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Case Report

Primary Carcinoid Tumor of the Ear

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Summary. A very rare case of primary carcinoid tumor in the left ear of a 35-year-old woman is described. The argyrophilic property and uniformity of the size and shape of neurosecretory granules in the cytoplasm of tumor cells, correspond to the characteristics of carcinoid tumors derived from foregut endoderm. Clinical and light microscopic observations suggest this tumor originated from middle ear mucosa.

Key words: Carcinoid tumor – Ear – Argyrophilic granules – Serotonin

It is generally accepted that carcinoid tumors arise from the enterochromaffin (Kulchitsky) cells. Two hypotheses have been proposed as to the origin of these cells, the neuroectodermal (Pearse 1974) and endodermal derivation theories (Robboy and Scully 1980). The occurrence of carcinoid tumor in the skin (Dijk and Seldam 1975) and occasional association of parathyroid adenoma with carcinoid tumor (Williams and Celestin 1962) may support the former hypothesis. The latter can explain the presence of argentaffin cells in adenocarcinoma of appendix (Warner and Seo 1979; Chen and Qizilbash 1979) and colon (Hernandex and Reid 1969), as well as the intimate admixture of argentaffin cells, thyroid epithelium and mucinous cells in ovarian teratoma (Robboy and Scully 1980).

Carcinoid tumors occur most commonly in gastrointestinal tracts and lung. However, ovarian (Robboy and Scully 1980), thymic (Chalk and Donald 1977) and urinary bladder (Colby 1980) carcinoid tumors have been reported. Although carcinoid tumors have been generally considered to be benign, it is widely recognized that extra-appendiceal carcinoid tumors are frequently malignant. This paper reports a case of primary carcinoid tumor in the ear and original site of this tumor is discussed.

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Case Report

A 35-year-old woman was admitted to a hospital with chief complaints of fullness, tinnitus and slight hearing loss in her left ear for 6 months prior to admission. Except for these complaints, she was completely asymptomatic and there was no history of previous otitis media. External ear examination revealed a sessile polypoid lesion arising from the anterior bony portion of the left external auditory canal. Under microscopic operation, polypectomy was performed and no continuity with the ear-drum was noted.

After one month she was then admitted to Kyushu University Hospital for removal of the skin of the external auditory canal. Serial histological examination of the tissue showed no invasion by the tumor cells. Conductive hearing loss, associated with otorrhoea, increased from 15 to 40 dB on an average during 16 months after her discharge. She was then re-admitted and a large, white, soft and fragile tumor filling the tympanic cavity and extending into the mastoid tract was proven by explorating operation. The ossicular chain was completely encased and therefore removal of malleus and incus was necessary to dissect the tumor. There was no bony erosion or destruction of the middle ear. Re-curretage of the middle ear was done 9 days later. The specimens showed only granulation tissue with no tumor cells.

Gastrointestinal tract series, chest X-ray and gallium scintigram revealed no remarkable changes. Quantitative analyses of blood serotonin (5-HT) and 5-hydroxyindoleacetic acid in urine were performed after the operations, and results were within normal limits. The operative course was uneventful. The patient was followed-up for 10 months with no recurrence of the tumor.

Microscopic Findings

The tumor taken from the external auditory canal showed similar findings in haematoxylin-eosin sections to those from the middle ear. The unencapsulated tumor masses were seen beneath the epithelium and were composed of regular cuboidal-to-columnar cells forming trabecular or anastomosing cords with thin fibrous stroma (Fig. 1). Neither haemorrhage nor necrosis was ob-

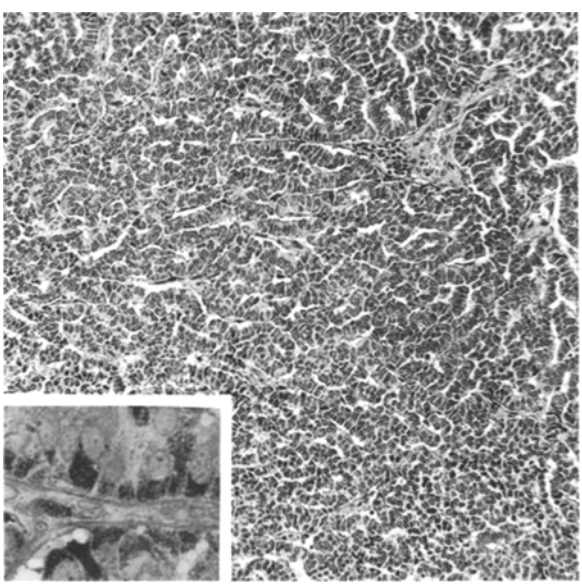

Fig. 1. Typical ribbon-like arrangement of tumor cells separated by thin fibrous stroma. H.E. ×114. *Inset:* Uniform tumor cells with subnuclear granules stained strongly with toluidine blue. Epon-embedded, ×520

