Congenital Atresia of the External Ear and Tinnitus: A New Syndrome

Abraham Shulman,1 Arnold M. Strashun,2 Barbara Goldstein,2 and Martin L. Lenhardt3

1Health Science Center at Brooklyn and 2Department of Otolaryngology, State University of New York, Downstate Medical Center, Brooklyn, and Martha Entenmann Tinnitus Research Center, Forest Hills, New York, and 3Virginia Commonwealth University, Richmond, VA

Abstract: Congenital atresia of the external ears and severe tinnitus has been reported by two patients to be contralateral to the atretic ear. The use of the nuclear medicine imaging technique of single-photon emission computed tomography (SPECT) of brain has demonstrated hypoperfusion in brain areas supplied by the middle cerebral artery on the side of the atretic ear. Ultra-high-frequency audiometry (UHFA) has revealed a bilateral loss of hearing greater than expected for the age of affected patients. Quantitative electroencephalography (QEEG) has shown a significant central nervous system electrical dysfunction correlated with the SPECT of brain findings. One case is reported in detail at this time. Completion of the medical audiological tinnitus patient protocol, including SPECT of brain, UHFA, and QEEG, accurately established the clinical tinnitus diagnosis of predominantly a central-type tinnitus, a clinical hypothesis that the medical significance of the tinnitus is a “soft” sign of cerebrovascular disease, and provided a rationale for treatment directed to a presumed ischemia of brain based on a receptor-targeted therapy targeted to the GABA-A receptor, resulting in significant tinnitus relief. Questions that have arisen include (1) the incidence of occurrence of hypoperfusion of the middle cerebral artery in congenital atresia patients; (2) implications and long-term consequences of this finding in this patient population for development of cerebrovascular disease; (3) brain plasticity for tinnitus relief (i.e., neuronal reprogramming, particularly in response to treatment recommendations for complaints of the cochleovestibular system in general and specifically for tinnitus); (4) the clinical significance of the UHFA thresholds of bilateral hearing loss greater than expected for the age of the patient; and (5) whether congenital atresia of the external ear may be part of a syndrome that includes hypoperfusion in brain areas supplied by the middle cerebral artery on the side of the atretic ear, ultra-high-frequency bilateral loss of hearing greater than expected for the age of the patient, and significant central nervous system electrical dysfunction. As far as we can determine, these findings, highlighted by the brain SPECT, have not previously been reported in patients with congenital atresia of the external ear.

Key Words: brain plasticity; congenital atresia; medical audiological tinnitus patient protocol; middle cerebral artery; quantitative electroencephalography; single-photon emission computed tomography

Our clinical experience since 1977 with tinnitus of the severe disabling type (subjective idiopathic tinnitus [SIT]) in more than 10,000 patients leads us to consider the establishment of a clinical accuracy for the diagnosis of tinnitus as the “key” to achieving tinnitus relief with therapeutic modalities now available. Multifactorial elements influence the clinical course of SIT and attempts for establishing tinnitus relief [1–3].

The completion of a medical audiological tinnitus patient protocol (MATPP) for SIT patients, with extensive testing of the cochleovestibular system, both peripheral and central, has been recommended to establish
(1) accuracy of diagnosis of tinnitus, (2) its medical significance, and (3) a rationale for treatment based on a correlation of structure and function [4–6].

The correlation of patients’ clinical history and otological and neurotological physical examination with the results of extensive cochleovestibular testing—including ultra-high-frequency audiometry (UHFA; 10–20 kHz), single-photon emission computed tomography (SPECT) imaging of brain, and quantitative electroencephalography (QEEG)—provided a basis for an accurate clinical tinnitus diagnosis (i.e., a predominantly central-type tinnitus [7]). We present these findings to support previous recommendations of extensive cochleovestibular and brain function testing to be completed in SIT patients. The clinical course of two cases of congenital atresia of the external ear and tinnitus supports this clinical experience. We report one case in detail.

Questions that have arisen highlight the implications of the incidence of hypoperfusion of the middle cerebral artery (MCA) in patients with congenital atresia of the ear and the long-term consequences for cerebrovascular disease and brain plasticity (i.e., neuronal reprogramming for complaints of the cochleovestibular system highlighted by the symptom of tinnitus). The UHFA results in two patients (i.e., identification of hearing loss greater than expected for the age of affected patients) supports previous recommendations for routine UHFA hearing testing in all patients.

The detailed single-case report includes (1) objective evidence (SPECT of brain) to support the hypothesis that the medical significance and etiology of the contralateral SIT in this patient with an ipsilateral congenital atretic ear is reflective of cerebrovascular disease; (2) objective evidence to support the recommendation for inclusion of UHFA, QEEG, and SPECT of brain in an MATPP; (3) the association of objective and subjective tinnitus in two cases of congenital atresia of the external ear; (4) a discussion of the long-term implications of SPECT of brain findings of hypoperfusion in brain areas of distribution of the MCA on the side of the atretic ear for patients with congenital atresia of the external ear; and (5) the results of a receptor-targeted tinnitus therapy [8].

As far as we can determine, these findings, highlighted by brain SPECT, have not previously been reported in patients with congenital atresia of the external ear.

**METHOD**

**General**

Patients with congenital atresia of the external ear and SIT completed the MATPP to establish an accurate diagnosis for the clinical type of tinnitus, to identify and treat factors influencing the clinical course of the tinnitus, and to establish a rationale for attempting tinnitus relief. The MATPP included recording patients’ neurotological and audiological history; a physical examination of the head and neck; and electrodiagnostic cochleovestibular testing, including UHFA, QEEG, and nuclear medicine imaging of brain with SPECT [1,3,4,9].

**History**

A right-handed white male, aged 39, was seen in initial consultation on November 30, 2004.

