

Research Article

The dynamics of diagnosis of salivary gland tumours: histopathology matters

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Received: 02 May 2016

Accepted: 09 May 2016

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ABSTRACT

Background: Tumours of salivary glands are rare neoplasms of head and neck region accounting for less than one percent of all tumours. Parotid gland accounts for majority of tumors followed by submandibular gland. As such many challenges are encountered in establishing histological diagnosis, classification, grading and management of salivary gland neoplasms. This study is taken up to study the incidence of salivary gland tumours in our institution and analyse histological criteria for diagnosis and grading systems in vogue for common malignant lesions.

Methods: Clinical data at presentation, resected specimens received from Government General Hospital, Guntur and tissue sections stained with Haematoxylin & Eosin are retrieved from the archives in the Department of Pathology for the study. Relevant Immunohistochemical markers are done in difficult cases. Salivary gland tumours reported between 2011 and 2015 in the Department of Pathology, Guntur Medical College, Guntur, are taken for the study.

Results: Majority of the salivary gland tumours in our study were observed in the fourth and fifth decades with a male preponderance (62.68%). Parotid gland was the most common site (83.63%) for all tumours and pleomorphic adenoma was the most common tumour with 76 out of 110 cases (69.09%). Other benign tumours in the study included three cases each of Warthin tumour and basal cell adenoma. Malignant tumours accounted for 28 out of 110 tumours (25.45%). Mucoepidermoid carcinoma (MEC) was the most common malignant lesion in the study with 13 cases (46.42%).

Conclusions: Salivary gland tumours are rare. But the wide spectrum of tumour entities and histological complexities lead to diagnostic problems in many cases. Pleomorphic adenoma was the most common tumour overall and parotid gland was the most common site for both benign and malignant tumours.

Key words: Salivary gland tumours, Histological diversity, Grading of salivary carcinomas, Mucoepidermoid carcinoma, Adenoid cystic carcinoma

INTRODUCTION

Tumours of salivary glands are rare constituting less than one percent of all tumours and 3% to 10% of the neoplasms of head and neck region.^{1,2} They are a heterogeneous group of tumours and present distinct clinicopathological features. Parotid gland accounts for 80% of salivary gland tumors followed by submandibular gland (10-15%).³ Majority of the primary tumours of salivary glands are benign but diagnosis of malignant

tumours pose many difficulties in routine practice due to a wide spectrum of entities with overlapping in morphology.

The histopathological features are intricate and differences between different types are very subtle and as such many challenges are encountered in establishing histological diagnosis, classification and grading of salivary gland neoplasms. The present work is taken up to study the incidence of salivary gland tumours in our

institution with the primary objective of analysis of criteria for diagnosis and grading of primary malignant epithelial tumours of salivary gland.

METHODS

Salivary gland tumours reported during the last five years in our institution were taken for this retrospective study. Clinical data and gross features of tumours were recorded and tabulated. Haematoxylin and eosin (H&E) stained sections and corresponding paraffin tissue blocks were retrieved from the archives and reviewed. Special stains were done wherever necessary. Immunohistochemistry was done in specific cases for confirmation. Sections of 4 micron thickness were used for H and E staining as well as immunohistochemical study. The tumours were categorized according to the WHO classification.³ Histological hallmarks for diagnosis of various malignant tumours and criteria for grading of mucoepidermoid carcinoma and adenoid cystic carcinoma were analyzed.

RESULTS

Majority of the salivary gland tumours in our study were observed in the fourth and fifth decades with a male preponderance (62.68%). Parotid gland was the most common site (83.63%) for all tumours and pleomorphic adenoma was the most common tumour with 76 out of 110 cases (69.09%) (Figure 1). Other benign tumours in the study included three cases each of Warthin tumour (Figure 2) and basal cell adenoma. Malignant tumours accounted for 28 out of 110 tumours (25.45%).