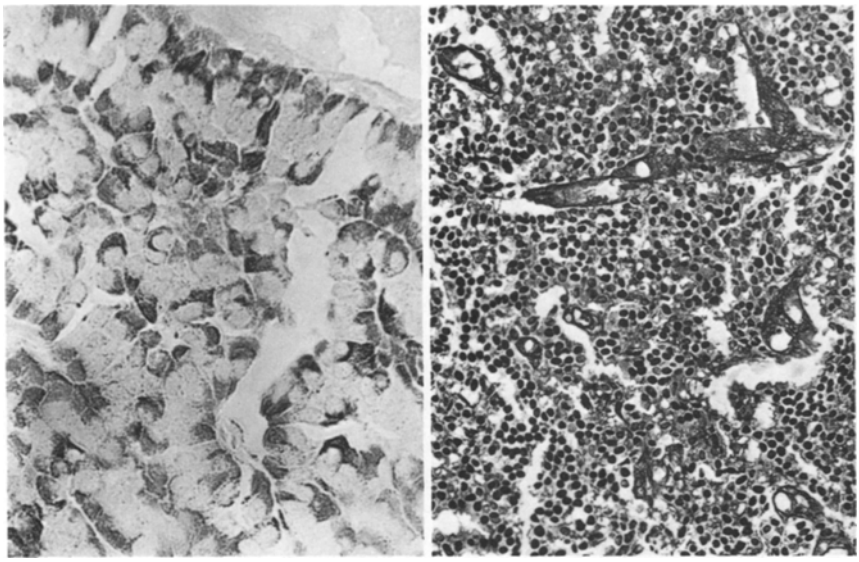

Fig. 2a. Argyrophilic granules in the basal portion of the cytoplasm of the tumor cells. Grimelius stain ×480. **b** Little increase of reticulin fibers around the tumor cell cords. Gomori's silver stain ×210

