Case Report

Carcinoid Tumors in the Middle Ear: a Case Report and Literature Review

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Abstract Middle ear carcinoid tumor (MECT) is rare. Only 46 cases of MECT have been reported in the literature since the first case of MECT was described in 1980. We present here a case of primary MECT initially diagnosed as inflammatory aural polyp. The case was a 43-year-old woman complaining of right ear chronic otorrhea and hearing loss over a period of five years, with a blockage sensation in the right ear for two years. Audiometry showed conductive hearing loss in the right ear. Physical examination and CT scans showed a mass in the right external auditory canal and middle ear, surrounding the ossicular chain. Pathologic study of surgically removed specimen revealed features of carcinoid tumor with positive staining to chromogranin A and synaptophysin in tumor cells. Local radiation of 60 Gy was applied. The patient has been followed up for more than one year. Postoperative histopathological examination showed no evidence of MECT recurrence one year after surgery, but inflammatory changes in the middle ear. Relevant literatures were reviewed. Clinical, histopathological, immunohistochemical and ultrastructural features of MECT, and strategies in MECT diagnosis and management are discussed.

Key words carcinoid tumor; middle ear; diagnosis; surgery

Introduction

Middle ear carcinoid tumor (MECT) is a rare form of neoplasm. Since the first case of MECT was reported by Murphy et al. in 1980 (Murphy et al, 1980), there have been only forty-six cases of MECT reported in the literature (Ramsey et al, 2005), with only three cases reported in China (Feng et al, 2001; Zhang et al, 2005; Chan et al, 2005). We present here a case of primary MECT, which was initially diagnosed as inflammatory aural polyp. The literature is reviewed. Clinical, histopathological, immunohistochemical and ultrastructural features of MECT, as well as strategies for diagnosis and management of MECT are discussed.

Case Report

A 43-year-old woman presented in November, 2004, with chronic otorrhea and hearing loss on the right for five years, and a gradually increasing blockage sensation for two years. Physical examination revealed a soft tissue mass blocking the right external auditory canal. Audiometry showed conductive hearing loss in the affected ear. High-resolution CT scans showed a soft-tissue density mass in the external canal and in the middle ear on the right side, surrounding a relatively intact ossicular chain, without mastoid involvement (Figure 1). Biopsy of the external auditory canal mass suggested inflammatory aural polyp.

The patient underwent resection of the external auditory canal mass. The mass was found to have originated from the middle ear through a perforation in the eardrum and was wrapped in a fibrous capsule. The lesion tissues were removed completely. Exploration of the middle after removed all the lesion revealed an intact ossicular chain. This was followed by a modified tympanoplasty.

Examination of the specimen with H & E staining demonstrated morphologic features of a carcinoid tumor. Immunohistochemical examinations showed positive staining to chromogranin A and synaptophysin, but not to S100, cytokeratin 20 and cytokeratin 7, in tumor cells(Figure 2), A diagnosis of MECT was made based upon these findings. Two weeks after the surgery, the patient received local radiation with a total dose of 60 Gy. At the 1 year follow-up visit, CT scan suggested
possible recurrence of MECT in the middle ear. The right middle ear was reopened and found where filled with granulation tissues with signs of ossicular chain erosion. After removed the lesion and the eroded ossicles including malleus, incus and stapes cruses, a modified tympanoplasty was conducted to reconstruct hearing. Histopathologic examination of the removed lesion showed no evidence of MECT recurrence, except features of inflammatory tissues.

Discussion

Carcinoid tumors are neuroendocrine neoplasms. They are relatively common in the digestive and respiratory systems. Carcinoid tumors are extremely rare in the middle ear (Soga, 2003). Only have 46 middle ear cases been reported since MECT was first described by Murphy et al. in 1980 (Murphy et al., 1980; Ramsey et al., 2005).

