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Original Research Paper

Pathology

THE SALIVARY GLAND ENIGMA: UNRAVELING RARE TUMOUR MYSTERIES

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ABSTRACT Salivary glands comprise of parotid glands found in front of and just below the ears, submandibular glands below the jaw, sublingual glands under the tongue and few minor salivary glands in upper aerodigestive tract. In spite of different locations, the glands share the same histology with acinar and ductal epithelial cells and myoepithelial cells. Salivary gland tumours are rare groups of complex heterogenous histology with wide range of tumour etiology, microscopy, growth patterns and tumour characteristics, which may be challenging to the pathologists. In this case series, we are presenting 3 cases of rare salivary gland tumours, mucoepideromoid carcinoma arising from Warthins tumour, Epithelial myoepithelial carcinoma presenting as multiple nodules around the parotid gland with H/O previous pleomorphic adenoma operated and Canalicular adenoma which is rare with our case having unique aspects like occurring in a younger age, bigger than average size reported, rare location in the parotid gland, cystic change and occurrence in a woman of Asian ethnicity.

KEYWORDS : Salivary gland, mucoepidermoid, warthins, epithelial, myoepithelial ,canalicular, adenoma.

INTRODUCTION

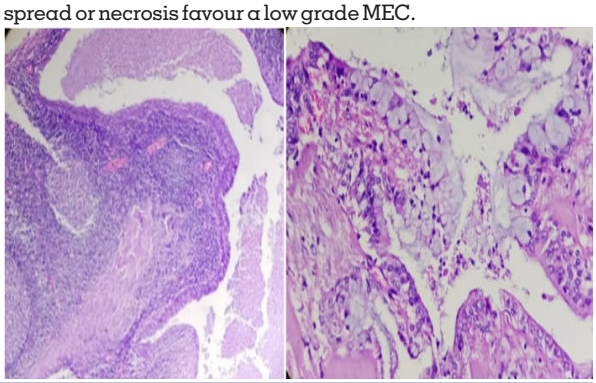
Salivary gland tumours are rare group of complex heterogenous histology with wide range of tumour etiology, microscopic histology, growth pattern and tumour characteristics .(1) Of these, the commonest benign tumour is pleomorphic adenoma and commonest malignant tumours being Mucoepidermoid carcinoma and adenoid cystic carcinoma with salivary gland malignancies representing 5% of head and neck cancers with 60% of arising from the parotid glands, 30% arising from the submandibular gland and 10-15% from minor salivary glands. Regarding etiopathogenosis, though the exact etiology is unknown, radiation exposure is an important cause for mucoepideromoid carcinoma. Other etiologies proposed are viruses (EBV and HIV) ultraviolet light exposure, occupational exposure in rubber and nickel industries and individuals with Sjogrens syndrome having a predisposition to lymphomas. Genetic mutations are also found to be associated with salivary gland neoplasms with most common genetic findings in mucoepideromoid carcinoma being translocation t (11,19) leading to fusion of MECTI and MAM L2 GENES AND 11P15.5 mutation in epithelial myoepithelioid carcinoma.Out of our 3 cases,2 cases needed IHC for definite diagnosis and molecular genetics study was not done for any of our cases.

METHODS

This study is retrospective study of rare salivary glands neoplasms over a period of 1 year from July 2023 to July 2024.As this is a case series we chose to describe cases received during this period at HISTO LAB Coimbatore .All the 3 patients presented with parotid swelling of which 2 needed IHC for definite diagnosis. Molecular genetic study could not be done for case 1.

