Carcinoid Tumor of the Middle Ear: A Report of Two Cases

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Background: Carcinoid tumors of the middle ear are rare and difficult to diagnose preoperatively. These low-grade malignant tumors require complete surgical removal; however, consensus on the amount of radicality required is lacking. Herein, we report two cases of carcinoid tumors of the middle ear.
Case Presentation: The first patient was a 40-year-old woman who presented with right-sided hearing loss and a white mass behind the tympanic membrane. The tumor was surgically removed using a transcanal approach, while maintaining an intact ossicular chain. The histopathological diagnosis was carcinoid tumor, and no additional treatment was administered. The second patient was a 28-year-old woman who presented with left-sided hearing loss and a white mass in the ear canal. Preoperative biopsy revealed a carcinoid tumor. The tumor was excised using the same approach as in Case 1 with tentative removal of the incus during surgery, and reconstruction with tympanoplasty type IIIc (Ost) was performed. No recurrence was observed in either case during > 3 years of follow-up.
Conclusion: Treatment algorithms for carcinoid tumor of the middle ear are lacking; therefore, surgical plans vary according to the tumor extension. Furthermore, because carcinoid tumors are low-grade malignant tumors, long-term follow-up after complete macroscopic removal is necessary.

Key words: neuroendocrine tumor, low-grade malignancy, surgical treatment, ossicular chain repair

INTRODUCTION

Carcinoid tumors occur mainly in the digestive system and rarely in the middle ear. Obtaining a precise preoperative diagnosis using either imaging or histopathology is usually difficult, as is an intraoperative pathological diagnosis. Furthermore, because carcinoid tumors are considered low-grade malignant tumors [1], determining the excision range in the middle ear, which contains important structures, such as the ossicular chain, chorda tympani, facial nerve, and oval and round windows, is difficult.

Herein, we report two cases of middle-ear carcinoid tumors: a case diagnosed after exploratory surgery in which the ossicular chain was preserved, and a case diagnosed by preoperative biopsy followed by tumor resection with ossicular chain repair.

CASE REPORT

Case 1

A 40-year-old woman experiencing gradual hearing deterioration in the right ear over 3 years was referred to our hospital by a nearby ENT clinic. Otoscopic examination revealed a non-pulsatile white mass behind the right tympanic membrane (Fig. 1A). Pure tone audiometry (PTA) revealed mixed hearing loss in the right ear with a threshold of 28.8 dB (Fig. 1B). Computed tomography (CT) of the temporal bone revealed a soft-tissue mass confined to the tympanic cavity without bone destruction (Fig. 2A). Magnetic resonance imaging (MRI) revealed a lesion with high signal intensity on T1-weighted images and an intensity identical to that of the brain tissue on T2-weighted images; enhancement with gadolinium contrast was uncertain (Fig. 2B, C, D).

Because an accurate preoperative diagnosis was difficult, we performed middle-ear surgery. The tympanic cavity was explored following a retroaural incision. The mass was soft, bled easily, and extended from the malleus handle to the posterior tympanic space (Fig. 3A). No invasion of the facial canal was observed; however, extension to the stapes and round window niche were observed without apparent bone erosion. The chorda tympani was involved in the mass; therefore, it was transected. Intraoperative pathological diagnosis revealed a neoplasm; however, we were unable to determine whether the tumor was benign or malignant. Macroscopic tumor resection was performed while preserving the ossicular chain (Fig. 3B). Postoperative histopathological examination revealed uniform proliferation of cells with rounded nuclei and eosinophilic cytoplasm on hematoxylin-eosin staining. Based on these findings, a neuroendocrine tumor characterized by a variable growth pattern was suspected, and immunohistochemical testing was added. Immunohistochemical staining for synaptophysin and

