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Audiology findings in patients with teprotumumab associated otologic symptoms

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ABSTRACT

Purpose: To report a case series of subjective and objective hearing function changes associated with teprotumumab treatment for thyroid eye disease.

Observations: A 74-year-old female with a history of Graves' disease with thyroid eye disease was treated with teprotumumab. She had a history of bilateral tinnitus and noticed a subjective improvement in her tinnitus after the second infusion. Audiology testing obtained before, during, and after completion of infusions showed symmetric and rapidly progressive worsening of the patient's sensorineural hearing loss. In contrast, a 42-year-old male with a history of Grave's disease endorsed worsening intermittent tinnitus and low-pitched hearing loss after initiation of teprotumumab. Audiology testing before, during, and after completion of infusions showed stable and normal hearing function bilaterally.

Conclusion and importance: This case series highlights the importance of objective testing in patients prior to and after teprotumumab initiation as subjective hearing changes may not accurately reflect objective hearing function. In addition, this report suggests that teprotumumab may play a role in potentiating sensorineural hearing loss.

1. Introduction

Thyroid eye disease (TED) is an orbital inflammatory condition that can lead to disfigurement, debilitation, and permanent vision loss. Teprotumumab (Horizon Therapeutics, Dublin, IRL), a human monoclonal antibody that inhibits insulin-like growth factor-1 receptor (IGF-1R), has been found to be effective at improving proptosis, diplopia, Clinical Activity Score, and quality of life in patients with TED.[1,2] In the inner ear, IGF-1R has been implicated in homeostatic regulation and may play a role in maintaining sensorineural auditory function.[3,4] Between 10 and 46% of TED patients receiving teprotumumab have been reported to experience subjective hearing symptoms including hypoacusis, autophony, and tinnitus, and cases of teprotumumab associated audiology testing changes have been reported.[1,2,5,6] This is one of the first reports to describe audiology testing results in patients before, during, and after teprotumumab treatment.

2. Findings

2.1. Case 1

A 74-year-old woman with a history of Graves' disease with TED received teprotumumab for proptosis and diplopia. Prior to presentation, the patient had a history of bilateral tinnitus and otherwise no known hearing or vestibular abnormality. A pre-treatment audiogram revealed symmetric mild to moderate sensorineural hearing loss (SNHL) that was more severe in high frequency ranges (Fig. 1A). After her second infusion (week 3), the patient described improved tinnitus and no other subjective hearing changes. Audiograms obtained after infusion 6 (week 15), and 2 weeks (week 23) and 8 weeks (week 29) after completion of therapy revealed symmetric and rapidly progressive worsening of SNHL, increased average functional hearing thresholds, and impaired word recognition (Fig. 1).

2.2. Case 2

A 42-year-old male with a history of Graves' disease with TED

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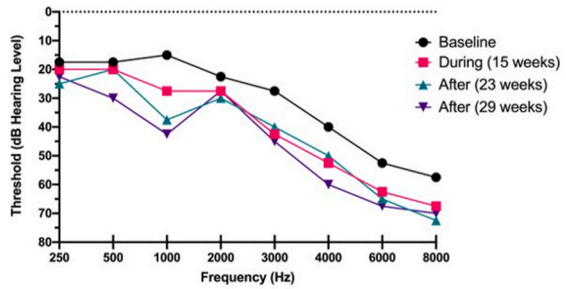
A.

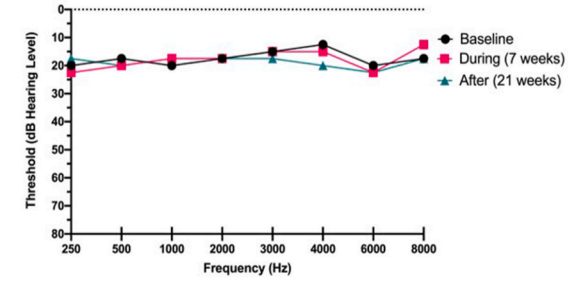


B.

