none of the patients whose tumor penetrated 6 mm or less beyond the capsule died of the disease but that all patients with invasion of 8 mm or more had a fatal outcome.

Carcinosarcoma in a eleomorehic adenoma (true malignant mixed tumor)

Carcinosarcoma is exceedingly rare (5). Many arise in a preexisting PA but they can also develop *de novo.* Microscopy shows that it is a biphasic tumor, composed of epithelial and mesenchymal components. The epithelial component is generally a poorly differentiated (adeno)carcinoma or salivary duct carcktoma. The mesenchymal element is usually a chondrosarcoma but osteogenic sarcoma, fibrosarcoma, malignant fibrous histiocytoma and pleomorphic rhabdomyosarcoma have also been described (3). It has still not been resolved whether myoepithelial cells have a role in the genesis of the multiple tissue differentiation; some immunocytochemical results support a myoepithelial histogenesis while others do not. In analogous neoplasms in the breast, there is experimental evidence that the sarcomatous elements derive from myoepithelial cells and the carcinoma from the epithelial cells.

Metastasizing oleomorohic adenoma

Metastasizing pleomorphic adenoma (MPA) (6) is histologically indistinguishable from benign PA but it metastasizes widely to distant sites and can kill the patient. It remains histologically "benign" in the primary site, local recurrences and metastatic deposits. The reported cases (<100) shared several similarities, such as long time intervals (up to 50 years) between the primary tumor and metastases, and simultaneous local recurrences and distant metastases. The recurrences are usually multiple, and although their morphology and that of the metastases are almost identical, they seem to play an important role in the genesis of systemic spread. This suggests that surgical manipulation may favor vascular implantation or invasion eventually leading to metastases but in many cases of MPA it was not possible histologically to demonstrate actual vascular permeation.

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Clear cell tumors

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Introduction

The unqualified term "clear cell tumor" (or carcinoma) is not a diagnostic category but a description of one of several neoplasms and tumor-like lesions of the salivary glands histologically characterized by a significant population of cells possessing clear cytoplasm. In Exeter they comprised 2.3% (14/608) of all salivary tumors over the last 21 years. Most salivary tumors can be diagnosed purely on hematoxylin and eosin morphology but clear cell tumors are an exception and generally require special stains, immunohistochemistry and even electron microscopy.

Table 1. Classification of clear cell tumors of the salivary glands.

Benign
Pleomorphic adenoma, myoepithelioma, sebaceous adenoma, oncocytoma and oncocytic hyperplasia (MNOH)
Malignant, primary
a) Carcinomas not usually characterized by clear cells, but with rare clear cell variants; *e.g.,* mucoepidermoid and acinic cell carcinomas
b) Carcinomas usually characterized by clear cells
i) Dimorphic epithelial-myoepithelial carcinoma
ii) Monomorphic hyalinizing clear cell carcinoma
clear cell malignant myoepithelioma (myoepithelial carcinoma)
Malignant metastatic
Carcinomas, especially kidney, thyroid. Also melanoma
MNOH = multifocal nodular oncocytic hyperplasia

Individual tumor tyDes

Pie omorohic adenoma and benign mygevithelioma

These are variants of the same tumor but only rarely are clear cells (usually myoepithelial) a significant component. Generally, there are areas of typical pleomorphic adenoma or other forms of myoepithelial cells.

Oncocvtoma and multifocal nodular oncocytic hyperolasia

Oncocytes sometimes have clear cytoplasm. This is often the case in multifocal nodular oncocytic hyperplasia, which may be bilateral. The cytoplasm shows granular positivity with phosphotungstic acid hematoxylin (PTAH) and antimitochondrial antibody, and large numbers of mitochondria are seen on ultrastructural examination.

Sebaceous adenoma and carcinoma

These are especially rare and resemble sebaceous neoplasms of the skin. Their cytoplasm has a "foamy" appearance due to lipid. The carcinomas may also include basaloid areas.

Acinic cell carcinoma

The clear cell variant is uncommon (6% in one large series), and even then they are never pure, and cells with the characteristic periodic acid-Schiff-positive and diastase-resistant cytoplasmic zymogen granules are also present. Their behavior is the same as that of other acinic cell carcinomas.

Mucoevidermoid carcinoma

The clear cell variant is generally low grade; true epidermoid and mucous cells may be few.

Adenoid cystic carcinoma

Clear cells are sometimes seen, usually due to myoepithelial cell participation.