**Chief and Associated Complaints**

The patient’s tinnitus was described as a noise in “spells of increased intensity of a constant rumble in the left ear,” fluctuant intensity, and increasing annoyance within 1–2 months before his neurotological consultation on November 30, 2004. The rumble was described as a “hot-tub motor” with “spells” of increased intensity. In addition, the patient experienced an occasional perception of “water rushing” 4–5 days after a reduction in the rumble intensity and a “ring” in the left ear. He reported an occasional pulsation in the right postauricular region of the head. The annoyance included interference in communication, concentration, performance, and participation in social activities. Steroid therapy and a low-sodium diet received prior to November 30, 2004, resulted in a reduction of spells of the rumble. The goal of the patient for this consultation was to obtain information about the tinnitus complaint, to obtain tinnitus relief, to identify the medical significance of the tinnitus, to maintain hearing in the left ear in view of right hearing loss associated with congenital atresia in the right external ear, and a concern for the need for long-term prednisone therapy.

We informed the patient that although no cure was available for tinnitus at this time, the goals of the consultation were to attempt to establish a clinically accurate tinnitus diagnosis and the medical significance of the tinnitus and to attempt to provide tinnitus relief by medication alone or in combination with instrumentation.

We recorded the left-ear tinnitus intensity reported by the patient on a tinnitus intensity index (TII) and a tinnitus annoyance index (TAI). This scale ranges from 0 to 7 (0 = absent, 7 = worst), and the incidence of occurrence is expressed as a percentage:

<table>
<thead>
<tr>
<th>Time</th>
<th>Average</th>
<th>Best</th>
<th>Worst</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–4 years ago</td>
<td>3</td>
<td>0 (10%)</td>
<td>7 (25%)</td>
</tr>
<tr>
<td>1–2 months before November 30, 2004</td>
<td>3</td>
<td>0 (10%)</td>
<td>7 (25%)</td>
</tr>
<tr>
<td>January 25, 2005</td>
<td>0 (80–90%)</td>
<td>1 (35%)</td>
<td>6–7 (65%)</td>
</tr>
</tbody>
</table>

Associated complaints included increased left-ear hearing loss, fluctuant left-ear blockage, and weight loss of approximately 20 pounds. Also demonstrated were memory...
interference and increased tinnitus intensity reported with increasing left-ear blockage. Communication ability was normal. The mood-affect of the patient was one of anxiety and questionable depression.

Onset and Clinical Course of Tinnitus
Sudden-onset tinnitus in the left ear occurred while the patient was at work on May 5, 2004, in a standing position. The patient described his tinnitus as an intermittent rumble. Left-ear blockage preceded the tinnitus onset. A sensation of “vertigo” of approximately 24-hour duration described as a “drunk feeling” followed the rumble sensation. The patient reported spells of tinnitus since August 2004.

Tinnitus originally was reported as an intermittent “high-pitched ring” in the left ear at age 21–25 after exposure to loud music. The TII at that time was reported as best (0; 95%) and worst (7) for 3 days after noise exposure. The patient reported an increased frequency of occurrence within the last 3–4 years and an increased intensity (average TII, 3) after left-ear rumble.

The patient’s significant history included congenital atresia of the right external ear, presence of allergies, presence of hearing loss following noise exposure (including to firearms), and reconstructive surgery to the right external ear at age 6–7 years, and hospitalization for kidney stones. No history of hyperacusis, malaria, typhoid fever, or tuberculosis was elicited. A review of symptoms revealed anxiety, memory interference of 3 months’ duration, and kidney stone. The patient was a nonsmoker and drank alcohol socially. The clinical course previously outlined describes the patient’s tinnitus history. The patient experienced imbalance beginning May 2004. His medication regimen included prednisone, 25 mg/day; gabapentin, 1,800 mg/day; and Flonase nasal spray, one spray daily to each nostril.

The patient’s family history was positive for allergy and asthma.

The physical examination included evaluation of the patient’s general appearance and an external inspection, both of which were found to be satisfactory.

Assessment of the eyes, ears, nose, and throat was conducted. Ocular examination revealed symmetrical eyelids, clear conjunctivae, heterochromic irises, and equally reactive pupils without sign of spontaneous labyrinthine irritation. During otoscopic examination, the external left-ear canal was found to be satisfactory, whereas signs of reconstructive external right-ear surgery and right external canal atresia were seen. Mild scarring was found on the left tympanic membrane. A screening test revealed mixed moderate-severe right-sided hearing loss and mild left sensorineural hearing loss. Pneumotoscopy showed left mobility to be reduced. On nasal assessment, mild right septal deviation and mild right-to-left hypertrophy of the turbinates were seen. Posterior rhinoscopy revealed no mass. Throat evaluation also revealed no masses in oropharynx or hypopharynx. No cervical lymphadenopathy was seen. Auscultation of the left ear side overlying the external auditory meatus and in the postauricular fold discovered a bruit (November 30, 2004).

A complete neurotological specialty examination was performed. The fistula test proved negative on the left side. Among the tuning-fork evaluations, the Weber test showed right lateralization, whereas the Rinne test was positive on the left and negative on the right. Spontaneous eye signs were negative; tracking was abnormal (reduced); nystagmus was negative; and the postural stability, regular Romberg, sharpened tandem Romberg, and nuchal tenderness tests were normal, whereas the Fukuda stepping test revealed a central abnormality. Cranial nerve examination showed the eighth cranial nerve on both sides to be abnormal and the remaining nerves normal.

Tinnitus Evaluation
Site-of-lesion audiometry identified severe hearing loss, which was mixed and predominantly conductive, on the right. The sensorineural loss in the left ear was a mild, predominantly cochlear-type loss (Fig. 1). There was bilateral involvement of the central auditory pathway. The masking curve produced incomplete results. The auditory brainstem response assessment showed abnormal short-latency responses to broadband stimulation, which we interpreted as a latency increase: P1; P3–P5 interpeak ipsilateral right; P1–P3; P1–P5 ipsilateral left. UHF electrical-acoustic testing revealed sensorineural hearing loss greater than expected for the age of the patient (Fig. 2).

