CASE STUDY

Middle-Ear Neuroendocrine Carcinoma

Carcinoma neuroendocrino de oído medio

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Clinical Case

This case was of a 42-year-old male who presented a 5-year history of sensation of hearing loss and tinnitus in the right ear. Otoscopy revealed a non-pulsatile bulge of the tympanic membrane. In audiometry testing, he had a fall in high-pitched sounds from 2000 Hz onwards. Initial diagnosis was set as congenital cholesteatoma or glomus. Magnetic resonance imaging (MRI) revealed a hypercapturing mass that occupied the entire tympanic membrane, antrum and attic, compatible with possible tympanic glomus. In the computed tomography (CT) of the petrous portion of the temporal bone, no bone erosions surrounding the ossicular structures were seen (Fig. 1). It was decided to carry out a tympanoplasty and a slightly bleeding, purplish-red mass was found in the operation.

Anatomopathological study indicated a neoformation with hyperchromatic cell groups and eosinophilic cytoplasm; the immunohistochemical study was positive for AE1-AE3, CAM5.2, chromogranin and synaptophysin (Fig. 2). The diagnosis was neuroendocrine carcinoma of low-grade activity. The possibility that it was a secreting tumour was posed to the Internal Medicine Service at this hospital. The X-ray study and that of the tumour markers (carinoembryonic antigen [CEA], alpha-1-fetoprotein, cytokeratin fragment [cyfra] antigen, prostate-specific antigen [PSA], CA 19.9, CA 125 and CA 72.4), along with the biochemical study of catecholamines in plasma and urine were normal. The patient appears for periodic follow-up and is disease-free 1 year after the otological surgery.

Discussion

Carcinomas of the middle ear are rare tumours with epithelial and neuroendocrine differentiation. The first to describe them was Hyams in 1976. They are composed of 2 types of cells (exocrine and neuroendocrine) in which neuroendocrine granules and sometimes neuropeptides (chromogranin, synaptophysin, serotonin and pancreatic polypeptide) are detected. Chromatin tends to align in a salt and pepper pattern. Electron microscopy reveals dark neurosecretory granules and intermediate filaments inside the cytoplasm.

Approximately 100 cases, plus the one described here, have been published. Mean onset age is located in the fifth decade of life.

Hearing loss is the most frequent symptom. The majority have conductive type. In otoscopy, redness or swelling of an intact tympanic membrane is seen.

Only 1 case of carcinoid syndrome arising from a neuroendocrine tumour of the middle ear has been published. That patient presented diarrhoea, abdominal pain, skin redness and bronchoconstriction.

Differential diagnosis of the condition includes cholesteatoma, chronic otitis media, parangangiomas, Schwannoma, hamartoma, squamous cell carcinoma.
Middle-Ear Neuroendocrine Carcinoma

Figure 1  CT of petrous portion of the temporal bone in which there are no osseous erosions surrounding the ossicular structures.

Table 1 Immunohistochemical Differential Diagnosis.

<table>
<thead>
<tr>
<th>Positive markers</th>
<th>Negative markers</th>
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<tbody>
<tr>
<td>Neuroendocrine carcinoma</td>
<td>Enolase</td>
</tr>
<tr>
<td>Cytokeratins AE1/AE3</td>
<td>Enolase, LCA, E-cadherin, CD99</td>
</tr>
<tr>
<td>CAM5.2, chromogranin, synaptophysin</td>
<td>CAM5.2, EMA</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>Cytokeratins</td>
</tr>
<tr>
<td>Vimentin, desmin, MyoD1, myogenin</td>
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<tr>
<td>Paraganglioma</td>
<td>Synaptophysin, chromogranin A, protein S-100</td>
</tr>
<tr>
<td>Papillary adenocarcinoma</td>
<td>Cytokeratins, EMA, protein S-100</td>
</tr>
<tr>
<td>Endolymphatic sac tumour</td>
<td>Cytokeratins, vimentin, EMA, protein S-100, enolase</td>
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<td>EMA, epithelial membrane antigen; LCA, leucocyte common antigen.</td>
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rhabdomyosarcoma, papillary adenocarcinoma and endolymphatic sac tumours.

Being able to identify various immunohistochemical markers has increased diagnostic precision. Table 1 presents a brief summary of the immunohistochemical markers that help us to differentiate this condition. Our case was positive for AE1/AE3, CAM5.2, chromogranin and synaptophysin cytokeratins; these data are similar to those described by other authors in the literature review, with percentages of 89.6%, 81.3%, 87.5% and 31.3% respectively.

The X-ray study using computed tomography (CT) of the petrous portion of the temporal bone usually reveals a soft tissue mass in the middle ear, with greater or lesser effect on the ossicular chain. Intraoperative description usually corresponds to a reddish polypoid or multilobulated mass. The tumours are generally well circumscribed but not encapsulated.

There are no differences between benign and malignant tumours detectable using CT.3 Magnetic resonance imaging (MRI) reveals tumours that are isointense or that they give a weak signal higher than the white matter in T1. In T2 tumours they have approximately the same signal of intensity as the grey matter.

The appearance of local recurrences is higher if transcant tympanotomy is performed rather than a radical mastoidectomy.4 Some cases have required a petrosectomy. The use and benefit of postoperative radiotherapy has not been established. There are no published cases in which chemotherapy or somatostatin analogues have been used.

Long-term follow-up is recommended because of late recurrences (18%)7 and metastases.

Nuclear medicine (thanks to scintigraphy for somatostatin receptors with octreotide8 and PET scanning6) has been shown to be a sensitive tool to determine tumour recurrences, primary tumour remains and metastasis.

The most frequently found metastases are located in the ipsilateral parotid gland,9 treated with parotidectomy.

References