

Sudden Hearing Loss and Autoimmune Inner Ear Disease

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Abstract

This case report describes the audiologic and medical diagnostic evaluations, results, and treatment options in a patient with a classic presentation of immune-mediated sensorineural hearing loss, commonly called autoimmune inner ear disease (AIED). It reviews findings of the basic battery, immittance audiometry, transient otoacoustic emissions, and auditory brainstem response measures and medical findings over more than 2 years. AIED generally causes asymmetric bilateral sensorineural hearing loss with atypical configuration. Although hearing loss is generally fluctuant, the overall pattern is usually rapid progression, particularly in the absence of early medical intervention. Word recognition is usually disproportionately poor. In our case, otoacoustic emissions and auditory brainstem responses suggest both cochlear and retrocochlear involvement and may initially appear to be inconsistent with pure-tone thresholds. Audiologists must be familiar with AIED because early identification is critical. Additionally, an immunologic basis may be a factor in other disorders, including many cases of Meniere's disease.

Key Words: Auditory evoked potentials, autoimmune inner ear disease, otoacoustic emissions, sensorineural hearing loss, sudden hearing loss

Abbreviations: AIED = autoimmune inner ear disease, FTA/ABS = fluorescent treponemal antibody/absorption, MLR = middle latency response, MRI = magnetic resonance imaging, TOAEs = transient otoacoustic emissions

Patients with sudden hearing loss can present a diagnostic dilemma for many audiologists and physicians. Sometimes, the cause is obvious (e.g., head trauma). However, more often the underlying cause is not immediately apparent, and there are no clear precipitating factors. Etiologies of sudden loss include Meniere's disease, perilymphatic fistula, labyrinthitis, herpes, or other viral infection. Autoimmune disease may also produce somewhat similar audiologic findings of unilateral or asymmetric sensorineural hearing loss, tinnitus, and frequently balance disorder.

Early differential diagnosis is critical. Because autoimmune inner ear disease (AIED) hearing loss is usually rapid, bilateral, and progressive, early appropriate medical and audio-

logic intervention is essential to preserve hearing and to counsel an understandably upset patient.

Autoimmune disease as an underlying cause of sensorineural hearing loss has been relatively recently identified as a clinical entity and is

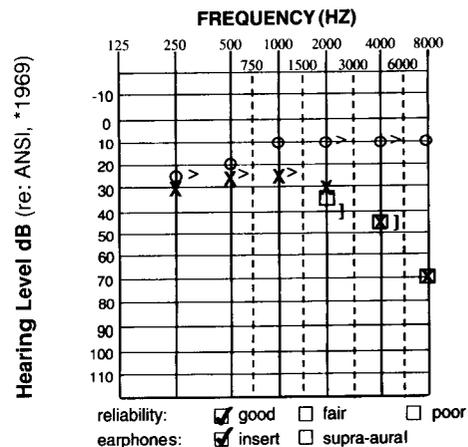


Figure 1 Pure-tone thresholds obtained on patient's initial evaluation on June 1, 1996.

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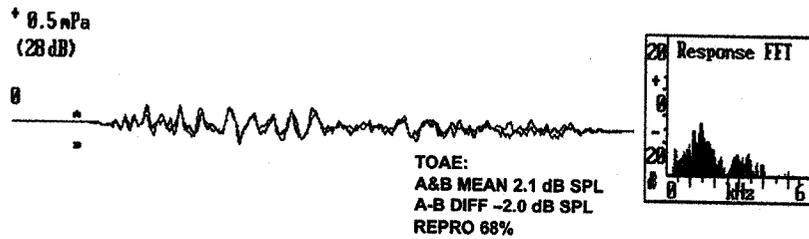


Figure 2 TOAEs for the right ear obtained on patient's initial evaluation on June 1, 1996.

still poorly understood. Consequently, many audiologists are not fully familiar with the patient and audiologic characteristics related to this disorder or with the appropriate test and management approaches. In fact, the term AIED, although commonly used, is something of a misnomer because its effects may also involve the retrocochlear pathway. Further, some propose that the term "immune-mediated" rather than "autoimmune" inner ear disease would be more accurate (Barna and Hughes, 1997).