Case 1

71/male presented with parotid swelling of 10years duration with sudden increase in size since one year. On examination left parotid area was diffusely enlarged with overlapping skin ulcerated and puckered and hard in consistency. Superficial parotidectomy was done and sent for HPE. Grossly skin with underlying fibrofatty tissue was received measuring 6.5x4.5x3.cm which on sectioning showed a mass measuring 3x3x2.5cm,that was greyish white and cystic on further sectioning .Also two lymphnodes were received from the adjacent fat. HPE showed a tumour with a DD of Warthins tumour(WT) with mucinous metaplasia/mucoepideromoid carcinoma(MEC)arising in Warthins tumour(fig1a,1b) . Also the IHC study,(though it does not have a major role) with CK 7 positivity of the luminal cells and P 40 positivity of squamous cells,(fig.1c,1d,1e) is in favour of the diagnosis of mucoepideromoid carcinoma-Low grade arising from Warthins tumour. Moreover encapsulation of the Warthins tumour focuses and desmoplasia surrounding mucoepideromoid elements and history of of swelling of 10 years duration with recent increase in size favours this diagnosis. Absence of intracystic component,atypia,capsular or vascular invasion,mitosis of more than 4/10HPF,perineural spread or necrosis favour a low grade MEC.



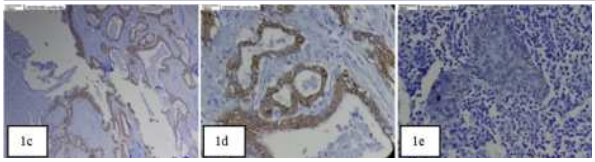


Fig.1 a showing warthins tumour low power,1b)showing mucoepidermoid component high power.,1c and 1d)low and high power of CK7 positivity of the luminal cells, 1e)low power of squamous cells showing P40 nuclear positivity

Case 2

34/M Presented with parotid gland swelling and also gave H/O of previous surgery for pleomorphic adenoma. Left total parotidectomy was done and sent for HPE. Grossly fibrofatty tissue measuring 10.5x9x6.5cms was received which on sectioning showed multiple nodular mass with cystic and solid areas with largest nodule measuring 5.5x5x5cm.HPE showed multiple nodules of tumour with infiltrative borders and composed of tubules of inner epithelial cells and variable layer of outer myoepithelial cells with scant fibromyxoid stroma. Foci of necrosis was seen. Tissue was taken up for IHC and CK 7 was positive, highlighted the epithelial component with S 100 and P63 positivity highlighting the myoepithelial component and with CD 117 negativity, a diagnosis of Low Grade epithelial myoepithelial carcinoma was made.

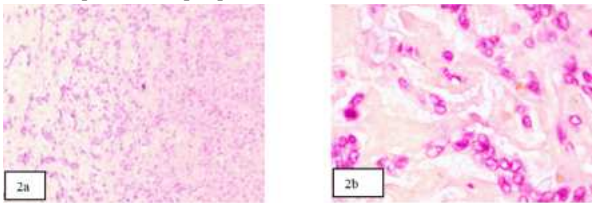


Fig.2a and 2b)low and high power of adenoma in canalicular pattern.

Case 3

38/Female presented with left parotid swelling of 2 years duration and segmental parotidectomy was done and sent for HPE. Grossly tumour tissue was received in multiple pieces, largest measuring 4.5x3.5x3cm.which on sectioning showed a mass measuring 3.5x3x3cm which on HPE showed an encapsulated neoplasm composed of multifocal strands, anastomosing cords, tubules and canalicular spaces of columnar to cuboidal cells with few of them appearing basaloid with uniform nuclei. The stroma has hyalinized with cystic change and with the above finding, a diagnosis of canalicular adenoma was made.

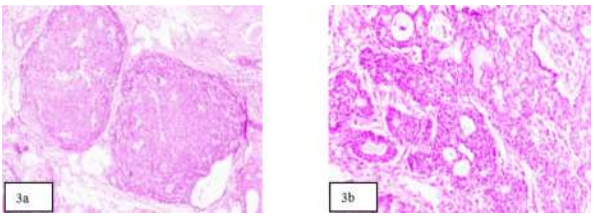


Fig 3a) scan power with nodular appearance of the tumour infiltrating the adjacent fat,3b)low power showing tubular and solid arrangement of the tumour cells.

DISCUSSION

Salivary gland neoplasms are rare in both pediatric and adult populations and demonstrate considerable histological, biological, and clinical diversity.The WHO histological classification of salivary gland tumors now includes over 40 variants as well as tumor-like lesions (e.g., salivary gland cysts). A simplified classification is presented below(1,2):

1. Benign: Pleomorphic adenoma, Warthin tumor (adenolymphoma), myoepithelioma, basal cell adenoma, oncocytoma, cystadenoma.

