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OTOPATHOLOGY REPORT

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Human otopathology in scleroderma

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Abstract

Objective: Scleroderma is a complex chronic progressive immune-mediated disease that causes fibrosis of the skin and internal organs, and vasculopathy.

Ear involvement has been poorly studied in patients with scleroderma. Vasculitic and autoimmune mechanisms are considered as possible etiologies on hearing impairment, however, this etiology still unclear.

Herein, we reviewed three cases of scleroderma from a temporal bone repository.

Methods: The national temporal bone database was reviewed for cases with scleroderma. Clinical case review and correlative otopathologic analysis. Middle and inner ear otopathologic analysis was performed following hematoxylin and eosin staining under light microscopy. Findings were compared to three age-matched controls.

Results: Two patients (three cases) with a history of serologically confirmed scleroderma were identified. Both individuals reported tinnitus and demonstrated bilateral moderate to severe down-sloping sensorineural hearing loss on audiometry. Histologically, the incudomallear joint space was diminished and ossicles appeared demineralized. A loss of hyaline cartilage, and obliteration of the incudomallear and incudostapedial joint synovial spaces was observed. Decreased caliber and intimal hyperplasia of arteries adjacent to ossicles was also identified. Mild diffuse atrophy of stria vascularis in the middle and apical turns of cochlea were found. Hair cell populations were normal. Total spiral ganglion neurons were lower in cases of scleroderma (range 29%–51%) compared to age-matched controls.

Conclusion: Fibrosis, inflammation, and vascular changes were observed in the middle and inner ear in patients with scleroderma. Findings have implications for understanding hearing and vestibular dysfunction in this patient population.

Level of evidence: Retrospective study.

KEYWORDS
otopathology, scleroderma, vasculitis

1 | INTRODUCTION

Scleroderma, also known as systemic sclerosis, is a complex immune-mediated disease characterized by obliterative vasculitis and extensive fibrosis of the skin and internal organs.[1,2] Although the etiology of scleroderma is not well understood, the prevailing hypothesis is that an inciting vascular injury occurs in a genetically susceptible individual and leads to a cascade of autoimmune dysregulation.[3] Auto-antibodies are produced which lead to worsening vascular injury that results in tissue hypoxia with subsequent collagen deposition throughout the skin, kidneys, lungs, and heart.[4]

From an otologic perspective, about 20%–40% of individuals with scleroderma develop hearing loss and related symptoms such as tinnitus and/or vertigo.[5–7] Sensorineural hearing loss predominates as was noted in a cohort study of 13 patients with scleroderma and hearing loss.[8] Whereas the association between scleroderma and hearing loss has been demonstrated, the mechanisms behind auditory dysfunction in scleroderma patients are not well understood. It is known that vasculitic and autoimmune mechanisms drive fibrosis throughout affected organs in scleroderma; whether these same mechanisms affect the ear is unknown.[9] In the single histopathologic report of temporal bone histology in scleroderma, Abou-Taleb and Linthicum report luminal narrowing of the peripheral vessels with perivascular fibrosis throughout the middle and inner ear.[10] Their findings from a single case of scleroderma are consistent with those reported in other vascular autoimmune diseases such as granulomatosis with polyangiitis (GPA) and suggest that vasculitic changes in the capillary network of the inner ear with resultant hypoxia of crucial inner ear structures including the endolymphatic sac, stria vascularis, and organ of corti may play a role in the pathogenesis of audiovestibular dysfunction.[10,11]

Herein, we hypothesize that cases of scleroderma will harbor vasculitic changes throughout the middle and inner ear when compared to controls. We also sought to specifically assess for differences in fibrous composition of the ossiclular chain/joints in scleroderma given the propensity for progressive fibrosis seen elsewhere in the body. We seek to add to the existing literature and report both qualitative and quantitative otopathologic findings in the middle and inner ear of three temporal bone specimens from two patients with scleroderma.

2 | MATERIALS AND METHODS

2.1 | Subject selection

The national temporal bone database was queried for histopathologic cases in the Mass Eye and Ear archive with a clinical history of scleroderma. Two patients with clinical and serologically confirmed scleroderma (anti-ro/SSA and anti-la/SSA positive) were identified from the temporal bone (TB) collection. Patient history was negative for mention of other rheumatologic conditions (e.g., rheumatoid arthritis, systemic lupus erythematosus (SLE), or Sjögren syndrome). From these two patients, three TB specimens were available for histopathologic analysis.

Two of the TB were fixed in 10% buffered formalin and one was fixed in Heidenhain's Susa for 3.5 and 23 h, respectively. All TB specimens were decalcified in ethylenediaminetetracetic acid, and then dehydrated and embedded in celloidin for sectioning. All sections were cut in an axial plane with a thickness of 20 μm and every 10th section was stained with hematoxylin and eosin.[11] All available, stained sections were examined under light microscopy and otopathologically described.