McCabe first named AIED as a clinical entity in 1979, although an immunologic basis for certain hearing losses had been hypothesized prior to that time (Lehnhardt, 1958; Kikuchi, 1959). Research into the mechanism behind autoimmune diseases has clarified many of the medical questions regarding these debilitating afflictions. Most evidence of the cause for AIED supports an antibody-mediated, type II hypersensitivity response to inner ear antigen, although all four types of hypersensitivity have been implicated (Griffith, 1992). Some of these patients have other generalized autoimmune disorders discovered either prior to or after the onset of hearing loss, whereas in others, the sudden onset of hearing loss is the first and only symptom (Hughes et al, 1986; Saracaydin et al, 1993).

CASE REPORT

The patient was a 40-year-old, athletic, Taiwanese female who presented June 1, 1996, with acute onset of left-sided hearing loss shortly after resolution of an upper respiratory infection. Her primary complaint was difficulty using the telephone on the left side. The patient, a physician, was not overly concerned about the sudden hearing loss as she suspected that it was related

to her recent upper respiratory infection, although she had experienced no hearing loss during that time. Further, she had no history of hearing loss, tinnitus, dizziness, vertigo, vestibular symptoms, or other neurologic symptoms and denied any history of head trauma, ototoxic drugs, or noise exposure. She had an active outbreak of oral herpes at the time of diagnosis. The patient was not a smoker and denied alcohol use. Her only medication was oral contraceptives. Past medical history was significant only for chronic sinusitis, which had been stable for 2 years, and a minor thalassemia, a form of anemia that is usually asymptomatic as in her case. She had been otherwise healthy.

Pure-tone air- and bone-conduction audiometry initially revealed essentially normal hearing in the right ear with borderline to normal hearing in the low frequencies and a mild sensorineural hearing loss in the left ear (Fig. 1). Word recognition was 100 percent in the right ear at 40 dB SL with a speech recognition threshold (SRT) of 10 dB and 92 percent in the left ear at 40 dB SL with a SRT of 25 dB. Both ears had normal tympanograms and normal acoustic reflex thresholds with no reflex decay.

In the right ear, transient otoacoustic emissions (TOAEs) were normal in the 1- to 2-kHz range, but no response was elicited in the higher frequencies of 3 to 5 kHz (Fig. 2). Initially, this appeared to be inconsistent with the pure-tone air- and bone-conduction thresholds, but all thresholds and TOAEs were clear and replicable. In the left ear, TOAEs were present at 1.5 kHz but absent at 2 kHz and above (Fig. 3), which was consistent with behavioral thresholds.

Initial medical treatment for AIED is generally high-dose steroids. Because AIED was suspected, the patient was started on 60 mg of

