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Ceruminous gland tumours: a reappraisal

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Abstract
Ceruminous glands should no longer be regarded as purely apocrine glands, but as apoeccrine glands with both apocrine and eccrine modes of secretion. We present two cases of pleomorphic adenoma of ceruminous glands, among the rarest of such tumours. The use of such terms as 'ceruminoma' and 'hidradenoma' should finally be abandoned, and 'ceruminous gland tumour' used instead as a generic term. Classification should be based on Wetli's prototype (adenoma, pleomorphic adenoma, adenoid cystic carcinoma and adenocarcinoma), with the addition of benign eccrine cylindroma and syringocystadenoma papilliferum; the inclusion of mucoepidermoid carcinoma should await full validation. Wide local excision is necessary for all tumours, with only follow-up for histologically benign neoplasms. Malignant tumours need early aggressive surgery and radiotherapy. If marginal invasion cannot be assessed histologically, then adenoma and adenocarcinoma cannot be distinguished and we suggest that the tumour be reported as 'of uncertain malignant potential'. Long-term studies are needed to confirm or refute the view that all ceruminous gland tumours are potentially malignant.

Introduction

Tumours of ceruminous glands, although common in cats and dogs (Habib, 1981), are not common in man, and when they occur they may give rise to difficulties in diagnosis and confusion over nomenclature. In this paper we present two cases of pleomorphic adenoma of ceruminous glands, which are among the rarest of such tumours. We review the literature on ceruminous gland tumours, discuss their clinical features, histopathology and histogenesis, and advance suggestions for the nomenclature and classification of such tumours. We also discuss the nature of normal ceruminous glands themselves and propose their reclassification.

Case reports

Case 1

A 52-year-old white male presented in 1978 with a six-month history of right-sided tinnitus. He also gave a history of deafness for 15 years in the same ear; this had been investigated and found to be sensorineural. He did not complain of otalgia or otorrhoea. On examination there was a smooth mass 1 cm diameter, thought to be an osteoma, occluding the right external auditory canal. No facial weakness, cervical lymphadenopathy or parotid mass was found. Sensorineural deafness in the right ear was confirmed, with some loss also on the left. X-rays showed no lesion at the base of the skull but possible sclerosis in the right mastoid. At operation, the mass in the right external auditory canal was removed via an endaural approach and was found to be of cartilaginous consistency, arising from the anterior wall of the outer ear canal. The tympanic membrane was intact but retracted anteriorly. The excision site healed uneventfully. At last follow-up, 12 years after the operation, there was meatal stenosis but no evidence of recurrence.

Histology

Seven fragments of pale, slighly glistening tissue, some partly covered by skin, were received, of total size approximately 1 cm^3. In the pieces covered by skin, the mid-dermal collagen merged with the myxoid, blue-tinged matrix which formed the bulk of the tumour. This matrix bore a strong resemblance to the stroma of hyaline cartilage, and accounted for the tumour's glistening appearance and cartilagenous consistency. No capsule was recognizable around the tumour, although the fragmented nature of the specimen made assessment difficult. No parotid tissue was included in any of the fragments. The majority of the tumour cells were round to oval, with a moderate amount of eosinophilic cytoplasm. The nuclei were vesicular, with finely-dispersed chromatin and one (sometimes two) small, regular nucleoli. There was no significant nuclear pleomorphism. Very occasional mitotic figures were present, which were of normal form. No perineural infiltration was identified. The tumour cells were arranged in tubules, short trabeculae and small aggregates of eight to 10 cells, or 'streamed' into the stroma in a haphazard fashion. The myxoid nature of the stroma was often intensified around groups of tumour cells, and some cells were vacuolated, heightening the resemblance to cartilage (Figs. 1 & 2). The stroma also showed patchy collagenization, and fibrous bands surrounding myxoid areas gave the tumour a vaguely lobulated architecture. PAS staining showed glycogen within epithelial cell cytoplasm, with diastase-resistant positivity (i.e. epithelial mucin) within tubule lumina. Alcian blue positivity was found within the stroma and in tubule lumina, and both appeared resistant to hyaluronidase digestion, indicating the presence of epithelial acid mucin. On immunoperoxidase staining with anti-S-100 antibody, strong positivity was found within both epithelial and 'stromal' cells, indicating a common origin from myoepithelial cells (Zarbo *et al.*, 1986; Collins and Yu, 1989). The overall appearance of the tumour was that of a pleomorphic adenoma of ceruminous glands.