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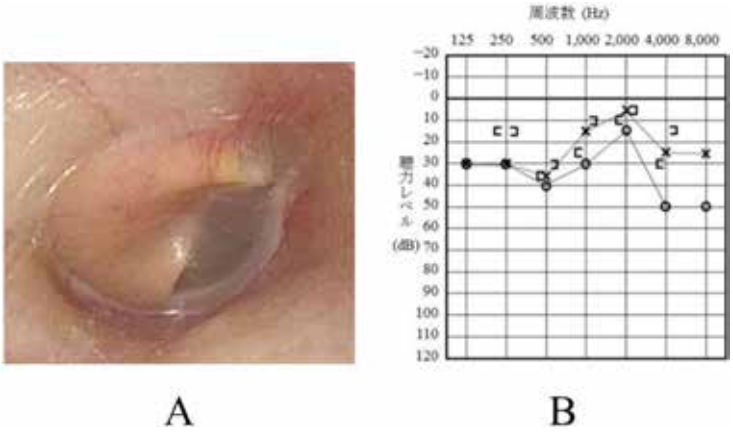

Fig. 1 Otoscopy and pure tone audiometry findings in Case 1
A: A non-pulsating white mass is observed behind the tympanic membrane. B: The right ear shows mixed hearing loss with a threshold of 28.8 dB.

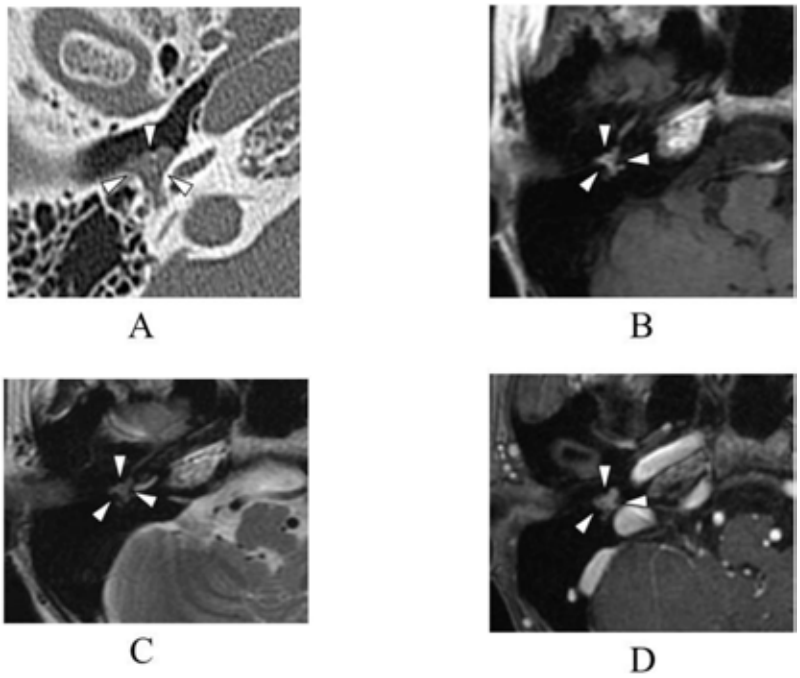

Fig. 2 Computed tomography (CT) and Magnetic resonance (MR) images of the temporal bone in Case 1. The arrowheads show the tumor extension.
A: CT axial view shows a soft-tissue lesion in the right posterior tympanic cavity without bone destruction. B: T1-weighted MR image shows a hyperintense lesion. C: T2-weighted MR image shows a lesion with intensity similar to that of the brain. D: T1-weighted gadolinium-enhanced MR image shows no enhancement.