Otoacoustic emissions were consistent with left inner-ear dysfunction.

Electronystagmography (December 1, 2004) revealed no spontaneous nystagmus, positional nystagmus, or neck torsion. A negative bilateral Hallpike test was found. Right-sided gaze testing showed a right-beating nystagmus with ocular fixation suppression (OFS), downward gaze testing resulted in vertical up-beating nystagmus with OFS, and left-sided gaze testing revealed dysrhythmia with no OFS. Caloric tests were deferred.

A computed sinusoidal harmonic rotation test (December 1, 2004) revealed left labyrinthine asymmetry, normal saccadic eye movement, and normal OFS. Optokinetic eye movements were normal at low frequency. Results of a computed pursuit tracking test (December 1, 2004) were normal.

QEEG (December 1, 2004) demonstrated significant electrical dysfunction in the central nervous system (CNS) (Fig. 3).

Auscultation of the neck and ears demonstrated a left-ear bruit overlying the external auditory meatus and postauricular fold, which the patient described as a “rumble.”

Baseline SPECT of brain findings (November 2, 2004) included bilateral parietal lobes hypoperfusion, more dom-
nant on the right side, and bilateral mesial temporal hypoperfusion, more prominent on the right (Fig. 4). We considered magnetic resonance imaging (MRI) or magnetic resonance angiography (MRA) for further evaluation.

Neuroradiology suggested findings may represent vascular deficiency as opposed to cortical atrophy. The perfusion asymmetries were considered to reflect cerebral ischemia or atrophy or both. A Diamox stress test could differentiate between the two but was deferred due to allergy to sulfa. Clinically, an ischemia was presumed to be present based on our past SPECT of brain experiences with tinnitus patients of the severe disabling type [10]. The GABA-A receptor, with its inhibitory activity in brain function, exerts a neuroprotective action [8,11]. The findings of SPECT of brain in areas of distribution of the MCA were the basis for recommending various tests. Computed tomography (CT) scan of temporal bones (January 7, 2005) revealed right external canal atresia but no CT abnormality of the right bony labyrinth. A dilated right internal auditory canal (IAC) showed no enhancing mass, but the right demonstrated abnormal pinna with calcifications. The left temporal bone was normal.

An MRI of the brain with gadolinium (May 10, 2004) showed none of the following: acute infarct or intracranial mass lesion, cerebellopontine angle mass or abnormal enhancement within the IAC or inner ears bilaterally, or otomastoiditis. Sinusitis was seen bilaterally, although it was more pronounced in the maxillary than the ethmoid sinus.

MRI and MRA scans (December 16, 2004) demonstrated a small area of flow gap or narrowing in the proximal portion of the straight sinus. A partial obstruction in this area was suspected, although artifact may have accounted for this finding. The left draining system (transverse and sigmoid) was found to be dominant. MRA of the circle of Willis showed it to be normal.

Impressions

Hearing was within normal limits for language and speech in the left ear. Hearing loss was mixed moderate-severe and predominantly of the conductive type in the right ear and of a mild sensorineural type in the left, with a bilateral cochlear component and involvement of the central auditory pathways bilaterally (see Fig. 1).

Tinnitus was diagnosed to be predominantly of a central type in the left ear but to be subclinical in the right ear.
and to have a bilateral cochlear component. An objective tinnitus and presumptive secondary endolymphatic hydrops (SEH) was diagnosed in the left ear. Central vertigo was diagnosed and clinically considered to be compensated at this time. Physical examination was consistent with the diagnosis of chronic vasomotor rhinosinusitis, chronic catarrhal otitis media, and Eustachian tube dysfunction on the left.

Additional diagnoses included an anxiety syndrome and bilateral heterochromia of the irises. SPECT of brain (December 2, 2004) reported hypoperfusion in regions of interest in brain consistent with distribution of the right MCA (see Fig. 4).

Arteriovenous (AV) fistula, dural fistula, bilateral SEH, autoimmune inner-ear disease, hereditary sensorineural hearing loss, anterior internal cerebral artery (AICA) syndrome (left-sided), and cerebrovascular disease all were recommended to be ruled out.
Interval of Care

The patient was seen by his primary physician 1 day after tinnitus onset (i.e., May 6, 2004). The examination results were satisfactory and reported no elevation in blood pressure. Recommendations included a trial of meclizine and a Medrol Dosepak. The patient reported an improvement, which included elimination of the vertigo and left-ear blockage and a reduction in the tinnitus intensity.

The initial ear, nose, and throat (ENT) consultation took place 2 days later (May 8, 2004). The examination showed the patient to have no sign of infection. An audiometric test (May 8, 2004) reported no response in the right ear but left-ear hearing within normal limits for language and speech and a mild sensorineural hearing loss at 4 kHz. Recommendations included a continuation of the steroids and meclizine. MRI of the IACs and brain (May 10, 2004) demonstrated no cerebellopontine or IAC angle tumor and no mass, otomastoiditis, acute infarct, or intracranial mass lesion. Bilateral maxillary and ethmoid sinusitis were noted. The antinuclear antibody titer was reported as normal (May 11, 2004).

The patient made an emergency room visit (May 9, 2004) for evaluation of recurrent and increased intensity of the rumble and with concern about left-ear hearing. Results of a review of systems were reported to be satisfactory. Intramuscular Decadron (10 mg) and continued Medrol Dosepak and Ativan (1 mg) for anxiety were recommended.

