Middle ear tumours, contribution to classification and diagnosis

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Introduction

Middle ear tumours are rare and a precise determination of their incidence is difficult. Figures range from one in 6 000 to one in 20 000 patients with ear diseases.[1] The middle ear is the least common site of malignancy in the hearing organ with an incidence varying from 9-12 %.[2] The chance of developing a middle ear malignancy in comparison with other sites is about one in 1 500.[3] Reports have also established that malignant tumours of the middle ear are more frequently encountered than benign ones.[1] Tumours may involve the middle ear cleft primarily, metastatically or by extension from a contiguous area. Occasionally, anomalous conditions such as intrapetrosal carotid aneurysma, aberrant carotid artery or jugular bulb and manifestations of systemic disease such as leukaemia or multiple myeloma, may mimic middle ear neoplasms. This paper is restricted to primary tumours of the middle ear and mastoid.

Classification of primary tumours of the middle ear cleft

Figure 1 presents a classification of benign and malignant primary tumours of the middle ear and mastoid, each with subdivisions into epithelial, non-epithelial and miscellaneous lesions.

An attempt is made to indicate the total number of cases of each histopathological entity reported in the literature. However, since a substantial number of cases do not reach the literature, figure 1 does not present an exact determination of the incidence of the various middle ear tumours. One of the problems not solved in middle ear tumours is the determination of the site of origin, when the partition between middle ear and external ear canal is unrecognisable or the tympanic membrane is perforated.

Squamous cell carcinoma is the most common neoplasm in the adult middle ear and mastoid. It is well-established that this tumour, as well as other malignant tumours, has an associated incidence of pre-existing chronic suppurative otitis media of 60-80 %.[4] Fifty per cent of patients give a history of chronic, and twenty per cent a history of intermittent infections.[2] One may only be alerted to the possibility of a malignancy if unusual symptoms such as pain, bleeding and facial paralysis develop. The correct diagnosis will be made early

Fig. 1. Primary middle ear tumours - **Malignant neoplasms**

Classification of tumours of the middle ear cleft, with the approximate number of cases reported in the literature.

Epithelial	**Approximate Number**
squamous cell carcinoma	450
adeno carcinoma	17-30*
adenocystic carcinoma	15
ceruminoma	7
malignant melanoma	10
undifferentiated carcinoma	10
Non-epithelial	
sarcoma, including subclassification	50
rhabdomyosarcoma	70
Miscellaneous	
lymphangioendothelioma	1

* related to classification of adenomatous tumours

Primary middle ear tumours - **Benign neoplasms**

Epithelial	**Approximate Number**
adenoma (adenomatous tumours)	40
choristoma	14
pleomorph adenoma	5
melanoma	10
carcinoid apudoma	4
Non-epithelial	
chemodectoma	400
meningioma	18
haemangioma	10
lymphangioma	10
giant cell tumour	5
osteoma	10
ossifying fibroma	1
odontoma	1
neuroma/fibroma (excl. N VIII)	130
myxoma	10
solit-plasmocytoma	10
teratoma, dermoid (epidermoid?)	40
Miscellaneous	
blue nevus	1

* rarely metastasize

if polyps, persistent granulations associated with chronic suppuration of the middle ear, are examined histopathologically. Bradley and Maxwell[5] suggested that any patient with middle ear discharge of more than 20 years duration should be under regular otologic supervision and routinely examined by Papanicolaou smears. Lewis[6] found that 10 out of 28 cases of carcinoma of the middle ear and mastoid operated upon were associated with cholesteatoma. However, primary middle ear squamous cell carcinoma behind an intact tympanic membrane has been reported.[7,8] Kleinsasser[9] observed two cases of squamous cell carcinoma which occurred 8 and 9 years after tympanoplasties. Histological grading is not important in determining the prognosis in squamous cell carcinomas of the middle ear cleft.

Glomus jugular tumours are next in frequency to squamous cell carcinoma of the middle ear. In the great majority of cases these tumours have a benign histology and clinical course. Some consider this tumour to be of low grade malignancy since it invades bone, recurs and occasionally metastasizes.

Rhabdomyosarcoma is the most common neoplasm in children and usually manifests itself after the age of five.

240 Adenomatous tumours of the middle ear and mastoid have only

recently been recognised as a distinct pathological entity by Derlacki and Barney in 1976.[10] Two of Derlacki and Barney's three cases showed microscopic infiltration, which initially prompted the diagnosis of adenocarcinoma. The biological behaviour and prognosis were not reflected by the histological appearance and this tumour was later referred to as adenomatous tumour. In the same year Hyams and Michaels[11] reported another twenty cases under the same name. In their report, the following diagnostic criteria were recorded: absence of bone destruction, tumour confined to the middle ear cleft and no evidence of invasion or metastasis.