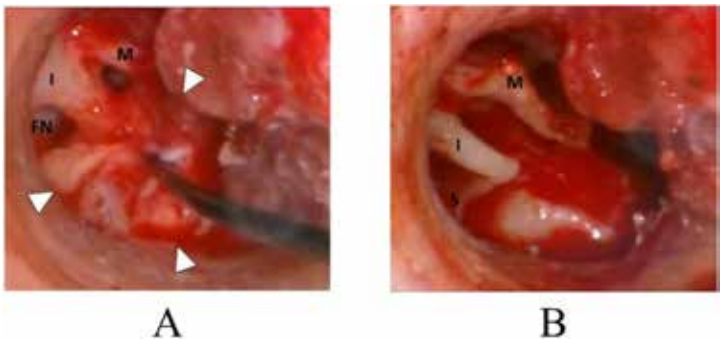

Fig. 3 Operative findings in Case 1
A: The tumor (arrowhead) in the right tympanic cavity does not adhere to the ossicles or facial nerve. B: Intact ossicular chain after resection of the chorda tympani and tumor.
(M: Malleus, I: Incus, FN: Facial nerve, S: Stapes)

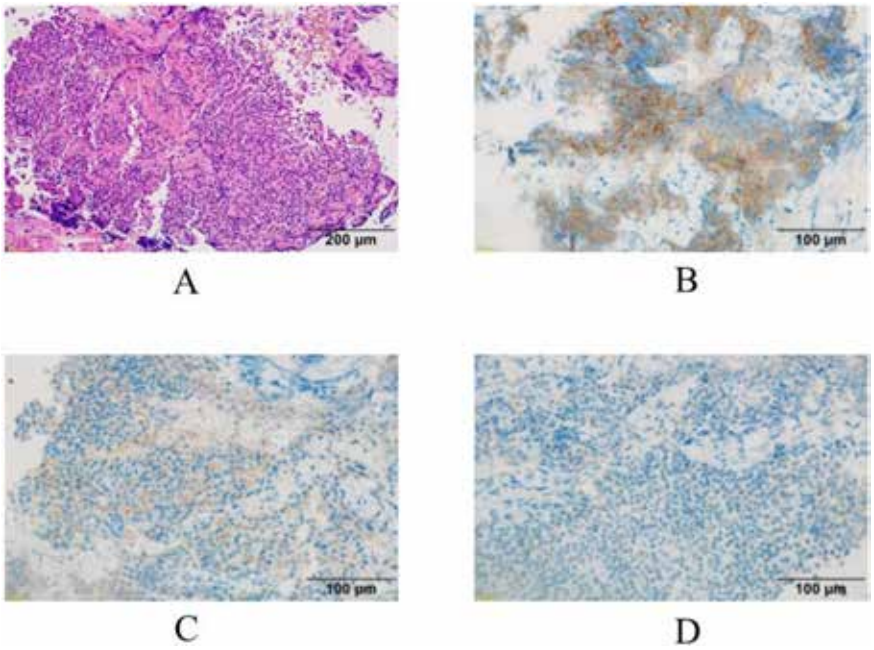

Fig. 4 Histopathological findings in Case 1
Hematoxylin and eosin staining shows uniform proliferation of cells with rounded nuclei (A). Immunohistochemically, the tumor is positive for synaptophysin (B) and CD56 (C). Tumor Ki-67(%) was estimated to be < 3% (D).

CD56 was positive, whereas that for chromogranin A was negative; the Ki-67 index was < 3% (Fig. 4). Based on the histological and immunohistochemical findings, the patient was diagnosed with a Grade 1 neuroendocrine tumor (carcinoid tumor). Although additional surgery was not attempted, no recurrence or metastases were observed during 4 years of follow-up.

Case 2

A 28-year-old woman was referred to our hospital by a nearby ENT clinic owing to left-sided hearing loss since 3 months. Otoscopy revealed a smooth white mass in the left ear canal, and the tympanic membrane was not observed (Fig. 5A). PTA revealed conductive hearing loss with a threshold of 30 dB in the left ear (Fig. 5B). CT revealed a soft-tissue mass in the left middle ear extending to the ear canal, without osteolysis (Fig. 6A). The mass showed high signal intensity on T1-weighted magnetic resonance images and isointensity on T2-weighted images, and a slight contrast effect was observed with gadolinium (Fig. 6B, C, D). Biopsy of the tumor in the ear canal performed under local anesthesia revealed a Grade 1 neuroendocrine tumor (carcinoid tumor).

