Carcinoid tumor of the middle ear: a case report and review of literature

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Abstract: Carcinoid tumors of the middle ear are very rare. Here we describe a 37-year-old man with multiple recurrent carcinoid tumor of the right middle ear. The CT demonstrated the recurrent mass that filled the tympanum and mastoid with osteolytic invasion, and the tumor was removed by surgery. The pathological findings showed the tumor cells, without necrosis and mitotic activity, had round, oval, or slightly irregular nuclei and finely-dispersed chromatin, arranged in cords, nests, and glandular structures. They were strongly positive for synaptophysin and CD56, but were negative for S-100 and chromogranin A. Ki-67 proliferation activity was low (<2%). With a review of the literature, the clinical, pathological characteristics and treatment modalities of this rare tumor are discussed.

Keywords: Middle ear, carcinoid, neuroendocrine carcinoma, immunohistochemistry

Introduction

Carcinoid tumors of the middle ear are very rare. Since Murphy described the first case in 1980 [1], there have been approximately 54 cases of middle-ear carcinoid reported. With an indolent course, middle-ear carcinoids have previously been considered as benign, usually confined to the tympanum and lacking any capacity for metastasizing [2]. However, several recent reports [3-5] suggest that the carcinoid should be classified as a low-grade malignancy supported by the evidence of local recurrence, regional cervical lymphatic metastasis and distant metastasis [3-8]. Here we present a patient with early local recurrence and osteolytic invasion of a middle-ear carcinoid and also review the previous studies.

Case report

A 37-year-old man, with no history of smoking or alcohol consumption, presented with a 2-year history of otorrhea and 6-month of tinnitus and hearing loss of right ear, but no complaint of pain, bleeding, dizziness and facial palsy. No symptoms of lymphatic metastasis and distant metastasis. No family history of cancer. Physical examination revealed a pink mass extending through the right tympanic membrane from the middle ear. A computer tomography scan showed that the tympanum and mastoid were filled with an isodensity mass without osteolytic invasion (Figure 1A); The patient was first considered as chronic otitis media with cholesteatoma and agreed to undergo the surgery. During the operation, frozen biopsy was taken and histology was indicative of a tumorous mass. Tympanomastoidectomy was performed that revealed a reddish mass with a slight yellowish hue occupying the tympanum and mastoid. The construction of the ossicular chain was conservative, although it was covered with tumor. The Fallopian canal and cochlea did not appear to be eroded. The tumor was completely removed.

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At one month post-surgery follow up, CT showed a heterogeneously enhanced mass that filled the tympanum and mastoid with osteolytic invasion (Figure 1B). Subtotal temporal bone resection was performed. A recurrent tumor with granulation eroded the fallopian canal and the wall of the tympanum was found. The tumor was completely excised and the wall of the carotid artery canal, cochlea and horizontal semicircular canal were also removed. Eight months later, a new mass similar to that found during the first month follow up on CT scan was found again (Figure 1C). There were no signs of regional or distant metastasis. The patient refused further treatment and was lost to follow up.

Discussion

Carcinoid tumors are currently categorized as well-differentiated neuroendocrine carcinomas that belong to a group of neuroectodermal neoplasms with epithelial differentiation. A typical carcinoid is considered as Grade I, according to the latest WHO classification of head and neck tumors [9]. Understanding the pathogenesis of middle-ear carcinoid is evolving and experienced three stages. Prevailing reports suggest that middle-ear carcinoid was considered to be benign, lacking any capacity for metastasizing before 2002 [2]. However, 5 cases from 2005 to 2012 demonstrated the presence of local lymphatic metastasis suggesting that the tumors may be classified as a low-grade malignancy [4, 10, 11]. Two cases with distant metastasis were reported in 2008 and 2013 [5, 12], respectively, indicating a more malignant nature of the tumor. Here we review the literature with focus on the differences between primary and metastatic middle-ear carcinoid.

Primary middle-ear carcinoids generally develop slowly, and its local invasion is usually non-destructive. More than 90% of the patients...
Carcinoid tumor of the middle ear

Some patients develop facial paralysis. Apart from these symptoms, metas-

complain of hearing loss, and 20%-30% of patients suffer from ear fullness, tinnitus, ear discharge [3]. Some patients develop facial paralysis. Apart from these symptoms, meta-

Figure 2. (A) The tumor cells, without necrosis and mitotic activity, have round, oval, or slightly irregular nuclei and finely-dispersed chromatin, arranged in cords, nests, and glandular structures. Hematoxylin and eosin. (B) Cells are strongly positive for synaptophysin and (C) positive for CD56, but (D) negative for chromogranin A. Original magnification, ×400.

Table 1. Review of literatures describing metastasis of the middle-ear carcinoid and treatment

