ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 11, Issue, 03, pp.2368-2373, March, 2019

DOI: https://doi.org/10.24941/ijcr.34937.03.2019

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

CYTOLOGY OF SALIVARY GLAND LESIONS WITH HISTOPATHOLOGICAL CORRELATION: A THREE YEAR STUDY IN A TERTIARY CARE HOSPITAL

[1,*]Samoon Nuzhat, [2]Syed Besina Yasin, [3]Bhat Nazia, [4]Bhat Irfan Hussain, [5]Huzaifa Nazier, [6]Umara Jan, [7]Hilal, [8]Sabiya Hafiz and [9]Saba Gul

[1,3,5]Senior Resident, Department of Pathology, SKIMS Soura, J&K, India
[2]Professor and Head, Department of Pathology, SKIMS Soura, J&K, India
[4,] Senior Resident, Department of Neurosurgery, SKIMS Soura, J&K, India
[6,7,8,9]Postgraduate Resident, Department of Pathology SKIMS Soura, J&K, India

ARTICLE INFO

Article History:
Received 16th December, 2018
Received in revised form
13th January, 2019
Accepted 17th February, 2019
Published online 31st March, 2019

Key Words:
Salivary Gland, Milan's System for Reporting Salivary Gland Cytology, Histopathology.

ABSTRACT

Back ground: Salivary gland lesions form about 2-6.5% of all head and neck neoplasms in adults. They are easily accessible for FNAC with lower risk factors compared to surgical biopsy. **Methods:** FNAC was done using 20 cc syringes and reporting was done according to Milan's system for reporting salivary gland cytology. Cases from the year 2016 and 2017 were retrieved and recategorised according to Milan's system for reporting salivary gland cytology. Histopathological examination was done on routine H & E (Haematoxylin and eosin) stained paraffin sections. Special stains and IHC was done where ever needed. **Results:** In the present study we had 47 cases of salivary gland lesions and histopathogical correlation was done in 43 cases as two were non diagnostic , two cases of metastatic melanoma and a single case of metastaic squamous cell carcinoma were not included. Male to female ratio was 1:1.7. Pleomorphic adenoma was the most frequent benign neoplasm while mucoepidermoid carcinoma was the most frequent malignant lesion. A statistical analysis was performed for the 43 cases histopathology of which was available. Sensitivity of 90% was observed, whereas the specificity was 95.65%. The positive and negative predictive values were 94.7% and 92%, respectively. **Conclusions:** FNAC being a simple, rapid, high patient compliance and cost effective, continues to have high diagnostic accuracy and is thus helpful for guiding management. Neoplasms with classic cytomorphology are easily diagnosed; however, in difficult cases showing overlapping features, the use of the Milan system could be beneficial.

***Citation*: *Samoon Nuzhat, Syed Besina Yasin, Bhat Nazia, Bhat Irfan Hussain, Huzaifa Nazier, Umara Jan, Hilal, Sabiya Hafiz and Saba Gul.* 2019.** "Cytology of Salivary gland lesions with Histopathological correlation: A three year study in a tertiary care hospital", *International Journal of Current Research*, 11, (03), 2368-2373.

INTRODUCTION

Salivary gland neoplasms represent less than 1% of all tumors and 2-6.5% of all head and neck tumors (Auclair, 1997; Ethunandan, 2009). They are rarely subjected to incisional or needle biopsy techniques because of the risks of fistula formation or tumour implantation . The initial diagnostic workup of a salivary gland nodule uses a multi-modal approach. Initial imaging using USG and/or MRI enables localization of the lesion within the salivary gland and provides information regarding the imaging characteristics including the contours of the lesion. Imaging assists with surgical planning for larger tumors within the salivary gland. However, to clarify the malignant potential of a lesion, FNAC remains the preferred diagnostic test.