Following the histopathological diagnosis, tumor resection was performed using the transcanal approach. After retroaural incision and tympanomeatal flap elevation, the posterior wall skin of the ear canal was incised to control the soft tumor filling the ear canal. The tumor was located in the tympanic cavity and extended into the ear canal through the anterosuperior quadrant of the tympanic membrane. The tumor bled easily and extended into the epitympanum medially to the malleus head (Fig. 7A); therefore, transcanal atticotomy was added. The incus, and head and handle of the malleus were removed (Fig. 7B), and the tumor was removed en bloc. The stapes and chorda tympani were not involved in the tumor; therefore, they were preserved. The ossicular chain was repaired with tympanoplasty type IIIc (Ost) [2]. Histopathological examination revealed tumor cells with rounded nuclei proliferating in a sheet-like pattern on hematoxylin-eosin staining. Since this was one of the variable growth patterns characteristics of neuroendocrine tumors, immunohistochemical testing was added. Immunohistological tests for synaptophysin, CD56, and chromogranin A were positive, and the Ki-67 index was < 3% (Fig. 8), which was consistent with a Grade 1 neuroendocrine tumor (carcinoid tumor). No recurrence or metastasis was observed during 3 years of follow-up.

DISCUSSION

Carcinoid tumors are derived from neuroendocrine cells and occur frequently in the digestive system; however, they have rarely been reported in the middle ear (< 0.7% of cases) [3]. In 1907, Siegfried Oberndorfer reported a tumor of the small intestine, calling it "carcinoid" [4]. Although carcinoids are considered benign tumors, non-benign carcinoid tumors with distant metastases have been reported [5]. Carcinoid tumors have been removed from the World Health Organization classification of neuroendocrine tumors of the digestive system, and these tumors are graded based on mitotic figures and the Ki-67 index. Neuroendocrine tumors generally present on HE staining as histology with rounded nuclei and pale cytoplasm, with a variety of growth patterns including glandular/tubular, sheet-like, trabecular and single cell [6]. Neuroendocrine cell markers used in immunohistochemistry include synaptophysin, CD56, chromogranin A, and Ki-67. Among these, the Ki-67 index is associated with degree of the malignancy; the higher the index, the higher the malignancy [7]. Grade 1 neuroendocrine tumors are regarded as conventional carcinoid tumors [1]. Therefore, carcinoids are now recognized as a low-grade malignant tumors. In addition, new categories of

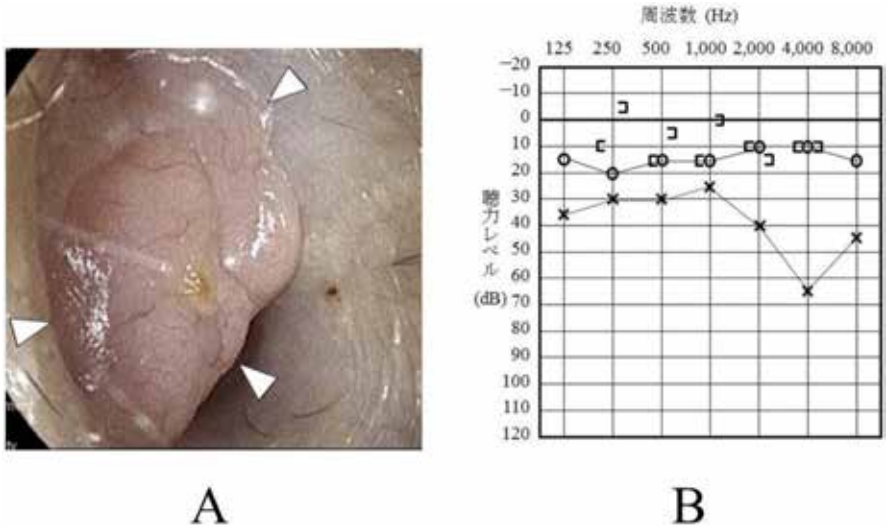

Fig. 5 Otoscopy and pure tone audiometry findings in Case 2
A: The left ear canal is occupied by a smooth white mass extending to the anterosuperior quadrant of the tympanic membrane (arrowhead). B: Pure-tone audiometry shows conductive hearing loss in the left ear, with a threshold of 30 dB.

