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Case Report

Middle Ear Neuroendocrine Tumor: Case Report of a Tympanic Adenoma

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Middle ear neuroendocrine tumors (MeNETs) are an exceptionally rare occurrence. These benign tumors stem from the tympanic mucosa and can easily be misinterpreted by the clinician and the pathologist. Clinical characteristics, otoscopic findings and medical imaging in these cases are non-specific. We present a case of a 60-year-old male patient with bilateral hearing loss following recent coronavirus disease 2019 disease. Diagnostic work-up revealed a soft tissue neoplasm of the left middle ear. Surgical resection of the tumor mass with implantation of a partial ossicular replacement prosthesis (PORP) was the main modality of treatment. Middle ear neuroendocrine tumors was confirmed through positive immunohistochemistry for neuroendocrine tumor markers. Follow-up magnetic resonance imaging 12 months after the surgery reported no tumor recurrence or significant residual disease with a stable PORP. Our report highlights challenges in diagnosing and treating these rare tumors, while emphasizing surgical resection pitfalls and resulting improvement of quality of life of the patient. We recommend a through follow-up of patients with unclear soft tissue masses in the middle ear to obtain a definitive diagnosis.

KEYWORDS: MeNET, middle ear, neuroendocrine, tumor, adenoma, case report

INTRODUCTION

There is a wide range of middle ear tumors described in the medical literature. Middle ear neuroendocrine tumors account for about 2%-9% of all middle ear tumors.[1] They arise from tympanic mucosa and have unclear pathogenesis and prognosis, since their varied pathologic characteristics show overlap with carcinoid middle ear tumors, with several cases showing metastatic spread documented in literature.[3] Middle ear mucosa is derived from the endoderm similar to pulmonary mucosa; however, cells with neuroendocrine characteristics are not routinely identified in the tympanic cavity.[2]

Hyams and Michaels were the first to describe a MeNET in 1976, followed by Murphy in 1980.[3,4,5] In modern literature, most information and the overall assessment of these tumors are found in case reports and small case series. Many authors insist that MeNETs and carcinoid tumors are different neoplasms with some similar biological characteristics. However, the latest histopathological research suggests that those labels actually represent a common pathological neoplasm.[3,5] That is why different labels further complicate tumor assessment. Middle ear neuroendocrine tumors is the latest definition of an adenoma in the middle ear constituted in the 5th Edition of the World Health Organization Classification of Head and Neck Tumors in 2022.[6]

Most patients affected by this tumor will commonly report hearing loss as the main symptom, leading to diagnostic difficulties due to an intact tympanic membrane, and a non-specific imaging finding.[3,7] The main point of this case report is to assist the clinician in the diagnostic and treatment decision-making process, and to sum up relevant knowledge in a straightforward way. Diagnostic and treatment pitfalls relevant to this rare entity are discussed, alongside outcomes.

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CASE PRESENTATION

A 60-year-old male patient reported bilateral hearing loss following a recent coronavirus disease 2019 infection. Hearing loss was more pronounced on the left side, while there were no other accompanying symptoms. Otoscopic finding resembled an acute serous otitis media, and pure-tone audiometry indicated bilateral conductive hearing loss, with a tympanometric Jerger B curve on the left side. There was no history of middle ear pathology or hearing loss in the patient and family history. A left-sided myringotomy with implantation of a ventilation tube was performed in local anesthesia. On a follow-up visit a month later, no improvement of hearing was noted, with persistent conductive hearing loss on the left side showing an air–bone gap of 35 dB (Figure 1).

Since no improvement in hearing was noted after a month, and there were no signs of chronic infection, a middle ear exploration procedure was scheduled under local anesthesia, with a possible ossiculoplasty or stapedotomy procedure possible. Upon raising the tympanomeatal flap, a white, lobulated bleeding mass was observed encasing the ossicular chain. Following the procedure, a contrast-enhanced multislice computed tomography of the left temporal bone revealed soft tissue formation obstructing the tympanic cavity and surrounding the ossicular chain, extending into the epitympanum, showing moderate contrast imbibition. Fluid content was observed in the mastoid antrum and mastoid cells. The facial nerve canal was perserved with left inner ear showing no morphological pathology (Figure 2). Magnetic resonance imaging (MRI) confirmed a mass with lower intensity on T2-weighted images (Figure 3). There was no facial or vestibulocochlear nerve infiltration observed. Differential diagnosis included a glomus tympanicum tumor, with other tumors being less probable (Figure 4).