Three cases (one 65-year-old female with two ears and one female 70-year-old female with one ear) were chosen as age matched controls. These cases did not report known middle or inner ear disease, nor clinical history of vasculitis, autoimmune disease, or scleroderma, and each case had post-mortem time of less than 24 h. Cases were analyzed independently by two researchers trained in otopathology. Controls were fixed in 10% buffered formalin for 5 and 19.5 h. All TB specimens were decalcified in ethylenediaminetetracetic acid, and then dehydrated and embedded in celloidin for sectioning. All sections were cut in an axial plane with a thickness of 20 μm and every 10th section was stained with hematoxylin and eosin.[11] All available, stained sections were examined under light microscopy and otopathologically described. Incudomallear and incudostapedial joints quantitative measurements as well as the stria vascularis area findings were compared to these age-matched controls. For spiral ganglion neuron counts, results were compared to historical controls.

The protocol was approved by the human subjects committee of the Mass General Brigham institutional review board: Protocol #2019P003272.

2.2 | Otopathology review

All three TBs were examined using both qualitative and quantitative methods for middle and inner ear analysis as detailed below. Images from areas of interest across slides were obtained at 1.6×, 4×, and 20× magnification. Length measurements were made in ImageJ (http://rsbweb.nih.gov/ij/). Qualitative assessment of the TBs involved review and commentary on the overall appearance of the middle and inner ear structures compared to controls.

2.3 | Middle ear quantitative analysis

2.3.1 | Incudomallear joint length analysis

To assess for fibrous change along the ossicular chain, and specifically at the ossicular joints, a method established by Fausch and Röösli[12] was adopted to evaluate 25 defined histological parameters along the incudomallear joint (IMJ). The distances between the osseus (B-line) and the cartilaginous (Discus) surfaces of both ossicles as well as the cartilage levels (hyaline, calcified, and total) along the IMJ were measured. Of the 8–10 histologic sections through the IMJ in each TB, the single section with the longest distance between the synovial membranes resting on the lateral ligaments of the joint capsule

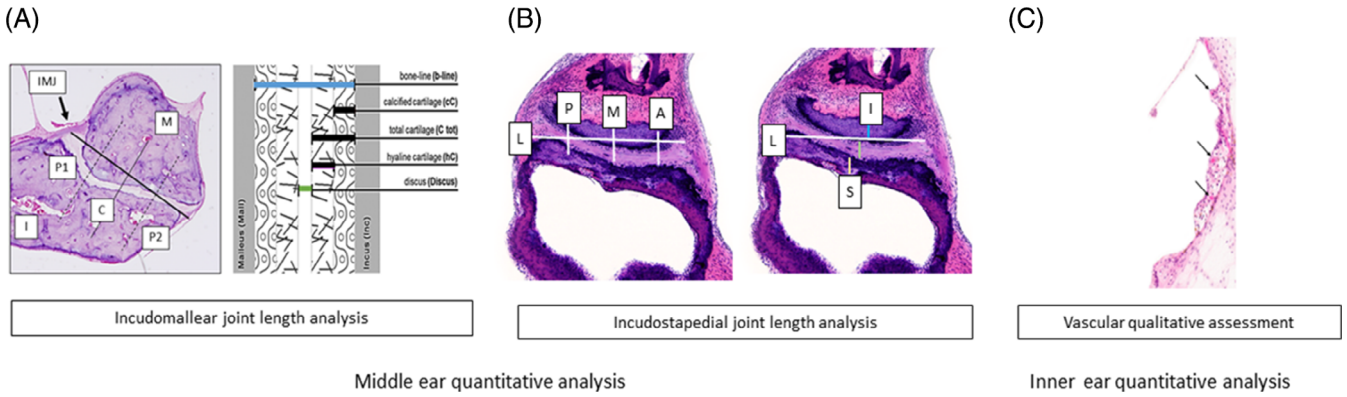

FIGURE 1 (A) Incudomallear joint length analysis (adapted from Fausch and Röösli[12]). (B) Incudostapedial joint length analysis (adapted from Ogando et al.[13]). IMJ: incudomallear joint. (C) Vascular quantitative assessment based on Kurata et al.[19] and Santos et al.[20] assessments.

(Longline) was selected for further analysis. The IMJ was subsequently quartered to visualize three equidistant positions at which eight measurements of the IMJ were made (Figure 1A).

