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Original Research Paper

Oral Pathology

HISTOPATHOLOGICAL ASPECTS OF SALIVARY GLAND TUMORS -A REVIEW

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ABSTRACT The salivary gland is the site of origin of a wide variety of neoplasms and is relatively uncommon and rare in occurrence due to various causes like congenital anomalies, inflammation, infections, cysts, or neoplasm which can be either benign or malignant. Salivary gland tumours account for 2-6.5% of all head and neck tumours. Salivary gland lesions always pose diagnostic dilemmas. Histopathological diagnosis with routine hematoxylin and eosin in conjunction with minimal assistance plays a considerable role in the diagnosis of the lesion. Once a tumour is identified, the differential diagnosis between more formidable, frequently requiring histological diagnosis Since optimum treatment is dependent on the histological aspects of the salivary gland a thorough knowledge of these characteristics allows an accurate diagnosis and provides the indications for proper treatment. Hence this review article focuses on the concepts of histopathological aspects of benign and malignant salivary gland tumours.

KEYWORDS : Salivary gland, neoplasm, histopathological aspects, benign, malignant.

INTRODUCTION:

Salivary glands are the specialized glands that will produce and secrete saliva. Saliva is produced by both major and minor salivary glands of the head and neck region and is secreted into the oral cavity. Saliva contains enzymes, antibodies and other minerals. Enzymes help in initiating the food digestion process and the antibodies help in preventing the infection. There are three pairs of major salivary glands namely the parotid, submandibular and sublingual glands in addition to numerous minor salivary glands in the oral cavity. [1]

Salivary Gland Development And Anatomy:

The development of the salivary gland starts from the 4-6 6th week, the submandibular gland at the 6th week, and the sublingual gland, including the minor salivary glands, develop at the 8-12 week of embryonic life. The diverse developmental stages are Bud formation, epithelial cord formation, branching, and glandular differentiation. The parotid is ectodermal, while the submandibular and sublingual are endodermal in their origins. The parotid represents the largest of the salivary gland, situated among the external acoustic meatus and the ramus of the mandible, sternocleidomastoid muscle. Each gland is encapsulated and is composed of fat tissue and cells that secrete specifically the serous fluids. The predominant duct of the parotid gland, known as the Stensen's duct, opens into the vestibule of the mouth, contrary to the crown of the upper second molar tooth. The submandibular glands are positioned alongside the lower jaw bone in the anterior part of the digastric triangle. Each gland has a primary duct called the Wharton's duct that opens on the floor of the mouth. On the summit of the sublingual papillae at the side of the frenulum of the tongue, each gland is covered by a capsule and is hence more dispersed throughout the surrounding tissue. Their secretions drain through many small ducts, such as Rivinus's ducts, that exist along the sublingual fold at the floor of the mouth. A few anterior ducts may join to form a common duct called Bartholin's duct. Their secretions, being mixed in nature, empty into Wharton's duct. The sublingual and minor salivary glands are primarily mucous in nature.[2], [3]

Classification

Key Changes In The 2017 Who Classification Of Salivary Gland Tumors [4],[5]

	KEY CHANGES	EXPLANATORY NOTES
	NEW ENTITIES	
1	1. Secretory carcinoma	First described in 2010. Formerly known as mammary analogue secretory carcinoma (MASC)
2	2. Sclerosing polycystic adenoses	First described in 1996. There is controversy over its status as a neoplasm
	NEW NAMES	
1	1. Polymorphous adenocarcinoma	Formerly polymorphous low-grade adenocarcinoma
	2.Intraductal carcinoma	Formerly low-grade cribriform cystadenocarcinoma, low-grade salivary duct carcinoma, Salivary duct carcinoma in situ
	3. Poorly differentiated carcinoma	The single category includes undifferentiated carcinoma, large and small cell neuroendocrine carcinoma
CLARIFICATIONS CHANGES		
1.Adenocarcinoma, NOS	Definition broadened to include rare entities, including cystadenocarcinoma, mucinous (cyst) adenocarcinoma, papillary cystadenocarcinoma	