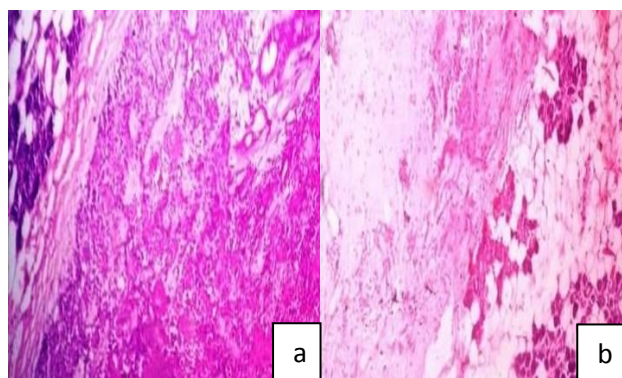


Figure 1: Pleomorphic adenoma; (a) epithelial differentiation 10x; and (b) chondroid differentiation 10x.

Mucoepidermoid carcinoma (MEC) was the most common malignant lesion in the study with 13 cases (46.42%). (Tables 1-3) Grossly, these tumours were multicystic with solid component. Infiltration of gland parenchyma was evident in most of the cases. The diagnosis of MEC was based on the presence of mucus cells, intermediate cells and epidermoid cells. The proportion of the cell types and their architecture varied within the same tumour and in between tumours. Cystic spaces were lined by large mucous cells interspersed by

basaloid intermediate cells and polygonal epidermoid cells (Figure 3).

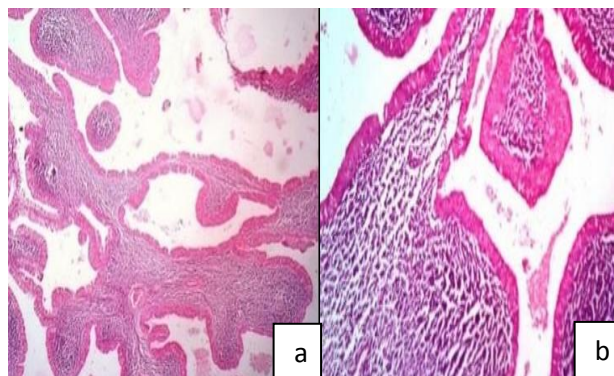


Figure 2: Warthin tumour; (a) papillary and glandular pattern 4x and (b) oncocytic change and subepithelial lymphocytes 10x.

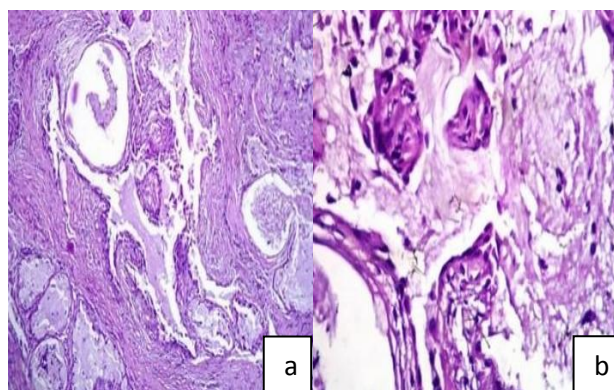


Figure 3: Mucoepidermoid carcinoma (MEC); (a) cystic spaces with mucin 10x and (b) squamous cells and mucin 40x.

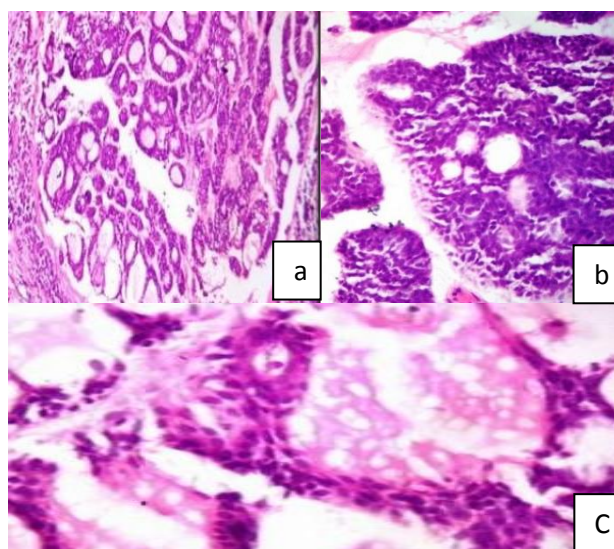


Figure 4: Adenoid cystic carcinoma; (a) cribriform pattern 10x, (b) small basaloid cells 40x and (c) mucin filled spaces 40x.