Precise classification of these adenomatous tumours as either benign or low-grade malignant neoplasms remains controversial. Terminology, classification and pathological criteria are not uniform in recent papers.[12,13,14] Although the collective term "ceruminoma" has been used in the past, four distinct patterns are now recognized for the middle ear cleft: adenoma, pleomorph adenoma, adenocarcinoma, adenoid cystic carcinoma.[15] Choristoma consists of heterotopic remnants of histologically normal salivary gland tissue, first described in the middle ear by Taylor and Martin.[16] The frequency of ossicular chain and facial nerve anomalies accompanying all except one of the 14 reported cases of choristoma has suggested

a syndrome with unilateral conductive hearing loss as the presenting symptom. The few pleomorph adenomas of the middle ear were not associated with middle ear anomalies.

Recently developed histochemical and histo-immune assays may be of value in resolving the controversies in the classification of middle ear tumours. The proper application of these diagnostic techniques usually requires fresh, i.e. unpreserved specimens which should be sent immediately to the pathologist. *"Oncological surgeons do it without formaldehyde, but if you must, do it with plenty of it (20:1)."*

Antibodies to intermediate filament proteins allow the immunohistochemical identification of the cellular origin of tumours.[17] Intermediate-sized filament proteins (IFP) are tissue-specific in that antibodies to keratin, vimentin, desmin, glial fibrillary acidic protein (GFAP) and the neurofilament proteins can distinguish between cells of epithelial and mesenchymal origin, as well as of myogenic and neural origin (fig-

ure 2). Malignant cells retain their tissue-specific IFP, which makes it possible to use these antibodies in tumour diagnosis. Carcinomas, for instance, are exclusively identified by antibodies to keratin. Monoclonal antibodies to keratin have allowed the differentiation between subgroups of epithelial tumours, usually between adenocarcinomas and squamous cell carcinomas.[17]

Recent developments in immunohistochemical visualisation of basal membranes could be of eminent value in the detection of micro-invasive growth of malignant tumours. Basal membranes are found at any side of the body as a continuous boundary between epithelial cells, capillaries, muscle- and nerve fibres respectively and the surrounding connective tissue. Collagen type IV and laminine are the most important and exclusive basal membrane biochemical constituents. It was found that polyclonal antisera against collagen type IV and laminine showed evidence of interruption and fragmentation of the basal membrane in the pres-

