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The clinical value of a thorough diagnostic evaluation for neurotologic complaints☆

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ABSTRACT

Purpose: Determine the clinical efficacy of comprehensive neurotologic testing in patients presenting with complaints of hearing loss, tinnitus and/or dizziness.

Methods: This is a retrospective analysis of 1170 consecutive charts of patients who presented between 1980 and 2013 with neurotologic complaints. Demographic data, chief complaint, diagnostic imaging, audiograms, and blood tests were evaluated.

Results: Retrospective analysis of 1170 patient charts was performed. 762/1170 (65%) patients presented with subjective hearing loss, 575/1170 (49%) with dizziness, and 657/1170 (56%) with tinnitus. Audiometric testing revealed hearing loss in 1059/1169 (91%) patients. 536/1120 (48%) patients had abnormalities on Magnetic Resonance Imaging, and 343/1087 (32%) on Computed Tomography imaging. Endocrine and immunologic testing revealed 108/1135 (9.5%) patients were hyperglycemic; 125/1124 (11%) patients had elevated TSH; 149/1141 (13%) patients had a positive ANA; and 82/1133 (7.2%) patients were positive for RF. 198/1083 (18%) of patients were positive for HLA-B35, 246/1083 (23%) for HLA-Cw4, 454/1083 (42%) for HLA-Cw7, and 747/1060 (70%) of patients had absent HLA-DR4. 112/1085 (10%) of patients were positive for anti-68kD antibodies and 154/936 (17%) for protein 0. Many patients were diagnosed with previously unrecognized medical conditions.

Conclusion: Comprehensive neurotological workup results in diagnoses that would go unrecognized otherwise, allowing patients to receive prompt treatment for medically important conditions, some of which may be causally related to their neurotologic complaints. However, the value of each study for routine testing of patients with neurotologic complaints remains controversial; and the evidence presented herein should help practitioners determine what studies should be included in their patient assessments.

1. Introduction

Neurotologic symptoms including hearing loss, tinnitus and dizziness account for a substantial number of presenting complaints to both primary care physicians [1] and otolaryngologists. Neurotologic complaints have many etiologies, some of which are treatable. Moreover, some conditions that cause hearing loss, tinnitus and/or dizziness may progress to cause worse neurotologic impairment or even death if not diagnosed and treated promptly. Otolaryngologists, otologists and neurotologists vary greatly in what they consider adequate, inadequate and excessive testing. Some are minimalists and rely almost entirely on physical examination. At the other extreme are specialists who order what many doctors would consider “too many tests”. Opinions within our specialty are strong, but unfortunately most of them are based upon

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anecdote rather than evidence. The senior author (RTS) joined a 35-year-old quaternary care otology practice in 1980 and established a quaternary care neurotology practice promptly as the first neurotologist in Philadelphia. Many of his patients already had consulted several excellent otolaryngologists. He established a goal of having no one he saw have a delayed or missed diagnosis. This resulted in a comprehensive test battery for any patient with sensorineural hearing loss, tinnitus and/or dizziness (other than young patients with classic benign paroxysmal positional vertigo and normal hearing who responded to repositioning movements). He also made a point of teaching his residents that this was not the only way to practice, or even the best, especially outside of a quaternary care setting. The routine evaluation included blood tests for many of the conditions associated with otologic dysfunction, including autoimmune inner ear disease (AIED) looking for patients who had early AIED before it caused classic symptoms and signs; magnetic resonance imaging (MRI) to investigate not only acoustic neuroma and other neoplasm, but also ischemia, demyelination and other pathologies; computed tomography (CT) to seek congenital malformation, mastoid disease, cochlear otosclerosis, internal auditory canal stenosis and other maladies; and electrophysiological tests of hearing and balance, when appropriate.

This study was designed to present on the outcomes of our comprehensive approach. This paper is not intended to advocate for or against comprehensive neurotologic assessment as we practice it. Rather, it is offered to present evidence regarding the results of the extensive studies obtained by a specialist who practices on the “too many tests” end of the continuum so that each practitioner can evaluate the data and determine whether any of these studies should be added to or removed from his/her neurotologic evaluation protocol.