Case 2

A 45-year-old white male presented in 1974 with left-sided deafness and otorrhoea. On examination, there was a suppurative otitis media of the left ear with a postero-central perforation, and a mixed hearing loss of 40–50 dB on that side. The right ear was essentially normal. Tomograms of both internal auditory meatus showed no abnormality. The patient declined the offer of tympanoplasty, and the otitis was treated by regular aural toilet. Following regular review, a smooth polypoid swelling was

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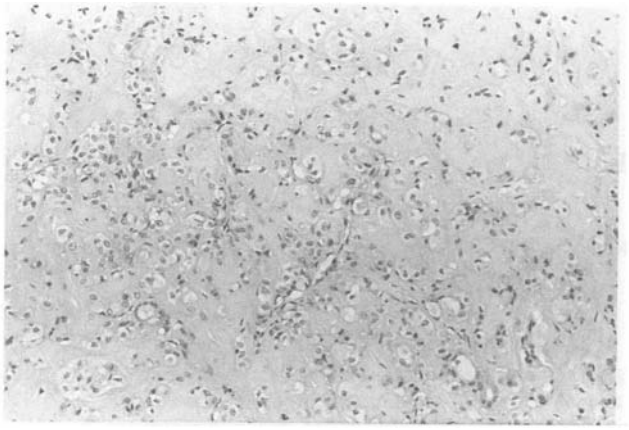

FIG. 1

Case 1, showing clumps of epithelial cells set in a myxoid, pseudocartilaginous stroma.

found arising from the roof of the external auditory canal on the opposite (right) side; the tympanic membrane was visible behind the swelling and was normal. The perforation of the left tympanic membrane was still present. There were no parotid masses, cervical lymphadenopathy or facial weakness. At operation in 1980 via an endaural approach, the swelling measured approximately 1.5 cm in diameter, arose from the superior aspect of the canal and extended from the annulus to within 1 cm of the meatal entrance. It was of bluish colour with a softish consistency. There was no middle ear extension. It was easily dissected from the bony canal; in its outer part it extended quite deeply into the tissue planes but was still dissectable. The excision site healed well and seven years later there was no evidence of recurrence.

Histology

The specimen was intact, and consisted of a nodule approximately 1.5 cm in diameter, partly covered with skin and with a bluish glistening cut surface. The tumour was well demarcated but not encapsulated, and was seen to lie within the dermis, surrounded by non-neoplastic ceruminous glands showing apocrine-type secretion. No parotid tissue was present. The histological features of this tumour were essentially the same as those in Case 1, namely the prominent myxoid matrix, the bland tumour cells arranged in a variety of patterns and the lack of any malignant features. The myxoid stroma was even more prominent, with little collagenization. Tumour cells showed less tendency to form tubules and were mainly arranged in fairly large aggregates and as scattered single cells. Some nuclei were smaller, darker and more angular in shape, probably a degenerative phenomenon (Fig. 3). Mitotic figures, pleomorphism or hyperchromatism were not seen. The appearances again were those of a pleomorphic adenoma of ceruminous glands. A small separate biopsy deep to the tumour consisted only of fibrovascular tissue containing nerves, with no invasion by tumour.

Discussion

The external auditory canal contains both sebaceous glands and ceruminous glands, the latter traditionally being regarded as modified apocrine glands (Fig. 4). The combined secretion of sebaceous and ceruminous glands is termed cerumen, and its low pH and content of lysozyme and immunoglobulins are important anti-microbial defences. Ceruminous glands are numerous in the cartilaginous part of the canal but sparse or absent in the bony part (Main and Lim, 1976; Hicks, 1983; Yamamoto *et al.*, 1987). They are located deep to the sebaceous glands and usually empty into hair follicles, only rarely emptying directly onto the skin surface.

