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Commentary

The Aural Canker-Ceruminous Adenocarcinoma

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Preface

Ceruminous adenocarcinoma is a commonly discerned entity, in contrast to benign neoplasms of the ceruminous gland. Malignant neoplasms of the ceruminous gland are designated as "ceruminous adenocarcinoma" by the world health organization (WHO). In descending order of frequency, ceruminous adenocarcinoma is categorized into adenoid cystic carcinoma, ceruminous adenocarcinoma- not otherwise specified (NOS) and mucoepidermoid carcinoma.

Mucinous carcinoma of the ceruminous gland is an extremely exceptional neoplasm. Ceruminous gland neoplasms are frequently a diagnosis of exclusion. Also, benign and malignant neoplasms emerging from ceruminous glands enunciate concordant clinical features and morphological characteristics.

Disease characteristics

Generally, ceruminous adenocarcinoma emerges at an estimated decade earlier than ceruminous adenoma. Besides, emergence of adenocarcinoma beyond > 60 years at initial representation is associated with enhanced disease-related morbidity and decimated survival. Ceruminous carcinomas usually arise within the male population between 30 years to 59 years although a comprehensive age range of disease incrimination is observed [1,2].

Commonly, the neoplasm arises from postero-superior quadrant of lateral aspect of external auditory canal. Tumour magnitude varies from 0.5 centimetres to 3.0 centimetres with a mean diameter of 1.55 centimetres [2,3].

Ceruminous adenocarcinoma exhibits a slight female predilection with a female to male proportion of 5:4. Typically, implicated females demonstrate miniature neoplasms with an average diameter of 1.4 centimetres, in contrast to males who display neoplasms of an average magnitude of 2.0 centimetres [2,3].

Ceruminous adenocarcinoma -not otherwise specified (NOS) enunciates significant infiltration into circumscribing soft tissue and nerves along with destruction of osseous and cartilaginous structures. Exceptionally, extra-mammary Paget's disease is associated with ceruminous adenocarcinoma [2,3].

Microscopic evaluation of ceruminous carcinomas lacks concurrence with prognostic outcomes. Comprehensive surgical eradication of the neoplasm with a tumour-free tissue perimeter may be frequently accompanied by tumour reoccurrence, regional and systemic tumour metastasis [2,3].

Adenoid cystic carcinoma arising from ceruminous glands is a frequent subtype of glandular malignancy which is proportionately twice as common to ceruminous adenocarcinoma-not otherwise specified (NOS) or mucoepidermoid carcinoma. A definitive gender predilection is absent [2,3].

Clinical elucidation

Ceruminous carcinomas are associated with localized pain. Generally, the neoplasm demonstrates localized reoccurrence and tumour metastasis to pulmonary parenchyma or regional lymph nodes is exceptional [3,4].

Ceruminous adenocarcinoma -not otherwise specified (NOS) is a frequent subtype of carcinoma arising from ceruminous glands in adults. Generally, tumefaction represents clinical symptoms as altered hearing, mass, otorrhea, tinnitus, haemorrhage from the ear,

pain, lymphadenopathy or paralysis of sixth, seventh, twelfth and associated cranial nerves [3,4].

Adenoid cystic carcinoma of ceruminous glands can manifest pain, a definitive tumefaction, altered hearing, otorrhea, recurrent or chronic otitis externa, haemorrhage and neural symptoms as facial nerve palsy. Duration of clinical symptoms exceeding > 2 years is associated with tumour reoccurrence [3,4].

Mucoepidermoid carcinoma is an infrequent subtype of ceruminous adenocarcinoma associated with pain, definitive tumour mass, tinnitus and dizziness [3,4].

Histological elucidation

Upon gross examination, mean tumour magnitude appears at nearly 1.7 centimetres. Characteristically, ceruminous adenocarcinoma demonstrates an infiltrating growth pattern. The deceptive neoplasm manifests as a well differentiated tumefaction or a high grade tumour with significant cellular and nuclear pleomorphism and prominent mitotic activity. Perineural tumour infiltration may ensue. Ceruminous adenocarcinoma demonstrates pertinent variants as pure glandular and papillary [5,6].