2.3.2 | Incudostapedial joint length analysis

Histological analysis of the incudostapedial joint (ISJ) involved measuring seven defined histological parameters as per the method established by Ogando et al.[13] The anterior–posterior distance limited by the synovial membrane was defined as the longline whereas the measurement of lateral (incudal) to medial (stapedial) distance at the midpoint of the Longline was considered the Midline. The measurement of incudal to stapedial distance at 1/3 anterior of the longline was defined as the Ant-line and the measurement obtained of the incudal to stapedial distance at 1/3 posterior of the longline was the Post-line. The measurement obtained of the calcified cartilage attached to the incus at its midpoint was the Incus line and the measurement obtained of the calcified cartilage attached to stapes at the midpoint was the Stapes line. The measurements obtained of the articular disk between the osseous surfaces of the incus and stapes at the midpoint of the longline were the Meniscus line (Figure 1B).

2.4 | Inner ear quantitative analysis

2.4.1 | Spiral ganglion neurons count

The lengths of the cochlear duct and Rosenthal's canal were calculated, and the spiral ganglion neurons (SGN) population was quantified along the length of Rosenthal's canal based on previously described methodologies by Otte et al.[14] SGNs were counted in all available TB sections and the counts for each segment were totaled, multiplied by 10 to account for sections not studied, and multiplied by a correction factor of 0.9 to account for neurons lying at the interface between the sections that were at risk for being double counted.[15,16]

The SGN populations were then compared with historical controls.[11] The control SGC population is based on 100 ears from individuals with useful hearing who ranged from 9 to 90 years (mean, 61 years).[15,16]

2.4.2 | Hair cell quantification

The presence or absence of hair cells were evaluated and reconstructed via cytocochleogram. The inner and outer cells, which form the tunnel of corti were assessed.

Methods were assessed as described by Mahmud et al.[17] The quantification of hair cell loss was done by creating three bins for each turn: basal (0–16 mm), middle (16–22 mm), and apical (22 mm to apex).

2.4.3 | Stria vascularis area

The stria vascularis area was quantified using the Pauler method.[18] The area was determined by tracing along the surface of the marginal cells at the point of attachment of Reissner's membrane down to the base of the spiral prominence. The tracing continued along a line between the basal cells of the stria vascularis and spiral ligament prior to returning to the vestibular crest. The mid-modiolar plane provided the optimal section for completing these measurements, as the stria was cut perpendicularly at this level. This measurement was completed in four adjacent sections as well (two above and two below the mid-modiolar section) and calculated the average area in each turn. The measurements were compared to normal controls (Figure 1C).

2.4.4 | Vascular quantitative assessment

The vessels in each turn of stria vascularis were evaluated for wall thickness by measuring the length between the basal and the intimal layer of the artery, as formalized by Kurata (Figure 1C)[19,20] and compared to normal controls. The presence of luminal occlusion was

qualitatively documented and congestion of the artery walls without luminal occlusion, was recorded as inflammation.[20] Large arteries such as the petrous carotid was assessed under light microscopy, with measurements of vessel thickness, presence of fibrosis, and local inflammation described.

2.4.5 | Statistical analysis

Statistical analysis was performed using Prism Software (Graph Pad V 8.0). Categorical and quantitative variables were described as frequencies and mean ± SD. Demographic data and clinical and measurements were compared with Wilcoxon Rank-Sum Test. Statistical significance for all tests was set at $p < .05$.

3 | RESULTS

Results obtained were reviewed by two researchers. These were concomitantly discussed in each case review. Methods were assessed by researcher #1 and proved by researcher #2. An Alpha-Crohnbach for intervariability in all methods described were of 0.8.

3.1 | Clinical history

Patient 1 was a 66-year-old female with a diagnosis of diffuse cutaneous systemic sclerosis of unknown onset. Clinical notes indicate she presented with hearing loss and tinnitus at age 22 and had no prior history of middle ear disease or otologic surgery. Pure tone audiometry at age 63 revealed moderate bilateral down slopping sensorineural hearing loss without a conductive component. The patient died from intestinal obstruction presumed to be due to scleroderma at age 66. Post-mortem time was 3.50 h.

Patient 2 was a 71-year-old female with a diagnosis of diffuse cutaneous systemic sclerosis beginning at age 45. She presented clinically with hearing loss at age 58 without any other symptoms and had no history of middle ear disease or otologic surgery. Pure tone audiometry at age 58 revealed moderate to severe bilateral downsloping sensorineural hearing loss. No conductive component was identified on pure-tone audiometry. Patient died due to infectious endocarditis, presumed to be a complication of scleroderma. Post-mortem time was 23 h.