***Corresponding author:* Samoon Nuzhat,**

Approximately 80% of the salivary gland tumors are found in the Parotid gland and 10 to 15% in the submandibular gland . Around 80% Parotid tumors and 50% of submandibular tumors are benign (Paparella's, 1991). Minor salivary gland tumors are infrequent, accounting for 10 to 15% of all salivary neoplasms and are fundamentally located in the palate (50%), lips (15%), buccal mucosa (12%), tongue (5%) and floor of mouth (5%), among other regions (Speight, 2002; Yih, 2005). Salivary gland tumors highest incidence observed in the 3rd and 4th decade for benign tumors and 4th and 5th decades for the malignant tumors (Ahrnad, 2002; Bashirs *et al*., 2013). The aim of this study was to analyse various salivary gland tumors on Fnac with histopathological correlation. FNA has high accuracy in distinguishing between benign and malignant salivary gland lesions; however, its precision varies when it

comes to subtyping neoplasms (Colella *et al*., 2010; Jain *et al*., 2013; Jayaram, 1994; Kocjan, 1990; Schindler *et al*., 2001; Chakrabarti, 2010). To develop a standardized terminology for reporting salivary gland cytopathology, the American Society of Cytopathology and the International Academy of Cytology initiated a project to propose an international classification scheme (the Milan system) for reporting salivary gland FNA(American Society of Cytopathology, 2016).

MATERIALS AND METHODS

The data for the present study was collected from the record section of the department of Pathology of our hospital. Three year period from January 2016 to January 2019 was taken for the present study, retrospective of two years and a prospective study of one year. A total of 48 cases were evaluated. Information about age, gender, tumor location and tumor size were determined for each salivary tumor type. The frequencies of different benign and malignant salivary tumors in both major and minor glands were identified. The histopathological diagnosis of surgical specimens was compared with the preoperative FNA diagnosis of salivary gland lesions, and the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of FNA for differentiating between benign and malignant disease were evaluated. The cytological diagnoses were also categorized according to the Milan System for Reporting Salivary Gland Cytopathology as follows: nondiagnostic, nonneoplastic, atypical, benign neoplasm, neoplasm of uncertain malignant potential (NUMP), suspicious for malignancy, or positive for malignancy.

RESULTS

In the present study a total of 48 cases were evaluated. The age of the patients ranged from 17 to 68, and the mean age was 39.5 years. The male to female ratio was 1:1.7.

The parotid gland was the most common site involved (29 cases / 60.41%), and it was followed by the submandibular gland (16 cases /33.3%) and the minor salivary gland (4 cases / 8.3%). There were no post-FNA complications in any of these cases. Nondiagnostic aspirations were found for (2 cases / 4.2%). The cytological diagnoses offered in different cases are listed in (Table 1 and table 2). Non neoplastic lesions accounted for (5 cases /10.4%), whereas (38 lesions / 79.2%) were neoplastic. (3 cases /6.25 %) were classified as cystic lesions. Of the 38 neoplastic lesions, (17 cases /35.4%) were benign, and (18 cases /37.5%) were malignant. 5 cases/10.4% were classified as suspicious of a malignant lesion. Follow-up histopathology was available for 43 cases (table 3) of the 48 patients (89.6%), and there was discordance in 4 of these cases (Table 4). A case reported as benign cystic lesion turned out to be a warthins tumor on histopathology. Two cases diagnosed as pleomorphic adenoma on cytology, one turned out as adenoid cystic carcinoma and other one as chordoma on histopathology a case diagnosed as adenoid cystic carcinoma on cytology came out to be a pleomorphic adenoma on histopathology. The cytological diagnosis was true-positive in 18 of 43 cases (41.85%) and true-negative in 23 of 43 cases (53.48%). There were 2 false-negative results (4.16%) and we had a single false-positive case (2.08%). A statistical analysis was performed for the 43 cases of which histopathology was available; a sensitivity of 90% was observed, whereas the specificity was 95.65%. The positive and negative predictive values were 94.7% and 92%, respectively (Table 5)

DISCUSSION

Benign salivary gland tumors were more common in age group of 51 to 60 years with a mean age of 43.63 years and the peak age incidence observed for malignant salivary gland tumors was 41 to 60 years with a mean of 51.54 years.