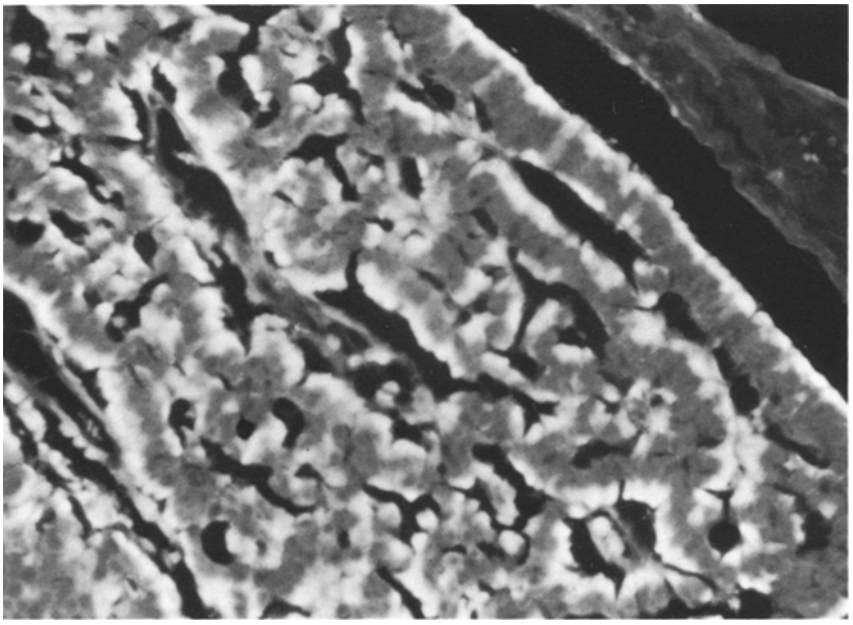

Fig. 3. Yellow fluorescence in cytoplasm fixed with aqueous formalin. ×800

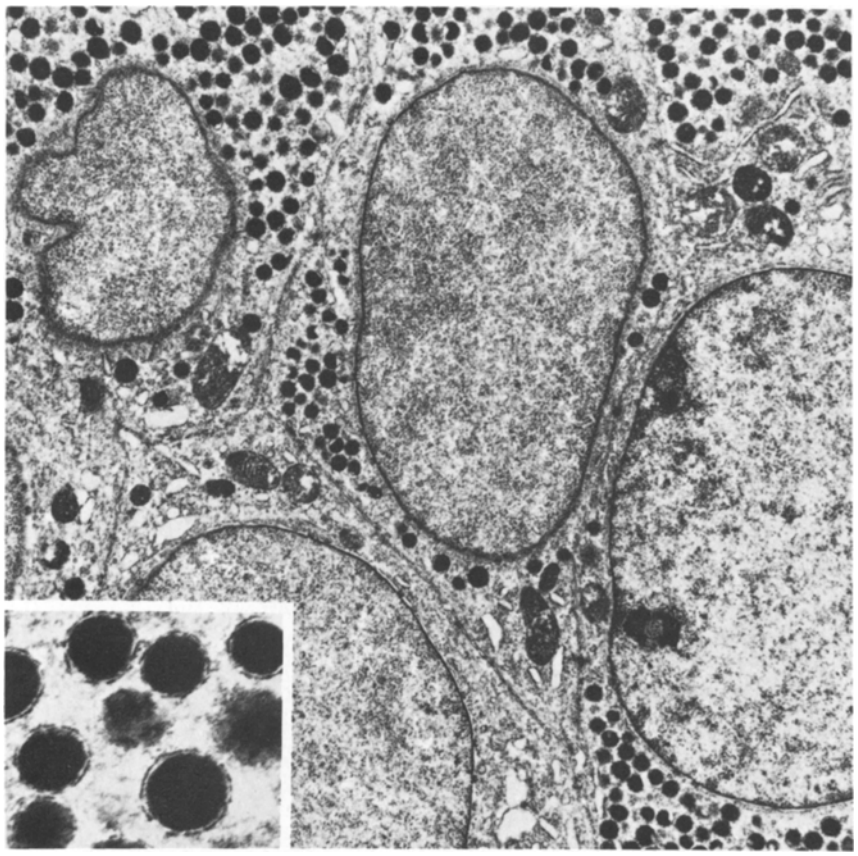

Fig. 4. Numerous dense granules in the cytoplasm of the tumor cells. ×14,700. *Inset:* Dense core granules limited by distinct membrane. ×61,700

served. Mitotic figures of tumor cells were seldom seen throughout the specimen. Strongly eosinophilic fine granules were noted chiefly at the subnuclear portion of the cytoplasm of the tumor cells (Fig. 1 inset).

The following examinations were performed on the tumor in the middle ear. The granules in the cytoplasm showed positive reaction with Grimelius staining for argyrophilia (Fig. 2a). Small amount of diastase resistant, PAS positive material was demonstrated in the lumen of some gland-like structure of the tumor cell nests. Fontana-Masson, PAS and alcian blue staining revealed negative reaction for these granules in the cytoplasm of the tumor cells. Prussian blue and Ziehl-Neelsen staining ruled-out ceruminous adenocarcinoma.

Formaldehyde-induced fluorescent studies on deparaffinized sections fixed in aqueous formalin (Enerbäck 1972) showed finely granular yellow fluorescence in the basal portion of the cytoplasm (Fig. 3), corresponding to the pattern of distribution of the granules with Grimelius staining. Yellow fluorescence was decreased by sodium borohydride reduction and was partly regenerated

by subsequent formaldehyde gas treatment. These findings indicated the presence of 5-HT in the tumor cells.

Ultrastructural studies of the tumor cells fixed with formalin revealed numerous spherical, well-defined dense granules with diameter from 150 to 220 nm, surrounded by distinct limiting membrane. Nuclei were oval and smooth but several showed indentations. Nuclear chromatin was finely granular and one or two small prominent nucleoli were occasionally seen. Lateral borders of the cell surface were rather straight and junctional complexes were occasionally found (Fig. 4). Lumen formation with microvilli was partly seen in the tumor cells.