2. Methods

This study was approved by the Institutional Review Board at Drexel University College of Medicine. A retrospective chart review was performed for demographic factors, chief complaint, history of present illness, otoscopic and other physical examination findings, laboratory results, electrophysiologic tests and imaging studies. Charts were identified using ICD-9 codes. Many charts were not available because patients had not been seen for > 7 years, and their charts had not been retained. 1170 patient charts were evaluated from patients who presented to the senior author (RTS) between 1980 and 2013 with neurotologic complaints including hearing loss, dizziness/vertigo and/or tinnitus. All patients for whom charts were available and who had undergone the tests prescribed were included. 645 females and 525 males were analyzed for the study.

Results of otoscopic examination, Histelberger's sign, Hennebert's sign, diplacusis, Weber test, Rinne test, gag, nystagmus and tandem Romberg testing were included. Audiogram results were reported as normal, or as demonstrating sensorineural, conductive, or mixed hearing loss. Results from auditory brainstem response (ABR), electronystagmography (ENG), MRI, CT, and single-photon emission computed tomography (SPECT) scanning were recorded. Results of central auditory processing studies were not included in this review because of the relatively small number of patients studied.

Laboratory studies obtained included fasting blood sugar (FBS), cholesterol, triglycerides, fluorescent treponemal antibody absorption (FTA-ABS), or an equivalent test, Lyme titer and Western Blot in some cases for diagnosis of Lyme Disease, T3, T4, thyroid stimulating hormone (TSH), ANA and titer when positive, rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), blood urea nitrogen (BUN), creatinine, Human Leukocyte Antigen (HLA) testing with particular attention given to HLA alleles B35, Cw4, Cw7, and DR4, and anti-cochlear antibodies (anti-68 kD antigen and myelin protein zero (p0)).

The percentage of abnormal results in our patient population was compared to the prevalence (or incidence when prevalence data were not available) of abnormal results in the general population, which was used as a control. These data were analyzed using Statplus:mac (AnalystSoft Inc., Walnut Creek, CA). Standard statistical analysis was used, including z-score and exact binomial test.

3. Results

3.1. Age

The average age of the patients at the time of evaluation was 52 years, with a standard deviation of 17 years, minimum age of 4 years and a maximum age of 92 years.

3.2. Presenting complaints

762/1170 (65%) patients presented with hearing loss. 575/1170 (49%) patients presented with dizziness, vertigo, or disequilibrium. 657/1170 (56%) patients presented with tinnitus. 148/1170 (13%) presented with otalgia, and 288/1170 (25%) presented with complaints of aural fullness. Many patients presented with more than one complaint.

3.3. Physical examination

291/1166 (25%) patients had an abnormal otoscopic exam. 190/1105 (17%) patients were found to have loss of sensation within the ear canal (Histelberger's sign). 65/1101 (6.0%) patients had dizziness (with or without ocular deviation) provoked by pneumotoscopy (Hennebert's sign) in the absence of clinical evidence of middle ear or mastoid disease. 166/999 (17%) patients were found by tuning fork to have diplacusis. 428/1040 (41%) patients lateralized on Weber testing, and 243/1034 (24%) patients were found to perceive bone conduction greater than air conduction when tested with a 512 Hz tuning fork (either bilateral or unilateral). 92/1118 (8.2%) patients exhibited decreased gag reflex. 44/1052 (4.2%) patients displayed nystagmus during physical examination (without Frenzel glasses). Tandem Romberg testing was found to produce at least mild unsteadiness and/or falls in 626 of 960 patients (65%).

3.4. Audiometric studies

1059 (91%) out of the 1169 patients who underwent audiogram evaluation were found to have hearing loss, leaving only 110 (9%) of patients with normal hearing. 870 (82%) of these patients were found to have sensorineural hearing loss (SNHL) only, in one or both ears, 34 (3.2%) patients had conductive hearing loss (CHL) only, in one or both ears, and 81 (7.6%) patients had mixed hearing loss (MHL) only, in one or both ears. 74 (7.0%) patients had a combination of diagnoses, such as SNHL in one ear and CHL in the other, SNHL in one ear with MHL in the other, or CHL in one ear with MHL in the other. Of the 1059 patients with documented hearing loss, 1025 had a component of SNHL (either SNHL alone, mixed hearing loss, or a combination of diagnoses). Of these, symmetric SNHL was seen in 293 (29%) patients and asymmetric SNHL (defined as a difference of 15 dB over three frequencies, 20 dB over two frequencies, or at least 25 dB at at least one frequency) was seen in 732 (71%). 189 (18%) patients had a component of CHL, while 121 patients had MHL (11%).