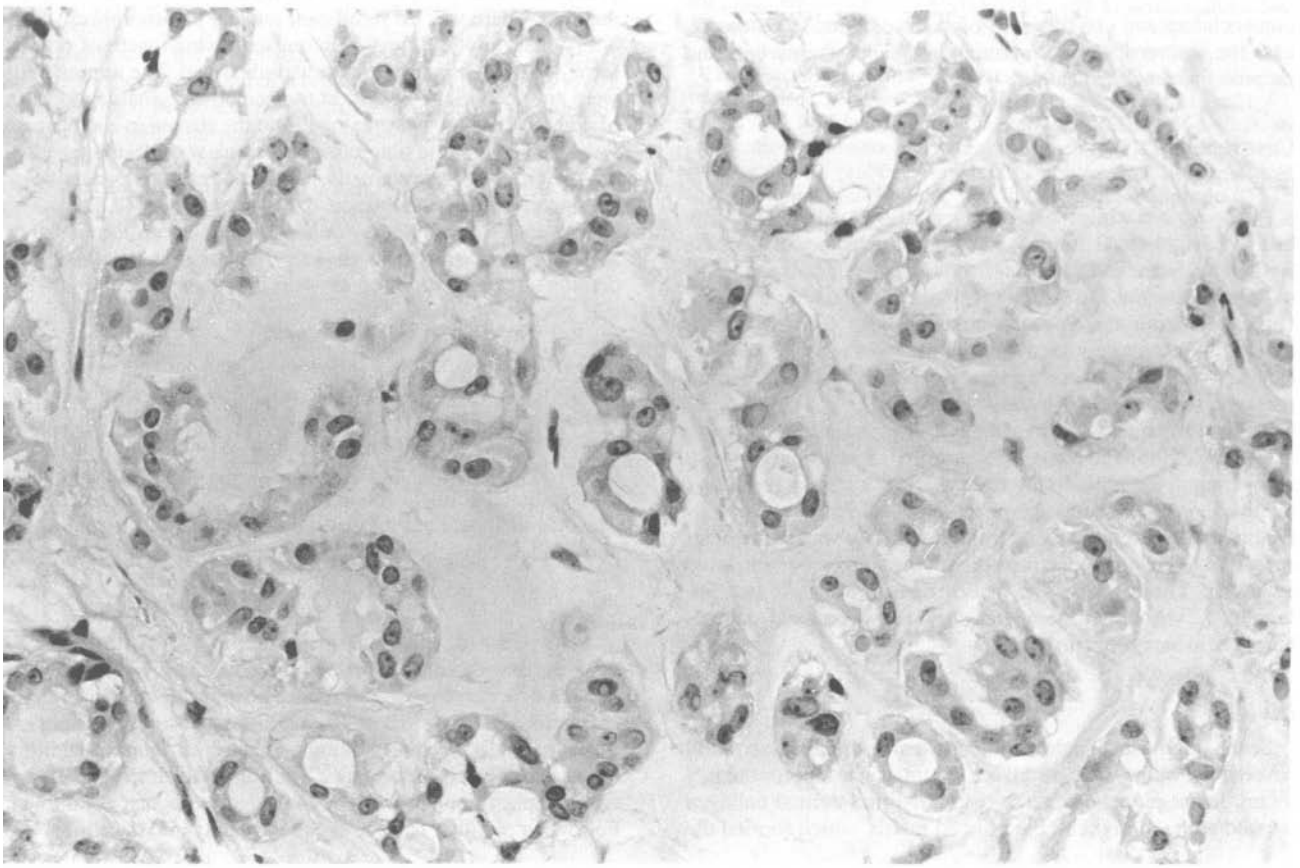

FIG. 2

Case 1, showing the myxoid nature of the stroma, especially around groups of cells. Cytoplasmic vacuolation is also present.

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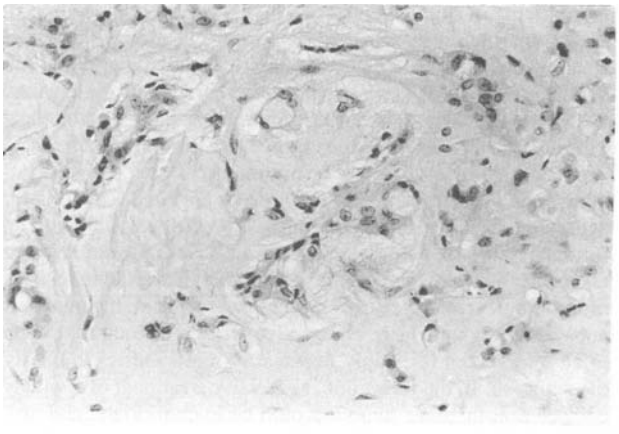

FIG. 3
Case 2, showing myxoid matrix and a population of small, dark, angular nuclei.