Adenoid cystic carcinoma was the second most common cancer in our study with seven cases in minor salivary glands and two cases in parotid gland (Table 3). Basaloid nature of the tumour with epithelial and myoepithelial cells arranged in tubular, cribriform and solid patterns

were evident in these cases. The cribriform pattern was the most frequent one with nests of cells and microcystic spaces filled with basophilic mucoid material (Figure 4).

Table1. Age distribution of malignant salivary gland tumours.

Age group in years	MEC	Ad CC	ACC	BCAC	Papillary cystadenocarcinoma	Epithelial myoepithelial carcinoma
11-20	1					
21-30	1	1				
31-40	3	2			2	
41-50	-	3	2			
51-60	5	-				
61-70	3	2				1
71-80		1		1		
All ages	13	9	2	1	2	1

Table 2: Sex distribution of malignant salivary gland tumours

Histological type	Male	Female	Total
Mucoepidermoid carcinoma	6	7	13
Adenoid cystic carcinoma	5	4	9
Acinic cell carcinoma	1	1	2
Basal cell adenocarcinoma	1	-	1
Papillary cystadenocarcinoma	1	1	2
Epithelial – myoepithelial carcinoma	-	1	1

Two cases of acinic cell carcinoma (ACC) were reported in the parotid gland, one in a 50 year old man and the other in a 41 year old woman (Tables 1 and 2). Gross examination showed capsulated nodular masses. Microscopy revealed large polygonal cells with basophilic granular cytoplasm and round eccentric nuclei. PAS positivity for mucin was characteristic but was patchy. Smaller intercalated duct type cells, and vacuolated cells were also seen (Figure 5). Other malignant entities in the study included two cases each of papillary cystadenocarcinoma and acinic cell carcinoma and one case each of basal cell adenocarcinoma and epithelial myoepithelial carcinoma, all arising in the parotid gland (Table 3).

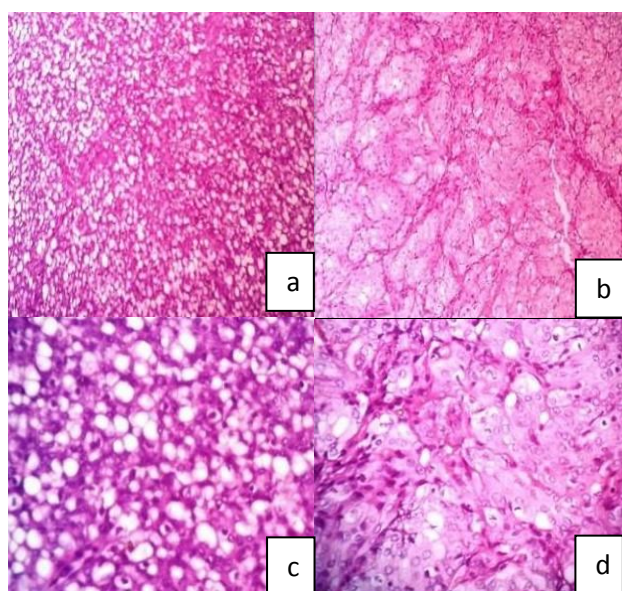


Figure 5: Acinic cell carcinoma (ACC); (a) solid pattern 10x; (b) solid pattern 10x; (c) cells with clear cytoplasm 40x and (d) granular cytoplasm 40x.

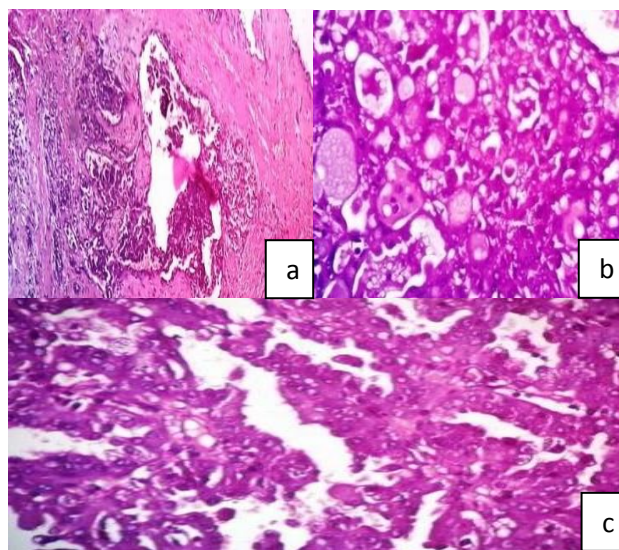


Figure 6: Papillary cystadenocarcinoma; (a) stromal infiltration 10x; (b) cystic spaces filled with mucin 40x and (c) papillary pattern 10x.

