Case Report

**Carcinoid Tumor of the Middle Ear**

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The patient was a 32 year-old man who was first seen in 2003 for 2 years hearing loss. On otoscopic examination, a whitish mass could be observed through the intact tympanic membrane. High resolution computed tomography showed a tumor like lesion in the middle ear with no evidence of bone destruction. A tympanomastoidectomy was performed. Light microscopy showed fragments of cellular tissue in which both glandular and trabecular growth pattern could be identified. Immunohistochemical examinations showed positive staining of the tumor cells for cytokeratin and chromogranin. The diagnosis of carcinoid tumor should be considered in all cases of adenomatous neoplasms of the middle ear and mastoid. Conservative surgical excision is the treatment of choice, and local recurrence following complete excision is uncommon.

**Keywords:** Carcinoid tumor, Middle ear

The middle ear (ME) is a rare site for primary malignant tumors. The neoplasms most commonly encountered at this site in adults and children are squamous cell carcinoma and rhabdomyosarcoma, respectively. Primary tumors with glandular structures, such as ceruminoma, choristoma, monomorphic adenoma, and adenoid cystic carcinoma, are uncommon(1-6). A carcinoid tumor of the middle ear is a very rare neoplasm that represents a class within the spectrum of adenomatous neoplasms. Their true incidence is probably greater than reported because they are very difficult to distinguish from other middle ear adenomatous tumors by histopathology. A correct diagnosis that includes immunohistochemical studies and ultrastructural techniques (electron microscopy, EM) to show neurosecretory granules is important(1-11).

The authors present a new case, together with a review of the literature.

**Case Report**

A 32 year old Thai male was first seen in January 2003 for hearing loss and fullness in his right ear that had persisted for 2 years. The medical and familial histories were unremarkable. On otoscopic examination, a whitish mass could be seen through the intact tympanic membrane at the upper quadrant. An audiogram showed a conductive hearing loss on the right side; the air conduction threshold was 18 dB and the bone conduction threshold was 5 dB. Tympanometry revealed a flat type B trace on the right ear. High resolution computed tomography demonstrated a mass of soft tissue density in the ME with no evidence of temporal bone or ossicles destruction. The initial diagnosis was congenital cholesteatoma. The operative finding showed a reddish mass occupying the upper half of the mesotympanum, epitympanum with extension to the mastoid antrum. The mass engaged ossicles but there was no erosion. A tympanomastoidectomy was done and the tumor was removed together with the head of malleus and incus. Ossicular chain reconstruction was also performed.

Histologically, the neoplasm was characterized by diverse growth patterns of uniform tumor cells. These cells were arranged in small cellular clusters, large sheets, well-formed glands, or short strands (Fig. 1). Individual cells tended to be round, ovoid or cuboidal and contain a mildly hyperchromatic, round to ovoid and occasionally angulated nucleus without discernable nucleolus. Mitosis and necrosis were not seen. The background connective tissue around these tumor cells
was infiltrated by many leukocytes, mainly plasma cells. On immunohistochemical staining, the tumor cells were strongly reactive to cytokeratin (AE1/AE3) and focally positive for chromogranin (Fig. 2). However, they were negative for synaptophysin.

The post operative course was uncomplicated without signs of recurrence during one year follow up.

**Discussion**

The carcinoid tumor of the middle ear is very rare. The first publication by Murphy et al on carcinoid tumors of the middle ear appeared in 1980¹. An accurate review of the literature has shown that since 1980-1999 only 37 cases of primary carcinoid tumor of the middle ear have been described².

Although the diagnosis of carcinoid tumors is based on morphological findings, pathological confirmation of the diagnosis relies on immunohistochemical reactions and to a lesser degree on ultrastructural studies³. The tumors characteristics are 1) cellular arrangement is in solid trabecular or tubule glandular pattern 2) the presence of argyrophilic granules or immunoreactivity for chromogranin/other neuroendocrine markers 3) the presence of neurosecretory granules detected by electron microscopy⁴. Murphy et al suggested that carcinoid tumors should be suspected.