776 patients underwent tympanometry. 532 (69%) of patients displayed normal Type A tympanograms for at least one ear, while 113 (15%) had Type As and 107 (14%) with Type Ad. 59 (7.6%) patients had Type B tympanograms and 50 (6.4%) had Type C tympanograms. A single patient could have more than one type given testing in both ears.

Acoustic reflexes were obtained in 524 patients, 151 (29%) of whom recorded absent reflexes on at least one side.

Auditory brainstem response (ABR) audiometry was performed in 911 patients, 461 (50%) of whom had normal results. 234 (26%) patients were reported to have possible retrocochlear pathology, 184

Table 1
Abnormal laboratory results of selected comorbidities in presenting patients compared to the general population.

Laboratory test (abnormal value)	Abnormal no. (%)	National rates (%)	Difference (%)	p
Fasting blood glucose (≥110 mg/dL) (n = 1135)	108 (9.5)	9.4[a]	0.1	0.04
Hypercholesterolemia (≥240 mg/dL) (n = 1129)	153 (14)	29.8[b]	−16.2	NS
Hypertriglyceridemia (≥150 mg/dL) (n = 1120)	260 (23)	25.1[c]	−1.9	< 0.01
FTA (positive) (n = 1141)	27 (2.4)	0.0087[d]	2.3913	< 0.01
Lyme (positive) (n = 1140)	39 (3.4)	0.039[e]	3.36	< 0.01
Elevated TSH (> 3.04 mIU/L) (n = 1124)	125 (11)	4.7[f]	6.4	< 0.01
ANA (≥1:80) (n = 1141)	70 (6.1)	13.8[g]	−7.7	< 0.01
Rheumatoid factor (positive) (n = 1133)	82 (7.2)	10[h]	−2.8	< 0.01
ESR (> 20 mm/h) (n = 1113)	154 (14)	5[i]	8.8	< 0.01

[a] This is the rate of diabetes in 2015. CDC Division of Diabetes Translation. Diabetes public health resource. http://www.cdc.gov/diabetes/statistics/prevalence_national.htm. Accessed February 9, 2018.
[b] CDC Health, United States, 2016. https://www.cdc.gov/nchs/data/hus/hus16.pdf#055. Accessed February 9, 2018.
[c] Carroll MD, Kit BK, Lacher DA. Trends in Elevated Triglyceride in Adults: United States, 2001–2012. NCHS Data Brief. 2015;(198):1–8.
[d] This is the national rate for syphilis. CDC Division of STD Prevention. Syphilis. http://www.cdc.gov/std/stats14/tables/1.htm. Accessed February 9, 2018.
[e] Centers for Disease Control and Prevention. Lyme disease. http://www.cdc.gov/lyme/stats/chartstables/incidencebystate.html. Accessed February 9, 2018.
[f] Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab. 2002;87:489–499.
[g] Satoh M, Chan EK, Ho LA, et al. Prevalence and sociodemographic correlates of antinuclear antibodies in the United States. Arthritis Rheum. 2012;64:2319–2327.
[h] Westwood OM, Nelson PN, Hay FC. Rheumatoid factors: what's new? Rheumatology. 2006;45:379–385.
[i] This is the national rate of the Norwegian population. Wetteland P, Roger M, Solberg HE, Iverson OH. Population-based erythrocyte sedimentation rates in 3910 subjectively healthy Norwegian adults. A statistical study based on men and women from the Oslo area. J Intern Med. 1996 Sep;240(3):125–31.

(20%) had cochlear/conductive pathology noted, and 21 (2.3%) had both. 11 (1.2%) patient results that could not be assessed due to poor wave morphology.

3.5. Other studies

Electronystagmogram (ENG) was performed on 1010 patients, of whom 285 (28%) had normal results. 344 (34%) patients had abnormalities suggesting a central etiology, 350 (35%) had results suggestive of a peripheral etiology, and 31 (3.1%) had results suggesting both central and peripheral etiologies.

3.6. Laboratory results

A summary of the laboratory results as compared to national rates is provided in Table 1.

3.6.1. Fasting blood glucose (FBG)

1135 patient laboratory results were collected for fasting blood glucose. Of these, 108 (9.5%) patients were found to be hyperglycemic at the time of testing (defined as a FBG of over 110 mg/dL), 24 (2.1%) were found to be hypoglycemic (defined as a FBG under 70 mg/dL), and 1003 (88%) patients were within normal limits.