Two cases of papillary cystadenocarcinoma were diagnosed in parotid gland one case in a male patient and the other in a female patient, both in the fourth decade of life. Gross examination showed irregular gray white masses with central cystic areas and papillary projections.

Microscopy showed cystic tumours with cuboidal and columnar cells proliferating in papillary pattern (Figure 6). Nuclei were bland though occasional nucleoli were seen.

Table3. Site wise distribution of malignant salivary gland tumours.

Histological type	Parotid gland	Sub mandibular gland	Sublingual gland	Minor salivary glands	Total
Mucoepidermoid carcinoma	11	2	-	-	13
Adenoid cystic carcinoma	2	-	-	7	9
Acinic cell carcinoma	2	-	-	-	2
Basal cell adenocarcinoma	1	-	-	-	1
Papillary cystadenocarcinoma	2	-	-	-	2
Epithelial myo epithelial carcinoma	1				1

In our study a case of basal cell adenocarcinoma (BCAC) was diagnosed in a parotid lesion in a 74 year old male. Gross specimen showed a lobulated gray white tumour with infiltrative margins. On microscopy, nests and islands of cells with peripheral palisading were evident.

A case of epithelial myoepithelial carcinoma was reported in a parotid lesion in a woman in seventh decade who presented with a slowly growing mass in the parotid gland. Grossly an irregular nodular mass was seen. The histological diagnosis was based on the typical biphasic nature with inner layer of duct lining epithelial type cells and outer layer of clear myoepithelial type cells. The biphasic pattern was conspicuous in papillary-cystic areas where as in solid areas exclusively vacuolated cells were noted. IHC markers cytokeratin and S 100 were positive in our case (Figure 7).

DISCUSSION

Age and sex incidence and localization

In our study, parotid gland accounted for most of the tumours with 92 out of 110 cases (83.63%) followed by submandibular glands with eleven cases (10.00%) and minor salivary glands with seven cases (6.36%). Literature shows that majority of salivary gland tumours arise in the parotid gland.⁴ About 64 and 80% of all primary epithelial salivary gland neoplasms are seen in the parotid gland, followed by submandibular glands and minor salivary glands. However the incidence in minor salivary glands account for 9-23% of total tumours as per world literature.^{5,6}

Most of the tumours in the study were seen in the sixth and seventh decades. This is in accordance with the literature.³ In case of malignant tumours, majority of our cases were diagnosed in seventh decade followed by fourth and sixth decades (Table 1). In our study, definite male preponderance was observed for benign tumours (66.66%). In malignant tumours, however male female ratio was even with 14:14. (Table 2) Though many studies show that females are more frequently affected, there is some gender variation in different types of tumour.³