2. Cystadenocarcinoma	Cystadenocarcinoma is removed as a separate entity (see above)
3. Mucinous adenocarcinoma	Mucinous adenocarcinoma is removed as a separate entity (see above)
4. Metastasizing pleomorphic adenoma	Moved from malignant category to a variant of benign pleomorphic adenoma
5. Carcinoma ex-pleomorphic adenoma	Clarifications on diagnostic terminology: should explicitly state the histological type of malignant component. Definition of minimally invasive changed from 1.5 mm to "<4-6 mm"
6.Sialadenoma papilleferum	Given its category. No longer a "ductal papilloma"
7. Ductal Papilloma	A single name for two variants: inverted ductal papilloma and intraductal papilloma
8. Lymphadenoma	A single category replacing sebaceous and non-sebaceous lymphadenomas. Sebaceous-type is regarded as a simple variant
9. Non-neoplastic epithelial lesions	A new category includes sclerosing polycystic adenosis, nodular oncocytic hyperplasia, lymphoepithelial sialadenitis, intercalated duct hyperplasia

Benign Salivary Gland Tumors

Pleomorphic Adenoma (benign Mixed Tumor):

It is a benign neoplasm comprised of a combination of glandular myoepithelium and epithelial components. It is the most common benign salivary gland neoplasm.[6]

Histopathological Features:

It is composed of mixtures of myoepithelial and epithelial/stromal components in various forms. Epithelial cells are usually arranged in nests, cords, sheets, and islands forming duct-like structures containing eosinophilic coagulum. Myoepithelial cells are the major component of pleomorphic adenoma. Myoepithelial cells are also responsible for characteristic mesenchyme-like changes, these changes are done by extensive accumulation of mucoid material around individual myoepithelial cells giving a myxoid appearance. Myoepithelial cells may be spindled, oval, epithelioid, clear, or plasmacytoid (hyaline cells). Foci of mucous cells, sebaceous differentiation, oncocytic phenotype, and squamous differentiation can be seen Stromal components are the result of myoepithelial differentiation. Chondroid, myxoid, lipomatous, and osseous stroma are common. Collagen-containing crystalloids and tyrosine-rich containing crystalloids can be seen in this neoplasm. These are glossy, eosinophilic, and petal-shaped structures that are refractile and show radial arrangement surrounding a central core. The crystals stain black with verhoeff's stain, pink with Millon's reaction, and deep purple with Masson's trichrome stain. Encapsulation and the presence of chondromyxoid stroma are characteristics of classic pleomorphic adenoma. Vascular degeneration of myoepithelial cells results in a cartilaginous appearance. [6]

Myoepithelioma:

It is a rare benign tumour composed almost exclusively of myoepithelial cells, it arises from the neoplastic myoepithelial cells located between the basement membrane and basal plasma membrane of acinar or ductal/luminal cells. [7]

Histopathological Features:

Neoplasm is composed exclusively of neoplastic myoepithelial cells; Neoplastic cells are predominantly spindle-shaped or plasmacytoid. Clear cells or epithelioid cells may also be seen. Either a single cell type predominates in the tumour or there may be a combination of cell types, tumor is often difficult to be diagnosed definitively at the light microscopic level. Myoepithelioma predominantly consisting of spindle cells tends to be more cellular than the tumour consisting of plasmacytoid cells it exhibits a basal lamina and fine intra-cytoplasmic myofilaments Desmosomes are encountered between the adjacent cells. [7]

Basal Cell Adenoma

It is a rare benign salivary gland tumour with a high recurrence rate. differentiation of BCA from other forms, involving the maxillofacial area is mandatory. [8]

Histopathological Features:

Basal cells that make up this lesion are fairly uniform and regular; two morphological forms can be seen small cells with scanty cytoplasm and deeply round basophilic nucleus and large cells with eosinophilic cytoplasm and ovoid pale staining nucleus. Despite the low-power appearance of monomorphous tumour cells, there is a mix of cellular differentiation, including ductal, basal, and myoepithelial cells, which have been identified by immunohistochemical and electron microscopic studies. Basal cell adenoma demonstrates the bi-layering of cells mimicking what is observed in intercalated ducts of the salivary gland unit, with an inner luminal (ductal) layer and outer abluminal (basal/myoepithelial) layer.