	Pure Tone Average (Bilateral mean dB Hearing Level)	Word Recognition Score
Baseline	21	96%
15 weeks	26	96%
23 weeks	30	86%
29 weeks	33.5	Did not complete*

Fig. 1. (A) Audiologic findings revealed baseline mild sensorineural hearing loss (SNHL) at mid-frequency range and moderate SNHL at high frequencies consistent with an age-related hearing loss pattern. A rapid worsening of hearing is observed over the surveillance period with no improvement after teprotumumab completion at 21 weeks. **(B)** Mean bilateral *pure tone average thresholds* of 500, 1000, 2000, and 4000 Hz demonstrated a progressive increase in decibel (dB) hearing level needed to detect sound in frequencies corresponding to human speech. *Word recognition score*, which assesses the ability to understand speech when presented at a level of 40 dB above the threshold when speech is first detected, illustrated progressive word recognition impairment.
*At 29 weeks, the patient required higher dB levels to successfully complete the test.

A.



B.

	Pure Tone Average (Bilateral mean dB Hearing Level)	Word Recognition Score
Baseline	21.5	96%
7 weeks	19	98%
21 weeks	19	98%

Fig. 2. (A) Audiology testing demonstrated baseline normal hearing function that remained stable during and upon completion of teprotumumab. **(B)** Mean bilateral *pure tone average* and *word recognition scores* at 40 dB above speech detection thresholds were within normal limits and stable before, during, and immediately upon completion of teprotumumab.

received teprotumumab for proptosis with worsening eye pain and injection. The patient had a history of right greater than left subjective hearing loss and occasional bilateral tinnitus. A pre-treatment audiogram revealed symmetric normal hearing bilaterally, defined as the ability to detect sounds of 0–25 dB across the full frequency range (Fig. 2A). Shortly after teprotumumab infusion 3 (week 6), he described intermittent tinnitus and low-pitched hearing difficulty. Audiograms obtained the following week (week 7) and on the day of therapy completion (week 21) revealed no changes in hearing, average functional hearing thresholds or word recognition (Fig. 2).

3. Discussion

Teprotumumab has shifted the treatment paradigm for TED but has been associated with several adverse effects including hearing impairment.[4–6] Hearing symptoms reported in the initial randomized controlled trials varied widely.[1,2] These two cases demonstrate that subjective hearing changes do not necessarily correlate with objective findings. Research has shown that subjective hearing changes correlate with objective hearing loss less than 72% of the time, emphasizing the need for objective measures for hearing performance.[7] Notably, the patient who reported decreased tinnitus with no subjective hearing loss demonstrated worsening of SNHL, while the patient who described increased tinnitus and hearing impairment did not have any objective changes on audiology testing. Despite hearing symptoms, audiologic findings, and other side effects, neither patient elected to discontinue treatment.

Although IGF-1 has been linked to inner ear development and multiple authors have suggested that a deficiency in IGF-1 can lead to presbycusis, it is unclear if there is a causal relationship between IGF-1R inhibition and hearing impairment.[3] The rapid hearing decline in Patient 1 far exceeded the expected rate of natural SNHL progression.[8] This suggests that IGF-1R inhibition may have a role in potentiating progressive forms of hearing loss. It is unclear whether IGF1-R inhibition affects patients without pre-existing SNHL.

4. Conclusions

These cases highlight the importance of objective testing in patients prior to and after teprotumumab initiation as subjective hearing changes may not accurately reflect objective hearing function. More studies are needed to investigate the effect of teprotumumab on hearing, identify patients at risk for hearing loss, and explore potential protective measures. Particular attention should be paid to patients with pretreatment SNHL as inner ear cells do not regenerate, and a risk of long-term irreversible hearing loss may exist.

Patient consent

Consent to publish this case report has been obtained from the patients in writing.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

CRediT authorship contribution statement

Caroline Y. Yu: Writing – original draft, preparation, Visualization, Investigation, Data curation. **Tatiana Correa:** Data curation, Visualization, Writing – review & editing. **Brittany A. Simmons:** Writing – review & editing, Conceptualization, Methodology. **Marlan R. Hansen:** Writing – review & editing, Supervision. **Erin M. Shriver:** Conceptualization, Writing – review & editing, Resources, Supervision.

Declaration of competing interest

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