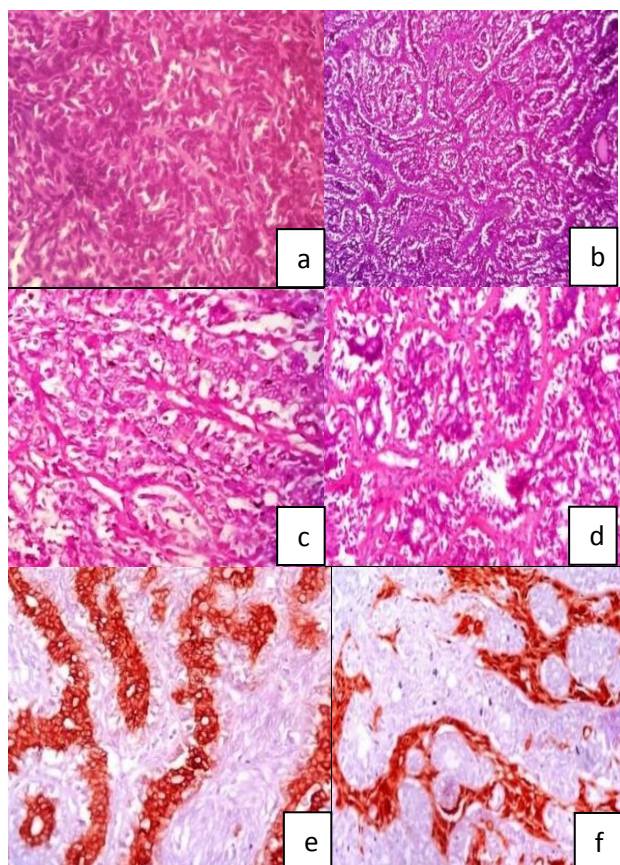


Figure 7: Epithelial myoepithelial carcinoma (EMC); (a) solid pattern 10x; (b) tubular pattern 10x; (c) bimodal morphology 40x; (d) bimodal morphology 40x; (e) cytokeratin positive and; (f) S 100 positive.

Pleomorphic adenoma was the most common tumour in the study with 76 out of 110 (69.09%). This compares well with other studies.³ Warthin tumour and basal cell adenoma accounted for three cases each. Literature shows that Warthin tumour is second in frequency among benign tumours and nearly all Warthin tumours occur in the parotid gland or periparotid lymph nodes while most canalicular adenomas and polymorphous low-grade adenocarcinomas arise from minor glands.⁷ In our study also all the three cases of Warthin's tumour were observed in the parotid gland.

The rate of malignancy varies a lot between various studies; this is attributed to geographical or distinct settings of the studies. General ENT clinics manage both benign and malignant lesions but head and neck and oral surgery clinics deal mainly with malignant tumours. Incidence of malignancy in these tumours ranges between 21 and 46% as per different studies.⁴ The distribution of malignant tumours also varies greatly by site. The parotid glands predominate, representing 45%, with 7% for submandibular glands and 1% in sublingual glands.^{3,8} The most frequent intra-oral sites are the palate and buccal mucosa. In our study the rate of malignancy was 28.12% (19 out of 64) in parotid gland, 25% (2 out of 8 tumours) in submandibular gland and 100% in minor salivary glands as all the seven tumours reported turned out to be malignant (Table 3).

It has been well documented in literature that, mucoepidermoid carcinoma is the most common malignant tumour.^{5,6} In our study also mucoepidermoid carcinoma accounted for 48% of the malignant lesions (13/28). Most of our cases were seen in the parotid gland. This is in accordance with other studies.³ It was observed that two low grade tumours in our study were recurrent lesions while one case occurred in the background of pleomorphic adenoma. Differential diagnosis of MEC includes necrotizing sialometaplasia, inverted ductal papilloma, cystadenoma, carcinomas composed of clear cells including adenosquamous carcinoma, squamous cell carcinoma and metastases.

Adenoid cystic carcinoma was the second most common cancer in our series with seven cases in minor salivary glands and two cases in the parotid gland. Adenoid cystic carcinomas (AdCC) constitute approximately 10% of all epithelial salivary neoplasms and most frequently involve the parotid, submandibular and minor salivary glands.³ In the study of Shrestha S et al submandibular gland was the most common site for adenoid cystic carcinoma.⁹ In contrast they comprise 30% of epithelial minor salivary gland tumours with the highest frequency in the palate.³ The tumour occurs in all age groups frequently in middle-aged and older patients. In our study also, adenoid cystic carcinoma affected different age groups with a peak incidence in the fifth decade and slight male preponderance. These cases usually presented as painful slow growing tumour due to the tendency of perineural invasion. The case of epithelial myoepithelial carcinoma

in our study occurred in a woman in the seventh decade of life which is in accordance with literature.¹⁰

Histological complexity and difficulty in grading of malignant tumours

Histological grade is an independent predictor of prognosis of malignant salivary gland tumours. But the diversity and the rarity of different tumours pose many hurdles in grading. In a review of grading systems of salivary gland cancers, Seethala RR opined that the current approach is prone to many challenges and an ideal system is still to emerge.¹¹ Salivary gland malignancies can be categorized into high risk and low risk groups basing on histological and biological profile but with a caveat that morphological grade of a salivary gland malignant lesion may not always predict its actual biological behaviour. High grade versions of intrinsically low grade tumours do exist as well as low grade versions of typically high grade versions and a case in point is carcinoma ex pleomorphic adenoma which is conventionally considered a high grade lesion, but intracapsular and minimally invasive variants behave in an indolent manner. In this context, Seethala RR recommends that in reporting of these tumours, additional comments regarding percentage of carcinoma and extent of invasion of carcinomatous component i.e. intracapsular, minimally invasive, and invasive should be included apart from histological type and grade for specified prognostic implications.