Figure 4. SPECT of brain: bilateral parietal lobes hypoperfusion, more dominant on the right than on the left side, and bilateral mesial temporal hypoperfusion, more prominent on the right. Findings may represent vascular deficiency as opposed to cortical atrophy.
A neurological consultation was completed (June 22, 2004). The diagnoses included atypical left-ear tinnitus, congenital right-ear deafness, structural anatomy of the seventh and eighth nerve complexes to be normal right as reported on the MRI obtained on May 10, 2004. The patient reported prior tinnitus relief associated with steroid intake. Initial neurological recommendations included continuation of the steroids in a tapered dosage and a trial of Topamax and verapamil if the tinnitus complaint persisted or recurred. Additional workup was planned if the tinnitus complaint persisted. Persistence of the tinnitus was the basis of a trial of verapamil. A follow-up neurological visit (July 9, 2004) reported the trial of verapamil for 2–3 days to be associated with an increased tinnitus intensity and was stopped by the patient. The patient also reported “steroid side effects of interference in sleep and sweating.” However, he did report that tinnitus continued to be influenced by the steroid dosage (i.e., tinnitus relief). The steroid dosage was recommended to be tapered in lowering doses; Topamax was started at 25 mg/day and was increased to four pills daily. At a follow-up neurological visit (August 16, 2004), the patient described his tinnitus as “better overall,” although “spells occurred.” The steroid prednisone, 20 mg/day by mouth, was reported by the patient to be effective for tinnitus relief. Neurology recommended a continued reduction of steroids in a tapered dosage and continuation of Topamax at 100 mg/day.

Neurotological consultation and follow-up visits (November 30, 2004–December 7, 2004) clinically established the following diagnoses: tinnitus of a predominantly central type in the left ear, with a left cochlear component, and subclinical in the right ear. Left-sided SEH was noted. Hearing loss in the right ear was predominantly mixed and involved a cochlear component, whereas there was a predominantly cochlear-type hearing loss in the left ear within normal limits for language and speech (see Fig. 1). The air conduction UHFA identified thresholds of sensorineural hearing loss greater than expected for the age of the patient (Fig. 2). The neurotological workup and particularly the SPECT of brain identified significant bilateral perfusion asymmetries, greater on the right than on the left (see Fig. 4), highlighted by the perfusion asymmetry in regions of interest in brain areas of distribution of the right MCA. The QEEG showed significant CNS electrical dysfunction (see Fig. 3).

Neurotological recommendations (December 4, 2004) for attempting tinnitus control included general rules pertaining to diet, such as elimination of stimulants and caffeine, and use of ear protection from noise, and specific recommendations of a combined therapy via medication and instrumentation, differentiating between sensory and affect components.

For the sensory component, we recommended medication initially, followed by introduction of instrumentation. Instrumentation recommendations were deferred pending tinnitus relief results and would include (if necessary) a trial tinnitus masker and UHF acoustic stimulation and external electrical stimulation and tinnitus retraining therapy.

Specifically, medication included treatment of factors identified in the clinical history, physical examination, and cochleovestibular test battery (i.e., maintenance of normal aeration of the left middle ear, with trial nasal steroid, and repeat pneumotoscopy; treatment of SEH with a low-salt diet and trial diuretic [Dyazide], one tablet daily, if no medical contraindication existed). Follow-up with an internist was recommended to maintain stable blood pressure and to complete a metabolic battery with appropriate treatment as necessary. A neuroprotective drug protocol was recommended of a receptor-targeted therapy, gabapentin (100-mg tablet in one dose to be titrated based on the TII), and clonazepam (Klonopin, 25 mg at bedtime), if not medically contraindicated, the dose to be titrated based on the TAI. Intratympanic drug therapy was deferred at this time.

For treatment of the affect component, we recommended follow-up with neuropsychiatry and psychology for the anxiety syndrome complaint and for fear. We further advised that the patient consider Klonopin use if no medical contraindication existed.

Follow-up neurological consultation was recommended (1) to establish the neurological significance of the SPECT of brain report and of the central cochleovestibular test findings; (2) to follow up locally completion of the diagnostic evaluation of the right and left temporal bones, using repeat MRI of brain, MRA, and MRV; (3) to consult with a neurologist regarding reduction or replacement of the Topamax and steroid dosage with a receptor-targeted therapy (i.e., gabapentin and Klonopin) directed to the GABA-A receptor; and (4) to acquire a neurological opinion of the indication (based on the remaining workup) of the need, if any, for a cerebral angiogram.

Close observation was advised to include clinical consideration of gradual, progressive cerebrovascular disease. Progression complaints of hearing loss, tinnitus, vertigo, and ear blockage, alone and or in combination, were to be clinically considered a “soft” sign of gradual, progressive CNS disease. Any deterioration in the patient’s condition was to be assessed by an internist, a neurologist, or an ENT specialist, and should include audiometry in an attempt to maintain hearing.

Neurological followup evaluation (December 9, 2004) reported the tinnitus to be associated with “pressure pulsations” in the left head area. The patient described his tinnitus relief to be intermittent and tinnitus to be increasing in frequency and intensity when the steroid dose was reduced to 6 mg/day. He reported tinnitus relief with steroid doses ranging from 9 to 20 mg/day. The Topamax dose was at 200–250 mg/day. The neurotological recommendations were being followed.
Neurological follow-up on January 14, 2005, reported persistent pulsation tinnitus on the left side of the patient's head. A gradual replacement of the Topamax with gabapentin followed. Neuroradiological follow-up including CT scan of the temporal bones confirmed right external-ear canal atresia, a dilated right IAC, and a normal left temporal bone. MRI results were normal, but MRA “demonstrated a small narrowing or flow gap of the proximal portion of the straight sinus, which may indicate a partial obstruction or artifact in this area.” Dominance was reported of the left sinus drainage pattern as opposed to the right, but considered to be “probably not significant.”

A neurotological follow-up visit on January 25, 2005, reflected attempts of tinnitus relief from December 7, 2004, to January 25, 2005, as initially recommended and which, by cooperation between the neurologist and the patient, were completed. Specifically, the Topomax had been replaced with gabapentin, 1,200 mg/day, prednisone was reduced to 25 mg/day, and Klonopin dosage was 0.25 mg at bedtime.