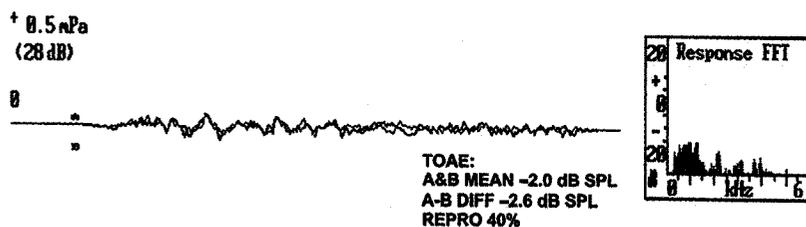
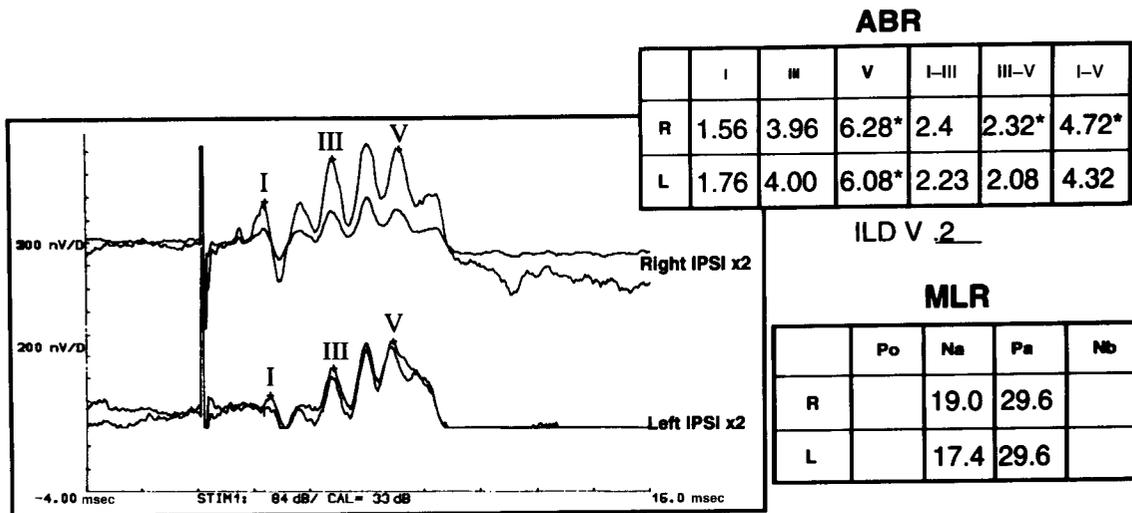


Figure 3 TOAEs for the left ear obtained on patient's initial evaluation on June 1, 1996.



RESULTS: RE: Wave V absolute latency is prolonged. Interpeak latencies III-V and I-V are prolonged. Results are suggestive of retrocochlear lesion AD.
 LE: Interpeak latencies are WNL but wave V latency is delayed. MLRs essentially WNL.

COMMENTS: Results suggestive of retrocochlear lesion. Further medical consultation planned.

Figure 4 Waveforms and latencies for ABR obtained after 6 days of steroid therapy. Latency values that are outside of 2 SD from laboratory norms are marked by an asterisk. MLR latencies are also listed. Comment on the date of assessment is also listed.

prednisone with a 2-week taper, or gradually diminishing dose. Although the patient did have an active outbreak of oral herpes, this was considered a less likely cause of the sudden hearing loss because the patient's symptoms were strictly auditory with no vestibular symptoms or involvement of the other cranial nerves.

The basic battery, repeated after 6 days of steroid therapy, showed no significant change in behavioral thresholds or in word recognition. Although improvement had been hoped for and can occur, a more realistic goal in cases of AIED is to stabilize the remaining hearing (Hughes et al, 1993). Consequently, the lack of improvement with steroids did not rule out the AIED diagnosis.

Auditory brainstem response (ABR) testing, performed on the same date (Fig. 4), revealed normal I-III interpeak latencies. However, prolonged absolute latency in wave V and prolonged III-V and I-V interpeak latencies suggested retrocochlear involvement on the right side. The left ear revealed wave V latency delay, but interpeak latencies were within normal limits. It should be noted that the interpeak ABR abnormalities were noted for the right ear that had an unusual audiometric configuration but essentially normal hearing and not the left where the hearing loss was noted. Mild latency

responses (MLRs) (not shown) were within normal limits bilaterally.

Following completion of the initial steroid trial, 11 days after the steroid taper was started, there was little change in audiologic findings. In the left ear, thresholds were improved by 10 dB at 250 Hz and 2 kHz but with no other change. Right ear thresholds were unchanged.

Serologic testing to rule out syphilis (FTA/ABS) was performed at this time and was nonreactive. Lymphocyte blast transformation antigen, which is an inner ear antigen, was also sent for testing at this time. The results showed that the inner ear antigen was normal, although this testing is generally more sensitive if performed prior to steroid treatment. False negatives and positives are also possible. Rheumatoid factor was positive, but the patient showed no other evidence of rheumatoid arthritis and has not done so as of this writing. Antinuclear Ab was negative. This test was performed because frequently results are positive with lupus or other systemic autoimmune diseases. The lipid panel revealed slightly elevated triglycerides (blood fats) and slightly low high-density lipids. Although lipid disorders have been related to hearing loss in large population and in animal studies (see review by Campbell et al, 1996), the