Table 1.Milan's system of reporting salivary gland cytology

Non diagnostic		2
Non neoplastic		6
Atypia of undetermined Significance AUS		2
Neoplastic	Beingn	17
	Sump(uncertain malignant potential)	0
Suspicious of malignancy		5
Malignant		16
Total		48

Table 2. Cytological Diagnoses Offered for Different Cases

Non neoplastic		Neoplastic						Tota l
Chronic Saladenitis	5	Benign		Malignant		Metastatic		
Cystic lesions	2	Pleomorphic denoma	17	Mucoepidermoid carcinoma.	6	Malignant melanoma	2	
				Adenoid cystic carcinoma	7	Squamous cell carcinoma	2	
				Suspicious of malignancy	5			
TOTAL	7		17		18		4	46

Table 3. Histopathological Diagnoses Offered for Different Cases

Non neoplastic		Neoplastic				Total
Chronic saladenitis	5	Benign		Malignant		
Cystic lesion	1	Pleomorphic adenoma	16	Mucoepidemoid carcinoma	10	
		Warthins Tumor	1	Adenoid cystic carcinoma	8	
				Epithelial –myoepithelial carcinoma	1	
				Chordoma	1	
Total	6		17		20	43

Table 4. Comparisons of Cytological Diagnoses With Histopathology (n=43)

Fnac diagnosis	Histopathological diagnosis							
	Chronic sailadeitis	Cysts	Pleomophic adenoma	Warthins tumor	Mucoepidermoid carcinoma	Adenoid cystic carcinoma	Epithelilal myoepithelial carcinoma	Chordoma
Chronic sailadenitis (5)	5							
Cysts (2)		1		1				
Suspicious of malignancy (5)					3	1	1	
Pleomorphic adenoma (17)			15			1		1
Mucoepidermoid carcinoma (6)					6			
Adenoid cystic carcinoma (7)			1			6		
Squamous cell carcinoma .(1)					1			
Total (43)	5	1	16	1	10	8	1	1

Table 5. Statistical analysis

True positive (18)	False positive (01)	Positive predictive value TP/TP+FP=94.7%
False negative (02)	True negative(23)	Negative predictive value TN/TN+FN=92%
Sensitivity TP/TP+FN=90%	Specificity TN/TN+FP=95.65%	

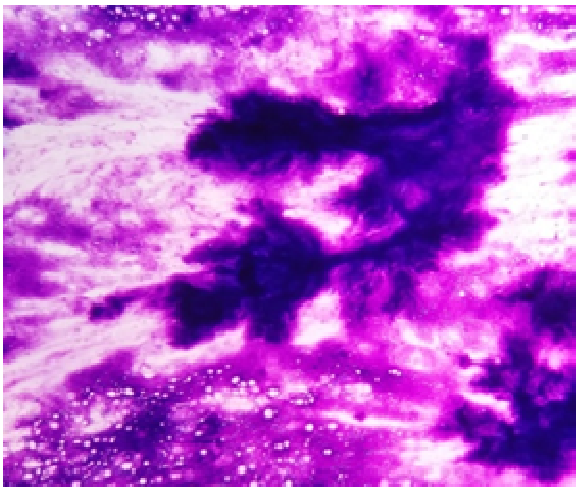

Fig 1. Photomicrograph shows mixed tumor of benign epithelial cells with blue myxoid matrix. Pleomorphic adenoma. (H&E ,10X)

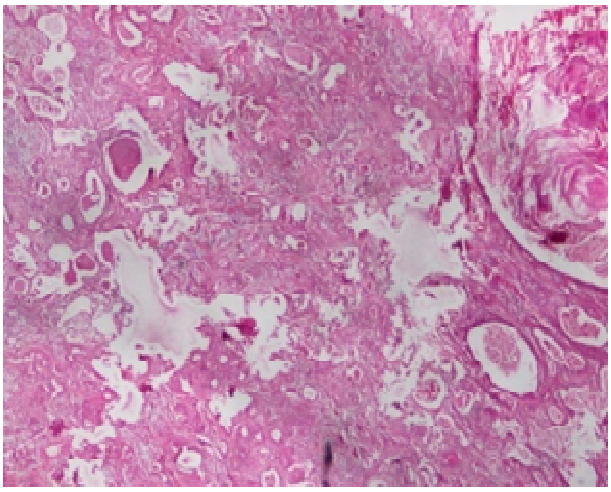

Fig 2.Photomicrograph shows squamoid areas, keratinization , cystic areas and intermediate cells .Mucoepidermoid carcinoma.(H&E , 40X)