Mucoepidermoid carcinoma

Mucous cells constitute less than 10% of the tumour whereas intermediate cells are the dominant population. Clear, columnar and/or oncocytic cell populations may also be present.³ In our cases, mucus extravasation with lymphocytic infiltrate at the tumour edge were noted. Lymphocytic infiltrate with germinal centre formation can mimic nodal invasion in some cases.¹²

Three different grading systems have been proposed, all based on cytomorphology and architecture to categorize MEC as low, intermediate or high grade lesions.¹³ Armed Forces Institute of Pathology (AFIP) scoring system and Brandwein system are point based, giving points to each histological feature.^{7,14} The AFIP system is based on five histologic features: intracystic component, neural invasion, necrosis, mitotic activity, and cellular anaplasia. Brandwein MS et al proposed an alternative grading scheme with additional criteria of lymphovascular and bony invasion and the pattern of tumor invasion in the form of small nests/islands to enhance predictability and reproducibility. The modified Healey system is based on certain qualitative histological parameters.^{14,15}

In our study, we applied AFIP grading system and nine out of 13 MEC were reported as low grade, three cases as high grade and one case as intermediate grade. In the three cases of MEC of high grade, the consistent features

were minimal intracystic component, presence of cellular atypia, necrosis and invasion by nests of tumour cell and they would be designated as high grade lesions in both AFIP and Brandwein systems. Nine cases of MEC were reported as low grade as there was no anaplasia or perineural invasion or necrosis in multiple sections and importantly there was no discordance between the two systems. But, the remaining one case of MEC in our study, which was reported as intermediate grade as per AFIP system, would come under high grade category if Brandwein system is to be applied. Seethala S et al also observed that AFIP system tends to down grade tumours while the Brandwein system appears to upgrade tumours especially in case of intermediate grade tumours whereas the Healey system does not have this limitations.¹¹

Jayasooriya PR et al felt that pitfalls in grading could be because of inadequate sampling of tumours and risk of false negativity in counting of mitotic figures.¹⁶ Application of grading schemes to sclerosing and oncocytic variants and submandibular gland tumours is subject to disagreement. Oncocytic mucoepidermoid carcinomas that are considered high grade may behave indolently but still these variants also should be graded.¹¹ In case of submandibular gland tumours even low grade MEC tend to behave more aggressively because of metastatic potential and AFIP grading may not predict accurately their outcome.¹³

Adenoid cystic carcinoma

Each of tubular, cribriform and solid patterns can be seen as the dominant feature or as a component of a composite tumour.¹⁷⁻¹⁹ The stroma within the tumour is usually hyalinized and may be mucinous or myxoid. Extensive stromal hyalinization with attenuation of the epithelial component may be seen in some tumours. Perineural invasion is a consistent feature of AdCC. Extension along nerves beyond the tumour margins and bone invasion are seen in some cases. AdCC should be distinguished from pleomorphic adenoma, basal cell adenoma, basal cell adenocarcinoma, basaloid squamous carcinoma, polymorphous low-grade adenocarcinoma and epithelial myoepithelial carcinoma. Diagnostic challenges are encountered when Adenoid cystic carcinoma occurs with other different neoplasms.^{20,21} In our study, one case of adenoid cystic carcinoma was seen to be associated with basal cell adenocarcinoma.