3.2 | Otopathologic analysis results

3.2.1 | Qualitative middle ear review

Scleroderma TBs demonstrated abnormalities of the middle ear, which were not observed in control ears. In the three scleroderma cases, no differences in ossification were evident at the malleus, but demineralization of the incus was found bilaterally in one patient (Figure 2A,B). One case revealed a complete obliteration of the space between the ossicles (Figure 2C) which was not seen in the controls (Figure 2D). A clear narrowing of the incudomallear joint space was observed in scleroderma cases (Figure 2A–C). In addition, narrowing of the incudostapedial joint space was seen in all the cases (Figure 3A–C) when compared to controls (Figure 3D). Evaluation of the stapes did not reveal any bony or connective tissue changes.

3.3 | Quantitative middle ear methods

3.3.1 | Incudomallear joint quantitative analysis

In ears with scleroderma, the distance between the cartilaginous surfaces of the malleus and incus was less than the controls at peripheral (Δ59 μm at P1, Δ54 μm at P2, and central Δ57 μm), locations ($p < .05$). Less hyaline cartilage was found along the malleus (Δ40.3 μm at P1, Δ44.9 μm at C, and Δ37.5 μm at P2) ($p < .005$) and incus (Δ55 μm at P1, Δ39 μm at C, and Δ49.7 μm at P2) ($p = .02$)

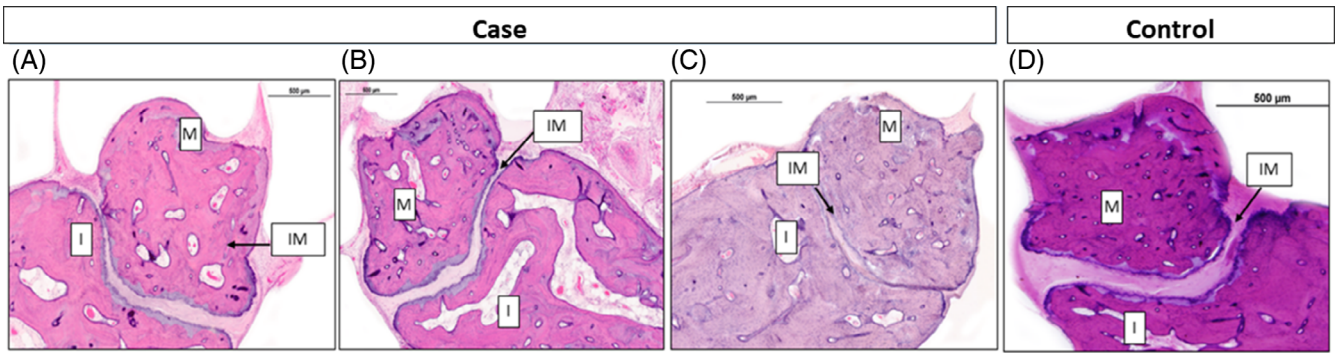

FIGURE 2 (A) A 66-year-old specimen, without any other rheumatologic condition, bone disorder, or surgical intervention, presented a diminished bone-to-bone space and cartilage along the IMJ right ear (4×). (B) Specimen with scleroderma during life with no surgical intervention or trauma, who shown demineralization of the ossicles and diminished bone-to-bone IMJ space (4×). (C) One of the specimens with scleroderma, who died at 71 years old who did not report during life trauma, surgeries, or any other metabolic or rheumatologic conditions shown a complete obliteration of the space between incus and malleus (4×). (D) Normal control (4×). I, incus; IMJ, incudomallear joint; M, malleus.