Surgical treatment in general anesthesia was then scheduled, with a left-sided canal-wall up tympanomastoidectomy performed through a retroauricular approach. Intraoperatively, the incudostapedial joint was shown to be eroded by tumor tissue, and the incus was removed to facilitate the extraction of the tumor from the attic. In addition, the tumor was carefully removed from the facial recess, stapes footplate, and intercrural space of the stapes. The manubrium was detached from the tympanic membrane and retropositioned over a PORP (MedEl mXACT PRO partial prosthesis) positioned between the manubrium of the malleus and the stapes. Fascia of the temporal muscle and auricular cartilage were used to reconstruct the tympanic membrane in an underlay position. Post-operative recovery was uneventful.

Histopathology confirmed a MeNET, according to the latest classification.[6] Immunohistochemical analysis showed a strong positive cytoplasmic reaction for neuroendocrine markers, especially synaptophysin and CD56. The Ki-67 expression was positive in less than 2% of the tumor cells. However, the S-100 and SOX10 markers were negative.

Two months after the surgery, the patient reported better hearing on the affected ear while no signs of visible recurrence were detected during otomicroscopic examination. Pure-tone audiometry showed conductive hearing loss in the left ear but with a notable improvement (Figure 5). Follow-up MRI reported no tumor recurrence or significant residual disease with a stable PORP 12 months after the surgery (Figure 6). Currently, the patient is without symptoms or signs of recurrence 20 months after the initial surgery.

Written informed consent was obtained from the patient and this submission was waived consent by our institutional bioethical board adhering to the Ethical Principles for Medical Research Involving "Human Subjects," adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964.

DISCUSSION

Throughout medical history, neuroendocrine tumors of the middle ear were mostly known as adenomas but were often mistaken for similar tumors in the same region. Their true nature, pathogenesis, classification, and prognosis are still a mystery. Hearing loss is the leading symptom, with few other symptoms leading to the eventual discovery of a neuroendocrine tumor. Nonspecific symptoms may include aural fullness, tinnitus, and otalgia.[7] These symptoms are not specific for MeNET and can mislead even a highly trained otologist. There are also asymptomatic patients described in the literature.[8] Middle ear neuroendocrine tumors are not encapsulated and tend to surround the ossicles, without major bony erosion. Nerve invasion

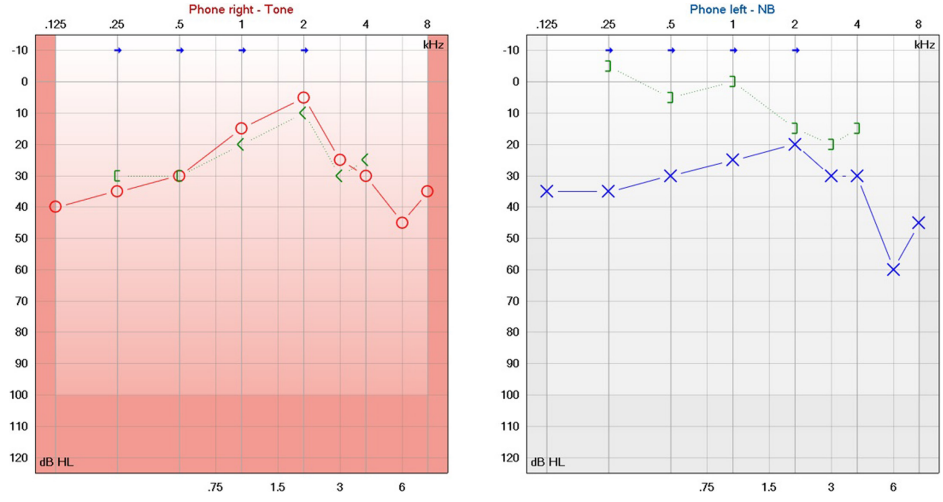

Figure 1. Control tonal audiometry image after the first line therapy showing there is still conductive hearing loss present in the left ear.