Typically, ceruminous adenocarcinoma exhibits irregular clusters, nests and solid sheets of atypical epithelial cells. Epithelial tumour cells exemplify a dual cell pattern, foci of glandular differentiation, an in-situ component or papillary articulations. Tumour cells are imbued with enlarged, hyperchromatic nuclei or vesicular nuclear chromatin and prominent nucleoli [5,6].

Upon microscopy, ceruminous glands are devoid of a dual cell layer. Singular layer of luminal epithelial cells is enunciated. Ceruminous carcinomas are associated with cellular and nuclear pleomorphism, nuclear anaplasia, mitotic activity and infiltrative patter of tumour growth. Nevertheless, well differentiated ceruminous carcinomas may simulate ceruminous adenomas although tumour invasion is present [5,6].

Tumour necrosis appears as a geographic expanse or configuration of a comedo pattern along with extensive infiltration into circumscribing soft tissue. Encompassing stroma is desmoplastic and incorporates a variable inflammatory cellular infiltrate. Perineural, lymphatic or vascular tumour infiltration may be observed [5,6].

Ceruminous adenocarcinoma can be classified as high grade or low grade neoplasms contingent to proportionate glandular differentiation and foci of solid areas. Exceptionally, a well differentiated tumefaction may emerge as mucinous carcinoma. Pagetoid pattern of tumour cell dissemination within superimposed epidermis is infrequent [5,6].

Adenoid cystic carcinoma of the ceruminous glands is an unencapsulated, poorly circumscribed neoplasm with a mean tumour magnitude of nearly 1.6 centimetres and diffuse infiltration into encompassing soft tissue. Tumefaction is composed of monomorphic, basaloid cells imbued with minimal clear cytoplasm and ovoid, hyperchromatic nuclei. Tumour cells configure irregular, tubular or cribriform nests of varying magnitude encompassing basement-like material which appears enmeshed within pseudoglandular spaces [5,6].

Basement- like material can be abundant and envelops tumour cell nests. Focal or extensive myxoid or mucinous alterations are commonly discerned [5,6].

Tumour cell proliferation configuring expansible nests or solid cell pattern is associated with an inferior prognosis. Foci of tumour necrosis or preponderant cellular and nuclear pleomorphism are exceptional. Multifocal perineural tumour infiltration is common [5,6].

Enhanced possible tumour reoccurrence and an inferior prognosis is associated with definitive histological pattern such as solid pattern of tumour growth, bony infiltration, perineural invasion, tumour-infiltrated surgical perimeter and secondary tumour extension into circumscribing organs as the parotid gland [5,6].

Morphologically, mucoepidermoid carcinoma demonstrates a mean tumour magnitude of 3.0 centimetres and is composed of varying admixture of squamoid, epidermoid or epithelioid cells imbued with dense, eosinophilic cytoplasm, focal keratinization and intercellular bridges, mucin-producing glandular or epithelioid cells incorporated with a miniature, peripheral nucleus compressed by intracytoplasmic mucin vacuoles which can be suitably discerned by mucin stains such as mucicarmine along with intermediate, ovoid cells with hyperchromatic nuclei and pale- pink cytoplasm with a potential for epidermoid or glandular differentiation [6,7].

Although debatable, the exceptional mucoepidermoid carcinoma of ceruminous glands can be graded into three distinctive categories denominated as low grade, intermediate grade and high grade, contingent to growth pattern with pushing or infiltrative tumour perimeter, occurrence of lymphatic and vascular invasion, perineural infiltration, coagulative tumour necrosis, predominant cellular pleomorphism, mitotic activity and proportionate cystic component. Prognostic outcome of ceruminous mucoepidermoid carcinoma is contingent to histological grade of the neoplasm [6,7].