Histogenesis of MECT

Although carcinoid tumors are labeled as neuroendocrine tumors, they can also originate in tissue lacking neuroendocrine cells, such as that in the middle ear (Nikanne et al., 2004). The cell origin of MECT is still speculative. MECT most likely originates from pre-existing neuroendocrine cells or a primitive precursor cell (Murphy et al., 1980).

Histologically, MECT exhibits both glandular and neuroendocrine differentiation. Based on immunohistochemistry and electron microscopy, three cell types may be found in MECT. Most frequent are B cells with an abundant pale cytoplasm containing neuroendocrine granules. Less frequent are A cells, which are slender, darkly staining and line the glandular lumina. Least frequent are amphicrine cells, which are characterized by both lumina and neuroendocrine granules in their cytoplasm and interpreted as the link between A and B cells (Manni et al., 1992; Faverly et al., 1992). It is believed that MECT represents a distinct entity and can be classified as adenocarcinoids or amphicrine tumors, i.e. demonstrating both exocrine and endocrine activities (Faverly et al., 1992).

Clinical Features of MECT

Recently, Ramsey et al. (2005) reviewed the literature to identify the clinical features of MECT. Symptoms of MECT are not characteristic. The most common presenting symptom is hearing loss (Ramsey et al., 2005; Manni et al., 1992). From a review of 30 reported
cases by Nyrop et al (1994), it seems that nearly all patients have progressive hearing loss, most often of the conductive type, and that about half of the patients complain of tinnitus and fullness of the ear. Systemic symptoms including carcinoid syndrome are uncommon (Ramsey et al, 2005; Nyrop et al 1994). On otoscopic examination, the eardrum is intact in most patients with MECT, and erythema or lateral bulging of the tympanic membrane is seen commonly. A whitish or reddish bulging mass can be observed through the intact tympanic membrane. In some cases, the eardrums may be perforated (Nikanne et al, 2004; Manni et al, 1992; Nyrop et al, 1994). The tumor is most often localized to the middle ear with varying degree of extensions into neighboring areas (Nyrop et al, 1994). The ossicular chain is often encased by the tumor, with or without ossicle erosion (Manni et al, 1992; Nyrop et al, 1994). MECT may erode facial canal resulting in facial palsy (Chan et al, 2005; Nikanne et al, 2004).

**Histopathology, immunohistochemistry and ultrastructure of MECT**

Microscopically, MECT shows histologic features of a carcinoid tumor, such as ribbon or festoon arrangement of tumor cells, formation of anastomosing cords and glandular spaces, presence of numerous argyrophilic as well as argentaffin secretory granules within many of the tumor cells. However, MECT shows a striking, heterogeneous aspect. Both solid trabecular and tubuloglandular growth patterns, resembling the classic carcinoid tumor and adenomatous tumor respectively, may be identified in MECT (Faverly et al, 1992).

MECT is typically keratin- and vimentin-positive immunohistochemically. Neuroendocrine cell differentiation, a carcinoid feature, may be demonstrated by the presence of numerous argyrophil granules in MECT cells. Immunohistochemically, the tumors are found to contain not only neuronal marker substances such as neuron-specific enolase, S-100 protein, synaptophysin, and chromogranin A, but also serotonin and multiple peptide hormones such as pancreatic polypeptide, glucagon, cholecystokinin and leucine-enkephalin (Nikanne et al, 2004; Mandigers et al, 1996; Devaney et al, 2003). Dense intracellular neurosecretory granules may be identifiable by electron microscopy (Nikanne et al, 2004; Devaney et al, 2003).

**Diagnosis and Differentiation**

Diagnosis of MECT is difficult since the tumors grow slowly and produce non-specific symptoms, easily leading to a relatively late diagnosis (Nikanne et al, 2004; Riddell et al, 1994). In many cases, primary MECT are identified by postoperative histological examinations. It is almost impossible to diagnose MECT solely based upon light microscopy. MECT should be considered in differential diagnosis when biologically low-grade tumors with glandular and trabecular architectures are encountered in the middle ear (Murphy et al, 1980). Diagnostic precision has increasingly improved over the years owing to the use of modern immunohistochemical techniques and electron microscopy, which are necessary for a definite diagnosis of MECT (Nyrop et al, 1994).