AdCC is graded basing on predominant growth pattern. Grade 1 is assigned to tubular pattern, Grade 2 to predominantly cribriform pattern with <30% and solid component and grade 3 is given in case of >30% solid component.¹⁹ But Spiro RH et al suggested a different grading scheme where in the cut off for solid component is 50% for Grade 2 and mostly solid for grade 3.¹⁸ In our study seven out of nine cases Ad CC were categorized as low grade, one case as high grade and one case as intermediate grade. However, regardless of the grade, all adenoid cystic carcinomas are managed with surgery and

radiotherapy as they are considered locally aggressive and high risk tumours. Rarely, dedifferentiation can occur in conventional adenoid cystic carcinoma of any grade. This transformation is represented by increased mitotic activity, necrosis and micro-calcifications and is associated with lymph node metastasis.

Other tumours

Other infrequent malignant tumours in the study included ACC, BCAC, Papillary cystadenocarcinoma and epithelial myoepithelial carcinoma all of which occurred in parotid gland. Acinic cell carcinoma is a malignant tumour characterized by serous acinar cell differentiation. Frequent mitoses, necrosis, neural invasion and pleomorphism indicate more aggressive course. In ACC, staging rather than grading is considered a better indicator of prognosis.²²

Basal cell adenocarcinoma is characterized by basaloid epithelial cells. Infiltration into adjacent salivary gland parenchyma and perineural invasion are the important features to distinguish it from basal cell adenoma as BCAC is associated with local invasion leading to destruction, recurrence and occasionally metastasis. Presence of tumour infiltration into salivary parenchyma is an important clue to papillary cystadenocarcinoma and hence multiple sections should be studied to clinch the diagnosis. Cystic MEC can be distinguished from papillary cystadenocarcinoma by the presence of a variety of cells in the former.

In our study, one case of EMC was reported (1/28) with an incidence of 3.57% in malignant lesions and 0.90% of all salivary gland tumours. According to literature EMC represents <1% of all salivary gland tumours and arises usually in the parotid gland.²³ Our findings are in concordance with these observations. Differential diagnosis includes clear cell tumours like pleomorphic adenoma, myoepithelioma, oncocytoma and MEC and metastatic tumours of renal and thyroid origin. Solid growth pattern, nuclear atypia, DNA aneuploidy, necrosis, positive surgical margins and high proliferative activity indicate more aggressive nature.^{24,25} The status of tumour margin is very important because inadequate surgical excision is associated with recurrence and metastasis.

CONCLUSION

Salivary gland tumours are rare. But the wide spectrum of tumour entities and histological complexities lead to diagnostic problems in many cases. Pleomorphic adenoma was the most common tumour overall and parotid gland was the most common site for both benign and malignant tumours. Histological grading of malignant tumours has independent prognostic value and should be applied meticulously. Various grading systems have been advocated for mucoepidermoid carcinoma though an ideal system is still to be evolved. The

prognostic outcome in the intermediate grade lesions of MEC depends on the specific grading system used. Adenoid cystic carcinoma is graded basing on the growth pattern with solid pattern indicating worse outcome. In other malignant tumours, assessment of tumour margin status and staging are considered better indicators of outcome than grading alone