Of the 108 patients with elevated FBG (> 110), 59 (%) had a FBG of 125 or above. 35/59 (59%) did not have a known history of diabetes mellitus, while 19/59 (32%) of patients had a past medical history of diabetes. 5/59 (8.5%) patients had unknown past medical history of diabetes based on chart review.

3.6.2. Lipid studies

153/1129 (14%) patients had elevated cholesterol (> 240 mg/dL), while 362/1129 (32%) had borderline results (200–239 mg/dL). 108/1121 (9.6%) patients had elevated triglycerides (> 200 mg/dL), while 162/1121 (14%) had borderline results (150–199 mg/dL).

3.6.3. Thyroid studies

977/1072 (91%) patients had normal T3 levels (70–195 ng/dL). 64/1072 (6.0%) patients had elevated T3. 31/1072 (2.9%) patients had low T3.

984/1121 (88%) patients had normal T4 levels (0.9–2.4 ng/dL). 22/1121 (2.0%) patients had elevated free T4. 115/1121 (10%) patients had low T4.

973/1124 (87%) patients had normal TSH levels (0.3–3.04 mIU/L). 125/1124 (11%) patients had elevated TSH, and 26/1124 (2.3%) had low TSH.

A summary of the laboratory results of patients presenting with SNHL as compared to national rates is depicted in Table 2.

3.6.4. Inflammatory markers and autoimmune studies

149/1141 (13%) patients were found to have a positive ANA, 38 of whom had an ANA titer of 1:160 or greater. 31 patients found to be positive for ANA did not have titers reported. 82/1133 (7.2%) patients were positive for RF. 154/1113 (14%) patients had an elevated ESR (> 20 mm/h).

3.6.5. Renal studies

72/700 (10%) patients had elevated creatinine (Cr) (> 1.2 mg/dL).

3.6.6. Infectious

27/1141 (2.4%) patients had reactive FTA-ABS. Of the 27 reactive FTA-ABS, microhemagglutination assay for Treponema pallidum antibodies (MHA-TP) data were available for 7 patients, of whom 5 were negative and 2 were positive. 39/1140 (3.4%) patients were found to have positive results on Western Blot testing for Lyme disease.

3.6.7. Autoimmune Inner Ear Disease (AIED) studies

3.6.7.1. HLA allele typing. 198/1083 (18%) of patients were positive for HLA-B35. 246/1083 (23%) patients were positive for HLA-Cw4. 454/1083 (42%) of patients were positive for HLA-Cw7. 747/1060 (70%) of patients had absent HLA-DR4. 935/1090 (86%) of patients had at least one high-risk allele (present HLA-B35, Cw4, Cw7 and/or absent DR4). Only 141/1090 (13%) of patients were found to have no high-risk results upon HLA testing. Table 3 outlines HLA allele typing results in patients with SNHL.

3.6.7.2. Inner ear antibody testing. 112/1085 (10%) of patients were positive for anti-68kD antibodies. 154/936 (17%) patients were positive for p0 (anti-30kD antibodies). 246/1091 (23%) of patients were positive for anti-68kD antibodies and/or p0. 706/1091 (65%) of patients were negative for both anti-68kD antibodies and p0. 211/246

Table 2
Abnormal laboratory results of selected comorbidities in patients presenting with sensorineural hearing loss compared to the general population.

Test (abnormal value)	Abnormal no. %	National rate (%)	Difference (%)	p
Fasting Blood Glucose (≥110 mg/dL) (n = 1135)	56 (5.5)	9.4[a]	−3.9	< 0.01
Hypercholesterolemia (≥240 mg/dL) (n = 1129)	140 (14)	12.1[b]	1.6	0.01
Hypertriglyceridemia (≥150 mg/dL) (n = 1120)	237 (23)	25.1[c]	−2.0	0.01
FTA (positive) (n = 1141)	23 (2.2)	0.0087[d]	2.1909	< 0.01
Lyme (positive) (n = 1140)	32 (3.1)	0.039[e]	3.061	< 0.01
Elevated TSH (> 3.04 mIU/L) (n = 1124)	113 (11)	4.7[f]	6.3	< 0.01
ANA (≥1:80) (n = 1141)	60 (5.9)	13.8[g]	−7.9	< 0.01
Rheumatoid factor (positive) (n = 1133)	72 (7.0)	10[h]	−3.0	< 0.01
ESR (> 20 mm/h) (n = 1113)	137 (13)	5[i]	8.4	< 0.01