<table>
<thead>
<tr>
<th>Literature</th>
<th>Case No.</th>
<th>Age (yrs)/sex</th>
<th>TDM</th>
<th>Location of metastasis</th>
<th>Treatment</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mooney et al. 1999</td>
<td>1</td>
<td>55/M</td>
<td>8 years</td>
<td>Right-sided cervical lymph node</td>
<td>MRND + RT</td>
<td>Free for 5 months follow-up</td>
</tr>
<tr>
<td>Menezes et al. 2001</td>
<td>2</td>
<td>51/M</td>
<td>20 years</td>
<td>Right parotid gland, parotid lymph node, cervical level II to IV lymph node</td>
<td>SPE + SND + RT (three months)</td>
<td>Further recurrence of The tumor in the right middle cranial fossa.</td>
</tr>
<tr>
<td>Ramsey et al. 2005</td>
<td>3</td>
<td>72/M</td>
<td>13 years</td>
<td>Right parotid gland</td>
<td>SPE</td>
<td>Free for 24 months follow-up</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>72/F</td>
<td>43 years</td>
<td>Left parotid lymph node</td>
<td>SPE</td>
<td>Free for 48 months follow-up</td>
</tr>
<tr>
<td>Pellini et al. 2005</td>
<td>5</td>
<td>55/F</td>
<td>3 years</td>
<td>Cervical level I V lymph node</td>
<td>MRND + RT</td>
<td>Unknown.</td>
</tr>
<tr>
<td>*Gaafar et al. 2008</td>
<td>6</td>
<td></td>
<td></td>
<td>Lymphatic and liver metastasis</td>
<td>-</td>
<td>Died</td>
</tr>
<tr>
<td>Richard et al. 2012</td>
<td>7</td>
<td>72/F</td>
<td>8 months</td>
<td>Left parotid and cervical level II to IV lymph node</td>
<td>SPE + SND + RT</td>
<td>Recurrence after 6 months follow-up</td>
</tr>
<tr>
<td>Fundakoski et al. 2013</td>
<td>8</td>
<td>52/M</td>
<td>11 years</td>
<td>Cervical lymph nodes and iliac crest</td>
<td>SND</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Abbreviations: yrs: years; F: female; M: male; TDM: the length of time between the first diagnosis and the metastasis; RT: radiotherapy; MRND: modified radical neck dissection; SND: selective neck dissection; SPE: superficial parotidectomy; *: no full text and detail.
Carcinoid tumor of the middle ear

static patients are mainly present with cervical level II to IV lymphatic mass (5 of 7 metastatic cases, 71.4%), followed by parotid gland mass (4 of 7 metastatic cases, 57.1%), according to our review (Table 1). One case reported iliac crest metastasis [5]. The length of time between first diagnosis and metastasis lasted from 8 months to 43 years, with a mean of 14.1 years, suggesting that a long follow-up is necessary.

There appears to have no difference in pathological findings between primary and metastatic tumors. Typical histologic features of the tumor include the presence of cuboidal or columnar cells—which have small, round, oval, uniform nuclei with finely stippled chromatin and form cords, nests, glandular or tubular structures-eosinophilic cytoplasm, but lack cellular pleomorphism, necrosis, and mitotic characteristics. Immunohistochemically, they are strongly stained positive for cytokeratin, chromogranin A, synaptophysin, CD56, and vimentin, but are negative for S-100. S-100 has been used to differentiate carcinoid tumors from parangangioma [2]. Ki-67 proliferative index of these tumors are generally less than 10%, whereas most small-cell carcinomas show a value that is substantially higher than 25% [3, 13]. Several investigators believe that Ki-67 serves as a significant predictor for local recurrence, osteolytic enlargement and metastasis [3, 14, 15]. A low Ki-67 index is associated with longer survival in carcinoid tumors. However, Fundkowski et al [5] argue that histologic and morphologic characteristics may not reliably predict tumor outcomes. An indolent middle-ear carcinoid with a low Ki-67 may also have undetermined malignant potential.

A complete removal of the tumor mass by surgery is considered to be the optimal treatment for primary and metastatic middle-ear carcinoids. Tympanomastoidectomy or radical mastoidectomy is recommended, especially in cases where tumors encase the ossicular chain. If the chain is involved and not removed, recurrence is much more likely [2]. A modified radical or selective neck dissection is used to remove cervical lymphatic metastasis, whereas superficial parotidectomy is suitable for the parotid gland. In some cases, operation may not be sufficient for multiple recurrent lesions or metastatic. Owing to its rarity, there is no standard approach to therapy. Adjuvant radiotherapy, which is not well documented in the literatures, is administered in some metastatic cases. But, the clinical efficacy has not been fully established [4, 7, 11, 16]. It has also been hypothesized that radiation therapy may induce malignant transformation of the tumor [2]. To date, only 4 patients have undergone the radiotherapy, 3 of them reported local recurrence and metastasis. There is still no sufficient evidence to confirm the hypothesis, but the possibility remains. Chemotherapy has not been reported so far.

A surgical recurrence rate is reported to be 18-22% [2, 11]. In 2005, Ramsey et al [10] reported 6 recurrences among 34 patients with primary middle-ear carcinoids that underwent surgery, with a relatively long period between initial tympanomastoidectomy or radical mastoidectomy and the recurrence (approximately 15-33 years). However, the tumor in the patient reported here had not only eroded the bones, but also rapidly recurred in a year, suggesting that primary middle-ear carcinoids may reappear rapidly following surgery.

The survival rate of primary middle-ear carcinoid remains optimistic. One of the largest case series (n = 48) reported 100% survival (including patients with recurrent tumor, n = 8), with a mean follow-up period of 15 years [2]. Another reported 10-year survival rate of 90% [3]. We are unable to calculate the accurate rate of metastatic cases because of the fragment data. The longest survival patient with metastasis is free for 48 months follow-up [10], according to our review.

In conclusion, carcinoid of the middle ear, an indolent tumor with undetermined malignant potential, is rare. Its possibility for regional and distant metastasis may present particular therapeutic challenge. Based on our case of a 37-year-old male who presented with this tumor rapidly recurred and bone erosion, we believe that the middle-ear carcinoids have more malignant potential.

Disclosure of conflict of interest

None.

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