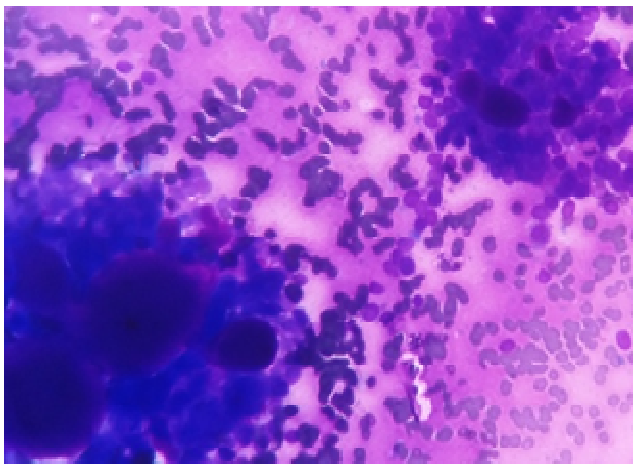

Fig 3. Photomicrograph shows small uniform epithelial cells with hyperchromatic nuclei and coarse chromatin, dispersed and adhering to a large, hyaline stromal globules. Adenoid cystic carcinoma. (MGG, 40X)

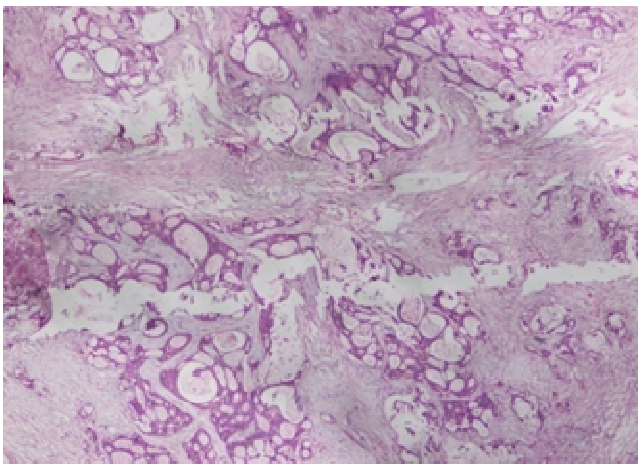

Fig 4.Photomicrograph shows gland like spaces filled with pink hyaline material representing Adenoid cystic carcinoma. (H&E, 40X)

Chatterjee *et al*. (Maj, 2000) observed large number of benign cases in third decade followed by fourth decade. Malignancy reported in his study was maximum in fifth decade. Potdar and Paymaster (Potdar, 1969) reported an age range of 9 to 81 years with average age for benign tumors as 40.1 years and for malignant tumors as 46.3 years.

In the present study a male preponderance was noted with a male: female ratio of 2.3:1. This is in agreement with the series reported by Potdar and Paymaster (Potdar, 1969), and Spiro *et al*. (1990). who reported a male preponderance in their series. However this was in contrast to series reported by Dandapat *et al*. (1991) and Rewsuwan *et al*. (2006).

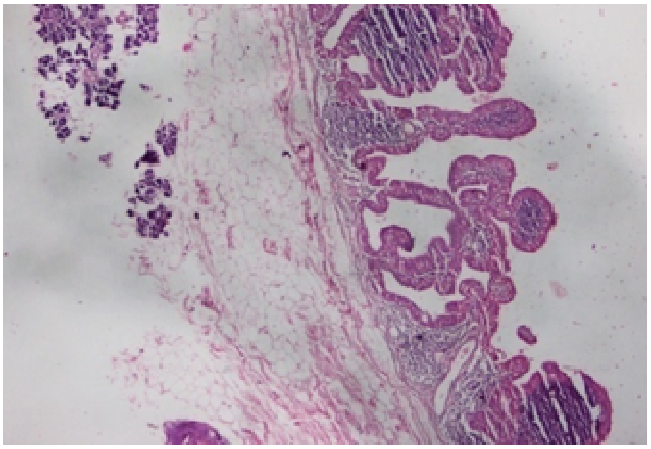

Fig 5. Photomicrograph shows presence of papillary projections into cystic spaces which have an epithelial lining composed of two layers of cells with oncocytic features and underling chronic inflammatory cell infiltrate. Warthins tumor (H&E, 40 X)