Differential diagnosis

Well differentiated ceruminous adenocarcinoma requires a segregation from

- Ceruminous adenoma which lacks an infiltrative tumour perimeter. Generally, a cystic lesion layered with epithelium is denominated. The lining epithelium is comprised of dual cell population wherein the intrinsic, luminal epithelial layer is composed of tubules of cylindrical, cuboidal or low columnar epithelial cells imbued with intensely eosinophilic cytoplasm, spherical nuclei and focal decapitation secretion. Tumour infiltration may be challenging to discern in miniature tissue samples. Ambiguous lesions can be designated as ceruminous adenoma with uncertain malignant potential and further evaluated is necessitated with an extensive tissue resection [6,7].
- Dermal eccrine cylindroma is composed of cellular cylinders and compact nests of intertwined basaloid cells circumscribed by dense, basement membrane-like material. Tumefaction is constituted of dual category of cells denominated as undifferentiated epithelial cells imbued with miniature, hyperchromatic nuclei and peripheral palisading along with centric clusters of differentiated ductal cells demonstrating enlarged, pale nuclei [7,8].
- Paraganglioma of middle ear demonstrates a classic, organoid pattern with the configuration of a “zellballen” or nesting of tumour cells. Tumefaction is constituted of centric, spherical or elliptical chief cells imbued with abundant, eosinophilic, granular or vacuolated cytoplasm and uniform nuclei with dispersed chromatin. Spindle-shaped, basophilic, peripheral sustentacular cells circumscribe tumour cell nests and appear immune reactive to S100 protein. Tumour cells may depict cellular and nuclear pleomorphism. Tumour cell aggregates are segregated by a prominent fibro-vascular stroma. Occasionally, dense fibrous stroma may encircle clusters of tumour cells. An infiltrative pattern of tumour evolution is encountered. Mitotic figures or foci of necrosis are exceptional. Glandular or alveolar differentiation is absent [7,8].

Additionally, ceruminous adenocarcinoma requires a segregation from epidermal neoplasms, tumours arising from external auditory canal, middle ear or mastoid region such as hidradenoma, cholesteatoma, choristoma, exostosis, osteoma, eosinophilic granuloma, branchial cleft cyst, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, neuroendocrine adenoma of the middle ear, meningioma and extension of benign or malignant salivary gland neoplasms from adjoining parotid gland. Comprehensive imaging and histological evaluation is paramount for precise tumour discernment [7,8].

Investigative assay

Upon imaging with computerized tomography (CT) and magnetic resonance imaging (MRI), a heterogeneously enhancing tumour is observed. Tumefaction appears to infiltrate and efface circumscribing soft tissues along with obliteration of external auditory canal. Tumefaction can extend into infratemporal fossa or adjacent parotid gland [8,9].

Therapeutic options

Comprehensive surgical extermination with a tumour-free surgical perimeter is an optimal treatment strategy for managing neoplasms of the external auditory canal. Trans-meatal resection is appropriate for treating miniature neoplasms whereas a retro-auricular approach is adequate for managing enlarged lesions [9,10].

Due to localized tumour infiltration, en bloc surgical resection with a broad, tumour-free tissue perimeter along with removal of osseous segment of external auditory canal and partial tympanomastoidectomy is a recommended procedure for treating ceruminous carcinomas. Radical surgical eradication can be employed for treating lesions with incrimination of middle ear or temporal bone [9,10].

Enlarged neoplasms or tumour reoccurrence may necessitate the adoption of surgical manoeuvers such as extended radical mastoidectomy and total parotidectomy. Intracranial extension mandates excision of incriminated dura [9,10].

Adjuvant radiation therapy is beneficial for treating enlarged or reoccurring neoplasms or high-grade carcinomas. However, adoption of radiation therapy is associated with decimated survival possibly due to advanced tumour stage of aggressive carcinomas [9,10].

Chemotherapy is an uncommonly employed therapeutic modality. Concomitant chronic otitis media can be satisfactorily treated with mastoidectomy and intervention of middle ear [9,10].

Ceruminous carcinomas frequently display localized tumour reoccurrence with regional lymph node and systemic metastasis. Adenoid cystic ceruminous carcinoma depicts a favourable prognosis although singular or multiple tumour relapse is observed in around 40% subjects. Distant metastasis occurs in roughly 27% neoplasms wherein pulmonary parenchyma, brain and bone are commonly implicated. Ceruminous adenocarcinoma delineates tumour reoccurrence and distant metastasis [9,10].