The diagnosis, nomenclature and behaviour of ceruminous gland neoplasms have traditionally been the source of considerable confusion. Doubtless this is partly the result of their relative rarity (although their true incidence is almost certainly underestimated by the number of cases documented in the literature) and any individual pathologist is likely to have limited experience of them; generally, the space devoted to them in standard texts has been similarly limited. Furthermore, the often small, fragmented nature of the specimens received by the pathologist tends to preclude accurate diagnosis and assessment of likely behaviour. A large part of the confusion, however, can be attributed to the use for many years of the term 'ceruminoma' as a description for all tumours of ceruminous glands, which are now known to form a heterogeneous group in terms of both morphology and behaviour.

This situation was addressed by Wetli *et al.* (1972), who proposed a simple classification based on a review of cases published since 1950. They suggested that ceruminous gland tumours be assigned to one of four categories: adenoma, pleomorphic adenoma, adenoid cystic carcinoma and adenocarcinoma. They considered the first two tumours to be benign and the second two to be malignant, in contrast to the previously held view that histological examination could not predict biological behaviour and that all tumours should be treated as potentially malignant. This latter view is still held by some authorities (Friedmann, 1986; 1990).

Since Wetli's paper, numerous case reports and series have used and validated this classification. In some, additional entities such as mucoepidermoid carcinoma and benign eccrine cylindroma have also been described (whichwill be considered later). Syringocystadenoma papilliferum, a benign tumour more often seen on the face and scalp (often in association with a nevus sebaceus), is known to occur in the external auditory canal where it is assumed to arise from ceruminous glands (Michaels, 1987). The most helpful review of the subject is that of Hicks (1983), who discusses fully the classification, presentation, histological diagnosis, behaviour and treatment of ceruminous gland tumours.

Incidence

Ceruminous gland tumours are certainly not common, but neither are they as rare as usually thought. Conley and Schuller (1976) reported a series of 273 malignancies of the ear (auricle, external auditory canal and middle ear) from 1945 to 1972; 61 arose in the external auditory canal, of which approximately 60 per cent were squamous carcinomas, 8 per cent were basal cell carcinomas, 5 per cent were melanomas and 20 per cent were 'adenocarcinomas of adenoid cystic or ceruminous gland origin'. Dehner and Chen (1980) reported a series of 92 neoplasms of the external and middle ear treated between 1964 and 1975, and 14 per cent of primary tumours were of glandular origin (although they did not distinguish between those of external auditory canal and middle ear origin).

Pulec (1977) collected a series of 37 ceruminous gland tumours at the Mayo Clinic between 1910 and 1976; 24 were adenoid cystic carcinomas, six were adenomas, five were adenocarcinomas and two were reported as mucoepidermoid carcinomas. (No detailed histological descriptions were given for these two tumours, and although the single low-power photomicrograph does appear to show both squamous and glandular features, squamous differentiation has been clearly described in both adenoid cystic carcinomas of the external auditory canal (Dehner and Chen, 1980) and in pleomorphic adenomas. We consider, therefore, that the existence of true mucoepidermoid carcinomas of ceruminous glands should be considered unproven to date). Otherwise, the relative frequency of each subtype in Pulec's series is supported by the experience of others, adenoid cystic carcinomas being the commonest and pleomorphic adenomas being the rarest of the four main subtypes. Wetli *et al.* (1972) stated that the ratio of malignant to benign tumours was 2.5:1, although this was based only on a review of published cases.

Presentation

The age range of published cases is from 12 to 87 years (both cases reported by Hicks, 1983), and younger patients are more likely to have malignant tumours. Males and females are represented equally. The presentation of benign tumours depends on the size of the mass and the degree of canal obstruction, causing hearing loss and possibly otorrhoea, while malignant tumours are more likely to cause pain. Either can become ulcerated and cause bleeding. Extramammary Paget's disease has been described in association with a ceruminous gland adenomcarcinoma (Fligiel and Kaneko, 1975). Ceruminous gland tumours extending onto the pinna may present to the dermatologists; Lynde *et al.* (1984) describe a series of seven such cases that presented between 1970 and 1982.