[a] This is the rate of diabetes in 2015. CDC Division of Diabetes Translation. Diabetes public health resource. http://www.cdc.gov/diabetes/statistics/prevalence_national.htm. Accessed February 9, 2018.
[b] CDC Health, United States, 2016. https://www.cdc.gov/nchs/data/hus/hus16.pdf#055. Accessed February 9, 2018.
[c] Carroll MD, Kit BK, Lacher DA. Trends in Elevated Triglyceride in Adults: United States, 2001–2012. NCHS Data Brief. 2015;(198):1–8.
[d] This is the national rate for syphilis. CDC Division of STD Prevention. Syphilis. http://www.cdc.gov/std/stats14/tables/1.htm. Accessed February 9, 2018.
[e] Centers for Disease Control and Prevention. Lyme disease. http://www.cdc.gov/lyme/stats/chartstables/incidencebystate.html. Accessed February 9, 2018.
[f] Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab. 2002;87:489–499.
[g] Satoh M, Chan EK, Ho LA, et al. Prevalence and sociodemographic correlates of antinuclear antibodies in the United States. Arthritis Rheum. 2012;64:2319–2327.
[h] Westwood OM, Nelson PN, Hay FC. Rheumatoid factors: what's new? Rheumatology. 2006;45:379–385.
[i] This is the national rate of the Norwegian population. Wetteland P, Roger M, Solberg HE, Iverson OH. Population-based erythrocyte sedimentation rates in 3910 subjectively healthy Norwegian adults. A statistical study based on men and women from the Oslo area. J Intern Med. 1996 Sep;240(3):125–31.

Table 3
sensorineural hearing loss and inner ear autoimmune laboratory testing.

Autoimmune marker	Percent (%)	Controls from Bowman et al. [6] (%)	Difference (%)	p
Present HLA-B35	17.7	15	2.7	< 0.01
Present HLA-Cw4	21.6	20	1.6	< 0.01
Present HLA-Cw7	38.8	21	17.8	< 0.01
Absent HLA-DR4	36.3	40	−3.7	< 0.01
Positive anti-68kD	10.1			
Positive P0	13.0			

This table depicts the results of HLA allele and inner ear antibody testing in patients with a component of SNHL. These results are compared to the control rate of positivity from Bowman et al. [6], a landmark study, which focused on those patients who presented with asymmetric, rapidly progressive SNHL.

(84%) of patients who were positive for anti-68kD antibodies and/or p0 also had at least one high-risk HLA allele. 96/1090 (8.8%) patients did not have high-risk results on HLA allele testing and were not positive on anti-68kD antibody or p0 testing. Table 3 outlines inner ear antibody testing results in patients with SNHL.

3.6.8. Imaging studies

3.6.8.1. MRI. MRI was obtained in 1120 patients. Findings are summarized in Table 4. We examined the relationship between patients presenting with SNHL and findings on MRI. Of the 1025 patients with a component of SNHL, 479 (47%) demonstrated abnormalities on MRI. Of the 735 patients with asymmetric SNHL, 347 (47%) demonstrated abnormalities on MRI. Table 5 details these findings. Of the 189 patients with a component of CHL, 94 (50%) demonstrated abnormalities on MRI.

3.6.8.2. CT. CT imaging was obtained in 1087 patients. Results of CT imaging are outlined in Table 4. Of the 1025 patients with a component of SNHL, 305 (30%) demonstrated abnormalities on CT imaging, while 102/198 (52%) patients with a component of CHL had abnormalities. Table 5 details these findings.

3.6.8.3. SPECT. 185/754 (25%) of patients who underwent SPECT

Table 4
MRI and CT imaging results as listed by diagnosis.