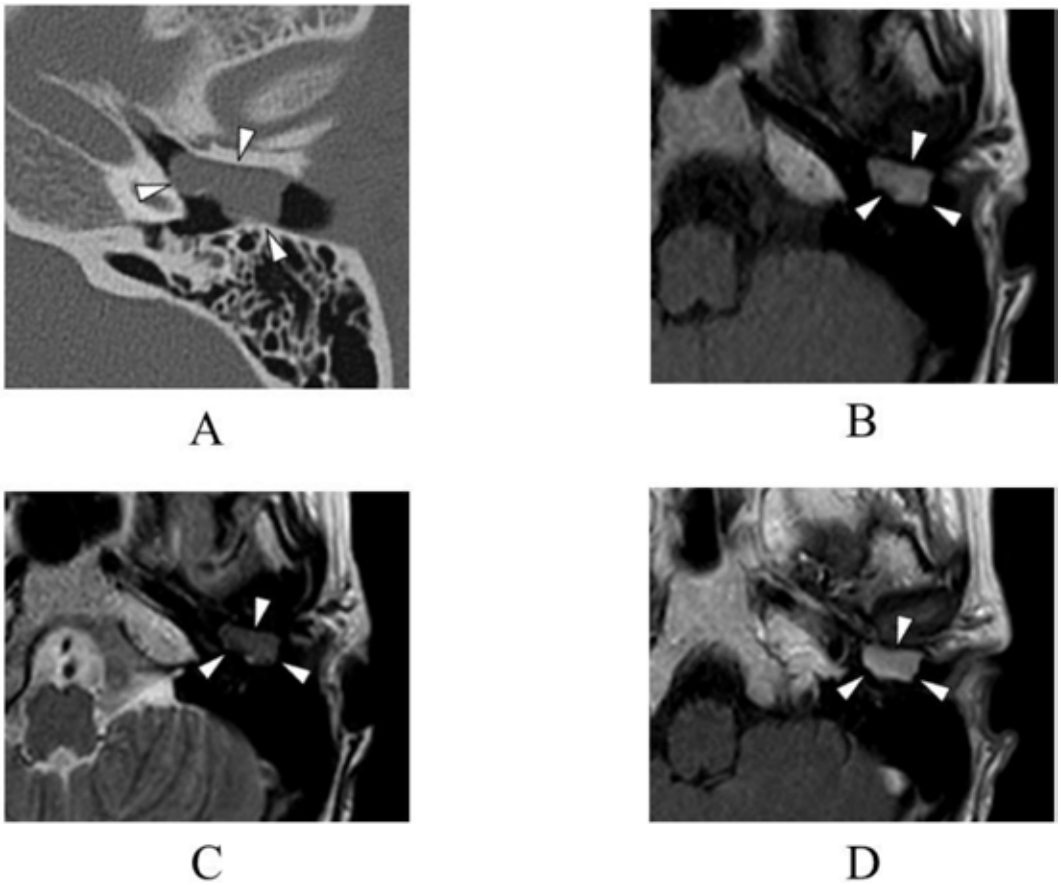

Fig. 6 Computed tomography (CT) and Magnetic resonance (MR) images of the temporal bone in Case 2. The arrowheads show the tumor extension.
A: CT axial view shows a soft-tissue lesion extending from the left middle ear to the ear canal without bone destruction. B: T1-weighted MR image shows a hyperintense lesion. C: T2-weighted MR image shows that the signal intensity of the lesion is similar to that of the brain. D: T1-weighted gadolinium-enhanced MR image shows contrast enhancement.