The patient reported overall improvement—“water sound in back of head” gone since December 14, 2004—and described the quality of tinnitus frequency as “midrange electric motor” and “80–90% gone.” Location of the tinnitus—left ear and back of the head on the right side—was significant. Auscultation of the ear, head, and neck provided negative results for bruit. The complaint of ear blockage was reduced in the left ear, and no vertigo or balance complaint remained.

Recommendations included continuation of the nasal spray and the diuretic. Significantly, the Fukuda stepping test was markedly improved. We recommended that the patient continue medication and attempt to taper down the steroid from 25 mg/day consistent with maintenance of the reported tinnitus relief. The gabapentin dosage at 1,200 mg/day was to be increased to 1,800 mg/day as the steroid was reduced. We also recommended discussion with a neurologist of an angiogram to rule out AV malformation or dural fistula if the tinnitus complaint persisted or progressed. On January 25, 2005, the TII for the left ear revealed the following: absent (0), 80–90%; best (1), 35%; and worst (6–7), 65%.

During telephone communication with the neurologist (February 4, 2005), the patient reported that he was “doing OK,” although concern about steroid dependence persisted in order to maintain tinnitus relief. The patient had increased his steroid intake to 30 mg/day. Our recommendations were to increase gabapentin from 1,800 to 2,400 mg/day, to substitute Imuran for the steroid, and to discuss an angiogram to rule out AV malformation or dural fistula.

In a telephone communication with the neurologist physician (February 15, 2005), the patient reported tinnitus relief was being maintained. When tinnitus was present, the TII was 1–1.5 (occasional). Steroid dosage was 25 mg/day, and gabapentin was being administered at 1,800 mg/day. The patient reported no associated complaint of hearing loss, vertigo, ear blockage, nausea, headache, drowsiness, or blurring of vision.

At a follow-up visit with neurotology (March 8, 2005), the patient reported tinnitus relief of 15–20% and increasing periods of “ignoring the complaint,” with associated reduction in anxiety. The spells of the rumble were approximately one every 5–6 days. The ringing in the left ear was “not a problem.” A water sensation in the back of the head was reported to occur “after a spell.” The TII in the left ear was reported to be gone (0) 70–80% of the time and the worst (6) only occasionally. Our advice was to follow the neurological recommendation of Mobic, 7.5 mg bid, to assist in prednisone reduction, which was reported by the patient to be effective. The neurotological recommendation was to continue gabapentin at 1,800 mg/day, to taper Dyazide to one tablet on alternate days, to continue Mobic 7.5 mg bid, to continue maintenance aeration of the middle ears with Flonase nasal spray, and to continue follow-up with neurology.

During telephone communications with the neurologist (March 15, 2005–April 12, 2005), the patient reported continued increasing periods and degrees of tinnitus relief. Steroid reduction continued to 10 mg/day, gabapentin dosage was increased to 2,000 mg/day, Mobic remained stable at 7.5 mg bid, and the diuretic was to be continued on alternate days. The patient was experiencing no tinnitus “spells.”

In telephone communication between the neurologist and the patient (September 13, 2005), the patient reported tinnitus relief in excess of 90%, absence of any spells, occasional ear blockage prior to or accompanying the tinnitus, no imbalance, and occasional hyperacusis with tinnitus. Steroid was reduced to 2.5 mg/day. Ongoing medication included gabapentin, 2,100 mg/day, Flonase as needed, and Mobic tablets, 7.5 mg bid.

During further telephone communication with the neurologist (December 20, 2005), the patient reported tinnitus “rumble” relief in excess of 90%. The last steroid was taken at the end of November 2005. The patient continued to take gabapentin, 2,100 mg/day, and Mobic, 7.5 mg bid. The diuretic was discontinued. No tinnitus spells were reported, and tinnitus overall was described as being “no bother.” No significant ear blockage was noted on either side, although the patient did note occasional left-ear tinnitus, which he described as a “high-pitched ring.”

**DISCUSSION**

The etiology of the symptom of tinnitus, as described at the time of and following completion of neurotological consultation (November 30, 2004–December 7,
2004), is considered to have a chiefly vascular basis, reflecting insufficiency of the anterior and posterior intracerebral circulation, and to be a predominantly “soft” sign of gradual, progressive cerebrovascular disease. The tinnitus as described is clinically considered to be of a combined type. The rumble sound was objectively auscultated over the left external ear (November 30, 2004). The clinical history of spells of this tinnitus, which are influenced by steroids, is considered to be mainly cortical in location. The subjective tinnitus described as an occasional ringing is thought to be mostly cochlear in location. Factors that are identified in the clinical history and can influence (and have influenced) the clinical course of the ringing tinnitus included fluctuation in bilateral aeration of the middle ears, SEH identified in the left ear, noise exposure, and stress. The affect component of the tinnitus (i.e., the behavioral response of the patient to the presence of the tinnitus) was clinically manifested as anxiety and depression. The affect component is complex and reflective of the frustration of patients with the complaint of tinnitus and fear of loss of hearing in the left nonatretic ear.

The clinical history of the original tinnitus, described as an intermittent high-pitched ring in the left ear, is traced to age 21–25 and occurred after exposure to loud music (TII: best = 0 [95%] and 7 [3 days in duration after noise exposure]). We hypothesized this original tinnitus to have been clinically predominantly a cochlear type before May 2004 and considered it to have become since age 21–25 years subclinical in the left ear. We further hypothesized that a cerebrovascular factor, gradual in onset, “triggered” the subclinical left-ear tinnitus to manifest itself as spells of noise at the brain cortex, located in the head, and as a “tone” in the left-ear cochlea. We considered both auditory perceptions to be a clinical reflection of altered hemodynamics in cerebrovascular circulation. The etiology of a cerebrovascular factor in this patient is clinically supported by three findings: (1) the MRA report of a questionable small area of flow gap or narrowing in the proximal portion of the straight sinus, possibly resulting from a partial obstruction in this area, and dominance of the left sinus drainage pattern in the transverse and sigmoid sinuses; (2) SPECT of brain results highlighted by hypoperfusion in regions of interest supplied by the right MCA, with resultant ischemia (i.e., temporoparietal cortices greater on the right than on the left); and (3) an intermittent left-ear brut.