Ceruminous muco-epidermoid carcinoma exhibits an inferior prognosis although low-grade lesions exemplify a relatively superior outcome. Disease- specific mortality varies from 22% (muco-epidermoid carcinoma) to 35% (ceruminous adenocarcinoma NOS). Adenoid cystic carcinoma of ceruminous glands exhibits a relatively superior 5 year survival percentage although 10 year and 20 year survival is inferior [9,10].

Extended monitoring is necessitated in order to appropriately recognize localized, regional and distant tumour reoccurrence and implement appropriate therapy [9,10].

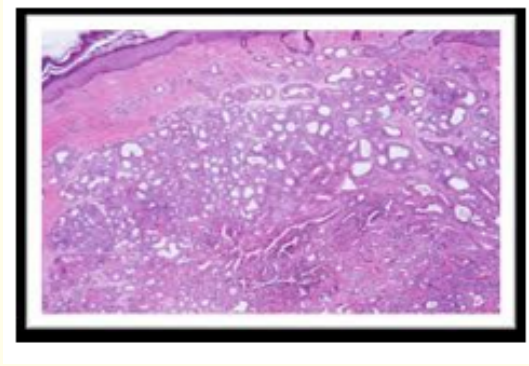

Figure 1: Ceruminous adenocarcinoma exhibiting irregular, tubular and cribriform nests layered by monomorphic, basaloid cells with hyperchromatic nuclei, surrounding fibrotic stroma and a superimposed epidermal layer [11].

Neoplasm	Clinical Symptoms	Histological Features	Immunohistochemistry
Eccrine cylindroma	Painless plaque or nodule	Circumscribed tumour with solid nests of luminal and myoepithelial cells admixed with hyaline substance surrounded by hyaline sheath	Luminal cells; CEA, CK7, CK19, EMA. Myoepithelial cell; S100, p63, SMA, CK5/6
Basal cell carcinoma	Bloody ear discharge, pain, nodular mass	Nests and infiltrative cords of basaloid cells with minimal clear cytoplasm, peritumoural clefts, myxoid stroma	p63, p40, CK5/6, Ber-EP4. CD10 (peripheral tumour cells)
Squamous cell carcinoma	Pain, discharge, haemorrhage, tinnitus, deafness, pruritus, exophytic, ulcerated tumour	Nested and infiltrative proliferation of epithelioid cells with eosinophilic cytoplasm, ovoid nuclei, keratin pearls	p63, p40, CK5/6, EMA
Malignant melanoma	Deafness, bloody ear discharge, variably pigmented, polypoid, ulcerated mass	Nests of variably pigmented, epithelioid, spindle or small cells with a frequent in-situ component in the superimposed epidermis	S100, SOX10, MART1/MelanA, HMB45, MITF, tyrosinase
Neuroendocrine adenoma	Ear fullness, tinnitus, deafness, pain, vertigo, retro-tympanic non-pulsatile mass	Cribriform, trabecular, nested, lobular or solid proliferation of small to medium epithelioid cells with finely speckled chromatin surrounded by fibrotic stroma	CK7, CK5/6, p63, CD56, chromogranin A, synaptophysin
Meningioma	Deafness, subcutaneous mass	Lobulated, whorled proliferation of epithelioid syncytial cells with psammoma bodies	Progesterone receptor, EMA
Paraganglioma	Deafness, firm subcutaneous mass, occasional haemorrhage	Organoid or nested growth of epithelioid (chief) cells with eosinophilic cytoplasm, ovoid nuclei, speckled chromatin. Inconspicuous sustentacular cells	Chief cells; synaptophysin, chromogranin A, cytokeratin, S100 Sustentacular cells; S100, GFAP

Table: Differential diagnosis of ceruminous adenocarcinoma [2].