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**Fig. 1**  Middle ear carcinoid composed of sheets, small clusters and glands of uniform epithelial cells (A, H&E *100), (B, H&E *400)

**Fig. 2**  Immunohistostaining, the tumor cells are strongly reactive to cytokeratin (A), and focally positive for chromogranin (B)
in cases of adenomatous lesions of the ME in which the histological appearance shows a trabecular growth pattern\(^1\). The relationship between middle ear adenoma and carcinoid tumors is controversial. Most authors consider the tumors as two separate entities\(^{6,7-9}\) while others favor the view that they are closely related and are epithelial glandular neoplasm with varying degrees of neuroendocrine differentiation\(^{4,6,10,11}\).

The histogenesis of ME carcinoid tumors remains unclear, particularly because neuroendocrine cells have not been described in normal or inflamed ME mucosa\(^{13,14}\). Carcinoid tumors have been classified according to their sites of origin as foregut, midgut, or hindgut lesions. The mucosa of ME developed embryologically from the foregut (ME epithelium is endodermally derived as an extension of the first pharyngeal pouch) and endocrine cells are known to be present in the bronchopulmonary and upper gastrointestinal tracts, which are also derived from the foregut\(^{1,5-7,9,11}\). ME carcinoid tumors may originate from preexisting but undetected neuroendocrine cells. An alternative mechanism is the origin from a precursor epithelial stem cell (a primitive uncommitted cell of the lining epithelium of the ME) that is capable of differentiation into both endocrine and non-endocrine cells\(^{5,7,8}\).

Nearly all patients had progressive hearing loss, most often of conductive type. About half of the patients complained of tinnitus and aural fullness. The typical otoscopic pictures show erythema or lateral bulging of the tympanic membrane, which was intact in most cases. The tumor was most often localized to the middle ear with varying degree of extensions into neighboring areas. It often encapsulated the ossicles, which sometimes were eroded. In addition, foregut carcinoids generally produce only small amounts of peptide hormones, and therefore are usually systemically asymptomatic. Systemic symptoms were only reported in two cases\(^{4,6,8}\).

The tumor is clinically benign and total excision ( tympanomastoidectomy or radical mastoidectomy) of the tumor and affected ossicles is an adequate treatment\(^{4,6,8}\).

**Conclusion**

The authors describe the first case of carcinoid tumor of the middle ear in Thailand. Carcinoid tumor of the middle ear is a very rare benign neoplasm, which may be mistaken for a malignant tumor. The correct diagnosis, which should be considered in case of adenomatous tumor of the middle ear, requires immuno- morphological and ultrastructural procedures. The tumor is clinically benign, conservative surgery with radical removal of the tumor is the treatment of choice.

**References**

เนื้องอกชนิดคาร์ซินอยด์ของหูชั้นกลาง

เพิ่มทรัพย์ อิสิประกิจ, เสาวรส อัศววิเชียรจินดา, สมบูรณ์ ศิลาวัฒน์

ชายไทยอายุ 32 ปี มาตรวจเมื่อ พ.ศ. 2546 ด้วยอาการการได้ยินลดลงเป็นเวลา 2 ปี ตรวจเจอหูซึมก้อนเนื้อสีขาวหลังเยื่อแก้วหูที่มีลักษณะปกติ การตรวจทางรังสีคอมพิวเตอร์พบก้อนเนื้องอกในหูชั้นกลางแต่มีลักษณะการทำลายของกระดูกบริเวณช่องเสียดได้ทำการผ่าตัดเอาเกลียวถิ่น (tympanomastoidectomy) การตรวจชิ้นเนื้อทางพยาธิวิทยาพบว่าเซลล์มีการเรียงตัวแบบ glandular และ trabecular การย้อมเชื้อศัพท์พบกับ cytokeratin และ chromogranin จึงให้การวินิจฉัยว่าเป็นเนื้องอกชนิดคาร์ซินอยด์ ซึ่งเป็นชนิดที่ควรระลึกเสมอในรายที่เป็นเนื้องอกชนิด adenoma ของหูชั้นกลางและกระดูกมาสตอยด์ การรักษาโดยวิธีการผ่าตัดเป็นวิธีการรักษาหลัก โดยการเกิดขึ้นในแนวหลัง การผ่าตัดพบโดนมาก