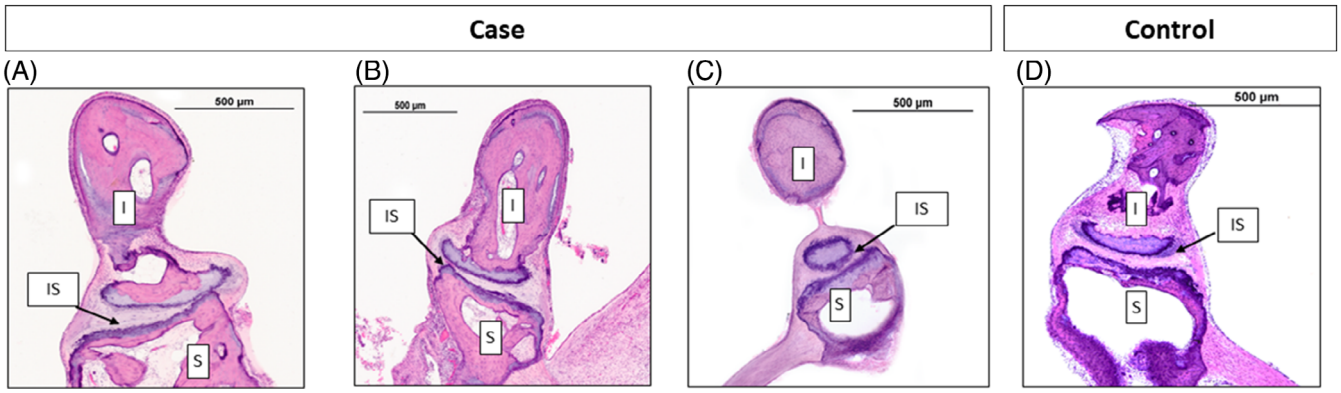

FIGURE 3 (A and B) Diminished bone-to-bone space at the ISJ with a clear narrowing at the distal incus were seen in both ears of one 66 years old specimen, reporting scleroderma during life (4×). (C) One ear of a patient 71 years old who was diagnosed with scleroderma during life shown a diminished space between distal incus and proximal stapes without any inflammatory response (4×). (D) Normal control (4×). ISJ, incudostapedial joint; S, stapes.

(Figure 2), whereas these findings were not observed in non-pathologic controls (Figure 2). Calcified cartilage compared to controls was less on malleus (Δ51 µm at P1, Δ66.5 µm at C, and Δ52.2 µm at P2) ($p = .03$). At incus, no difference was observed at calcified cartilage was found (Δ63.9 µm at P1, Δ58.6 µm at C, and Δ47.3 µm at P2) ($p = .42$). Narrowing of the discus was found in pathologic ears (Δ105 µm at P1, Δ108.5 µm at C, and Δ100.2 µm at P2) compared to controls ($p = .001$). Results are shown per each case in Table 1.

3.3.2 | Incudostapedial joint quantitative analysis

Less cartilage was found along the incus (Δ11.3 µm) ($p = .02$) and stapes (Δ18 µm) ($p < .04$) in scleroderma ears when compared to controls. Along the ISJ, the meniscus was narrower in the scleroderma cases (Δ9.2 µm) ($p = .024$). (Figure 3) than in non-pathologic specimens (Figure 3). Results are shown per each case in Table 1.

3.4 | Quantitative inner ear methods

3.4.1 | Spiral ganglion neurons quantification

Reduced population of spiral ganglion neurons was found in all cases of scleroderma with an average of 41% survival (range 29%–51%) compared to historic age-matched controls.[16] The loss along segment IV of the Rosenthal's canal was most notable in comparison to the remainder of the segments. Results are shown per each case in Table 1.

3.4.2 | Hair cell quantification

Scleroderma cases did not demonstrate notable loss of inner and outer hair cells and pillar cells along the length of the cochlea in the basal (segment I, which refers to 0–16 mm), middle turn of the cochlea (16–22 mm), and to the apex (22 mm to apex). Results are shown per each case in Table 1.

3.4.3 | Stria vascularis area

Compared to age-matched controls, scleroderma ears demonstrated a significant loss of strial area. These areas of decrease were found in the lower basal (440 ± 677 μm^2 vs. 6070 ± 1283 μm^2; $p = .05$), lower middle (4614 ± 606 μm^2 vs. 5947 ± 22 μm^2; $p = .0009$), upper middle (3859 ± 285 μm^2 vs. 6075 ± 1116 μm^2; $p = .02$), and apical (4214 ± 1432 μm^2 vs. 6550 ± 198 μm^2; $p = .04$) turns of the cochlea. No significant changes were found in the upper basal turn (5050 ± 342 μm^2 vs. 4058 ± 1908 μm^2; $p = .36$). Results are shown per each case in Table 1.

3.4.4 | Stria vascular vessel assessment

Qualitatively in the stria vascularis, the vessels in the lower basal turn were occluded in all examined ears (Figure 4A–C). This finding was not seen in any of the age-matched controls (Figure 4D). The middle turns of the cochlea did not demonstrate evidence of occlusion or inflammation in the three ears with scleroderma. However, inflamed vessels were found in the apical turn in the scleroderma cases. On the vascular quantitative assessment, vessels in the scleroderma cases had greater wall thickening in the lower basal turn of cochlea when compared to age-matched controls. Mean vessel wall thickness of the lower basal turn was 1.47 ± 0.23 µm in scleroderma ears compared with 1.31 ± 0.28 µm to age-matched controls ($p < .05$). No differences were found in the wall thickness of the vessels in the upper basal turn (1.52 ± 0.23 µm vs. 1.45 ± 0.15 µm; $p = .74$), lower middle turn (1.38 ± 0.27 µm vs. 1.29 ± 0.16 µm; $p = .65$), and upper middle turn (1.22 ± 0.15 µm vs. 1.08 ± 0.19 µm; $p = .43$), or in the

TABLE 1 Summary of quantitative measurements at the middle and inner ear.