neuroendocrine tumors have been reported not only in the digestive system, but also in the head and neck [8]. Carcinoid tumors of the middle ear were first reported by Murphy *et al.* in 1980 [9]. In 1976, Hyams *et al.* first reported adenomatous tumors of the middle ear [10]. The characteristics of carcinoid tumors and adenomas are similar, and Torske *et al.* concluded that these two tumors are indistinguishable [11]. Saliba *et al.* reviewed the literature on carcinoid and adenomatous tumors of the middle ear [12] and reported that differentiating

Fig. 7 Operative findings in Case 2
A: A tumor (arrowhead) is observed in the tympanic cavity that protrudes into the ear canal. The tumor extends medially to the malleus (arrow). B: The tumor has been removed following excision of the incus and head and handle of the malleus; the chorda tympani is preserved. (M: Malleus, I: Incus, CT: Chorda tympani)

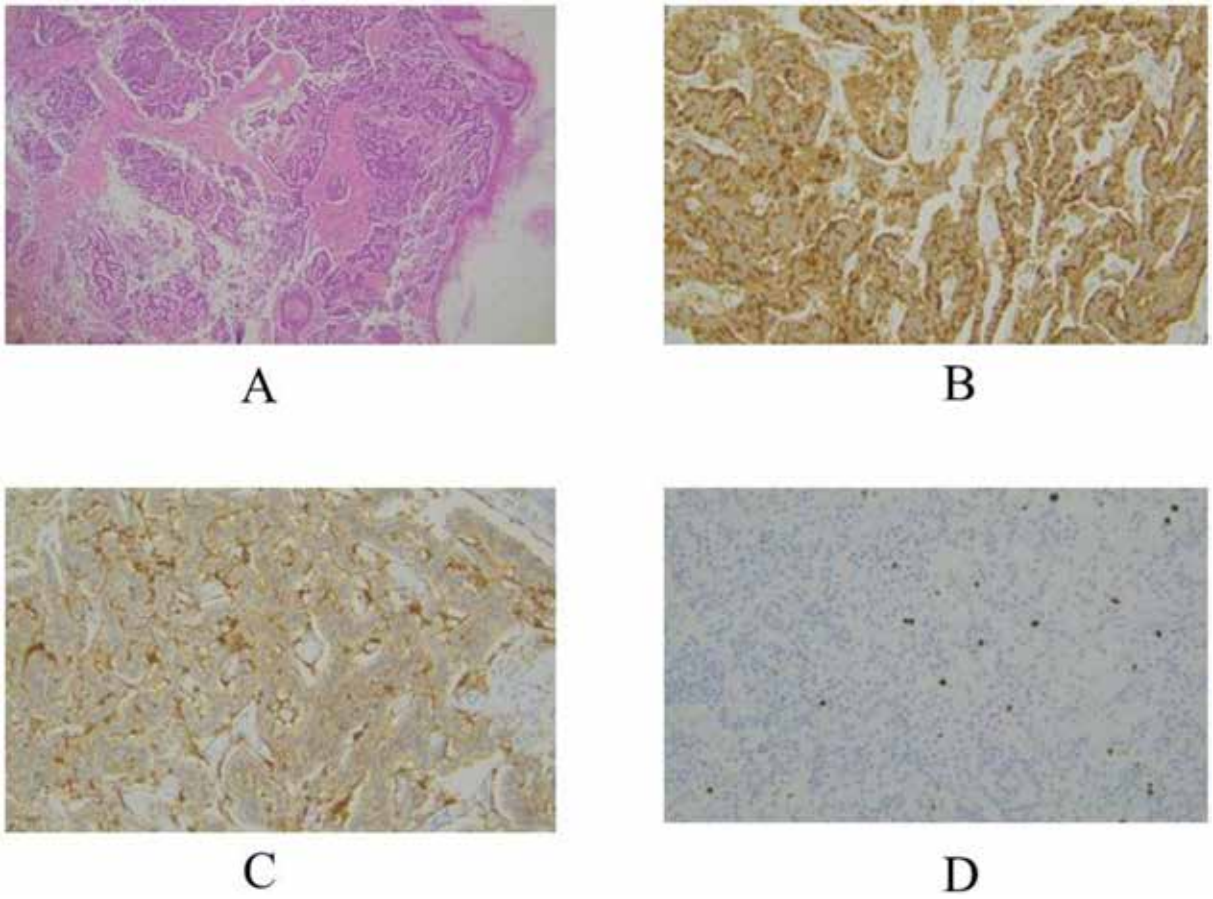

Fig. 8 Histopathological findings in Case 2
Hematoxylin-eosin staining shows tumor cells with round nuclei proliferated in a sheet-like structure (A). Immunohistochemically, the tumor is positive for Synaptophysin (B) and CD56 (C). Ki-67 index is less than 3% (D).

these tumors based on imaging findings is difficult.

Preoperative diagnosis of middle-ear carcinoid tumors based on imaging findings is challenging because of their rarity and nonspecific radiological features. In both the cases presented here, the imaging findings were nonspecific, making a definitive diagnosis based on imaging findings alone difficult. Often, these tumors cannot be distinguished from other middle-ear lesions, such as paragangliomas or cholesteatomas, based on imaging findings alone. Although CT and MRI provide useful information about the characteristics of the lesion, they are insufficient for a definitive diagnosis. Therefore, postoperative histopathological confirmation is essential to accurately diagnose middle-ear carcinoid tumors.

Surgery is the primary treatment modality for neuroendocrine tumors because of their poor sensitivity to radiation and chemotherapy. Surgical procedures for