Treatment

The management of ceruminous gland tumours is comprehensively described by Hicks (1983). All tumours should be completely excised with an adequate margin of normal tissue. If histological examination reveals a benign tumour (and examination of the tumour edge for invasion is of paramount importance), then no further treatment is necessary. Malignant tumours must be treated aggressively even in their early stages, for it is then the possibility of cure is greatest. For those tumours limited

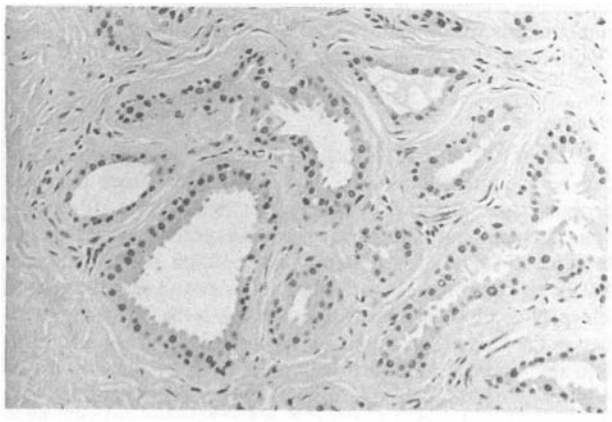

FIG. 4
Normal non-neoplastic ceruminous glands, showing luminal snouting ('capitate secretion'). The myoepithelial layer is inconspicuous.

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to the external auditory canal, a wide *en bloc* excision of the entire ear canal, surrounding bone, associated cartilage, mastoid, middle ear, parotid and all contingent muscle (with preservation of the facial nerve if possible) is necessary, followed by irradiation. Wider invasion necessitates more radical surgery, again with radiotherapy. While there may be understandable reluctance on the part of the surgeon to perform such aggressive surgery for what is often a small tumour, the high incidence of local recurrence and systemic metastasis in both adenoid cystic carcinoma and adenocarcinoma makes such treatment mandatory. (Despite Wetli's statement that only adenoid cystic carcinomas spread systemically, several subsequent cases of widely disseminated adenocarcinomas have been described (Pulec, 1977)). Both tumours tend to follow an indolent course, and five-year survival rates may be misleading when metastases can become evident up to 30 years after presentation (Hicks, 1983).

Histopathology

The ceruminous adenoma is well differentiated and consists of proliferating glands similar to non-neoplastic ceruminous glands, although solid, acinar or trabecular patterns may be seen. Glands are typically double layered, with an outer layer of myoepithelial cells which may show proliferation. The pleomorphic adenoma is identical to the corresponding salivary gland tumour, and the two presented cases exemplify the histological features. The adenoid cystic carcinoma is again identical to that seen in salivary glands, with a typical 'Swiss cheese' pattern caused by large cysts amonst darkly staining masses of basaloid malignant cells. More poorly differentiated cases show a greater predominance of solid areas with or without anaplastic cytological features. Ceruminous adenocarcinomas show a spectrum of malignancy, ranging from well to poorly differentiated, and the well differentiated examples may be very difficult to distinguish from adenomas; the only differentiating feature in many cases is the presence or absence of invasion at the tumour margin. For this reason, it is essential that the primary excision of all tumours is as far as possible complete with a margin of normal tissue; incisional biopsies alone may not only be difficult to interpret but also misleading. If the tumour margin is not included in the specimen, and if there is doubt as to whether the tumour is an adenoma or a well differentiated adenocarcinoma, we would suggest that the pathologist reports 'a ceruminous gland tumour of uncertain malignant potential'. Other diagnostic modalities then assume greater importance in guiding further treatment.

In all cases, a primary parotid tumour (and occasionally a primary middle ear tumour) must be excluded, largely by clinical means. Primary parotid tumours almost always present in the pre-auricular region or at the angle of the mandible before involving the ear, while ceruminous gland tumours present as masses in the external auditory canal (Peel, 1985). Where the origin of an adenocarcinoma is in doubt, cytoplasmic eosinophilia of tumour cells would tend to confirm a ceruminous gland origin (Wetli *et al.*, 1972; Friedmann, 1986).