BCA has a variety of cellular arrangements: Trabecular, tubular, solid, and membranous, and mixtures of these patterns are common. Recognition of the membranous patterned BCA is important; they have a greater propensity to recur. BCA can have a spindled stroma. .[8]

Warthins Tumor (papillary Cyst Adenoma Lympho matosum, Adenolymphoma):

It is one of the first salivary gland tumours to be described and the second most common tumour of the salivary gland. Warthin's tumours, characteristically occur in the superficial lobe of the parotid gland at or below the lower pole. [9]

Histopathological Features:

Microscopically, an oncocytic epithelium having a tubule-papillary cystic architecture within lymphoid tissue or a lymph node is seen. A lymph node has sinuses, an organized structure, and usually an embracing connective tissue capsule or connective tissue condensation. Warthin's tumours histologically classified Warthin's tumours into four subtypes. In subtype 1 Warthin's tumour ratio of the epithelium to lymphoid stroma is 1:1. Epithelial cells are in an irregular two-row alignment and possess acidophilic oncocytic cytoplasm. The basal-row cells are cuboidal, often pyramidal, in shape, in contrast to the taller cylindrical apical cells. In subtypes 1 and 2, areas of nonpapillary oncocytic proliferation are found. This tendency is much more pronounced in stroma-poor type 2. Warthin's tumour can suggest an oncocytoma. Subtypes 3 and 4 are characterized by a relative paucity of oncocytic cells. In the former, the lymphoid stroma dominates; in the latter an extensive squamous metaplasia, often accompanied by regressive changes, is characteristic. Oncocytic foci are few. Regressive changes consist of areas of hyalinization, liquefaction, and necrosis. The epithelial (oncocyte) elements of Warthin's tumours exhibit a heterogeneity of keratin expression, with the cells on the luminal side colouring differently than cells on the basal side. [9]

Oncocytoma (oncocytic Adenoma, Oxyphilic Adenoma, Acidophilic Adenoma):

It is a Rare benign tumour composed of oncocytes with granular eosinophilic cytoplasm and a large number of atypical mitochondria. [10]

Histopathological Features:
The oxyphilic adenoma is microscopically characterized by large cells which have eosinophilic granular cytoplasm and distinct cell membranes arranged in tightly packed narrow rows and cords. Oncocytes are arranged in sheets or cords which form an alveolar or organoid pattern, and some degree of cellular Atypia nuclear hyperchromatism and pleomo rphism has been accepted These cells exhibit few mitotic figures, are closely packed, and there is little supportive stroma Lymphoid tissue is frequently present but does not appear to be an integral part of the lesion. [10]

Cystadenoma:
It is a rare benign epithelial tumour of the salivary gland and is divided into papillary and mucinous subtypes, mainly characterized by polycystic growth, with the epithelial component showing adenomatous hyperplasia. It is a slow-growing, painless, slightly compressible swelling. [11]

Histopathological Features:
Epithelial proliferation results in various-sized cystic structures. The lining of cystic structures differs from flattened to tall columnar cells but mucous, cuboidal, and oncocytic cells may also be present. The thickness of the lining varies from one to three epithelial cells. Limited papillary growth with central connective tissue core is observed. Eosinophilic or slightly hematoxyphilic secretions are seen in the stroma. A Dense fibrous connective tissue stroma with scattered inflammatory cells is present. [11]

Ductal Papilloma:
They represent adenomas with distinctive papillary features and arise from the salivary gland duct system. They represent three types with unique histological features which include inverted ductal papilloma, intraductal papilloma, and sialadenoma papilleferum. [11]

Inverted Ductal Papilloma
Histopathological Features:
It consists of basaloid and squamous cells arranged in thick, bulbous papillary proliferation that project into the ductal lumen. The lumen of the tumour is generally narrow and, in some tumours, transmits with the exterior of the mucosal surface terminated by a constricted opening.

Intraductal Papilloma
Histopathological Features:
It exhibits a unicystic dilated structure, The cyst wall is lined with a single or double row of cuboidal and columnar cells which extend into the cyst lumen as papillary projection having thin fibrovascular cores.

Sialadenoma Papilleferum:
It most commonly involves the minor salivary gland. It is a rare benign salivary gland neoplasm that encompasses about 0.4 to 1.2% of all salivary gland tumours. Its name stands peculiar due to its microscopic resemblance to the syringo cystadenoma papilliferum, an uncommon benign tumour of sweat gland origin. [12]

Histopathological Features:
Multiple exophytic papillary projections are covered by stratified squamous epithelium. This epithelium is connected with the papillomatous ductal epithelium found below the surface and extends downward into the deeper connective tissues. Multiple ductal lumina are formed, which are lined by a double-rowed layer of cells comprising a layer of tall columnar cells and a basilar layer of smaller cuboidal cells. These ductal cells are known to have an oncocytic appearance. An inflammatory infiltrate of plasma cells, lymphocytes, and neutrophils is characteristically present. [12]