Within the limits of examination at this time, we hypothesized that the clinical course of the tinnitus as described is a reflection of a gradual alteration in the hemodynamics of the intracerebral circulation, highlighted at this time by SPECT of brain of hypoperfusion in regions of interest supplied by the right MCA. We further conjectured a resultant ischemia at brain cortex with noisy spells at the brain cortex owing to left cortical activation and a cochlear tone (as previously outlined), reflecting activation of a subclinical left-ear tinnitus, due to possible interference in AICA blood flow to the left cochlea. Alteration in underlying homeostatic mechanisms maintaining normal function of the fluid compartments of the blood-brain and blood-labyrinth barriers are hypothesized to have contributed to the left-ear SEH. The cortical activation is objectively demonstrated by QEEG (see Fig. 3). We considered this vascular hypothesis to be supported by the central cochleovestibular test findings (auditory brainstem response, QEEG), the SPECT of brain report (December 2, 2004), and the clinical response of the patient to treatment with steroids and antiseizure medication. Both medications have a GABAergic effect (i.e., increase in inhibition) [8].

We were sensitive to the concern of the patient over progression of left-ear hearing loss. Alteration in aeration of the middle ears secondary to Eustachian tube dysfunction or SEH (or both) identified in the left ear may result in fluctuation in hearing or progressive sensorineural hearing loss (or both). The UHFA findings of a loss of hearing greater than expected for the age of the patient may be a reflection not only of noise exposure in the past but, more significantly, together with the heterochromia of the irises, of a hereditary sensorineural hearing loss.

We considered a presumptive left SEH to be clinically related to alteration in homeostatic mechanisms between the fluid compartments of the brain and inner ear, with the resultant accompanying imbalance and reported left-ear hearing loss (May 5, 2004). The hearing in the left ear has been stable clinically and confirmed by audiometric testing since November 30, 2004, and when the patient was last seen (September 13, 2005).

We identified the complaint of right- or left-ear blockage in this patient as secondary to Eustachian tube dysfunction and left inner-ear dysfunction (i.e., left-ear SEH). When seen in initial neurotological consultation (November 30, 2004), the ear blockage had been predominantly located in the left ear and clinically related to left inner-ear SEH. The patient has reported no significant ear blockage since December 7, 2004. Normal Eustachian tube function control has been maintained with decongestant nasal steroid spray. The complaint of ear blockage will be recurrent in this patient, and accurate diagnosis will determine the selection of treatment. Close attention by patient and ENT specialists will improve the ability to maintain hearing and balance. The extensive medical evaluation, to the limits of examina-
tion, has excluded coagulopathy and autoimmune disease. Control of the foregoing factors highlighted by control of blood pressure is considered to provide an increased prognosis to maintain hearing and balance and tinnitus relief.

Acknowledged was the clinical history of a sudden onset of the tinnitus and the clinical history of tinnitus described as an increase in left-ear ringing 3–4 years ago. The report of interference in memory 3 months before November 30, 2004, was considered significant. To be considered at this time was a left-ear AICA syndrome associated with gradual, progressive cerebrovascular disease. We recommended neurological consultation follow-up to establish the neurological significance of these complaints and correlation with SPECT results, MRI reports, and central cochleovestibular test findings.

We recommended SPECT of brain in an attempt to improve the accuracy of the tinnitus diagnosis, to monitor the efficacy of modalities of therapy attempting tinnitus relief, and to provide a basis for neuroprotective drug therapy. The report of SPECT perfusion asymmetries in the brain was the basis for recommending a neuroprotective receptor-targeted therapy directed at the GABA-A receptor, in an attempt to treat a presumptive ischemia of the affected cortical areas. Recommendations included replacing the antiseizure medication topiramate (Topamax) with gabapentin (Neurontin) in combination with clonazepam (Klonopin). QEEG improved the accuracy of the tinnitus diagnosis for a central type of tinnitus. Also recommended was that complaints of progressing or deteriorating hearing loss, tinnitus, vertigo, and ear blockage, alone or in combination, be followed up by repeat ENT and neurological consultation in an attempt to maintain hearing and to maximize attempts at tinnitus relief.

In an attempt to establish a specific vascular etiology, to exclude AV dural fistula, AV malformations, and cisternal and venous sinus anomalies, we recommended MRI, MRA, and MRV, which were reported to be essentially normal. We also recommended an angiogram to exclude the presence of an AV dural fistula. We advised the patient to enter into this decision-making process if the tinnitus complaint persisted and the significance of the tinnitus complaint outweighed the incidence of potential complications of angiography.

In summary, we considered the tinnitus complaint in the left ear (as described on November 30, 2004) and its clinical course predominantly to be a “soft” sign of CNS dysfunction, on a vascular basis, superimposed on a preexisting sensorineural hearing loss. We considered the medical significance of the tinnitus symptom to be gradual, progressive cerebrovascular disease. Accurate tinnitus diagnosis by inclusion of peripheral and central tests of cochleovestibular function or dysfunction combined with tests of brain function (SPECT, QEEG) provided a rationale for tinnitus treatment that resulted in significant tinnitus relief, maintenance of hearing, and control of balance.

Questions

Questions that have arisen are highlighted by determining the incidence of hypoperfusion of the MCA in patients with congenital atresia and by the implications and long-term consequences of this finding for cerebrovascular disease and brain plasticity (i.e., neuronal reprogramming), particularly in response to treatment recommendations for complaints of the cochleovestibular system in general and specifically for tinnitus.

SPECT of Brain and Tinnitus

Is the reported SPECT of brain finding of hypoperfusion of the MCA in patients with a congenital atresia of the external ear an anomaly or a coincidence of occurrence [10–12]? What is the incidence of the hypoperfusion in brain areas of distribution of the MCA in patients with a congenital atresia of the external ear?