Behaviour

In contrast to the view that most ceruminous gland tumours can be accurately classified on a histological basis as either benign or malignant, some authorities believe that all ceruminous gland tumours should be regarded as potentially malignant. Friedmann (1986; 1990) states that 'opinion has hardened in favour of regarding all such tumours as potentially malignant, irrespective of whether or not invasive growth has been identified in the biopsy specimen'. However, we have been unable to find any report of a reliably diagnosed, completely excised adenoma which has recurred or spread. It should be mentioned here that one case of an 'aggressive chondroid syringoma' has been described (Botha and Kahn, 1978). (The term 'chondroid syringoma' or 'mixed tumour of the skin' is used in dermatological practice to describe tumours, identical to pleomorphic adenomas, arising in skin appendages). In this case, a nodule arose in the external auditory canal of a 15-year-old girl, with several smaller satellite nodules surrounding it. Following excision (no details are given of completeness or otherwise of the primary excision), the tumour recurred three years later. Histological examination on both occasions showed a pleomorphic adenoma, with focal severe cytological atypia and occasional mitoses. Satellite nodules, cellular atypia and mitoses are cited as criteria for aggression in chondroid syringomas. The girl was well with no further recurrences three years later. This case should not be taken as proof of the unreliability of histological examination, as morphological evidence of aggression was present. It would perhaps be timely for a large prospective series with long follow-up to be undertaken (probably necessarily multicentric) to clarify the situation. In the meantime, aggressive treatment of a widely excised non-invasive tumour would be inappropriate, and prolonged follow-up a wise precaution in any case.

Histogenesis

The origin of glandular tumours of the external auditory canal from ceruminous glands is supported by several circumstantial characteristics of these tumours: the cytological similarities between many tumours and normal ceruminous glands; the close physical proximity of tumours to non-neoplastic glands (although any tumour in the canal would be expected to show such a juxtaposition), sometimes with areas of transition, and the correlation between the concentration of ceruminous glands and the frequency of tumours in the cartilaginous and osseous parts of the canal respectively. In addition, two cases have been reported of ceruminous gland adenomas arising in association with cutaneous sweat gland tumours (Habib, 1981). The histogenesis of pleomorphic adenomas has always been the subject of controversy. It is generally accepted that both the epithelial and apparently mesenchymal elements of these tumours have a common origin from myoepithelial cells (which are a normal component of ceruminous glands), a view supported by the ubiquitous S-100 positivity of pleomorphic adenomas (Zarbo *et al.*, 1986; Collins and Yu, 1989). The postulated origin of adenoid cystic carcinomas from ceruminous glands is more problematic. Although such an origin is generally accepted, the high incidence of malignancy in ceruminous gland tumours compared with the rarity of malignancy in cutaneous apocrine tumours has been noted (Wetli *et al.*, 1972). The similarity of ceruminous gland tumours to salivary gland tumours has prompted suggestions that they arise in ectopic salivary gland tissue; such ectopic tissue has never, however, been identified in the external auditory canal. (In contrast, several cases of ectopic salivary gland tissue (salivary gland choristomas) have been reported in the middle ear, with convincing embryological explanations (Saeger *et al.*, 1982), and it is now accepted that the origin of glandular tumours resembling ceruminous gland tumours in the middle ear is from such ectopic tissue.)

Partial eccrine differentiation in tumours of the external auditory canal, an apparent anomaly given the absence of eccrine glands from the normal canal (Main and Lim, 1976; Hicks, 1983), has been noted and discussed (Wetli *et al.*, 1972), and metaplastic processes have been invoked. Indeed, one external auditory canal tumour has been described which appears identical to the benign cutaneous eccrine cylindroma (Wilson and Johnson, 1980). (The term cylindroma here is unfortunately confusing, as it has also been used in the past to describe the adenoid cystic carcinoma). Although traditionally ceruminous glands have been assumed to have a purely apocrine method of secretion, this has been based on light microscopical features of the secretory cells such as luminal snouting, cytoplasmic iron granules and ceroid-like pigment (Wetli *et al.*, 1972; Hicks, 1983). While Wetli also demonstrated apocrine features at the ultrastructural level, others have been unable to do so and have demonstrated eccrine features only (Kawabata, 1964). Main and Lim (1976) reconciled these findings by describing both apoc-