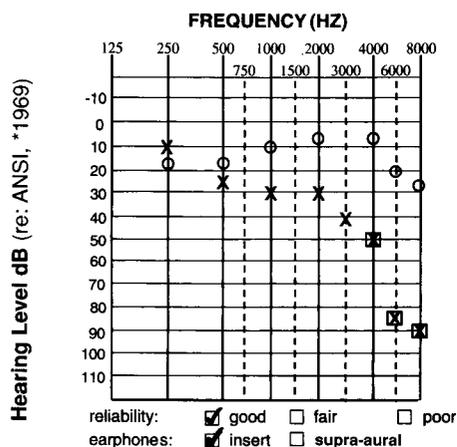


Figure 5 Pure-tone thresholds obtained on January 2, 1997.

lipid abnormalities in this patient were relatively minor.

One month later, hearing thresholds and word recognition were still stable, and the patient was told to return in 6 months or earlier if a change in hearing was noted or other symptoms developed.

Six months later, on January 2, 1997, hearing thresholds were largely unchanged, except for a bilateral drop in sensitivity for 8 kHz (Fig. 5). Word recognition remained normal bilaterally.

The patient was sent for magnetic resonance imaging (MRI) of the head, with contrast, which revealed normal otic capsules, internal auditory canals, and cerebellopontine angles. There was no evidence of multiple sclerosis or space-occupying lesions.

On March 9, 1998, the patient noticed a sudden decrease in her left ear hearing. Audiologic assessment revealed a worsening in thresh-

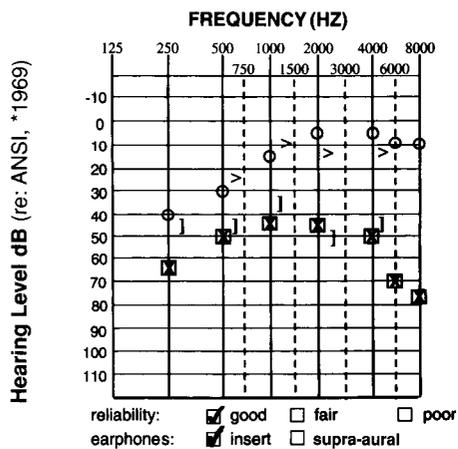


Figure 6 Pure-tone thresholds obtained March 9, 1998.

olds across all frequencies in the left ear and at 250 and 500 Hz in the right ear (Fig. 6). Word recognition was still 92 percent in the left ear and 96 percent in the right ear, although the patient's SRT in the left ear had increased to 40 dB HL. Recruitment was evident with a most comfortable listening level (MCL) in the left ear of 65 dB HL. The patient was counseled that she could be fit with hearing aids but felt that she was functioning fairly well with the hearing in the right ear.

The patient was started on high-dose steroids (methylprednisolone peak and taper). Repeat MRI at this time was again entirely normal. Three weeks later, the patient showed no hearing improvement, and 60-mg prednisone was started for 10 days with a fast taper, which also yielded no hearing improvement.

In April 1998, left ear hearing thresholds decreased 10 dB across all frequencies. Word recognition dropped to 46 percent with a SRT of 45 dB, although the SL was limited due to the patient's recruitment. The right ear showed no significant change in thresholds or word recognition.

The patient's steroid treatment was considered to be unsuccessful at 60-mg prednisone per day, and the use of methotrexate or cyclophosphamide was recommended. The patient declined these cytotoxic treatments at that time.