Canalicular Adenoma:
It is an uncommon tumour that occurs in the minor salivary gland and has a marked predilection for the upper lip. [13]

Histopathological Features:
It consists of uniform columnar or cuboidal cells forming canal-like ductal structures. The cells may appear in a double row and enclose cystic spaces of varying sizes. These spaces are filled with eosinophilic coagulum, and the supporting stroma is loose and fibrillar with fine vascularity. Large cystic spaces may be created and the epithelium may demonstrate papillary projections into the lumina. [13]

Malignant Salivary Gland Tumors:
Mucoepidermoid Carcinoma:
It is a malignant neoplasm comprised of epidermoid and mucous-secreting epithelial cells. It is the most common malignant neoplasm of the salivary gland [14]

Histopathological Features:
The mucous cells portray a diversity in shapes and possess an abundant pale and foamy cytoplasm that stains positively for mucin stains. Epidermoid cells have squamoid features that demonstrate a polygonal shape, intercellular bridges, and rarely keratinization, highly prolific basaloid cells referred to as intermediate cells. These cells seem to be larger than basal cells but smaller than squamous cells. Occasionally, clusters of clear cells can be present and are generally mucin and glycogen-free, epidermoid cells together with intermediate and mucous cells line cystic spaces or form solid masses or cords. Epidermoid and mucous cells are arranged in a glandular pattern.

LOW-GRADE: low- grade tumours are well differentiated and are made up primarily of mucous secreting and squamous epithelial cells

INTERMEDIATE: consisting of solid areas of epidermoid or squamous cells with intermediate basaloid cells

HIGH-GRADE: poorly differentiated and made up primarily of squamous epithelial and intermediate cells. [14]

Adenoid Cystic Carcinoma (cylindroma, Adipocytic Carcinoma, Adenocystic Basal Cell Carcinoma, Basaloid Mixed Tumor, Pseudo Adenomatous Basal Cell Carcinoma
It is an aggressive yet slow-growing neoplasm with an exceptional capacity for reversion. It is characterized by the proliferation of ductal (luminal) and myoepithelial cells in cribriform, tubular, solid, and cystic patterns. [15]

Histopathological Features:
It is composed of myoepithelial cells and ductal cells which have varied arrangements Morphologically, three growth patterns have been described: cribriform (classic), tubular, and solid (basaloid). The tumours are classified according to the principal pattern. The cribriform pattern shows basaloid epithelial cell nests that form multiple cylindrical cysts-like patterns resembling a Swiss cheese or honeycomb pattern, which is the most classic and best-recognized pattern. The lumina of these spaces are found to have periodic acid-Schiff (PAS) positive mucopolysaccharide secretion. The tubular pattern unveils tubular structures that are lined by stratified cuboidal epithelium. The solid pattern displays solid groups of cuboidal cells with little tendency towards duct or cyst formation. The cribriform pattern is the most familiar one, whereas the solid pattern is the mere common of all. Solid adenoid cystic carcinoma is a high-grade lesion with reported recurrence rates of up to 100% compared with 50–80% for the tubular and cribriform variants. [15]

Polymorphous Low-grade Adenocarcinoma (PLGA)
It is a malignant salivary gland tumour that is essentially

limited in occurrence to minor salivary glands and histopathologically has many growth patterns, is bland and has an infiltrative and low metastatic potential, henceforth the name speaks for itself. Following mucoepidermoid carcinoma, it is the second most common malignancy affecting the minor salivary glands. [15]

Histopathological Features:
cytologic uniformity and histologic blandness are seen in the tumour cells. The cells are cuboidal or columnar, with indistinct cell borders and with a pale to eosinophilic cytoplasm. The nuclei may perhaps, be round, ovoid, or spindle-shaped. The tumour cells show solid, ductal, cystic, and tubular-like growth patterns, hence the name polymorphous. The peripheral cells happen to usually be infiltrative and invade the adjacent tissue in a single file fashion or Indian file fashion. The stroma is generally mucoid or it may at times demonstrate hyalinization. Perineural invasion as well is a common feature that replicates adenoid cystic carcinoma

Acinic Cell Carcinoma (serous Cell Adenocarcinoma):
It arises from the neoplastic transformation of the reserve cells in the intercalated duct cells with histo-differentiation into serous acinar cells. [16]