TABLE I
CLASSIFICATION OF CERUMINOUS GLAND TUMOURS

Benign	Malignant
Adenoma	Adenoid cystic carcinoma
Pleomorphic adenoma	Adenocarcinoma
Syringocystadenoma Papilliferum	(Mucoepidermoid carcinoma)
Benign eccrine cylindroma	
Ceruminous gland tumours of uncertain malignant potential	

rine (apical cap formation) and eccrine (fusion of secretory granules with the luminal cell membrane) modes of secretion on electron microscopy. Such a hybrid form of sweat gland has also recently been described in the axilla, where they make up 45 per cent of the sweat glands and have been termed 'apoeccrine' glands (Santa Cruz, 1989). It seems apparent that the ceruminous glands of the external auditory canal are also apoeccrine glands, and should no longer be regarded as purely apocrine. This concept of apoeccrine glands explains not only eccrine differentiation in ceruminous gland tumours, but also the existence of 'pure' eccrine tumours such as benign eccrine cylindroma in the external auditory canal. From the detailed description and the photomicrograph given in their paper, and the histogenetic basis outlined above, there seems no reason not to accept Wilson and Johnson's benign eccrine cylindroma (1980) as valid. It must be made absolutely clear that this is a separate entity and not a synonym for adenoid cystic carcinoma, and for this reason the full title 'benign eccrine cylindroma' should always be used. (An eccrine hidrocystoma has also been described at this site (Hawke and van Nostrand, 1987); this is actually a retention cyst rather than a true ceruminous gland neoplasm).

Nomenclature

The use of a single but apparently specific term, such as 'ceruminoma', to describe the whole range of ceruminous gland tumours has been the cause of much confusion, and is a legacy of the period before a useful classification was available. The term 'hidradenoma' has also been used in this context (Johnstone *et al.*, 1957; Pahor and O'Hara, 1975). Such terms are now misleading, in that they suggest that ceruminous gland tumours form a homogeneous group, and they retain the meaning of tumours which behave in an unpredictable fashion. Furthermore, the suffix '-oma' (in the context of epithelial tumours) strongly implies a benign neoplasm. Neither can we agree with the suggestion (Moss *et al.*, 1987) that 'ceruminoma' still be used to describe the benign ceruminous adenoma; the word carries such a historical weight of controversy that its continued use in any context can only be unnecessarily confusing.

We are pleased to note that the term 'ceruminoma' has been dropped in the latest edition of the World Health Organization classification of tumours of the external ear (Shanmugaratnam and Sobin, 1991). The WHO classification is intended to be a working classification and to encourage uniformity of reporting, and so is based on morphological and explicitly not on histogenetic grounds. Therefore, in the body of the classification, only 'ceruminous adenoma' and 'ceruminous adenocarcinoma' are identified as arising from ceruminous glands. The accompanying explanatory notes state that: '[Besides ceruminous adenoma and ceruminous adenocarcinoma,] other glandular neoplasms occurring in the external auditory meatus, namely pleomorphic adenoma, syringocystadenoma papilliferum, adenoid cystic carcinoma and mucoepidermoid carcinoma, may also arise from ceruminous glands'.

Undoubtedly there is a need for a generic term for tumours of ceruminous glands, and in the same way that breast tumours or salivary gland tumours are so called, it seems perfectly logical to use the term 'ceruminous gland tumour' in this fashion (Collins and Yu, 1989). Individual tumours are then classified further as accurately as possible, with an admission in doubtful cases (by the classification 'of uncertain malignant potential') that prediction of behaviour is not possible.

Conclusion

We have presented two cases of pleomorphic adenoma of ceruminous glands, among the rarest of these tumours with only nine previous cases reported in the English literature (one by Pahor and O'Hara, 1975). Our experience confirms their benign nature.

We have stressed the difficulties encountered by the pathologist in attempting to predict the behaviour of some tumours when the margins cannot be adequately examined for evidence of invasion. In the case of pleomorphic adenomas, adenoid cystic carcinomas and poorly differentiated adenocarcinomas, the nature of the tumour is usually evident, even if adequacy of excision cannot be assessed. However, in a tumour which would otherwise be called an adenoma, a well differentiated adenocarcinoma cannot be excluded if the margins cannot be examined. It is in these circumstances that we suggest the classification 'ceruminous gland tumour of uncertain malignant potential'. Otherwise, Wetli's basic classification should still be used, with the addition of syringocystadenoma papilliferum as a benign ceruminous gland tumour. The existence of the mucoepidermoid carcinoma needs further validation. However, having supplied a histogenetic basis for eccrine differentiation in ceruminous gland tumours (with the concept that ceruminous glands are apoeccrine in nature), we see no reason not to accept the existence of the benign eccrine cylindroma (with a caveat concerning the use of the unqualified term 'cylindroma'). Our proposed classification is given in Table I.

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