MRI results (n = 1120)	No. (%)	CT results (n = 1087)	No. (%)
Normal	584 (52)	Normal	744 (68)
Abnormal	536 (48)	Abnormal	343 (32)
Tumors, masses, etc.		**External ear**	
Acoustic neuroma/schwannoma or CPA mass	68 (6)	Otitis Externa	2 (0.2)
Enhancement of CN VII or VIII	13 (1)		
Meningioma	11 (1)		
Glomus tumor	1 (0.1)		
Mass, tumor or cyst not listed above, e.g. pituitary adenoma, arachnoid cyst	44 (4)		
Vascular		**Middle ear**	
White matter changes, including ischemia	216 (19)	Cholesteatoma	41 (4)
Vascular loop	27 (2)	Tympanic membrane pathology	34 (3)
Infarct	10 (1)	Ossicular chain pathology	23 (2)
High riding jugular bulb	2 (0.2)	Otosclerosis	18 (2)
		Stapes prosthesis malposition	4 (0.4)
Other		**Inner ear**	
Mastoiditis or mastoid disease	85 (8)	Semicircular canal dehiscence	26 (2)
Cholesteatoma	5 (0.5)	IAC widening, enlargement or changes	25 (2)
Sinus pathology	33 (3)	Cochlear aqueduct enlargement	4 (0.4)
Paget's Disease	1 (0.1)	Vestibular aqueduct enlargement	3 (0.3)
Petrous apex pathology	10 (0.9)		
		Other	
		Mastoid pathology	134 (12)
		Mass	16 (2)
		Tegmen dehiscence	13 (1)
		Traumatic fracture	3 (0.3)
		Petrous apex pathology	12 (1.1)
		Vascular loops	3 (0.3)

Table 5
MRI and CT imaging results in relation to hearing loss, tinnitus and dizziness.

MRI imaging findings	SNHL (n = 1025) no. (%)	Asymmetric SNHL (n = 735) no. (%)	Tinnitus (n = 657) no. (%)	Dizziness (n = 575) No. (%)
Vascular loop	18 (1.8)	9 (1.2)	14 (2.1)	12 (2.1)
CN VII/VIII enhancement	11 (1.1)	8 (1.2)	6 (0.9)	8 (1.4)
White matter changes/ischemia	198 (19)	136 (19)	112 (17)	104 (18)
Infarct	8 (0.8)	6 (0.8)	2 (0.3)	6 (1.0)
CPA mass (including schwannoma/acoustic neuroma)	62 (6.0)	56 (7.6)	41 (6.2)	41 (7.1)
Mass/cyst/tumor not otherwise discussed	38 (3.7)	25 (3.4)	23 (3.5)	18 (3.1)

CT imaging findings	SNHL (n = 1025) no. (%)	Asymmetric SNHL (n = 735) no. (%)	CHL (n = 189) no. (%)	Tinnitus (n = 657) no. (%)	Dizziness (n = 575) no. (%)
Otitis media	5 (0.5)	5 (0.7)	6 (3.2)	1 (0.2)	2 (0.4)
Cholesteatoma	36 (3.5)	33 (4.5)	23 (12)	21 (3.2)	16 (2.8)
Mass	15 (1.5)	14 (1.9)	6 (3.2)	7 (1.1)	4 (0.7)
Petrous apex pathology	10 (1.0)	10 (1.4)	0 (0)	8 (1.2)	10 (1.7)
Otosclerosis	16 (1.6)	10 (1.4)	9 (4.8)	10 (1.5)	7 (1.2)
Stapes prosthesis malpositioning	2 (0.2)	2 (0.3)	4 (2.1)	2 (0.3)	3 (0.5)
Ossicular chain pathology	21 (2.0)	14 (1.9)	15 (7.9)	11 (1.7)	9 (1.6)
Tympanic membrane pathology	31 (3.0)	25 (3.4)	14 (7.4)	15 (2.3)	9 (1.6)
Tegmen dehiscence	9 (0.9)	8 (1.1)	6 (3.2)	6 (0.9)	7 (1.2)
Semicircular canal dehiscence	21 (2.0)	16 (2.2)	2 (1.1)	12 (1.8)	13 (2.3)
Mastoid pathology	117 (11)	91 (12)	58 (31)	71 (11)	52 (9.0)
Cochlear aqueduct enlargement	4 (0.4)	4 (0.54)	0 (0)	3 (0.5)	2 (0.4)
Vestibular aqueduct enlargement	3 (0.3)	3 (0.41)	1 (0.5)	2 (0.3)	3 (0.5)
Vascular loops	3 (0.3)	2 (0.27)	0 (0)	2 (0.3)	2 (0.4)
Traumatic fracture	2 (0.2)	1 (0.14)	0 (0)	0 (0)	2 (0.4)
High riding jugular bulb	16 (1.6)	12 (1.6)	4 (2.1)	9 (1.4)	8 (1.4)
IAC widening, enlargement or changes	23 (2.2)	20 (2.7)	4 (2.1)	12 (1.8)	9 (1.6)

imaging were found to have decreased perfusion.