We consider to be clinically significant the objective demonstration of hypoperfusion in brain areas of distribution of the MCA on the side of the congenital atretic ear in two patients. Follow-up nuclear medicine imaging studies in the atretic ear population with and without tinnitus will determine its incidence of occurrence. We identified no cerebrovascular anomaly or malformation within the limits of examination (i.e., MRI of brain and CT of temporal bones). The MRA results (December 16, 2004) showed a small area of flow gap or narrowing in the proximal portion of the straight sinus, leading to suspicion of a partial obstruction or artifact in this area. We hypothesized that the original left-ear bruit was an objective tinnitus found on auscultation, reflecting predominance of the left vascular drainage. Furthermore, the predominance of the left-ear drainage may be reflected in a new syndrome of the atretic ear (i.e., atresia of the external ear; hypoperfusion of the areas of distribution of the MCA on the side of the atresia; and a sensorineural hearing loss, including the UHFA results greater than expected for the age of the patient).

Over the long term, the inclusion of nuclear medicine imaging of brain and follow-up in cases of congenital atretic ear wherein this finding was demonstrated will determine the significance of the clinical course of cerebrovascular disease and cochleovestibular complaints in atretic and nonatretic ears. Specifically, the questions to be answered with respect to the clinical course of cerebrovascular disease are whether the pa-
tient with a congenital atresia of the external ear is predisposed to cerebrovascular disease; whether the hypoperfusion is identified with nuclear medicine imaging of brain, when ischemia, atrophy, or both are present; and whether complaints of the inner ear highlighted by tinnitus are a soft sign of gradual, progressive cerebrovascular disease and a gradually increasing hearing loss in the nonatretic ear.

**Brain Plasticity (Neural Programming)**

*Is brain plasticity altered in the patient with a congenital atretic ear for tinnitus therapies hypothesized to occur at brain cortex [13–20]?*

We hypothesize that brain plasticity (i.e., neural programming at the cortex) explains the efficacy of some modalities of therapy attempting tinnitus relief (i.e., UHF stimulation) [21–24]. Nuclear medicine positron emission tomography imaging of brain before and after UHF stimulation revealed a correlation of metabolism of brain at the cortex, with residual neuronal function in the 10- to 20-kHz range of hearing [25]. Specifically, brain plasticity at the cortex was most effective with UHF acoustic stimulation when the integrity of the brain at the cortex was intact and the residual neuronal function in the 10- to 14-kHz range of hearing did not exceed audiometric thresholds (30–40 dB). Clinically, such tinnitus patients reported tinnitus relief as most effective and demonstrated hypometabolism at the cortex. This suggests that for the tinnitus population and, in particular, the atretic ear population, modalities attempting tinnitus relief (e.g., acoustic masking, electrical stimulation, UHF acoustic stimulation, or medication), the determination of the residual neuronal function in the 10- to 20-kHz range of hearing can be routinely established. In both atretic ear cases, the residual neuronal function in the 10- to 20-kHz range of hearing was greater than expected for the age of the patient, and the residual neuronal function in the 10- to 14-kHz range of hearing did not exceed audiometric thresholds (30–40 dB). The UHF stimulation was not effective for tinnitus relief.

**UHF Testing and Tinnitus**

*What are the UHFA thresholds in patients with congenital atresia of the external ear [26]?*

Electrical and air conduction UHF thresholds of hearing (10–20 kHz) in the two cases of congenital atresia of the external ear (in both the ipsilateral and contralateral ears) were greater than expected for the age of the patient. Additional considerations to explain differences in UHF thresholds include exposure to loud noise and a hereditary sensorineural hearing loss. For the future, routine hearing testing, including establishment of UHF audiometric thresholds in all patients with congenital atresia of the external ear, will provide an answer to the question of whether this observation is special for patients with congenital atresia of the external ear and will assist in the determination of its medical significance for hearing conservation in general.

**Identification of a UHF Sensorineural Hearing Loss**

*Is the identification of a UHF sensorineural hearing loss greater than expected for the age of a patient, particularly a tinnitus patient with a congenital atresia of the external ear, a sign of predisposition to the effects of noise exposure and gradually increasing sensorineural hearing loss?*

A review of the literature has not resulted in a definitive answer to this question. Follow-up studies by hearing conservation programs in general and specifically for the population of tinnitus patients with a congenital atresia of the external ear will provide answers to this question.

**SEH and Tinnitus**

*Is the finding of hypoperfusion in brain areas of distribution of the MCA in congenital atresia of the external ear a predisposition or a factor (or both) in the development of SEH [27–31]?*

We considered the SEH and tinnitus in the contralateral ear to be a sign of the effect or presence of a vascular anomaly or an alteration in the intracerebral circulatory pattern on the side of the brain contralateral and secondary to the hypoperfusion in brain areas of the MCA in the atretic ear. The results of MRI, MRA, MRV, and CT of the temporal bones were reported as normal.

The diagnosis of a delayed SEH in patients with tinnitus of the severe disabling type has been reported to be frequent and to influence the clinical course of tinnitus [27]. Alterations in homeostatic mechanisms controlling the normal hemodynamics of the intracerebral vascular and spinal fluid systems have been hypothesized to influence perilymph and endolymph production and function of the inner ear, resulting in a particular type of endolymphatic hydrops (i.e., the secondary [delayed] endolymphatic hydrops) [30,31]. It is considered clinically significant that the diagnosis of a secondary (delayed) endolymphatic hydrops was identified in two cases of congenital atresia of the external ear, in the tinnitus ear contralateral to the side of the atresia. The diagnosis of SEH was supported by the subjective complaint of ear blockage in the tinnitus ear and its reduction with diuretic therapy. The etiology of the SEH (delayed) in both cases of congenital atresia of the external ear is considered to be cerebrovascular. In addition, the alteration in the hemodynamics of the cere-
brovascular circulation has been hypothesized also to involve the AICA, a long-term effect that may include SEH.