In August 1998, the patient complained of roaring left ear tinnitus. Audiologic assessment showed no decrease in hearing thresholds (Fig. 7). Tympanometry and acoustic reflex thresholds yielded bilaterally normal results. Reflex decay was present in the left ear at 1 kHz but not at 500 Hz. Right ear thresholds and word recognition were unchanged other than a 10-dB

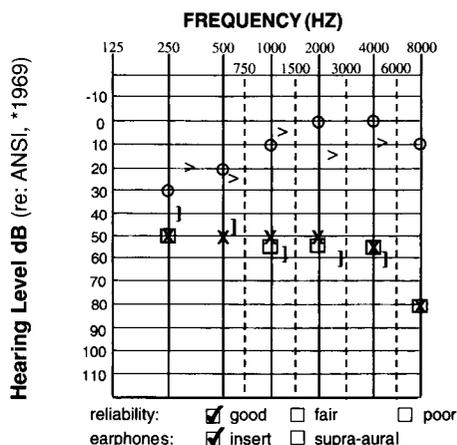


Figure 7 Pure-tone thresholds obtained on August 20, 1998.

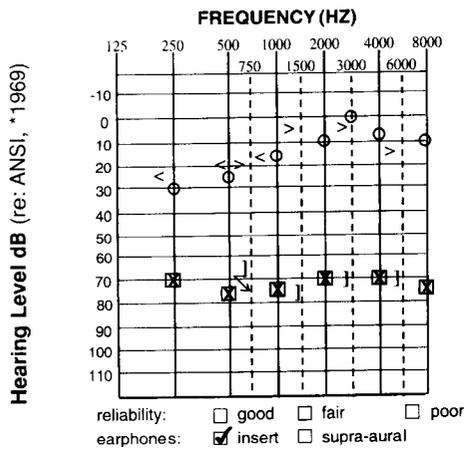


Figure 8 Pure-tone thresholds obtained on November 9, 1998.

improvement at 500 Hz. Normal word recognition, tympanometry, and reflex studies were found for the right ear at that time.

In November 1998, at follow-up, the patient's tinnitus had abated but the hearing in her left ear had decreased significantly to a flat 75 dB HL hearing loss (Fig. 8). Word recognition was 54 percent, but the patient's MCL was only 80 dB. There was no significant change in the right ear. Because she relied almost entirely on the right ear, the patient had not noticed the change in hearing. The ABR was repeated (Fig. 9). The ABR for the right ear was essentially normal for both absolute and interpeak latencies. The III-V interval was somewhat shortened, but the identified wave V is probably the peak of a IV-V com-

plex. The waves after the identified V, however, were labile and more poorly replicable. The ABR for the left ear was grossly abnormal with only delayed waves III and V present and an ILD V of 0.97 msec. TOAEs were normal in the right ear (Fig. 10) and absent in the left ear (Fig. 11). The patient was started on methotrexate therapy (20 mg once per week). The patient continues on this therapy at present. Hearing has remained relatively stable over the last year (1999) with some fluctuation within the 10- to 15-dB range in the right ear, but word recognition has deteriorated to 12 percent at a 5 dB SL tested at MCL. The right ear has generally stable thresholds, although there has been some fluctuation and thresholds at 250 Hz and 500 Hz have worsened 10 dB. The patient has tried hearing aids on a demonstration basis but feels that she is coping well with unilateral hearing.

COMMENT

This case of AIED demonstrates some fairly typical characteristics. According to a prospective series of 47 patients by Hughes et al (1983), the disease was more common in females in the age range 20 to 50, with an average age of onset of 44. Involvement was usually bilateral but unilateral in 19 percent of cases. Unilateral disease usually progressed to bilateral disease within weeks or months. However, Harris and Aframian (1994) reported that contralateral delayed endolymphatic hydrops, secondary to