3.6.9. Chief complaints as they relate to imaging findings

3.6.9.1. Hearing loss. Of the 762 patients who presented with hearing loss as a complaint, 359 (47.1%) were noted to have abnormalities on MRI and 246 (32%) on CT imaging. Details related to hearing loss and imaging results are outlined in Table 5.

3.6.9.2. Dizziness, vertigo, disequilibrium. Of the 575 patients who presented with dizziness, vertigo or disequilibrium, 262 (45.6%) had abnormalities on MRI and 154 (27%) on CT imaging. These are detailed in Table 5.

3.6.9.3. Tinnitus. Of the 657 patients who presented with tinnitus, 282 (43%) had abnormalities on MRI and 185 (2.8%) on CT imaging. These are summarized in Table 5.

3.7. Cost/benefit analysis

Cost analysis has been omitted from this paper because data to calculate a meaningful and valid comparative cost/benefit analysis are not available. More pertinent to this work is the reality that the patients evaluated by the senior author often already had undergone evaluation elsewhere, and their diagnoses remained unclear or incompletely defined. Hence, comprehensive evaluation was considered medically necessary and by extension, cost effective. Thus, calculating the cost of tests, and the costs of negative tests for each positive test, provides only part of the picture and does not analyze the cost to society of diagnoses that would have been delayed or missed if comprehensive evaluation had not been performed. Finding a tumor when it is small enough to save hearing, or at least small enough to minimize the risks of major surgical complications, might well be cost-effective and beneficial not only for the patient, but also for his/her employer and for society in general, though possibly not the health insurance provider based on the number of negative tests obtained to find each positive study. There are almost no data available to determine the human or economic toll of delayed diagnoses of acoustic neuromas, syphilis, Lyme disease, autoimmune disease or other abnormalities diagnosed in our patient cohort. These complicated considerations are the reasons that we believe including cost/benefit analysis in the paper would be misleading. A long-term, prospective, multi-institutional study of patients undergoing evaluations of various complexity (ranging from minimal evaluations performed in some centers to the comprehensive evaluation performed at centers such as ours) would be necessary to determine the true costs of performing or not performing comprehensive testing. We encourage such an inter-institutional research endeavor.

4. Discussion

There are many causes for neurotologic complaints, some potentially treatable. Metabolic disturbances that might cause hearing loss and tinnitus include hypertension, hypercholesterolemia, diabetes and thyroid disease. Elevated blood lipids may be a cause of inner ear malfunction [2]. Elevated triglycerides particularly have been associated with reduced hearing [3], and hypercholesterolemia is potentially associated with auditory dysfunction [4]. Metabolic syndrome, which includes hypertension, hyperglycemia, hypertriglyceridemia and abdominal obesity, was found to be involved in the development of vertigo in males, and also may be a risk factor for vascular vertigo (e.g. vertebral basilar insufficiency) in males [5].

In our experience, immunologic studies, specifically HLA and inner ear antibody (anti-68kD and p0 [anti-30kD]) testing have been important components of a comprehensive autoimmune workup for hearing loss that might be caused by AIED [6–8]. Ultimately, AIED is a clinical diagnosis made on the basis of symptoms and signs and supported by laboratory data and treatment response. Abnormal testing, e.g. positive anti-68kD antibody or p0 and high-risk HLA alleles, are suggestive of autoimmune pathology. Negative laboratory results are less helpful. We have found confirmed AIED (including response to treatment) in patients with all audiometric patterns, including normal

hearing. Some patients with AIED have presented with dizziness or tinnitus in the absence of hearing loss and have experienced symptom relief with corticosteroids and/or cytotoxic drugs after blood tests assisted with establishing the diagnosis. Diagnosis in this group of patients probably would have been missed if testing were limited to patients with classic AIED symptoms of sudden or rapidly progressive, asymmetric sensorineural hearing loss. In cases of hearing loss, dizziness and/or tinnitus, FTA-ABS should be considered as a screening tool for otologic syphilis [6,9], and etiologies such as Lyme disease should be investigated. Although a diagnosis of suspected otologic syphilis has often prompted cerebrospinal fluid (CSF) analysis, lumbar puncture is not necessary, as treatment for otologic syphilis exceeds that which is required to treat tertiary neurosyphilis; and treatment can be instituted without CSF sampling [9].

