precipitate in the endolymphatic or perilymphatic spaces. None of the 8 patients had a documented diagnosis of Meniere's disease, but 8 (61.5%) of the 13 samples revealed the presence of endolymphatic hydrops (involving the cochlea in 4 samples, the saccule in 4 samples). Of the 8 patients, 2 (25%) had cochlear hydrops, and 4 (50%) had saccular hydrops in any side. The overall rate of cochleosaccular hydrops was 75% (6 patients).

The mean area of the stria vascularis *did not* significantly differ between the 2 groups; however, it was lower, in our syphilis group, in the lower basal turn, the upper basal turn, the lower middle turn, the upper middle turn, and the apical turn of the cochlea in the midmodiolar sections (Table 2). Of the 12 samples in our final syphilis group, 7 (58%) showed complete loss of the organ of Corti in several sections of the cochlea. And of those 7 samples, 3 (43%) did not show any type of endolymphatic hydrops.

Out of 12 samples in our final syphilis group, 4 had a significant loss of spiral ganglion cells. Of those samples with loss of spiral ganglion cells, the total numbers of spiral ganglion cells were 10314, 7587, 11079, 13509 respectively and the percentages of loss of spiral ganglion cells were calculated as 54.9%, 66.8%, 51.6%, 41% using age matched normative data (22900 for age range of 61–70 years) [6]. In the cytochleograms of the 12 samples in our final syphilis group, the mean percentage of *outer hair cell loss* was higher in the basal and middle turns of the cochlea, but *did not* significantly differ from our control group. Yet the mean percentage of *outer hair cell loss* in our final syphilis group was *significantly higher* in the *apical turn* of the cochlea than in our control group (Fig. 2). Moreover, in all turns of the cochlea in our final syphilis group, the mean percentage of *inner hair cell loss* was *significantly higher* than in our control group (Fig. 3).

Fig. 4 shows the outer and inner hair cell loss in a human temporal bone section from a syphilis patient with a slight cochlear hydrops and without complete loss of the organ of Corti. Fig. 5 shows a flattened organ of Corti, as well as a missing organ of Corti, in a human temporal bone section from a patient with syphilis without cochlear hydrops.

DISCUSSION

Both congenital and acquired syphilis can be associated with endolymphatic hydrops and with otologic symptoms similar to Meniere's disease [8, 9]. Ootosyphilis can be presumptively diagnosed in patients with a history of syphilis who also have otologic symptoms. In our study, 75% of the patients in our syphilis group had cochleosaccular endolymphatic hydrops. We cannot clearly confirm the presumptive diagnosis of ootosyphilis in our syphilis patients because of the limited information in their medical records; nonetheless, the presence of endolymphatic hydrops in 75% of them supports the diagnosis of ootosyphilis. Still, the mechanism of variable otopathologic symptoms in patients with ootosyphilis and endolymphatic hydrops remains a matter of debate.

Sensorineural hearing loss and tinnitus are the most common otologic symptoms of syphilis [10–13]. But the mechanism of otologic symptoms remains unclear. Degeneration of both the cochlear and vestibular neuroepithelium has been reported in patients with syphilis [14]. Vestibular otopathology in syphilis patients was also studied previously, and in addition to endolymphatic hydrops, a significant loss of type II vestibular hair cells was detected in syphilis patients using differential interference contrast microscope, similar to Meniere's disease [15, 16]. In our study, of the 12 temporal bone samples in our syphilis group, 7 showed complete loss of the organ of Corti; 3 of those samples did not show any type of endolymphatic hydrops. Thus, the loss of the organ of Corti might not be associated with the presence of endolymphatic hydrops. In addition, we did not observe any significant temporal osteitis or microgumma in any sample under light microscopy. Thus this study suggests that cochlear changes might be seen in syphilis even without any obvious temporal osteitis or microgumma under the light microscopy.

We also found significantly higher inner hair cell loss in all turns of the cochlea in the temporal bone samples in our syphilis group, as compared with our control group. We considered sections with a flattened or absent organ of Corti to indicate the absence of both outer and inner hair cells, so our finding of higher inner hair cell loss can be attributed to the loss of the organ of Corti.

But outer hair cell loss was significantly higher only in the apical turn of samples in our syphilis group—a result with possible clinical implications. According to the cochlear traveling-wave model first described by Von Békésy, the base of the cochlea is sensitive to high-frequency sounds, whereas its apex is more sensitive to lower-frequency sounds [17]. Our finding of higher outer hair cell loss in the apical turn of samples in our syphilis group is consistent with low-frequency hearing loss, which is a common symptom of Meniere's disease [18, 19].

In Meniere's disease, the vascularity of the stria vascularis has been found to be reduced [20]. Degeneration of the stria vascularis has also been reported as a possible cause of progressive sensorineural hearing loss [21]. As the main producer of endolymph, the stria vascularis is expected to be affected in otosyphilis. However, in our study, we observed no changes in the area of stria vascularis in our syphilis group.

This study has several limitations. Samples were evaluated under light microscopy. In addition, audiovestibular history, electrophysiologic testing, and imaging results were not available for all of our patients, impeding our ability to fully correlate our findings with clinical manifestations.

CONCLUSION

In this study, syphilis led either to complete loss of the organ of Corti or to significant loss of cochlear hair cells (namely, of outer hair cells in the apical turn of the cochlea and of inner hair cells in all turns of the cochlea), in addition to cochleosaccular hydrops. But the area of the stria vascularis (measured with light microscopy) did not change.