Clinically, the tinnitus described as a ringing in the ear contralateral to the atresia is considered a soft sign of inner-ear dysfunction. It is considered to be a reflection of the SEH: the result of failure to reestablish "normal" homeostatic mechanisms controlling the hemodynamics of the intracerebral vascular and spinal fluid systems in response to hypoperfusion in the areas of distribution of the right MCA.

Steroid Therapy and Tinnitus Relief

What pathology in this tinnitus patient is reflected in the action of the drugs selected for attempting tinnitus relief (i.e., specifically steroids)?

Clinically, spells of subjective tinnitus were reportedly influenced by steroid dosage taken by mouth (i.e., the higher the steroid dose, the greater the reduction in tinnitus intensity and increased interval between tinnitus spells). We clinically identified four stages of tinnitus relief in the tinnitus case reported at this time: (1) initial minimal relief of tinnitus, demonstrated as reduced intensity, with combination therapy including the antiseizure drug Topamax and a steroid; (2) minimally increased tinnitus relief reflected as reduced intensity of tinnitus and reduced tinnitus spells, with increased dosing of steroid, gabapentin, and Klonopin, and elimination of Topamax; (3) moderately increasing tinnitus relief seen as reduction in spells and tinnitus intensity with increased dosing of gabapentin, maintenance dosing of Klonopin, and reduced steroid dosage; and (4) significant long-term tinnitus relief (elimination of spells) via maintenance dosing of gabapentin and Klonopin, introduction of Mobic, and elimination of the steroid.

In addition to therapy directed at factors identified as influencing the clinical course of the tinnitus, therapy directed to the GABA-A receptor is hypothesized to increase inhibition at the brain cortex and provide neuroprotection, with resultant increased tinnitus relief and reduction or elimination of the steroid. We considered the underlying pathologies to be inflammation and brain hyperactivity. The steroid is considered to modulate the GABA-A receptor inhibitory activity. A maintenance dose of Klonopin and a gradually increasing dosing of the antiseizure drug gabapentin replaced the Topamax. A mild reduction in steroid dosage accompanied the increased tinnitus relief. The introduction of Mobic—a nonsteroidal antiinflammatory agent, on a neurologist’s recommendation—in combination with gabapentin and Klonopin, was accompanied by elimination of the steroid and an increase in and maintenance of long-term tinnitus relief. Paradoxically, the “dependence” on the steroid for tinnitus relief may have been a sign of a steroid toxicity related to increasing stress before and during the initial course of the tinnitus.

Autoimmune Inner-Ear Disease and Tinnitus

What is the incidence of an autoimmune etiology in patients with sensorineural hearing loss?

The clinical history of the tinnitus in association with an alteration in hearing in the nonatretic ear introduces the consideration of autoimmune inner-ear disease. Within the limits of examination and supported by blood testing, we did not identify any evidence of autoimmune inner-ear disease.

Subjective and Objective Tinnitus

What is the incidence of occurrence of objective and subjective tinnitus in the tinnitus population and, in particular, in the tinnitus patient with an atretic ear?

In the patient in this report, the objective tinnitus was the rumble auscultated with the stethoscope at the left lateral neck overlying the external ear and left postauricular fold. We considered the subjective tinnitus clinically to be a combination of a predominantly central-type tinnitus (i.e., spells) with a cochlear component (i.e., ringing). Follow-up studies by hearing conservation programs in general and specifically for the population of tinnitus patients with a congenital atresia of the external ear will provide answers to this question.

Congenital Atretic External Ear as Part of a Syndrome

Is the congenital atretic external ear part of a syndrome that includes the MCA and a loss in the UHFs (10–20 kHz)?

The reported findings of nuclear medicine imaging (SPECT of brain), UHFA assessment of the loss of hearing in the UHFs (10–20 kHz), and QEEG in the evaluation of tinnitus in this patient form the basis for suggesting that the diagnosis of the congenital atresia of the external ear is part of a syndrome involving the intracerebral circulation (i.e., MCA on the side of the atretic ear), inner-ear bilateral (i.e., UHFs at 10–20 kHz) hearing loss, and SEH. Correlation of the findings of the neurootological workup with extensive testing of the cochleovestibular system (both central and peripheral and objective testing of CNS metabolic and electrophysiological responses) provided for accuracy of the tinnitus diagnosis and a rationale for achieving significant tinnitus relief.

CONCLUSIONS

SPECT of brain has demonstrated hypoperfusion in brain areas of distribution of the MCA on the side of an atretic ear. The medical significance of an objective
and subjective tinnitus of the severe disabling type, as demonstrated with SPECT of brain, may be a soft sign of gradual, progressive cerebrovascular disease. We recommend conducting a complete evaluation of the cochleovestibular system, both peripheral and central, including nuclear medicine imaging (SPECT of brain, UHFA, and QEEG), in an MATPP for SIT patients to improve the accuracy of the tinnitus diagnosis, to provide a rationale for treatment, and to monitor the clinical course of the tinnitus complaint.

A neuroprotective drug therapy strategy targeting the GABA-A receptor (RTT-GABA), for treatment of a severe, disabling, predominantly central-type tinnitus, with a clinical diagnosis of brain cortical ischemia based on brain SPECT, resulted in significant long-term tinnitus relief.

The incidence of hypoperfusion in brain areas of distribution of the MCA on the side of the atretic ear in patients with congenital atresia of the external ear remains to be established. We suggest that the findings of hypoperfusion in brain areas of distribution of the MCA on the side of the atretic ear and hearing UHF thresholds in the ear contralateral to the atresia are part of a syndrome in patients with congenital atresia of the external ear. As far as we know, the finding of hypoperfusion in brain areas of distribution of the MCA on the side of the atretic ear has not been previously reported.

ACKNOWLEDGMENT

The authors gratefully express their appreciation to the Martha Entenmann Tinnitus Research Center, Inc., for support of this educational and research effort.

REFERENCES