Additional evaluations may provide information not found with blood testing; auditory-vestibular testing and radiological studies may reveal a cause for neurotologic complaints [10]. SPECT [11,12] is a useful tool, in addition to MRI and CT, for determining the site of a lesion and central etiologies of hearing loss, dizziness and tinnitus. In quaternary practice, patients commonly are referred after failing to benefit from more limited evaluation or treatment. Therefore, the practitioner must consider the limitations of previous evaluation, which may necessitate an expanded approach to assessment and consideration of a widened differential diagnosis including pathologies often overlooked as etiologies for neurotologic complaints, including ischemia [11,12] and many other conditions.

As found in this study and in a recent paper evaluating vocal fold movement disorders [13], a comprehensive workup can produce a considerable amount of useful diagnostic information. The neurotological workup has largely remained unchanged at the senior author's (RTS) practice over the period of time reviewed, with the exception of the addition of new tests (such as those for autoimmune inner ear disease) as they became available. The information garnered from a comprehensive workup may affect the diagnosis and treatment of patients who present with neurotologic complaints. Negative, or normal, results may be as beneficial as those that reveal abnormalities, often providing important insight and allowing narrowing of the differential diagnosis. Furthermore, the diagnostic data gleaned from a comprehensive workup may play an important role in the systemic health of the patient. Patients not previously diagnosed with elevated fasting glucose or hyperlipidemia may be identified with these problems, thereby allowing for early referral for care, even if the maladies diagnosed are not causally related to the neurotologic complaint in a specific individual. Additionally, many of our patients were found to have autoimmune abnormalities. It appears that any patient, not just those patients with sudden or profound, rapidly progressive sensorineural hearing loss, may benefit from testing for AIED and possibly other autoimmune conditions. Testing for HLA typing, anti-68kD and anti-30kD antibodies in patients without the classic symptomatology of AIED may prove to be beneficial, as seen in our data, as there was a high rate of positivity. We suspect that such early cases of AIED are missed commonly because most practitioners do not consider or test for AIED until the disorder is more advanced. In our experience, mild, early AIED responds to treatment better than far advanced disease; and we believe that recognizing the disorder early is worthwhile.

The association of positive laboratory results and diagnostic studies with SNHL needs to be interpreted with caution given that most of the population studied has hearing loss and was selected due to neurotological complaints. The predictive value of a test, positive or negative, is dependent on the prevalence of the disease, as well as the sensitivity and specificity of the test. Patients with known diagnoses of diabetes, hypercholesterolemia, hypertriglyceridemia and/or autoimmune disease should undergo a more focused laboratory evaluation. Several studies (fasting glucose, hypercholesterolemia, hypertriglyceridemia, ANA and RF) had rates of abnormal results that were similar to or lower than the general population, a finding that might support selective ordering of these studies rather than their routine inclusion as has been our practice. The role of tests such as the ANA [14] that have rates of abnormal results lower than the general population and poor positive predictive value warrants reevaluation, although there is evidence that a positive ANA with a speckled pattern is associated with autoimmune inner ear disease in those without other systemic autoimmune disease [15]. The same may be said of Lyme disease testing, as even in endemic areas, Lyme disease testing has been shown to have a poor predictive value [16]. The testing for syphilis and anti-68 kD antibody, whose testing regimens both have high positive predictive values, would be supported using the same rational [17].

5. Conclusions

Comprehensive neurotological workup results in diagnoses that would otherwise go unrecognized. Diagnosing and treating potentially progressive conditions such as syphilis and AIED, as well as other systemic autoimmune and metabolic diseases, may prevent not only progressive neurotologic symptoms, but also adverse systemic health effects. We believe that recognizing such conditions is valuable whether or not they are causally related to the neurotologic complaints. However, the decision about what studies to include in or omit from the evaluation of patients with neurotologic complaints should be guided by an understanding of local disease prevalence, as well as the positive and negative predictive value of the tests performed. We hope that the data presented in this study are helpful in basing as many of those judgments as possible on evidence rather than anecdote.

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