Acknowledgments

Source of funding:

This project was funded by NIH (NIDCD), grant number U24 DC011968-01; the International Hearing Foundation; the Starkey Foundation; and the 5M Lions International. Ömer Hızlı and Serdar Kaya received the Scientific and Technological Research Council of Turkey (TUBITAK) Scholarship.

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Figure 1.
Light photomicrograph of the cochlea from a 68-year-old woman with syphilis: (a) lower-magnification image, (b) magnified view of boxed area
Arrow = complete loss of the organ of Corti

Figure 2.
Outer hair cell loss

Inner hair cell loss (%)

Figure 3.
Inner hair cell loss

Figure 4.
Light photomicrograph of the cochlea from a 68-year-old woman with syphilis: (a) lower-magnification image, (b) magnified view of boxed area.
Thick arrow = outer hair cell loss, thin arrow = inner hair cell loss

Figure 5.
Light photomicrograph of the cochlea from a 68-year-old woman with syphilis
Thin arrow = missing organ of Corti, thick arrow = flattened organ of Corti

Table 1

Qualitative and quantitative otopathologic observations of syphilitic ears.

Age /Sex	Evidence of Syphilis	Sx	Histopathologic findings				Area of Stria vascularis at mid-modiolar section (µm ²)				Outer hair cell loss (%)		Inner hair cell loss (%)						
			Side	PR	CH	SH	UH	LBT	UBT	LMT	UMT	AT	BT	MT	AT	BT	MT	AT	
63 /F	History of syphilis Clinical and laboratory diagnosis	NA	Left	-	+	-	-	-	7823	10186	8157	4845	2383	14	39	0	18	38	0
			Right	-	+	-	-	-	8163	4996	3175	6386	5870	10	6	33	6	0	33
68 /F	Latent syphilis history Reactive VDRL Significant TPI	Vertigo Tinnitus SNHL	Left	-	+	-	-	-	3452	4608	4644	3621	4930	77	67	85	54	42	14
			Right	-	+	-	-	-	5156	3454	5093	5024	4452	77	68	76	69	39	14
76 /M	Syphilis history Reactive FTA-ABS	Dizziness Nausea Vomiting	Right	-	-	+	-	-	9697	9357	7509	6755	6516	86	88	92	19	8	12
70 /M	History of syphilis Clinical and laboratory diagnosis	Tinnitus SNHL	Left	+	-	+	-	-	9247	10767	8794	7482	9474	75	83	60	10	18	0
78 /M	History of syphilis Reactive VDRL in cerebrospinal fluid Reactive FTA-ABS	SNHL	Right	-	-	-	-	-	6457	8413	4916	6388	4261	16	85	100	12	83	100
58 /F	History of syphilis Clinical and laboratory diagnosis Reactive VDRL	NA	Left [*]	-	-	-	-	-	*	*	*	*	*	*	*	*	*	*	*
			Right	-	-	-	-	-	9327	7886	7199	8427	5972	58	74	75	3	23	25

Age /Sex	Evidence of Syphilis	Sx	Histopathologic findings				Area of Stria vascularis at mid-modiolar section (μm^2)				Outer hair cell loss (%)			Inner hair cell loss (%)		
			PR	CH	SH	UH	LBT	UBT	LMT	UMT	AT	BT	MT	AT	BT	MT
75 /M	History of syphilis Reactive FTA-ABS	SNHL	Left	-	-	-	-	9345	8806	5847	6685	7053	48	51	87	6
			Right	-	-	+	-	5495	8464	6364	9965	5558	28	3	83	17
73 /M	History of syphilis Reactive VDRL Reactive FTA-ABS	NA	Left	-	-	+	-	8773	8103	6209	5280	7037	49	64	73	21
			Right	-	-	-	-	9704	11298	7722	9226	4063	29	35	42	20

Footnote for Table 1. * Excluded from evaluation of stria vascularis area and cochleocytogram because of purulent otitis media. Sx: symptoms reported in case history file; PR: precipitate; CH: cochlear hydrops; SH: saccular hydrops; UH: utricular hydrops. For precipitate and hydrops, + indicates presence, - indicates absence; NA: not available; VDRL: venereal disease research laboratory test; FTA-ABS: The fluorescent treponemal antibody absorption test; TPI: Treponema pallidum immobilization test; SNHL: Sensorineural hearing loss; LBT: Lower basal turn; UBT: Upper basal turn; BT: Basal turn; LMT: Lower middle turn; UMT: Upper middle turn MT: Middle turn; AT: Apical turn.

Table 2Mean area of stria vascularis for both groups (μm^2)

	Syphilis group	Control group	P value
	Syphilis group	Control group	P value
Lower basal turn	7719.9 $\pm$ 2090	8642.8 $\pm$ 2449.2	0.332
Upper basal turn	8028.2 $\pm$ 2475.3	8443.8 $\pm$ 2942.9	0.712
Lower middle turn	6302.4 $\pm$ 1653	6615.5 $\pm$ 3180.6	0.765
Upper middle turn	6673.7 $\pm$ 1872.5	7727.1 $\pm$ 1642.8	0.157
Apical turn	5630.8 $\pm$ 1821.4	5663 $\pm$ 2195.7	0.969