2. Malignant: Mucoepidermoid carcinoma, adenoid cystic carcinoma, acinic cell carcinoma, adenocarcinoma, squamous cell carcinoma (SCC), undifferentiated carcinoma, carcinoma ex-pleomorphic adenoma, polymorphous low grade carcinoma

3. Hematolymphoid: Hodgkin lymphoma, diffuse large B cell lymphoma, extranodal marginal zone B cell lymphoma.

4. Non-epithelial: Haemangioma, lymphangioma, neurofibromas

Mucoepidermoid Carcinoma Arising In A Warthins Tumour

Mucoepidermoid carcinoma (MEC) and Warthins tumour are two entirely different salivary gland neoplasm with distrinct histomorphologic features. WT ranks as the second most common benign tumor of the salivary glands and has morphologic characteristics consisting of (i) cystic structures with papillary projections lined by bilayered oncocytic and basaloid epithelium; and (ii) underlying lymphoid stroma.In contrast, MEC is the most common malignant salivary gland tumor, which is histologically composed of a mixture of mucous cells, intermediate cells, and squamous-like or epidermoid cells. (3,4) Our case showed coexistence of features of both WT and MEC. The differential diagnosis in such cases are(i) Warthin like variant of MEC (ii) Coexistance of both WT and MEC (iii)) Malignant transformation of WT (iv) Squamous and mucinous metaplasia of WT. Warthin-like MEC is a newly recognized entity. Ishibashi *et al.* analysed 15 tumors originally diagnosed as metaplastic Warthin tumor and found that five of them were positive for specific t(11:19) translocation resulting in *CRTC1–MAML2* gene fusions and suggested that 'Warthin-like' should be considered as a variant of MEC. (5)This variant has got better prognosis compared to conventional MEC. The coexistence of WT and MEC is rare, with only 29 cases reported.(6) Malignant transformation of Warthin's tumor is more common in the lymphoid component than the epithelial component, although malignant carcinoma is very rare (0.3%) .Malignant transformation of the epithelial component of WT, such as squamous cell carcinoma, MEC, adenocarcinoma, and undifferentiated, poorly differentiated, and anaplastic carcinoma is extremely rare and only seen in 0.3% of cases. (7) Direct evidence of malignant transformation is infiltration of lymphoid tissues and encapsulation of WT by MEC.(8) The pointers which suggest malignant transformation of WT are presence of a pre-existing benign WT,transition zones from benign oncocytic to malignant epithelia and infiltrating growth. (9)WT which has both mucous and squamous epithelium metaplasia, lacks the MAML2 rearrangement that is frequently present in WT-like MEC and conventional MEC.(3)

Epithelial Myoepithelial Carcinoma

Epithelial-myoepithelial carcinoma (EMC) is an infrequent tumour of the salivary glands, distinguished histologically by dual-layered tubular formations consisting of inner ductal epithelial cells and outer clear myoepithelial cells [10]. Typically, EMC shows a recurrence rate ranging from 30% to 50%, lymph node metastasis occurring in 15% to 20% of cases, with 5- and 10-year survival rates ranging from 80% to 94% and 72% to 90%, respectively[11]. EMC accounts for less than 1% of all salivary gland tumors and typically originates in the parotid gland, although cases have also been reported in the submandibular gland, minor salivary glands, and palate[12]. It predominantly affects females, with most cases occurring in the seventh decade of life. Clinically, EMC typically presents as a slowly enlarging mass within the parotid gland[13]. Due to its diverse histological presentation, complexity,and variability, accurately diagnosing it can sometimes be challenging.