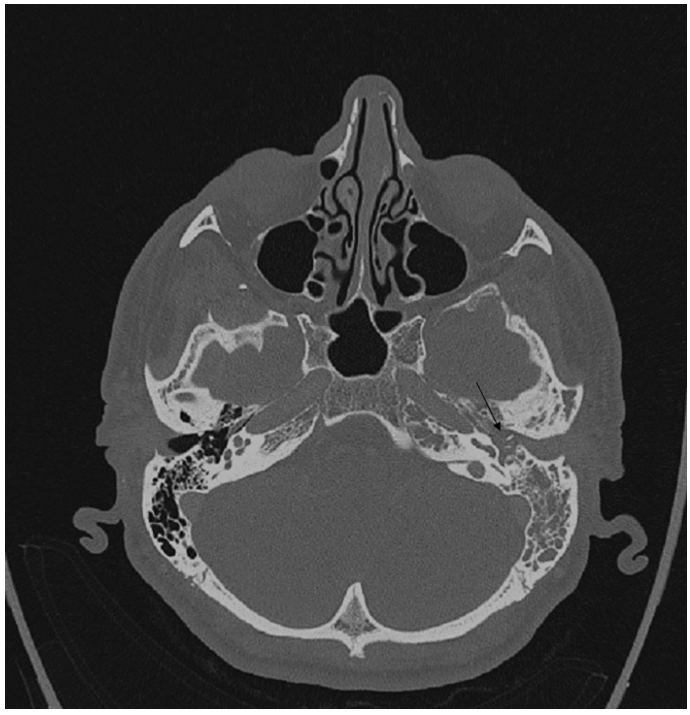

Figure 2. Axial multislice computed tomography image of the temporal bones, native and with contrast (arrow pointing to the tumor mass of the left middle ear).

is highly uncommon but was described in several cases, alongside malignant transformation and metastatic spread.[3,6,9]

Malignant transformation is very low in MeNETs.[9] There are some regional metastasis reports but those are highly controversial and extremely rare. We hypothesize that poor vascularization and the relatively small size of these tumors contribute to their lack of biologic potential to spread and transform into more aggressive tumors.

Computed tomography scans will show a well-defined lesion of the temporal bone, hypodense after implementation of the contrast. Middle ear neuroendocrine tumors can extend in any direction and can protrude through the tympanic membrane. There is no clear characteristic difference between benign or malignant MeNETs.[10] Magnetic resonance imaging with contrast is mostly used in neuroendocrine tumors that extend to the posterior fossa or when recurrence occurs, showing an iso/hypodense signal on T1 and hyperdense signal on T2 images.[11] Since only audiometry or otoscopy are insufficient to rule out recurrence after a long-term follow-up, the best strategy for long-term disease control is contrast-enhanced MRI scaning.[12]

Symptoms, clinical signs and radiologic findings mimic other middle ear diseases. Immunohistochemical staining is a powerful tool in separating MeNET from other neoplasms, with the most similar neoplasm being paraganglioma. Negative protein marker S-100 incorporated with positive staining for keratin can eliminate a diagnosis of