Histopathological Features:
Usually, the tumour is surrounded by a thin capsule and composed of cells of varying degrees of differentiation. Well-differentiated cells resemble normal acinar cells while Less-differentiated cells resemble embryonic ducts and immature acinar cells. The individual cells can be categorized as acinar, intercalated duct-like, vacuolated, clear, and nonspecific glandular cells. Acinar cells: These cells are large, round to polygonal in shape with an eccentric nucleus and a granular basophilic cytoplasm. Intercalated duct-like cells: These cells are smaller than acinar cells, cuboidal in shape with eosinophilic cytoplasm and consist of centrally placed nuclei. Vacuolated cells: They are distinct and peculiar cells. The cells are just the size of well-differentiated acinar cells and have eccentric nuclei that are less chromatic and more pleomorphic. several vacuoles or a single large vacuole present in the cytoplasm. Nonspecific glandular cells: The most difficult to describe and are defined by the absence of features that are characteristic of the other four cell types. These usually form a group of multinucleated cells with indistinct cell boundaries and eosinophilic cytoplasm. The nuclei are naturally larger, pleomorphic and more vesicular than those of the other types. Mitotic figures are more evident It exhibits four growth patterns:

1. Solid growth pattern: Classic pattern, it consists of numerous well-differentiated acinar cells arranged in a pattern that resembles normal parenchyma. The absence of striated ducts distinguishes it from normal parenchyma. and the cells are distinguished and surrounded by thin fibrous septa that contain small invisible capillaries.

2. Microcystic pattern: More common pattern, it has numerous small cystic spaces.

Acinar cells are the dominant cell type; however, vacuolated and intercalated duct-like cells can also be prominent. Microcystic spaces have increased chances to result from the coalescence of intracellular vacuoles of ruptured cells. Proteinaceous or mucinous material may puddle in microcystic spaces

3. Papillary cystic growth pattern: It is characteristic of one or more cystic structures that contain proliferations of epithelium. Usually, cysts may appear small with a few folds of lining epithelia projecting into the lumina. At times cystic structures can be large with long stalks, fronds, or masses of glandular epithelium within the lumina. Intercalated duct-like and nonspecific glandular cells are prominently seen. Some of the epithelial projections have thin fibrovascular cores, whereas others appear to have masses of epithelium without supporting stroma.

4. Follicular pattern: Least frequently encountered, this pattern has a definite thyroid-like appearance. Differently-sized, ovoid to round cystic spaces are lined by cuboidal to low columnar epithelial cells. Many of the cystic spaces contain an eosinophilic proteinaceous material. [16]

Carcinoma Ex Pleomorphic Adenoma
It is a malignant variation of a pre-existing pleomorphic adenoma.

Histopathological Features:
In the initial phase, carcinoma cells with large atypical nuclei replace the neoplastic ductal luminal cells while retaining an intact layer of non-atypical myoepithelial cells of the pre-existing pleomorphic adenoma. This can be contemplated as a form of carcinoma in situ and there is no metastatic potential. With time, carcinoma cells may flare up from the confines of the neoplastic myoepithelial sheath and invade the surrounding stroma. The prognosis is excellent with complete excision. The carcinoma ex pleomorphic adenoma is considered to be invasive if the invasion extends beyond the fibrous capsule. The malignant component is most probably poorly differentiated adenocarcinoma (salivary duct type or not otherwise specified) or undifferentiated carcinoma. histopathologic documentation of a previous pleomorphic adenoma or areas of pleomorphic adenoma are evident within the malignant tumour, a diagnosis of carcinoma ex pleomorphic adenoma is given. The infiltrative, destructive growth pattern is the most reliable diagnostic criterion, and minimal cellular atypia is seen. malignant cells exhibit nuclear hyperchromatic and pleomorphism. [16]

Adenocarcinoma:
The tumour exhibits ductal differentiation but still lacks histopathological features that resemble any classifiable salivary gland tumour.

Histopathological Features:
The Glandular or ductal structures with infiltrative growth are features of this tumour. the tumour is graded as low, intermediate, and high grades histopathologically depending on the ductal differentiation. Tumour cells are cuboidal to ovoid in shape, nuclear pleomorphism or hyperchromatic and rare mitosis is evident in these cells. High-grade tumours exhibit more features of anaplasia, an increase in mitotic figure, and cellular and nuclear pleomorphism. In a few areas, cords and nests of cells are also seen. [16]

Epithelial–myoepithelial Carcinoma
It is an abnormal, biphasic low-grade epithelial neoplasm consisting of variable proportions of ductal and large, clear-staining, differentiated myoepithelial cells. It comprises approximately 1% of all epithelial salivary gland neoplasms.