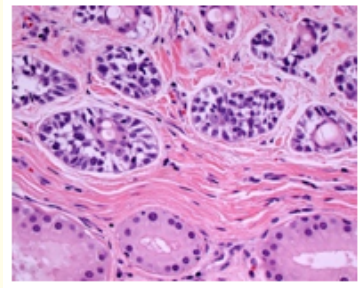

Figure 2: Ceruminous adenocarcinoma demonstrating tubules, small glands and cribriform structures lined by basaloid cells and ovoid, hyperchromatic nuclei scattered within a fibrotic stroma [12].

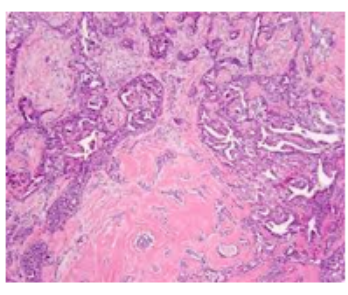

Figure 3: Ceruminous adenocarcinoma exhibiting, tubules, irregular structures and a cribriform pattern lined by monomorphic cells and hyperchromatic nuclei surrounded by an abundant fibrous tissue stroma [13].

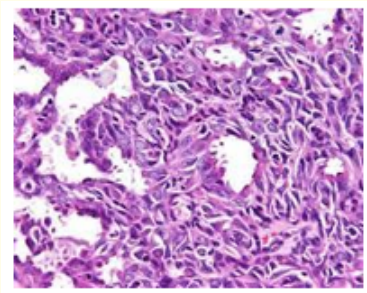

Figure 4: Ceruminous adenocarcinoma exemplifying scattered glandular structures layered by a two-layered of luminal and basal cells with pleomorphism and hyperchromatic nuclei admixed within a fibrotic stroma [13].

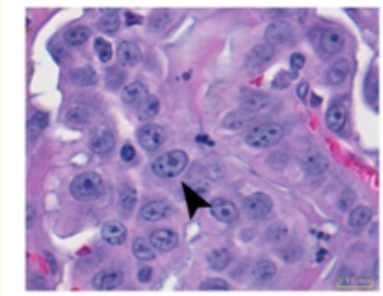

Figure 5: Ceruminous adenocarcinoma demonstrates glandular layering of luminal cells with nuclear hyperplasia and hyperchromasia, pleomorphism and mitotic figures [14].

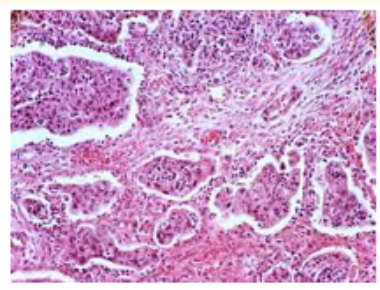

Figure 6: Ceruminous adenocarcinoma exhibiting tubular, irregular and cribriform structures lined by monomorphic cells with hyperchromatic nuclei and encompassing fibrous tissue stroma [15].

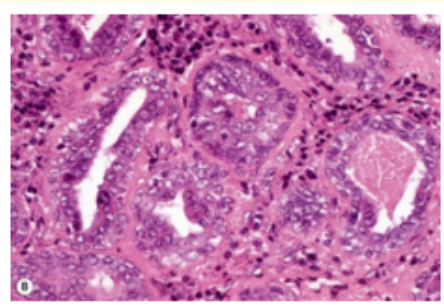

Figure 7: Ceruminous adenocarcinoma exhibiting glandular and tubular structures lined by luminal and basal cells with hyperchromatic nuclei enmeshed within a fibrotic stroma [16].

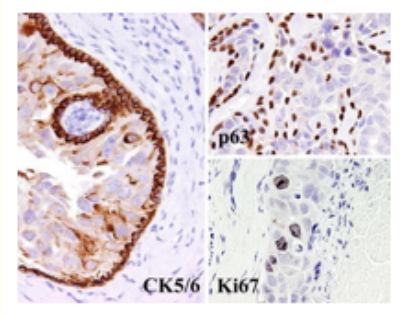

Figure 8: Ceruminous adenocarcinoma demonstrating epithelial tumour cells immune reactive to cytokeratin 5/6 and p63 with minimal Ki-67 immune reactivity [17].

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17. Image 8 Courtesy: Springer link.

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