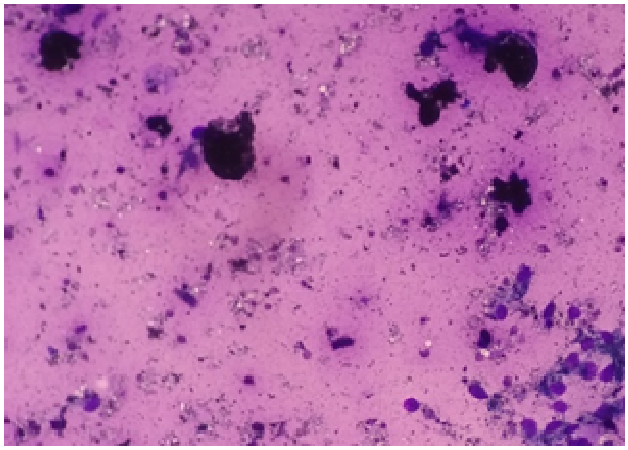

Fig 6. Photomicrograph shows metastatic tumor cells with intracellular as well as extacellular melanin pigment deposition. Malignant melanoma .(MGG, 40X)

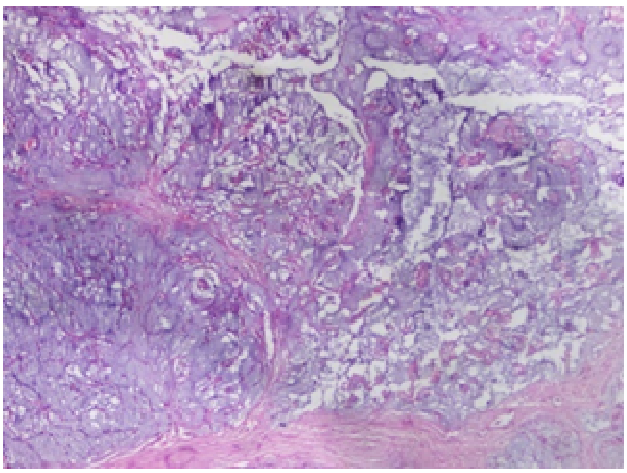

Fig 7. Photomicrograph shows lobules of vacuolated, eosinophilic to clear tumor cells embedded in a myxoid matrix. Chordoma.(H&E, 40X)

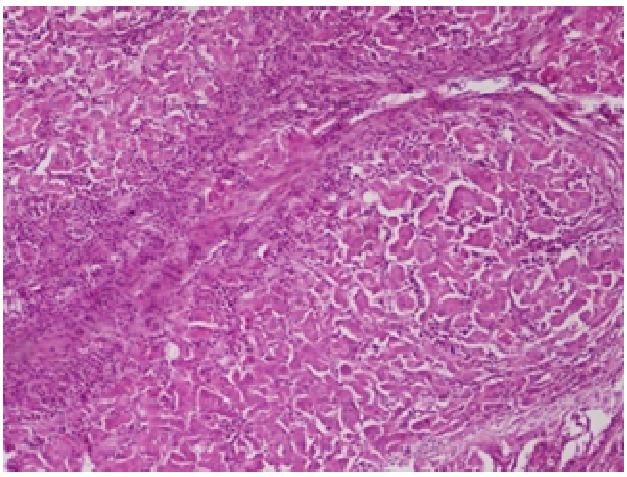

Fig. 8. Photomicrograph shows epithelial cells with abundant eosinophillic cytoplasm with a few clear myoepithelial cells . Epithelial myoepithelial carcinoma. (H&E, 40X)