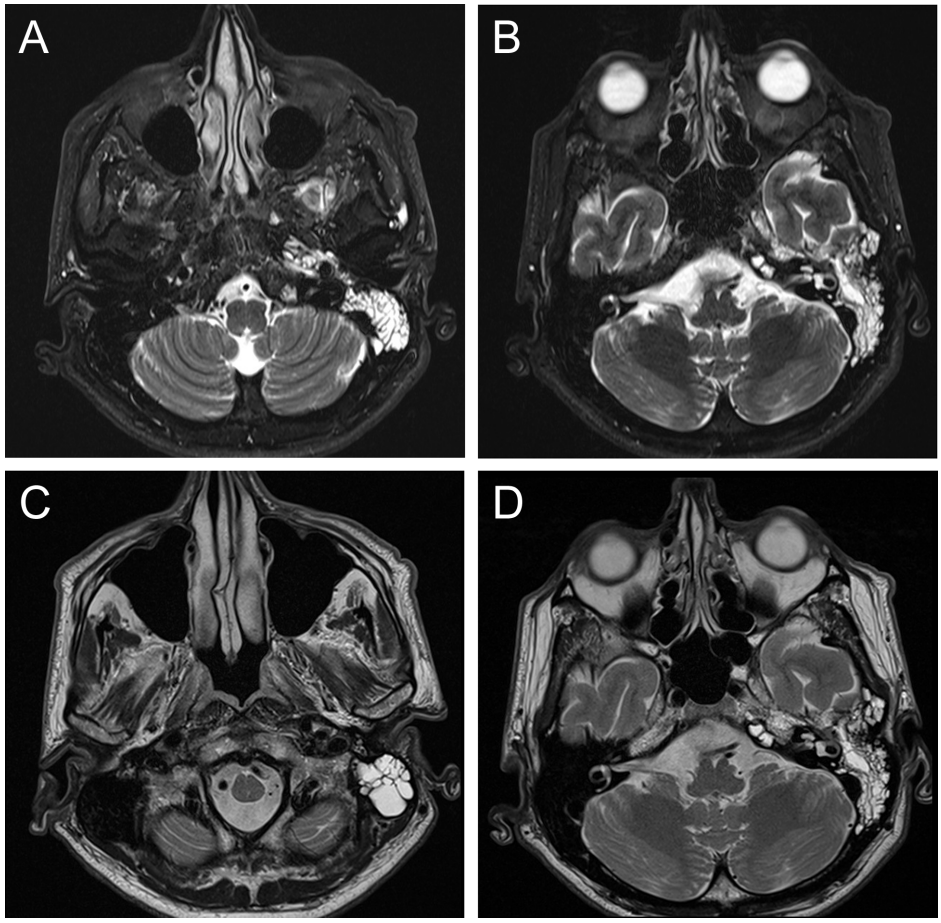

Figure 3. Axial T2-weighted (A, B) and T1-weighted magnetic resonance images (C, D) showing pre-operative scans of the temporal bones showing a tumor mass filling the middle ear space and fluid retention in the mastoid.

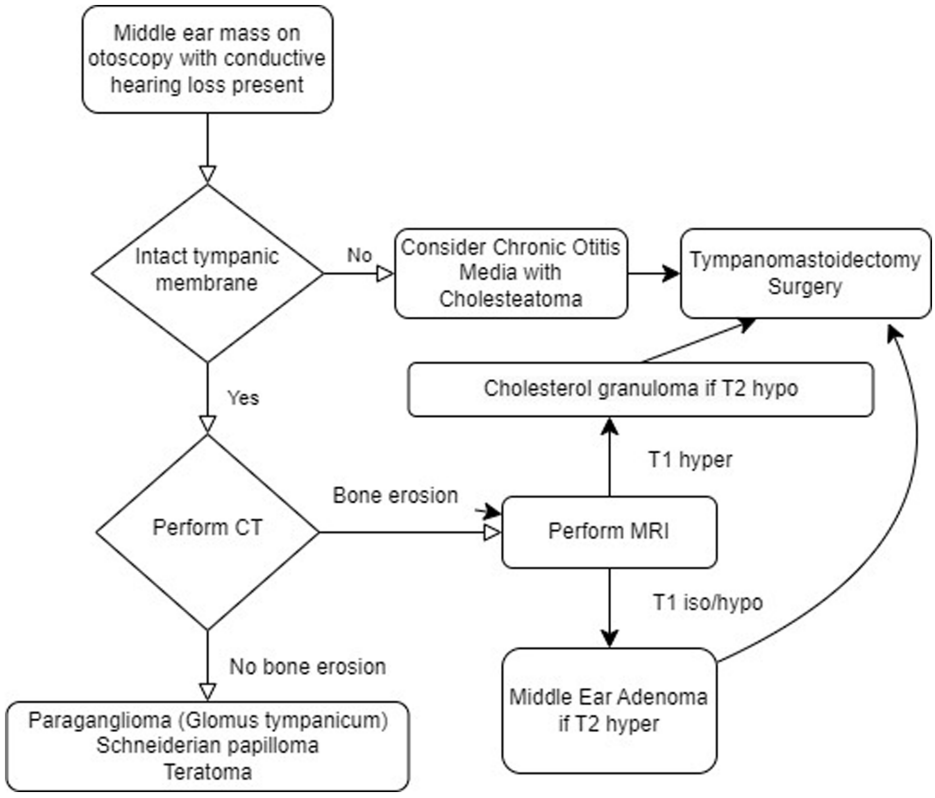

Figure 4. Possible diagram of diagnostic work-up and treatment concerning middle ear adenomas.

paraganglioma.[13] There have been many attempts to classify these rare neoplasms. One specific classification for MeNET's proposed by Saliba and Evrard is used by many authors.[6] This classification is mainly based on immunostaining results and possible regional spread of the adenoma.