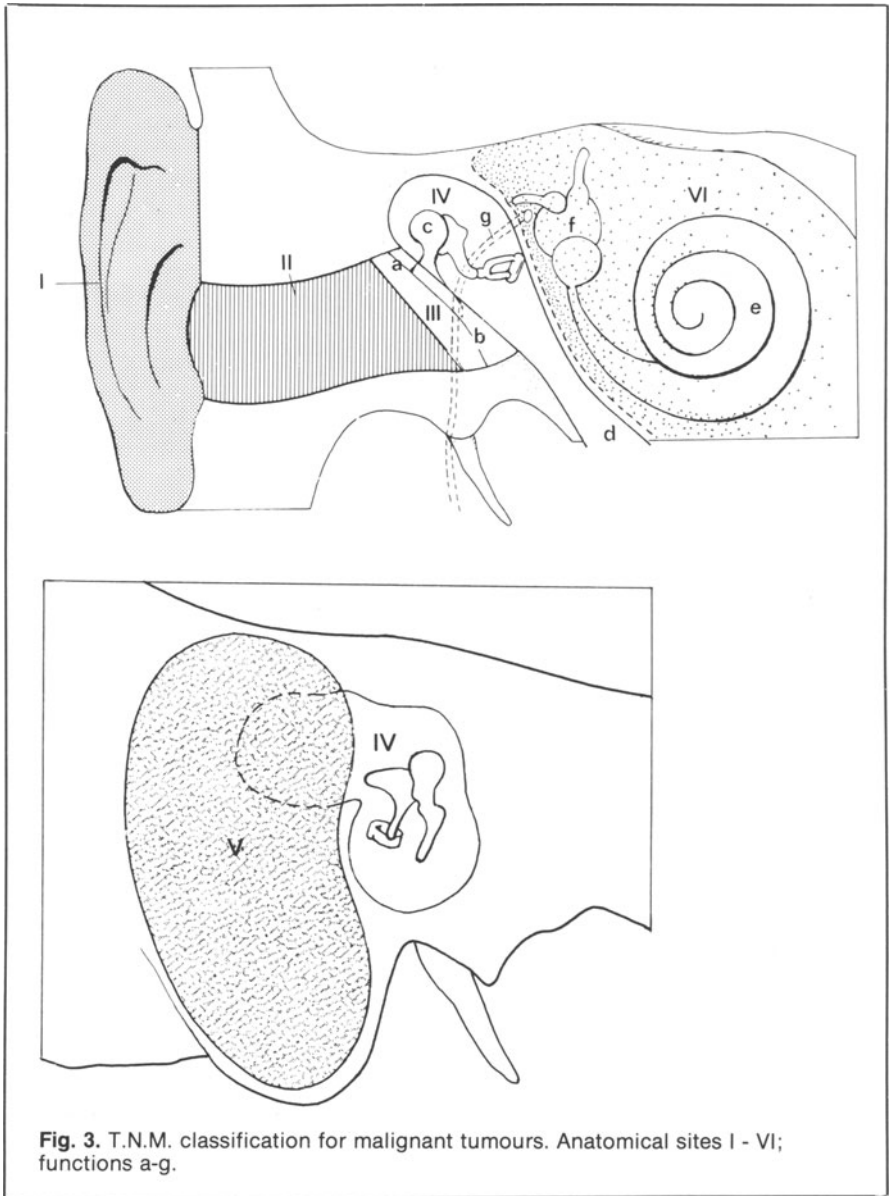| **Fig. 2.** Tissue specifity of intermediate-sized filament proteins (IFP). Malignant cells retain their tissue-specific IFP.	
Cell type	**Intermediate filament protein**
Epithelial cells	Keratin
Mesenchymal cells	Vimentin
Muscle cells	Desmin
Neuronal cells	Neurofilament proteins (NF)
Astrocytes	Glial fibrillary acidic protein (GFAP)

Fig. 3. T.N.M. classification for malignant tumours. Anatomical sites I - VI; functions a-g.

ence of micro-invasive growth, one of the characteristics of malignancy.[18] The histopathological differentiation of glomus tumours, with or without a tendency to malignant growth, or of adenomatous tumours and low grade malignant adenocarcinomas could benefit from the application of this new technique.

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Frozen sections of tumours of the middle ear cleft are often difficult to diagnose when inflammatory lesions are encountered. Definite surgery should be deferred pending a final histopathological diagnosis.

Electron microscopy should be routinely performed for middle ear tumours. In the differentiation between adenoma, "adenomatous tumours", adenocarcinoma, adenoid cystic carcinoma, rhabdomyosarcoma and carcinoid, electron microscopy could lead to the ultimate diagnosis.

The most recently described middle ear tumour is the carcinoid Apudoma.[19,20] The presence of intracellular membrane-bound neurosecretory granules varying in size from 120-300 nm demonstrated by electron microscopy, and argyrophily in the Grimelius stain are characteristic. The carcinoid tumours of the middle ear reported until now have behaved clinically benign.

All neoplasms of the hearing organ are rare. This precludes anyone from acquiring sufficient experience to reach meaningful conclusions regarding natural history, diagnosis and treatment. Centralized registration of tumours at this anatomical site and the use of the TNM classification of malignant disease are therefore advisable. We propose the TNM classification as is shown in figure 3.

The sites and functions include: I earlobe, II external auditory canal, III a.b. deep external auditory canal, middle ear adjacent to tympanic membrane, a. eardrum intact, b. eardrum perforated, IV C.D. middle ear, c. destruction of ossicular chain, d. dysfunction of Eustachian tube, V mastoid cavity, VI e.f.g. petrosal bone, e. cochlear involvement f. vestibular involvement, g. facial nerve impairment.

For staging of the disease we suggest:
T_1 malignancy is confined to the epithelium or mucosa; T_2 lesions include involvement of cartilage or radiologically confirmed bone destruction; T_3 reveals disease at sites other than defined for the middle ear.

Minimal requirements for assessing TNM category could be defined as follows: T category: clinical examination, tomography/CT scanning, audiometry, vestibulography, facial nerve topodiagnostic and electrical test; N and M category according to the regulations of UJCC or AM.J.C.

Example: $T_2N_0M_0$ III b IV cg. Primary cancer of the middle ear with bone destruction and extension to the external ear canal. The eardrum is perforated, the ossicular chain destructed, the facial nerve function impaired.

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