Histopathological Features:
The histologic features of this tumour exhibit a wide range of variations from solid lobules that are separated by bands of hyalinized fibrous tissue to irregular, papillary cystic arrangements with tumour cells that partially or fill cystic spaces but most of them show a multinodular growth pattern with islands of tumour cells separated by dense bands of fibrous connective tissue. The islands of tumour cells consist of small ducts lined by cuboidal epithelium that is surrounded by clear cells which form a common boundary with a thick, hyaline-like basement membrane. The inner luminal cuboidal

cells have a finely granular, dense eosinophilic cytoplasm and a central or basally located nucleus. The outer, clear myoepithelial cells show a wide variety of shapes from columnar to ovoid and have a vesicular nucleus located towards the basement membrane.

Basal Cell Adenocarcinoma

It is an unusual and lately defined entity occurring in the major salivary glands. It is a low-grade malignant neoplasm that is cytologically just like basal cell adenoma however it is infiltrative and has a small potential for metastasis.

Histopathological Features:

The subtypes are

(1) solid
(2) ductal
(3) trabecular
(4) membranous

The tumour pattern shows solid neoplastic aggregates with a basement membrane-like material that delineates the peripheral cell palisading arrangement, a trabecular or membranous arrangement is seen in a few places. The neoplastic clusters are shaped by two cell populations: the small dark cell type, one predominant, and a large pale cell type, larger paler cells are present peripherally to small dark cells. The tumour extends to the surrounding tissues by local infiltration as nodules, nests and cords. Perineural and vascular invasion is also seen. [17]

Sebaceous Carcinoma:

It is a malignant neoplasm consisting chiefly of sebaceous cells, which are arranged in sheets and/or nests with different degrees of pleomorphism, nuclear atypia, and invasiveness.

Histopathological Features:

The Tumour is well-circumscribed with locally infiltrating margins. Cellular pleomorphism and cellular atypia are seen and are more common than sebaceous adenomas. Tumour cells may be arranged in multiple large foci or sheets and have hyperchromatic nuclei surrounded by abundant clear to eosinophilic cytoplasm. cellular necrosis and fibrosis are seen. At times, Perineural invasion has been observed in more than 20% of tumours. vascular invasion is extremely unusual. Oncocytes are rare and foreign body giant cells with histiocytes are seen.

Papillary Cystadenocarcinoma

It is a rare malignant epithelial tumour characterized histologically by prominent cystic and, frequently, papillary growth that signifies cystic variants of various salivary gland neoplasms.

Histopathological Features:

A cystic growth pattern must dominate the histologic appearance for the diagnosis to be considered these cystic spaces vary in size between tumours as well as within the same tumour. These neoplasms are circumscribed and the lumina are filled with mucus and dystrophic calcifications are sometimes focally evident. The lining cells vary from cuboidal to tall columnar, and a single tumour filled with basaloid, oncocytic, clear, and rarely mucous cells, forms adenomatous or nodular, solid epithelial areas which occupy the space between the cystic structures. Nuclear hyperchromatism and nuclear variability are minimal, and mitotic figures are rarely present. Nucleoli may be obvious. Incomplete encapsulation is seen, and salivary gland parenchyma infiltration is seen. The tumour invades as cyst-like structures or as solid islands. Even though the vast majority of cystadenocarcinomas are low-grade lesions, moderate/ intermediate-grade tumours still exist.

Oncocystadenoma

It is a rare oncocytic neoplasm and its abnormal morphologic features and infiltrative growth reveals the malignant nature of the tumour. [17]

Histopathological Features:

The foci of oncocytic cells are present in all types of benign and malignant salivary gland tumours but the oncocytic component contains a small portion that is meant to be confused with oncocytic carcinoma. Tumours with a significant oncocytic component include Warthin's tumour, oncocytoma, and d by oncocytes with marked cellular atypia, frequent mitosis, destruction of adjacent structures, perineural or vascular invasion, and distant or regional lymph node metastasis. Histochemical or electron microscopic confirmation of the oncocytic (mitochondrial) nature of the cytoplasm is necessary because the cytoplasmic accumulation of smooth endoplasmic reticulum, lysosomes, or secretory granules may have a similar appearance. [17]