Eq/the//al-rn voevithellal carcinoma

Clear cells are usually part of the myoepithelial component and form a mantle around an inner layer of small cuboidal epithelial cells. This dimorphic pattern can be highlighted immunohistochemically. This tumor generally behaves as a low-grade malignancy.

Hyalinizina clear cell carcinoma

Monomorphic clear cell carcinomas are either epithelial or myoepithelial; the former, hyalinizing clear cell carcinoma, usually arises in the minor glands and is of low-grade malignancy. Microscopically, there are groups and trabeculae of polygonal glycogen rich cells separated by dense collagen bands. At times, particularly in the deeper parts of the tumors, the cells may lose their clarity when their cytoplasm appears weakly eosinophilic. Immunohistochemistry reveals positivity with cytokeratins but myoepithelial markers [S-i00 protein and a smooth muscle actin (SMA)] are negative.

Clear cell malignant mvoeoithelioma (mvoeoithelial carcinoma

The other form of monomorphic clear cell carcinoma is myoepithehal; relatively few cases have been described, mainly in the major glands. Microscopically, it is composed of sheets of clear cells, sometimes mixed with spindle shaped and other myoepithelial cells. Collagenous spherules and areas of necrosis are usual. The cells usually express cytokeratins, 5-100 protein and rrSMA. It is too early to comment on behavior but distant metastases and death due to disease have been reported.

Metasta tic renal cell carcinoma

Metastases composed of clear cells in the salivary glands include especially renal carcinoma. There are no specific markers as yet and it is best diagnosed (or excluded) by imaging the kidneys.

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Squamous and oncocytic metaplasia in salivary gland tumors

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Oncocytic lesions of salivary glands

Oncocytic change is where cells develop intensely eosinophilic granular cytoplasm due, typically, to increased numbers of mitochondria (1). Most oncocytic lesions show two types of cells: light and dark. The former are large and round or polygonal and have finely granular, pink cytoplasm and a vesicular nucleus. The dark cells are usually more sparse and have deeply eosinophilic, compressed cytoplasm and densely hyperchromatic nuclei.

Benign lesions

Focal and diffuse oncocytosis

Foci of oncocytosis, usually of ducts but sometimes also acini, are increasingly common with advancing age. Diffuse oncocytosis of the parotid is rare and can involve the whole gland.

Ductal oncocytosis

Extensive oncocytic metaplasia of ducts, often with cystic dilation, is seen mainly in the larynx and rarely elsewhere. These lesions can be regarded as oncocytic papillary cystadenomas. Microscopically, they resemble Warthin's tumor without lymphoid stroma. A similar appearance is seen in cheilitis glandularis (stomatitis glandularis).

Multifocal nodular oncocvtic hyperolasia

Multifocal nodular oncocytic hyperplasia (MNOH) comprises nodules of oncocytes, often with clear cytoplasm. The nodules may appear to engulf normal acinar tissue, giving a false impression of invasion.

Oncocvtoma

This tumor is rare and 50% are associated with MNOH. It comprises a well-demarcated mass of light and dark oncocytic cells with a solid, frabecular, or tubular configuration. A fibrous capsule may be incomplete, and there is little internal fibrous stroma. A rare clear cell variant typically consists of a circumscribed mass of polyhedral cells with clear cytoplasm and small eccentric hyperchromatic nuclei; phosphotungstic acid hematoxylin (PTAH) staining may be unreliable.

Warthin's tumor

Warthin's tumor has several variants, one being the stroma poor type with sparse lymphoid stroma; it forms a solid nodule of oncocytic cells rather than a papillary cystic lesion (2).

Oncoc vt/c tumor metaplasia

Oncocytic metaplasia in other benign salivary gland tumors (mainly pleomorphic and basal cell adenomas) is more common than oncocytoma itself (3).

Malignant oncocytic tumors

Mucoevidermoid carcinoma

Oncocytic change, either focal or diffuse, is a rare feature of mucoepidermoid carcinoma.

Oncocytic carcinoma

Oncocytic carcinoma is a rare tumor, found mainly in the parotid gland. The histological features are dysplastic, mitotically active oncocytic cells with soft tissue, perineural and vascular invasion. It is aggressive, and over half of the reviewed cases either died from the tumor or were alive with active disease, although this may not always be so, even in lesions with perineural invasion (4).

Sauamous metaDlasia and tumors of salivary alands

Squamous differentiation is common in reactive salivary gland lesions and can be seen in several tumors, either as metaplasia, or as an integral feature of the tumor.