Discussion

Up to the present, to our knowledge, there was only 1 reported case of primary carcinoid tumor from the middle ear (Murphy et al. 1980). Fayemi and Toker (1975) reviewed 11 cases of adenocarcinoma of the middle ear and reported 2 more cases of adenocarcinoma with histological characteristics similar to carcinoid tumor. However, neither histochemical nor electron microscopical evidences were documented (Table 1). On the other hand, only one case of primary carcinoid tumor of the skin has been reported in the literature, in which biochemical and radiographical examination strongly suggested that the tumor primarily developed in the skin of the scalp, not from other internal organs (Dijk and Seldam 1975).

Characteristic light and electron microscopic features of the tumor and the presence of 5-HT proven by fluorescent studies left no doubt as to the histological diagnosis of our case as carcinoid tumor. In addition, failure to discover the primary tumor in other organs indicated this tumor was primary in the external auditory canal or middle ear. However, it is uncertain whether it originated from the skin of the external auditory canal or mucosa of the middle ear, or if both lesions were primary.

Multicentric carcinoid tumors have been infrequently seen in gastrointestinal tracts (Godwin 1975) and bronchus (Krawisz and Ludwig 1980). But there has been no report of the tumor originating from both ectoderm and endoderm. The tympanic cavity develops from the first pharyngeal pouch and its mucosa originates from foregut endoderm. On the other hand, the external auditory canal is derived from the first branchial groove and is covered by ectoderm-derived skin (Anson 1973). Therefore, multicentric development of carcinoid tumor seems to be unlikely in our case. The tumor was first noticed in her external auditory canal, but audiometric examination after the polypectomy revealed slight conductive hearing loss, suggesting that the lesion might have already been present in her middle ear. In addition, light microscopic findings of our tumor well coincided with those of foregut-type carcinoid tumor, namely argyrophilic property and trabecular or ribbon-like arrangement of tumor cells (Black 1968; Soga and Tazawa 1971). In contrast, cutaneous carcinoid tumor reported by Dijk and Seldam (1975) had argentaffin granules and showed nodular solid nests of tumor cells, i.e. midgut-type carcinoid tumor. Although the continuity between the two tumorous lesions was not demonstrated by serial

Table 1. Clinical and pathological findings of carcinoid tumor and related conditions reported in literature

	Fayemi et al.		Murphy et al.	Inoue et al.
	case 1	case 2		
Age and sex	35y F	40y M	30y F	35y F
Initial symptoms	tinnitus, slight hearing loss	tinnitus, hearing loss	severe hearing loss	slight hearing loss, tumor in EAC
Ear-drum	intact	intact	intact	intact
Destruction of bone	no	jugular bulb	no	no
Extension	promontory Eustachian tube	anterior TC	TC, AAA, EAC	TC, AAA, EAC
Macroscopic	not available	not available	soft	soft, fragile, white
Light microscopic	anastomosing cords or sheets with glandular formation		trabecular or anastomosing cords with glandular formation	
mitoses	no	no	no	no
pleomorphism	no	no	no	no
cytoplasm	eosinophilic	eosinophilic		eosinophilic
stroma	rich	rich	rich	scanty
Grimelius	n.p.	n.p.	positive	positive
Fontana-Masson	negative	negative	negative	negative
Mucicarmine	positive	positive	positive	n.p.
PAS	n.p.	n.p.	negative	positive
5-HT	n.p.	n.p.	positive	positive
Electron microscopic	n.p.	n.p.	numerous neurosecretory granules	
Pathological diagnosis	adeno-carcinoma	adeno-carcinoma	carcinoid tumor	carcinoid tumor

n.p. = not performed; TC = tympanic cavity; AAA = aditus ad antrum; EAC = external auditory canal

histological examination, it might be reasonable to consider that the polypoid lesion of external auditory canal came from the middle ear tumor.

Electron microscopic studies of normal (Hentzer 1970) and inflamed (Møller and Dalen 1981) mucosal epithelium of middle ear have not confirmed the presence of cells with neuroendocrine characteristics. Murphy et al. (1980) speculated that carcinoid tumor of the middle ear might be derived from primitive precursor cells capable of differentiation into either neuroendocrine or glandular tissue, or from neuroendocrine-type cells of jugular paraganglia and melanocytes.

The Grimelius stain is indispensable when making a diagnosis of carcinoid tumor in adenomatous lesions showing trabecular arrangement, when these are found in the middle ear or even in the external auditory canal. Electron microscopic study and formaldehyde-induced fluorescence can confirm the diagnosis of carcinoid tumor. Additional cases are necessary to evaluate the exact incidence or prognosis of this rare neoplasm in the ear.

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