Mucinous Adenocarcinoma, (primary Colloid Carcinoma):

It is a rare malignant neoplasm characterized by a large amount of extracellular epithelial mucin that contains cords, nests, and solitary epithelial cells. [18]

Histopathological Features:

The tumour is mucoid, with a slimy texture and they are well circumscribed and unencapsulated. The islands and cords of tumour cells that appear to be floating within pools of pale staining mucin are revealed in low magnification. The pools of mucin may be divided into irregular lobules by fibrous connective tissue septa that Pierce through the tumour, which is also unencapsulated. They are large, cuboidal, and polygonal cells with eosinophilic to amphophilic cytoplasm. The nuclei are vesicular, and scattered mitotic figures are seen. There is a pale-staining mucoid substance which surrounds the tumour. Mucicarmine, periodic acid-Schiff, and alcian blue at pH 2.0 are the stains present in the mucoid substance. Many tumour cells contain intracytoplasmic mucin which is revealed by Mucicarmine stain. [18]

Salivary Duct Carcinoma

It is an extremely rare, high-grade malignant epithelial neoplasm that contains structures that are similar to the expanded salivary gland ducts.

Histopathological Features:

The infiltrative tumour elements contain clusters of tumour cells and small lumina or cribriform arrangements, solid, irregularly shaped tumour cell aggregates are also present. The epithelial cells are cuboidal and polygonal with a moderate amount of eosinophilic cytoplasm and co-exist with a dense fibrous connective tissue stroma which is hyalinized in some areas. Invasion of the nerves and blood vessels may often lead to infiltration of salivary gland lobules and extra-salivary gland tissues, such as fat, muscle, and bone. Mucicarmine and Alcian blue stains are negative, except for a small amount of luminal staining. Immunohistochemical and ultrastructural studies have identified ductal cells but myoepithelial cells are not found. [18]

Malignant Myoepithelioma (myoepithelial Carcinoma):

It is an extremely rare, malignant salivary gland neoplasm in which the tumour cells where Myoepithelial differentiation is manifested. It represents the benign counterpart of Myoepithelioma. The Parotid gland is the major gland to be affected. [19]

Histopathological Features:

The cytologic features and the morphologic features are similar to the tumour cells in benign myoepithelioma and the myoepithelial cells of mixed tumours. The cells are either spindle-shaped or plasmacytoid. The cell types are intermixed but sometimes the other cell type predominates.

The tumours are more cellular and highly suggestive of sarcoma than carcinoma. The tumours are more conspicuous and myxoid in the stroma of other areas. These tumours are renowned for benign myoepithelial neoplasms by their infiltrative, destructive growth. They generally demonstrate increased mitotic activity and cellular pleomorphism. Some tumour cells could be immunoreactive for cytokeratin, S100 protein, smooth muscle actin, and occasionally, glial fibrillary acidic protein. [19]

Squamous Cell Carcinoma:

It is a common malignant neoplasm of the major salivary glands which is composed of squamous (epidermoid) cells.

Histopathological Features:

The gross and microscopic appearance resembles squamous cell carcinoma of other primary sites and differentiates from well-differentiated to poorly differentiated. Salivary gland squamous cell carcinoma shows aggressive behaviour with rapid growth and primarily spreads to regional lymph nodes.

Small Cell Carcinoma

It was first described in 1972. Small cell carcinomas arising in salivary glands are extremely rare, high-grade malignant tumours and are subclassified into neuroendocrine and ductal types.20]

Histopathological Features:

The tumour cells have oval, hyperchromatic nuclei and a sparse amount of cytoplasm and are organized in sheets, strands, and nests microscopically. The tumour is highly aggressive, even though the prognosis may be better than that for extra-salivary neoplasms. Mostly, small cell carcinomas exhibit neuroendocrine differentiation, which is suggested by previous studies. Small cell carcinomas of the lung have a low survival rate when compared to the Neuroendocrine carcinomas of minor salivary glands. The undifferentiated equivalent to the neoplasm is the small cell undifferentiated carcinoma. [20]

CONCLUSION:

Histopathological diagnosis plays a major role in the diagnosis of the lesion and pays a way for assigning the proper treatment. Since optimum treatment is dependent on the histological aspects of the salivary gland, a thorough knowledge of these characteristics allows an accurate diagnosis and provides the indications for proper treatment.

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