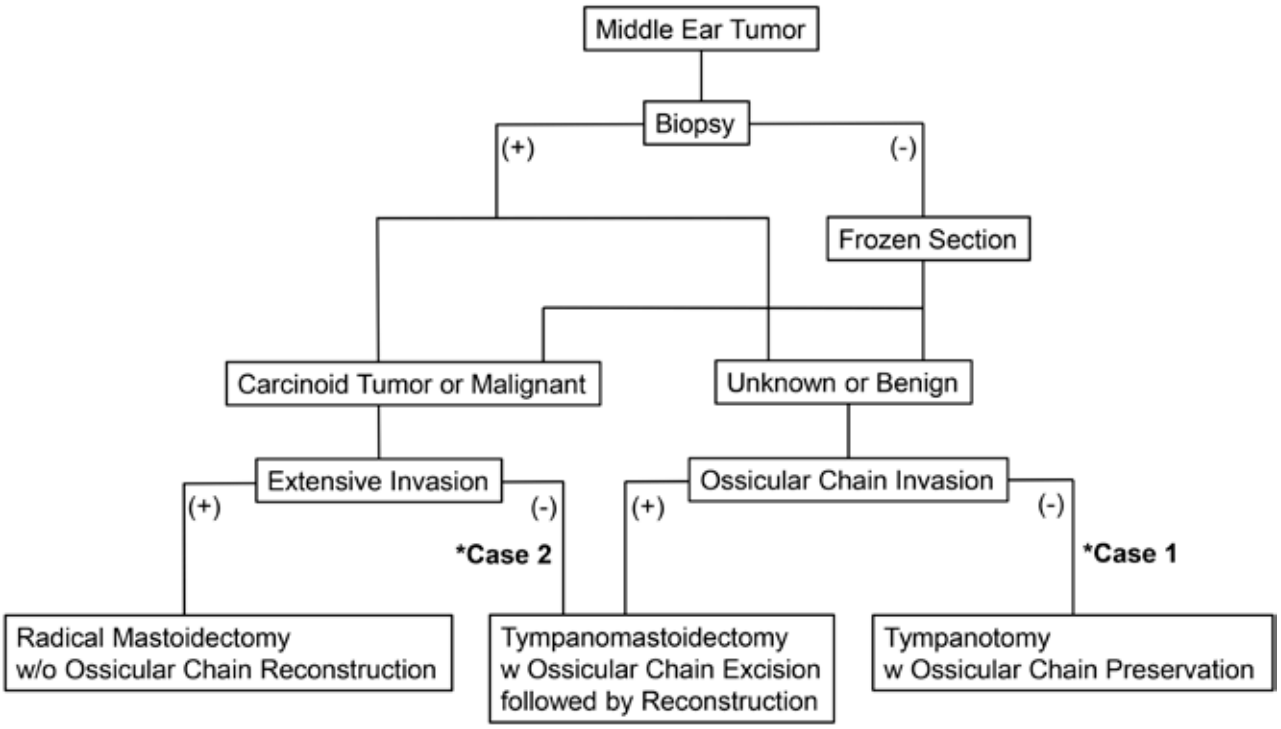

Fig. 9 Proposal of Flowchart of Surgical Treatment Strategies for Middle Ear Tumors
This flowchart outlines the decision-making process for surgical treatment of middle ear tumors.
Case 1: As the tumor was located in the middle ear, preoperative biopsy was not feasible, and intraoperative frozen section diagnosis was performed. Since the diagnosis remained unknown, a palliative resection was performed as tympanotomy with preserving the ossicular chain.
Case 2: A preoperative biopsy was possible, and a carcinoid tumor was diagnosed. Consequently, a tympanomastoidectomy was performed along with excision of the ossicular chain to allow for wider access to the tumor.

carcinoid tumors of the middle ear should be selected based on the extent and malignant grade of the tumor; however, consensus on the need for radical surgery is lacking. As a guide for surgical treatment strategies in middle ear tumors, a flowchart illustrating the approach is proposed (Fig 9). In Case 1, the preoperative and intraoperative diagnoses were uncertain, and macroscopic removal could be performed without removing the ossicular chain, despite the tumor extending to the stapes and round window niche. Following the histopathological diagnosis of a carcinoid tumor (neuroendocrine tumor grade 1), we contemplated additional surgery; however, revision surgery has not been performed till date. In Case 2, the lesion was preoperatively diagnosed as a carcinoid tumor (Grade 1 neuroendocrine tumor); therefore, wider access to the tumor was attempted by removing the ossicular chain. Previous studies recommend aggressive surgery with ossicular chain excision owing to the lower recurrence rate [13, 14]; however, the recurrence rates are not significantly different between tympanotomy, tympanomastoidectomy, and radical mastoidectomy [15]. In Case 1, the ossicular chain should have been removed as in Case 2; however, determining the appropriate resection range without long-term follow-up was impossible even in Case 2.