		Incudomallear joint (mean per case compared to controls)					Incudostapedial joint (mean per case compared to controls)						
	Ear		Hyaline Cartilage (μm)	Calcified Cartilage (μm)	B-line (μm)	Discus (μm)		Cartilage (μm)	Meniscus (μm)	Spiral ganglion neurons (survival rate) %	Hair cells (loss)	Stria vascularis area (mean) (μm^2)	Strial vascular vessel assessment (mean) (μm)
Case 1	Right ear	Malleus	P1 Δ20.2, C Δ27, P2 Δ52.5	P1 Δ71, C Δ86.7, P2 Δ72.2	P1 Δ79, C Δ75, P2 Δ74	P1 Δ125, C Δ128.5, P2 Δ120	Incus	Δ20	Δ10	29%	No OHC and IHC loss	Lower basal 470 ± 707	Lower basal 1.77 ± 0.26
		Incus	P1 Δ75, C Δ54, P2 Δ69.7	P1 Δ83.9, C Δ78.6, P2 Δ67.3			Stapes	Δ14				Upper basal 5090 ± 383	Upper basal 1.72 ± 0.23
												Lower middle 4654 ± 606	Lower middle 1.52 ± 0.44
												Upper middle 3899 ± 285	Upper middle 1.40 ± 0.15
												Apical 4255 ± 1472	Apical 1.80 ± 0.95
Case 2	Right ear	Malleus	P1 Δ60.5, C Δ61.9, P2 Δ15	P1 Δ31, C Δ46.5, P2 Δ32.2	P1 Δ40, C Δ40, P2 Δ37	P1 Δ85, C Δ86, P2 Δ85	Incus	Δ8	Δ7.5	51%	No OHC and IHC loss in both ears	Lower basal 410 ± 647	Lower basal 1.18 ± 0.22
		Incus	P1 Δ20, C Δ15, P2 Δ20.1	P1 Δ43.9, C Δ38.7, P2 Δ27.3			Stapes	Δ11				Upper basal 5010 ± 307	Upper basal 1.28 ± 0.25
												Lower middle 4574 ± 606	Lower middle 1.16 ± 0.17
												Upper middle 3819 ± 285	Upper middle 1.18 ± 0.15
												Apical 4174 ± 1392	Apical 1.40 ± 0.70
	Left ear	Malleus	P1 Δ41, C Δ44.8, P2 Δ45	P1 Δ50, C Δ80.2, P2 Δ62	P1 Δ60, C Δ 45, P2 Δ59	P1 Δ105, C Δ107, P2 Δ103	Incus	Δ5	Δ10	43%	No OHC and IHC loss	Lower basal 470 ± 325	Lower basal 1.52 ± 0.25
		Incus	P1 Δ68, C Δ50, P2 Δ60	P1 Δ62.5, C Δ80, P2 Δ55			Stapes	Δ20				Upper basal 5050 ± 1463	Upper basal 1.40 ± 0.32
												Lower middle 4605 ± 587	Lower middle 1.42 ± 0.10
												Upper middle 3703 ± 276	Upper middle 1.20 ± 0.07
												Apical 4508 ± 1576	Apical 1.50 ± 0.01