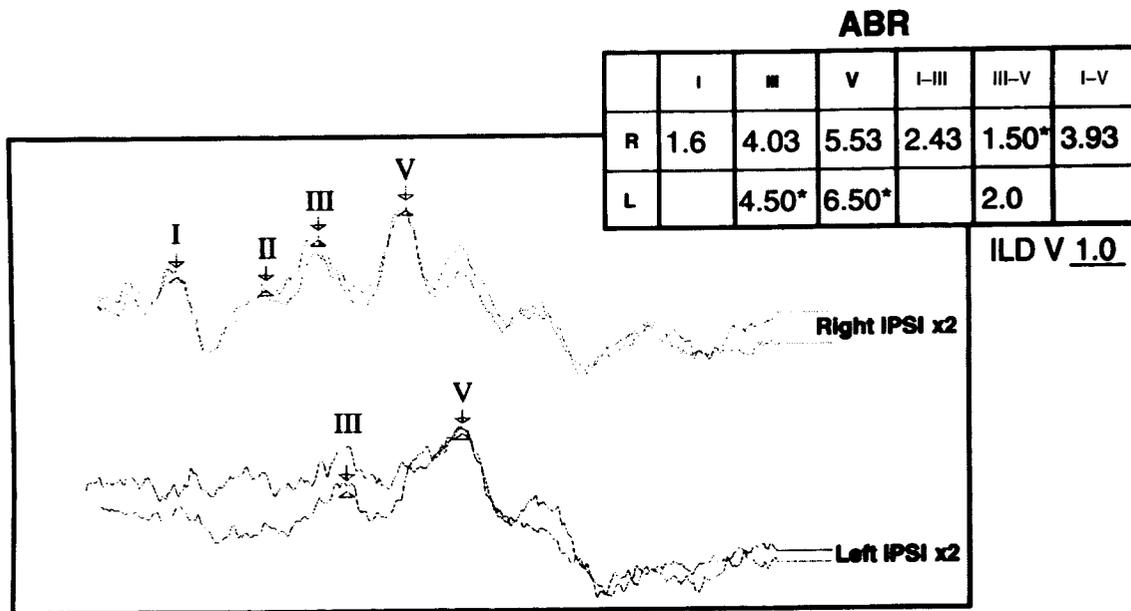


Figure 9 ABR results obtained November 9, 1998. Absolute and interpeak latency values that are outside of 2 SD from laboratory norms are marked by an asterisk. The ILD V is also clearly outside normal limits.

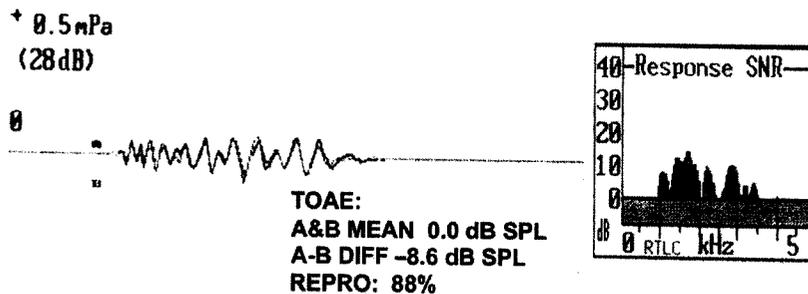


Figure 10 TOAEs for the right ear November 9, 1998.

AIED, may occur years after the initial onset of unilateral disease. However, as in the Hughes et al (1983) study, disease progression was usually rapid over several weeks and often had episodes of improvement and exacerbation. The audiometric pattern was usually up-sloping, flat, or down-sloping. The up-sloping pattern was more common in early immune Meniere's disease. The hearing loss was often asymmetric, particularly in early disease. Fluctuations in hearing loss with AIED are unpredictable.

Fifty percent of patients had symptoms of dizziness, light-headedness, or ataxia, although true vertigo was rare and usually associated with unilateral disease. Balance symptoms parallel auditory symptoms. These patterns are consistent with McCabe's earlier report of 18 patients (McCabe, 1979). Fortunately, this patient has not, to date, developed a balance disorder. She also has not developed aural fullness, which has been frequently noted in this patient population (Hughes et al, 1988).

Medical diagnosis of AIED is difficult, and no definitive tests have been developed. McCabe (1979) described positive findings in lymphocyte migration inhibition assay and leaned heavily on this evidence in his landmark paper describing AIED. This test assumes that a patient's lymphocytes are stimulated to combat an inner ear antigen. Tests of humoral immunity include indirect immunofluorescence, enzyme linked immunoassay, and Western blot immunoassay. None of these tests have been shown to be reliably sensitive or specific for AIED (Griffith, 1992). Any immunologic testing that is to be performed should be done in the

acute phase of the disease, prior to initiation of treatment (Hughes et al, 1993). The most common medical tests currently used for AIED are listed in Table 1.