Although the efficacy of post-operative treatments for middle ear carcinoid tumors remains unclear due to the rarity of cases, treatments such as radiation therapy, chemotherapy, somatostatin analogs, and peptide receptor radionuclide therapy have been reported in other areas [16]. These options could be considered in the event of recurrence.

In our two cases, long-term follow-up is essential, with careful attention to distant metastasis and local recurrence. Previous reports have highlighted that both local recurrence and distant metastasis can occur after prolonged disease-free intervals [15, 17]. Notably, it has been reported that "the average interval from initial treatment to the first recurrence was 13 years, with a range of 16 months to 33 years," illustrating the potential for recurrence even after extended periods of remission.

While the collection of additional case reports of carcinoid (neuroendocrine) tumors in the middle ear could contribute to a broader understanding of the disease, it may not directly establish a definitive follow-up period. Therefore, based on the currently available data and the unpredictable nature of this tumor, we plan to follow up these two cases for more than 10 years.

CONCLUSION

We encountered two cases of carcinoid (neuroendocrine) tumors in the middle ear. In one patient, the tumor was removed without a preoperative diagnosis; the ossicular chain was preserved, and revision surgery was not required. In the other patient, in whom the diagnosis was established preoperatively, the ossicular chain was removed prior to tumor excision, followed by ossicular chain repair. Long-term follow-up is necessary in both cases because carcinoid tumors are low-grade malignancies, and a definitive treatment policy is lacking.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this article.

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