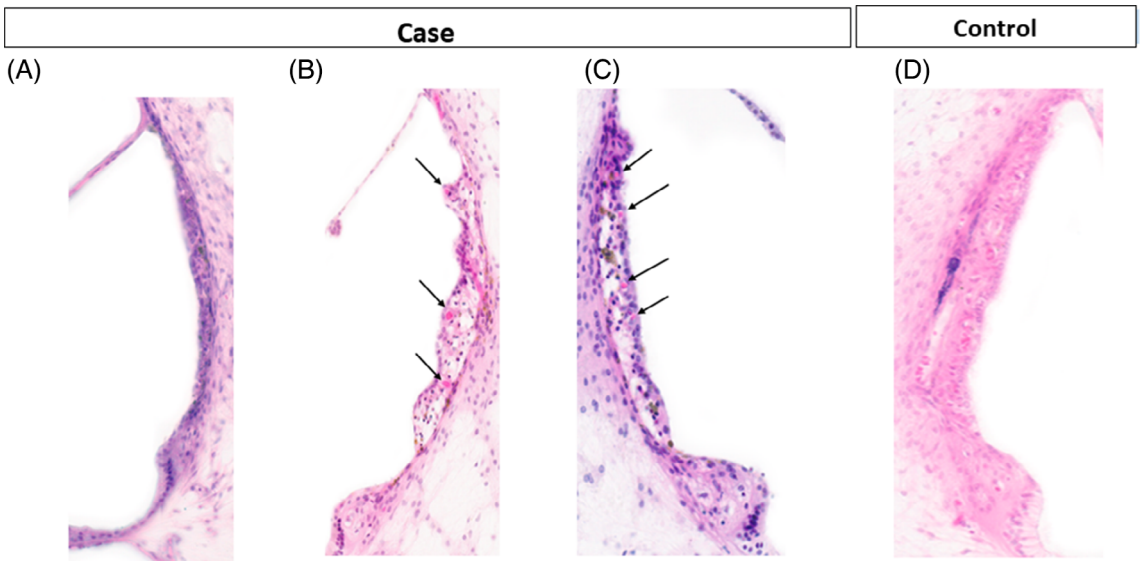

FIGURE 4 (A) Specimen of 66 years old diagnosed with scleroderma during life, who presented a moderate sensorineural hearing loss, shown a profound stria vascularis atrophy in the lower basal turn on its right ear (10×). (B) In the apical turn of this same patient, inflamed and occluded vessels were found (10×). (C) On the apical turns of one 71 years old specimen, without vascular disorders during life and scleroderma, occluded vessels were observed (10×). (D) Normal control (10×).

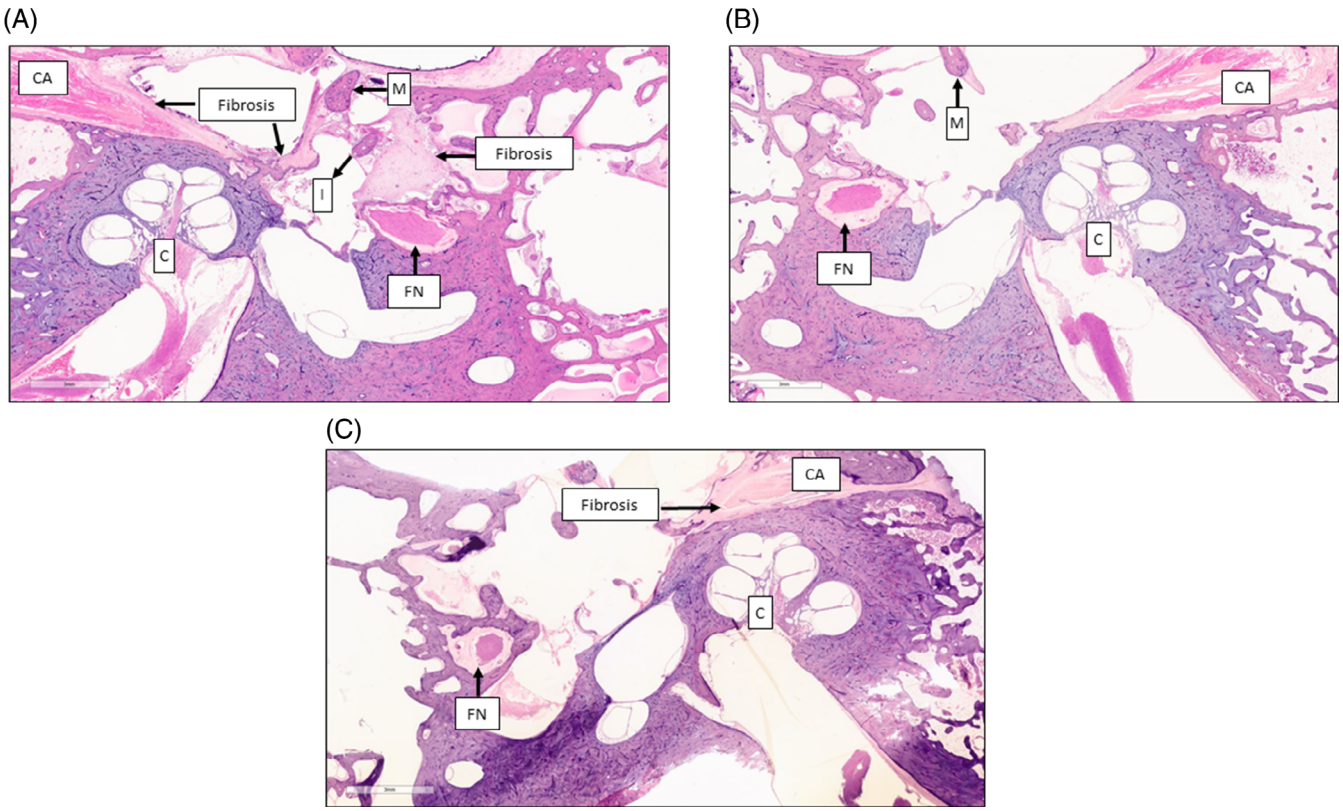

FIGURE 5 (A) A 66 years old patient presenting scleroderma during life, without any cardiovascular disorder, shown an increased thickening on the carotid artery and fibrosis within its layers, also a fibrous layer is seen between malleus, incus and part of facial nerve on its right ear (1.25×). (B) The contralateral ear of this 66 years old patient shown no presence of fibrosis in middle and inner ear instead of the diagnosis of scleroderma during life (1.25×). (C) Fibrosis was observed within the perivascular structures of carotid artery in one specimen of 71 years old who presented scleroderma before death (1.25×). C, cochlea; CA, carotid artery; FN, facial nerve; I, incus; M, malleus.

apical turn (1.60 ± 0.35 μm vs. 1.45 ± 0.21 μm; $p = .5$). Results are shown per each case in Table 1.