Many physicians consider treatment to serve as the best diagnostic aid. It is often recommended that while waiting for the results of the above-mentioned tests, a trial of steroids, if not medically contraindicated, should be started. Improvement while on immunosuppressive therapy is considered the best evidence that the hearing loss is immunologically mediated (Hughes et al, 1992). Hughes et al recommend a 1 mg/kg dose of prednisone for 1 month, although minimum doses and treatment lengths have not been delineated. McCabe (1979) has recommended cytotoxic agents as a first-line agent against AIED. No consensus has been reached on the proper agents, therapy duration, or other aspects of therapy regimens. However, the pathogenesis of AIED is complex (Ruckenstein and Harrison, 1991). The pathogenesis, diagnostic tests, and treatment options are still an ongoing area of research.

Audiologically, AIED usually causes bilateral asymmetric sensorineural hearing loss with disproportionately poor word recognition (Hughes et al, 1993). Most commonly, the audiometric configuration is atypical for sensorineural hearing loss but follows no consistent pattern. Rapid progression and/or fluctuation, particularly without early appropriate medical intervention, is common. Recruitment, frequently severe as in this case, may be present.

Few reports review otoacoustic emission and electrophysiologic findings in the AIED

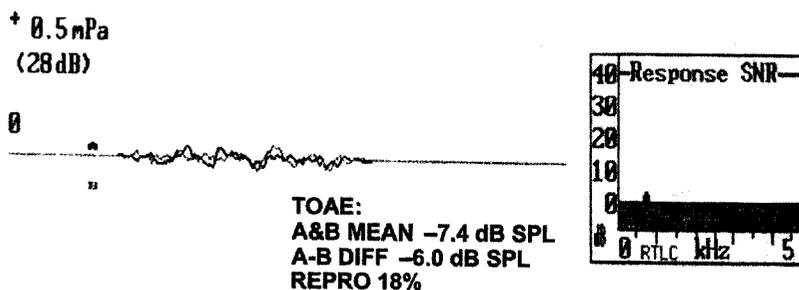


Figure 11 TOAEs for the left ear November 9, 1998.

Table 1 Medical Tests Commonly Used to Test for Autoimmune Inner Ear Disease

CBC (complete blood count) to check for leukemia or other hemolytic disorders
FTA/ABS to screen for syphilis
MRI, with contrast, of brain and cerebellopontine angle to check for multiple sclerosis, vascular lesions, and space-occupying lesions
Lymphocyte blast transformation to check for inner ear antigen, which may underlie AIED. The efficacy of this test is controversial.
Rheumatoid factor is a marker for rheumatoid arthritis and other autoimmune diseases
Antinuclear antibody is used to check for lupus and other autoimmune diseases
Lipid panel to check for dyslipidemias
Trial of steroids is also used as a test

population. Induced AIED models in guinea pigs immunized with homogenous inner ear antigen to simulate AIED demonstrated reduced amplitude or absence of otoacoustic emissions (Gloddek et al, 1994; Zou et al, 1996).

To our knowledge, this is the first report of otoacoustic emissions in a patient with AIED. Of particular interest are the discordant findings of TOAEs and behavioral threshold and the fluctuation of TOAEs. Perhaps this type of discrepancy could be used to more distinctly identify AIED in the early stages, if it also occurs in other AIED patients rather than an isolated occurrence.

Similarly, the ABR findings initially showed greater abnormality on the side with only minimal threshold involvement. Although retrocochlear involvement in AIED has been previously reported (Veldman, 1986; Zhai, 1993), the ABR findings that fluctuated over time and that were seemingly inconsistent with threshold were a particularly interesting finding.

Unfortunately, the long-term prognosis for this type of case is usually bilateral progression as has already occurred in the left ear. The very poor word recognition and recruitment render hearing aid fitting difficult. The prognosis for cochlear implants with an inflammatory process such as AIED would have to be carefully considered, but no comprehensive patient database exists in the area.

It is essential for the audiologist to recognize the audiologic signs and symptoms of AIED in patients and to work closely with the physician to prevent or delay progression as long as possible. Patient counseling and support are critical.

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