The main treatment modality should be complete surgical resection of the tumor with safe margins when possible. Ossiculoplasty should be performed in patients where ossicular chain is disrupted or incorporated in the tumor mass. There are many examples of higher rates of local recurrence (up to 20%) in cases where the ossicular chain was left intact. Lower incidence of recurrence (9%) was observed in patients who were treated with radical mastoidectomy compared to transcanal tympanotomy removal of the tumor (14%).[7]

While there is no definitive evidence which type of procedure should be primarily used, we strongly recommend the one mentioned above in our case. Adjuvant oncological therapy is not recommended, especially when considering cases in the literature where malignant transformation of the tumor occurred after higher doses of radiotherapy. There are no cases in the literature where primary oncologic therapy was used to treat MeNETs.

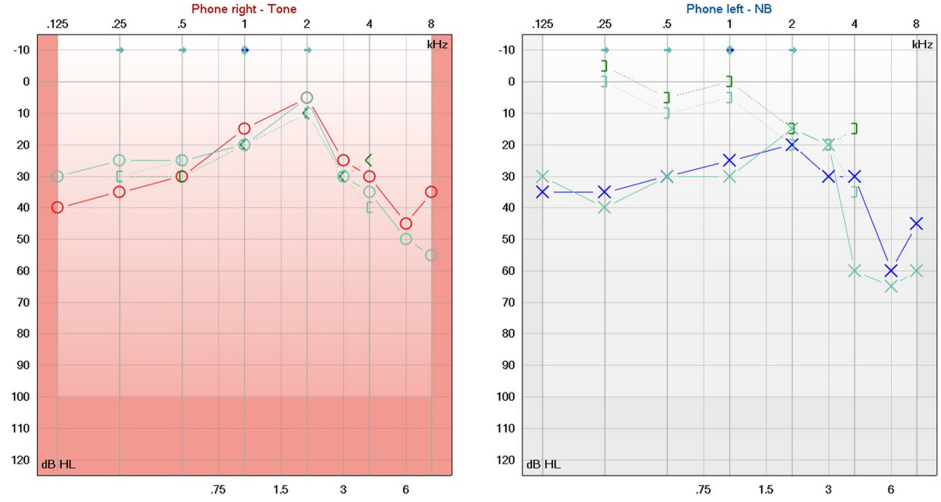

Figure 5. Pure-tone audiometry 2 months after the surgery. Curve colored with light green represents the follow-up hearing threshold, confirming residual conductive hearing loss in the left ear with some improvement in high-frequency hearing.

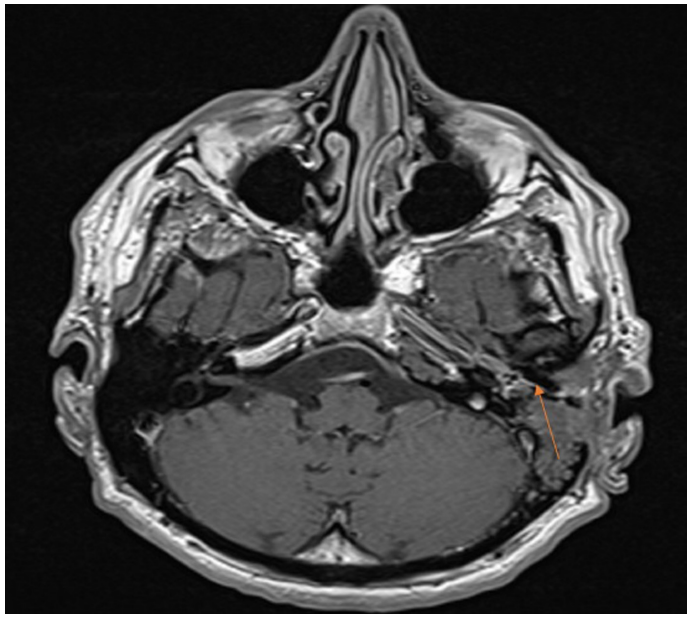

Figure 6. A, B. Axial T1-weighted magnetic resonance images showing postoperative scans of the temporal bones 12 months after surgery (arrows pointing to the left cavum tympani with no signs of tumor recurrence).

CONCLUSION

Neuroendocrine tumors of the middle ear are unusual and difficult to diagnose. Establishing a straightforward diagnosis is very challenging due to the lack of specific signs or symptoms, while surgical resection of the tumor should be the main treatment modality. We strongly recommend a long follow-up period with contrast-enhanced MRI performed routinely so any potential recurrence can be detected.

Informed Consent: Informed consent was obtained from the patient who agreed to take part in the study.

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