The differential diagnosis for EMCs primarily includes adenoid cystic carcinoma, canalicular and basal cell adenoma, myoepithelioma, and myoepithelial carcinoma. Adenoid cystic carcinoma, akin to EMC, is a tumor

characterized by a dual-cell composition of epithelial and myoepithelial cells. It may exhibit a trabecular pattern resembling that of EMC, with a notable hyalinized stroma encasing and compressing the tumor cells into delicate strands[14]. However, in contrast to EMC, these cells tend to be smaller with more hyperchromatic, irregular with angulated nuclei. What distinguishes myoepithelioma and myoepithelial carcinoma from EMC is the absence of ductal cell elements. Therefore, despite similar morphology that could lead to misdiagnosis, immunohistochemistry results are crucial in distinguishing between these entities[15]. Canalicular and basal cell adenoma are benign tumors consisting of basaloid, relatively uniform cells organized in canaliculi, trabeculae, and cords. Their morphology can sometimes resemble that of EMC, leading to potential confusion. However, the stroma of these tumors is typically loose and contains few cells, especially in canalicular adenoma. Moreover, they are composed solely of epithelial cells without a myoepithelial component, as confirmed by immunohistochemistry[16].

Since EMC is classified as a low-grade malignant tumor, complete resection with clear margins in surrounding soft tissues is the minimum recommended and essential treatment. Neck node dissection should be contemplated for cases showing lymph node involvement. Chemotherapy and radiotherapy are options for patients with advanced disease, positive margins after surgery, or tumors that cannot be surgically removed, although there is limited clinical data supporting these treatments[17].

CANALICULAR ADENOMA

Canalicular adenoma is a rare benign tumor of the salivary glands. Initially believed to originate from the terminal duct, there has been debate regarding its source and differentiation from other salivary gland tumours[18,19]. These neoplasms have experienced changes in classification, with various terms used to describe them over time(Canalicular tumour , Canalicular form of mixed tumour,Papillary cystadenoma of the upper lip, multifocal carcinoma of accessory salivary gland, adenomatosis of accessory salivary glands of the lip)[20,21,22,23,24]However, it is now universally accepted that Canalicular adenoma represents a distinct type of salivary gland tumor, distinguished from other monomorphic adenomas in the latest editions of the World Health Organization classification. Monomorphic adenoma, a benign tumor of the salivary glands, manifests in three distinct histological patterns: canalicular, basal cell, and trabeculo-tubular[25]. Among these, canalicular adenoma (CA) is notably uncommon, comprising only 1% to 3% of all salivary gland tumors[26]. This subtype predominantly affects older women and is characterized by its asymptomatic, slowly enlarging mass, occasionally appearing multinodular[27]. CA most commonly occurs in the minor salivary glands, particularly the upper lip, cases in the buccal mucosa have been reported, though infrequently. Instances in the parotid gland are exceptionally rare. Histologically, CA is identified by its well-encapsulated cluster of columnar epithelial cells surrounded by loose connective tissue[27].

In this case report, we describe a rare case of CA located in the parotid gland. As far as we know, this is only the eighth documented occurrence in recent literature[28]. Additionally, it is very rare within the Asian population[29]and rarely presents with cystic characteristics[30]. The size typically varies from 0.2 to 3 cm, averaging 1.2 cm, and originates from the luminal cells of the intercalated duct[26].

Our case has unique aspects like occurring in a younger age, bigger than average size reported, rare location in the parotid gland, cystic change and occurrence in a woman of Asian ethnicity.

CONCLUSION

Salivary gland tumours are rare in both pediatric and adult population and demonstratic considerable histological, biological and clinical diversity. There cases presented have are tumours with mucoepideromoid carcinoma arising in warthins tumour is extending rare with only 0.3% incidence. Canalicular adenoma with atypical presentation occurred in 38year female (common in old age) Asian rare in Asian population),size of 0.3cms (average size being 1.2cm) location in parotid (common in minor salivary gland)cystic areas (uncommon),introducing a new dimension to this case.

Epithelial myoepithelial carcinoma is presented as it is following a surgery for pleomorphic adenoma and multinodular presentation in this patient and also accuterlely1% of salivary gland tumour.

Abbreviations

HPE Histopathogical examination,IHC immunohistochemistry,H/O history of,WT-Warthins tumour,MEC-Mucoepidermoid Carcinoma,WHO World Health Organisation ,EBV Epstein Barr virus,HIV Human Immunodeficiency virus, DD differential diagnosis

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