Primary MECT are very difficult to distinguish from adenomas and adenocarcinomas using conventional histological stains. There are some differences but also some similarities between carcinoid tumors and adenomas of the middle ear (Murphy et al, 1980). Both of them share a sufficient number of overlapping pathologic features and similarities of clinical behavior to warrant their collapse into a single diagnostic category (Chan et al, 2005; Devaney et al, 2003). Also MECT may commonly be mistaken for an adenocarcinoma because of its histological heterogeneity. The diagnosis of carcinoid tumor should be considered in all cases of adenomatous neoplasm of the middle ear and mastoid (Krouse et al, 1990). Additionally, there is a strong clinical and endocrinological resemblance between MECT and functioning paragangliomas. As distinction from the more common paraganglioma may be difficult on morphologic grounds alone, immunohistochemical studies should be performed (Mandigers et al, 1996; Menezes et al, 2001). Immunohistochemical and electron microscopic studies are of great value in distinguishing carcinoid from other tumors of the middle ear (Riddell et al, 1994).

**Treatment and prognosis of MECT**

A broad range of diverse therapeutic measures have been employed in the reported cases of MECT. The tumor is primarily treated surgically and radical mastoidectomy is the most common procedure (Ramsey et al, 2005; Nikanne et al, 2004). Surgical treatment should be tailored to the extent of disease (Ramsey et al, 2005). MECT, a low-grade malignant tumor histologically, is clinically benign and total excision of the tumor and affected ossicles is an adequate treatment (Nyrop et al, 1994; Krouse et al, 1990). A conservative surgery with complete removal of the primary or recurrent tumor appears also to be the treatment of choice for MECT, but clinical follow-up on a
regular basis is recommended (Manni et al., 1992; Devaney et al., 2003; Riddell et al., 1994). As MECT is very rare, there is no statistical evidence as to whether further treatment is necessary after surgical resection of the tumor. However, it has been reported that additional radiotherapy was applied to MECT after surgery (Krouse et al., 1990; Kodama et al., 1989).

In general, the prognosis of MECT is excellent with radical excisions from middle ear. Local recurrence following complete excision is quite uncommon (Menezes et al., 2001). Successful treatment of MECT requires complete excision of the tumor mass, along with the ossicles if they are involved with disease, in order to prevent local recurrence (Krouse et al., 1990). However, local recurrence of a primary MECT 15 years after radical tympanomastoidectomy has been reported, indicating that primary MECT can recur years after radical tympanomastoidectomy (Knerer et al., 1998). But local recurrence of MECT may still be treated successfully with surgery (Manni et al., 1990). MECT may metastasize to cervical lymph nodes although with a low metastasize rate (Mooney et al., 1990). These tumors also have a low propensity for distant metastasis (Krouse et al., 1990). One case of metastatic disease has been reported, thus MECT has a low but definite metastatic potential (Mandigers et al., 1996).

MECTs show benign behaviors and most of them have an indolent biological course, with little destruction of surrounding tissues, therefore, some authors believe that MECT is a rare benign tumor (Nyrop et al., 1994; Devaney et al., 2003). A recent review of the literature has shown that in the 46 reported cases, 10 (22%) patients developed locally recurrent disease, and four (9%) developed regional metastases (Ramsey et al., 2005). Despite previous assertions of benignancy, those studies suggested that MECT is indeed a potential low-grade malignancy with documented metastatic potential. Patients with MECT require indefinite follow-up for possible recurrence or metastasis (Ramsey et al., 2005). In the follow-up of patients, octreotide scanning has proved to be a sensitive method in cases of both recurrence and metastasis (Nikanne et al., 2004).

References