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Pons-Vicente O, Almendros-Marqués N, Berini-Aytés L, Gay Escoda C. Minor salivary gland tumors: A clinicopathological study of 18 cases. *Med Oral Pathol Oral Cir Bucal.* 2008;13:582-8.
2. Ethunandan M, Davies B, Pratt CA, Puxeddu R, Brennan PA. Primary epithelial submandibular salivary gland tumors-Review of management in a district general hospital setting. *Oral Oncol.* 2009;45:173-6.
3. Everson JW, Auclair P, Gnepp DR, El-Naggar AK. Tumors of the salivary glands. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. *World Health Organization Classification of Tumours. Pathology and Genetics of Head and Neck Tumors.* Lyon: IARC Press. 2005;209-81.
4. Kızıl Y, Aydıllı U, Ekinci O, Dilci A, Köybaşıoğlu A, Düzlü M, et al. Salivary Gland Tumors in Turkey: Demographic Features and Histopathological Distribution of 510 Patients. *Indian J Otolaryngol, Head Neck Surg.* 2013; 65(Suppl 1):112-20.
5. Eveson JW, Cawson RA. Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. *J Pathol.* 1985;146(1):51-8.
6. Spiro RH. Salivary neoplasms: overview of a 35 year old experience with 2807 patients. *Head Neck Surg.* 1986;8(3):177-84.
7. Ellis GL, Auclair PL. Tumors of the salivary glands. *Atlas of tumor pathology, 3rd series, fascicle 17.* Washington DC: Armed Forces Institute of Pathology; 1996.
8. Tian Z, Li L, Wang L, Hu Y, Li J. Salivary gland neoplasms in oral and maxillofacial regions: a 23-year retrospective study of 6982 cases in an eastern Chinese population. *Int J Oral Maxillofac Surg.* 2010;39:235-42.
9. Shrestha S, Pandey GK, Pun CB, Bhatta R, Shahi R. Histopathological Pattern of Salivary Gland Tumors. *Journal of pathology of Nepal.* 2010;520-4.
10. Silvers AR, Som PM, Brandwein M. Epithelial - Myoepithelial C arcinoma of the Parotid Gland *AJNR.* 1996;17:560-2.
11. Seethala RR. An update on grading of salivary gland carcinomas. *Head and Neck Pathol.* 2009;3:69-77.
12. Auclair PL. Tumor-associated lymphoid proliferation in the parotid gland. A potential diagnostic pitfall. *Oral Surg Oral Med Oral Pathol.* 1994;77(1):19-26.
13. Goode RK, Auclair PL, Ellis GL. Mucoepidermoid carcinoma of the major salivary glands: clinical and histopathologic analysis of 234 cases with evaluation of grading criteria. *Cancer.* 1998;82:1217-24.
14. Brandwein MS, Ivanov K, Wallace DI, Hille JJ, Wang B, Fahmy A, et al. Mucoepidermoid carcinoma: a clinicopathologic study of 80 patients with special reference to histological grading. *Am J Surg Pathol.* 2001;25(7):835-45.
15. Healey WV, Perzin KH, Smith L. Mucoepidermoid carcinoma of salivary gland origin. Classification, clinical-pathologic correlation, and results of treatment. *Cancer.* 1970;26:368-88.
16. Jayasooriya PR, Karunathilake PRCL, Siriwardena BSMS, Amaratunga EAPD, Attygalla AM. Comparison of grading systems of mucoepidermoid carcinoma and the impact on patient survival *Journal of Diagnostic Pathology.* 2012;7(1):42-9.
17. Perzin KH, Gullane P, Clairmont AC. Adenoid cystic carcinomas arising in salivary glands: a correlation of histologic features and clinical course. *Cancer.* 1978;42(1):265-82.
18. Spiro RH, Huvos AG. Stage means more than grade in adenoid cystic carcinoma. *Am J Surg.* 1992;164(6):623-8.
19. Szanto PA, Luna MA, Tortoledo ME, White RA. Histologic grading of adenoid cystic carcinoma of the salivary glands. *Cancer.* 1984;54(6):1062-9.
20. Croitoru CM, Suarez PA, Luna MA. Hybrid carcinomas of salivary glands. Report of 4 cases and review of the literature. *Arch Pathol Lab Med.* 1999;123(8):698-702.
21. Seifert G, Donath K. Hybrid tumors of salivary glands. Definition and classification of five rare cases. *Oral Oncol Eur J Cancer.* 1996;32:251-9.
22. Batsakis JG, Luna MA, El-Naggar AK. Histopathologic grading of salivary gland neoplasms: II. Acinic cell carcinomas *Ann Otol Rhinol Laryngol.* 1990;99:929-33.
23. Batsakis JG, El - Naggar AK, Luna MA. Epithelial – myoepithelial carcinoma of salivary glands. *Ann Otol Rhinol Laryngol.* 1992;101:540-2.
24. Seethala RR, Barnes EL, Hunt JL. Epithelial-myoeplithelial carcinoma: A review of the clinicopathologic spectrum and immunophenotypic characteristics in 61 tumors of the salivary glands and upper aerodigestive tract. *Am J Surg Pathol.* 2007;31:44-57.
25. Tralongo V, Daniele E. Epithelial-myoeplithelial carcinoma of the salivary glands: A review of literature. *Anticancer Res.* 1998;18:603-8.

Cite this article as: Venugopal M, Devi CP, Deepthi K, Mutte K. The dynamics of diagnosis of salivary gland tumours: histopathology matters. *Int J Res Med Sci* 2016;4:1855-61.