Parotid was the commonest site of neoplasia (65%) in this series followed by submandibular gland (25%) and minor salivary glands (10%).This is in conformity with other workers, viz., Dandapat *et al*. (1991) Spiro *et al*. (1991) Gore *et al*. (20) and Richardson *et al*. (1975). All the cases diagnosed as pleomorphic adenoma on fnac were correctly diagnosed on histopathology as well. Pleomorphic adenoma is a mixed tumor of benign epithelial cells with blue myxoid matrix. (Fig1). Pleomorphic adenoma was the most frequent benign neoplasm (34%). Literature also reveals that primary tumors of sublingual salivary glands are extremely uncommon. Richardson *et al*. (1975), Vargas *et al*. (Pablo Agustin Vergas, Rene Gerhard, 2002), and Nagarkar *et al*. (2004), Pleomorphic adenoma was the most common benign salivary gland tumor encountered in parotid, submandibular and minor salivary glands. Similar findings were observed in the present study where pleomorphic adenoma was the most common benign salivary gland tumor at all locations. Mucoepidermoid carcinoma was the most common malignant neoplasm . 6 cases were diagnosed on Fnac with histopathological correlation. 3 cases were diagnosed as malignant lesion not specified on Fnac showed mucoepidermoid carcinoma on histopathological examination characterized by the presence of the three different cell types:mucous,sqamoid,and intermediate,present in variable proportions (Fig 2). A cytologic diagnosis of mucoepidermoid carcinoma requires a background of mucus and debris and a variable population of cells. In our study a case of high grade mucoepidemoid carcinoma was diagnosed as squamous cell carcinoma on Fnac. Adenoid cystic carcinoma is relatively uncommon tumour of salivary glands and are characterised by a prolonged clinical course and a fatal outcome. It was first described as 'cylindroma' by Billroth in 1859. Half of these tumors: occur in glandular areas other than the major salivary glands, principally in the hard palate, but they also arise in the tongue, minor salivary glands and lacrimal glands (Mohd Atha, 2012). 6 cases of Adenoid cystic carcinoma diagnosed on histology (Fig.4) were correctly diagnosed as Adenoid cystic carcinoma on Fnac however 1 case was diagnosed as pleomorphic adenoma and other as non specific malignant lesion. One case of pleomorphic adenoma was incorrectly diagnosed as adenoid cystic carcinoma on fnac. The distinction between pleomorphic adenoma and adenoid cystic carcinoma on Fnac may be difficult on account of several features-myxoid acellular material may be found in both and hyaline globules characteristic of adenoid cystic carcinoma (Fig 3) may also be seen in pleomorphic adenoma. Two cases of metastatic deposits of malignant melanoma (Fig 6) one in parotid gland and one submandibular gland were diagnosed on Fnac only as they were known cases of malignant melanoma no futher histopathological investigation was done. A single case of Chordoma (Fig 7) was diagnosed on Histopathology hich was diagnosed was pleomorphic

adenoma on Fnac. One case of epithelial myoepithelial carcinoma was diagnosed on histopathology which was diagnosed as malignant lesion not specified on cytology. There were 2 cases reported as cystic lesions; one case turned out to be a warthin tumor (fig 5)on histopathology, however, no histopathological or significant clinical follow-up was available of the other case. Salivary gland cystic lesions can be either nontumorous or tumorous (benign or malignant). Retention cysts, mucoceles, and lymphoepithelial cysts are the common nontumorous cysts, whereas MEC, Warthin's tumor, acinic cell carcinoma, cystic PA, and cystadenoma are examples of tumorous cystic lesions. In cystic lesions, fluid is aspirated, and the cellularity of the smear is generally low; therefore, malignant cells can be missed, and this can lead to a false-negative report. Postevacuation FNA with multiple passes from different planes is helpful for substantially reducing sampling errors. (Rajwanshi, 2006). The sensitivity of FNA, as mentioned in different previous studies, varies from 54% to 98% with high specificity values of 88% to 99% for separating benign lesions from malignant lesions (Kim *et al*., 2013; Stewart, 2000; Orell, 1995; Ashraf, 2010; Daneshbod *et al*., 2009; Jafari *et al*., 2009; Schmidt *et al*., 2011). Similarly, in the current study, the sensitivity was 90%, and the specificity was 95.5%.

Conclusion

Salivary gland FNA is a safe, minimally invasive, cost efficient, and effective diagnostic technique for salivary gland lesions. It edges over frozen sections because it proves the nature of the lesion before surgery and thus acts as a useful triage tool and prevents patients with non neoplastic lesions from undergoing surgery. Most of the salivary gland lesions can be accurately diagnosed by FNA with adequate sampling and cytopathologist experience. It can be used to differentiate benign from malignant lesions preoperatively thus helping further surgical management of the patient.

Conflict of interest: None\

Funding: None

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