3.4.5 | Petrous carotid artery

The intimal layers of carotid artery in the petrous segment were found to be thickened in two of the three temporal bone, consistent with vasculitis and fibrotic deposition (Figure 5A). No atherosclerotic areas were seen within any of the three specimens.

4 | DISCUSSION

In this otopathology study, middle and inner ear changes were observed in patients with a history of diffuse cutaneous scleroderma during life. Middle ear findings revealed demineralization and narrowing of the incudomallear and the incudostapedial joints, however no conductive involvement in the available pure-tone audiometry was observed. A notable loss of spiral ganglion neurons and atrophy of the stria vascularis was noted in all three cases of scleroderma. We identify vasculitic changes in the stria including increased arterial wall thickness and luminal occlusion in the lower basal turns of the cochlea. We hypothesize that spiral ganglion neuronal losses may be potentially due to vasculitis changes to the blood supply to the cochlear nerve, or from the loss of the endocochlear potential due to the observed damage to the stria vascularis. Available audiograms demonstrate high frequency sensorineural hearing loss in both cases, which is consistent with inner ear histologic findings.

To date, only one otopathology case report has provided data about middle and inner ear involvement in scleroderma.[10] Our findings are consistent with those reported by Taleb and Linthicum—where spiral ganglion neuron loss, hair cell loss along the organ of Corti, and focal strial atrophy were reported. We also present quantitative evidence of vasculitic changes including luminal wall thickening in the stria vascularis and perivascular fibrosis in the surrounding small arterioles and venules as well as thickening of the intima of the internal carotid artery. Of note, we did not appreciate the same degree of hyalinization of the mastoid air cells, bone marrow spaces, endolymphatic sac as in this prior case.[10] This may be due to differences in disease progression, or potentially differences in contemporary management of scleroderma.

Although inner ear involvement is suspected to play a role in the pathogenesis of hearing impairment in scleroderma, less is known about the middle ear.[21] Herein, we provide several examples of middle ear involvement including narrowing of the incudomalleolar and incudostapedial joint spaces as well as a decrease in the ossicular cartilage levels throughout. Significant narrowing of both joint spaces were seen and may represent articular manifestations of the disease. We suspect these changes may be secondary to the alteration blood supply to the ossicles and cartilage in the joint space. From a sound conduction standpoint, such stiffening of the IMJ and ISJ may not impact middle ear transfer function, as no conductive component to the patient's hearing loss was identified. Further audiometric and tympanometric work is necessary to characterize pathology at the ossicular chain and address the possibility of accompanying conductive deficits.

Prior clinical studies have described a variety of otologic symptoms in scleroderma including hearing loss, hyperacusis, aural fullness, tinnitus, and vestibular disturbances.[22–24] Both patients in this study reported hearing loss and one reported tinnitus. On the audiometric testing, bilateral sensorineural hearing loss is the most common finding followed by mixed hearing loss.[24] These audiometric features are consistent with our findings of decreased spiral ganglion neurons in the cases of scleroderma. We also report vascular involvement of the stria vascularis in the lower basal cochlear turns, which is consistent with lesions reported in other vasculitides such as granulomatosis with polyangiitis.[25]

There are several limitations in this otopathologic study of scleroderma. First, the progressive, insidious onset of the disease makes it difficult to perform early audiologic evaluation and consistent monitoring over time is necessary to effectively capture the change in hearing with respect to the natural history of disease. Second, the incidence of scleroderma is low and major organ involvement leads to significant morbidity, especially in patients with pulmonary and cardiac involvement, and as such audiovestibular symptoms may go overlooked.[26] In addition, as prior study of scleroderma has revealed profound variability in its clinical presentation, we suspect that inner and middle ear findings may vary by individual and may not be as generalizable as other systemic diseases. Further prospective clinical studies are necessary to describe the tempo of auditory and vestibular involvement throughout the duration of disease in patients with scleroderma.

5 | CONCLUSION

Otopathologic analysis of three temporal bones with scleroderma revealed changes in the middle and inner ear when compared to age-matched controls. In particular, vasculitic and fibrotic changes were observed in the stria vascularis and may represent the source of spiral ganglion neuronal loss. Future research will contribute to the understanding of ear involvement in scleroderma and its variable clinical presentations.

CONFLICT OF INTEREST STATEMENT

None.

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