

Original Research Article**Fine Needle Aspiration Cytology of Salivary Gland Lesions****Sushma K.^a, Sunita S. Vernekar^b, Sujata S. Giriyan^c**

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Abstract

Objectives: FNAC has been used in the pre-operative diagnosis of salivary gland lesions for many years. Existing literature has shown wide range of sensitivity, specificity and diagnostic accuracy of cytological diagnosis. This study was aimed at evaluating salivary gland FNAC for sensitivity, specificity and diagnostic accuracy at a tertiary care center.

Materials and Methods: This study included 203 patients from January 2012 to June 2015 who underwent FNAC of salivary gland lesions. The cytological diagnosis was correlated with histopathology wherever possible. The appropriate statistical results were analysed.

Results: Total 203 cases were studied. parotid gland-135, submandibular gland-62, intraoral glands-5 and upper lip-1. FNAC categorised 58.6% of the salivary gland lesions as nonneoplastic and 41.4% as neoplastic. Among nonneoplastic lesions 83.9% were sialadenitis. Among neoplastic lesions 80.95% were benign and 19.05% were malignant. Cytohistopathologic correlation was available for 32 cases. Overall 25 cases showed 80.6% correlation. There were 3 false positive cases. Specificity, sensitivity, positive and negative predictive values for malignant lesions were 100%, 50%, 100% and 89.65% respectively. Further statistical analysis showed a good cytohistologic agreement with kappa value of 0.619.

Conclusion: Adequate sampling, high quality smear preparation and established diagnostic criteria can help to diagnose majority of common benign and malignant salivary gland swellings with high level of accuracy. The findings of FNAC should be read in conjunction with clinical findings and in doubtful cases the true nature of the lesion should be confirmed by histopathological examination.

Keywords: Fine Needle Aspiration Cytology; Salivary Glands; Sensitivity; Specificity.

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Introduction

Fine needle aspiration is a widely accepted, safe, and accurate method for preoperative diagnosis of palpable lesions. Salivary glands due to their location are easily accessible for aspiration. This technique assumes greater importance considering the lack of characteristic clinical or radiologic features that may suggest a particular

diagnosis. Though few symptoms and signs may suggest malignancy, most malignant salivary gland lesions cannot be differentiated from their benign counterparts on clinical criteria alone [1]. Moreover salivary gland lesions are not generally subjected to incisional or needle biopsy techniques because of the risks of fistula formation or in case of neoplasm of tumor implantation. There is no evidence that these complications occur with FNAC [2].

Salivary gland lesions account for 3-10% of all neoplasms of the head and neck regions [3,4]. The characteristic cytological features of the common salivary gland lesions are well delineated in literature. However there also exist cytological pitfalls and overlapping features that make an accurate diagnosis difficult in few cases. This has led to a wide range of sensitivity (50% to 97%) and specificity (80% to 100%) of the cytological diagnosis [1,5,6,7,8]. The reported diagnostic accuracy is high for benign neoplasm, but lower for malignant tumors [7,8].

In the present study, various salivary gland lesions were studied clinicocytologically. The cytological diagnosis is compared with the histologic diagnosis wherever possible to assess the sensitivity, specificity and diagnostic accuracy of FNAC, with emphasis on discordant cases.

Materials and Methods

The present study is total three and half year study with one and half year retrospective and two years prospective with sample size of 203 patients from January 2012 to June 2015 in the department of pathology KIMS Hubballi. All patients with clinical history of salivary gland swelling were included in the study. Patients with head

and neck swellings other than salivary gland swelling were excluded from the study. Relevant clinical details were elicited in all cases and findings of local examination noted. After taking an informed consent, under aseptic precautions FNAC was performed by using 5-10 ml disposable syringe with 22-24 gauge needle. The character of the aspirate was noted. When cyst was encountered, the fluid was completely aspirated and the residual mass if palpated in these cystic lesions were reaspirated. The papanicolaou, H&E and air dried wright stain slides were studied. Following preoperative cytological diagnosis surgical specimens were available for only 32 cases. The specimens were submitted for histopathologic examination. Cytohistologic correlation was done and appropriate statistical tests were applied.

Results

The study includes 203 patients of salivary gland swellings (108 females, 95 male with M;F=1; 1.14) with age ranging from 3 years to 90 years with mean age of 38 years for all lesions considered together.

Of the 203 cases, 135 (66.5%) occurred in parotid gland, 62 (30.5%) in submandibular gland, 6 (3%) in minor salivary glands.

Table 1: Cytologic distribution of non neoplastic lesions

FNAC diagnosis	Total No/(%)	Parotid No/(%)	Submandibular No/(%)	Minor salivary gland No/(%)
Acute sialadenitis	19(16%)	12(10.1%)	7(5.9%)	-
Chronic sialadenitis	82(68.93%)	44(37%)	38(31.93%)	-
Benign cystic lesion	11(9.3%)	9(7.6%)	2(1.7%)	-
Lymphoepithelial cyst	2(1.7%)	1(0.84%)	1(0.84%)	-
Intraparotid lymphadenitis	2(1.7%)	2(1.7%)	-	-
Necrotising sialometaplasia	1(0.84%)	-	-	1(0.84%)
Sialadenosis	1(0.84%)	1(0.84%)	-	-
Unsatisfactory	1(0.84%)	-	1(0.84%)	-
Total	119	69	49	1

Table 2: Cytologic distribution of salivary gland tumours

FNAC diagnosis	Total	Parotid Gland No. of cases	Submandibular Gland No. of cases	Minor salivary Gland No. of cases
Pleomorphic adenoma	61(72.62%)	48	9	4
Basal cell adenoma	4(4.76%)	4	-	-
Warthin's tumour	2(2.38%)	2	-	-
Oncocytoma	1(1.19%)	1	-	-
Mucoepidermoid carcinoma	5(5.95%)	4	1	-
Acinic cell carcinoma	2(2.38%)	2	-	-
Adenoid cystic carcinoma	2(2.38%)	-	1	1
Adenocarcinoma NOS	2(2.38%)	2	-	-
Carcinoma Ex Pleomorphic adenoma	2(2.38%)	1	1	-
Squamous cell carcinoma	1(1.19%)	1	-	-
Poorly differentiated carcinoma	1(1.19%)	1	-	-
Malignant tumour unspecified	1(1.19%)	1	-	-

Table 3: Comparison of FNAC with histopathologic study

Cytologic Diagnosis	Histopathologic Diagnosis							Total
	Chronic sialadenitis	Chronic sclerosing sialadenitis (Kuttners tumor)	PA	BCA	MEC	AdCC	SCC	
Chronic sialadenitis	1	2	-	-	1	-	-	4
Necrotising sialometaplasia	-	-	1	-	-	-	-	1
Benign cystic lesion	-	-	-	-	1	-	-	1
PA	-	-	19	-	-	1	-	20
BCA	-	-	-	3	-	-	-	3
Ad CC	-	-	-	-	-	1	-	1
MEC	-	-	-	-	1	-	1	2
Total	1	2	20	3	3	2	1	32

PA=Pleomorphic adenoma, MEC=Mucoepidermoid carcinoma, BCA=Basal cell adenoma, AdCC=Adenoid cystic carcinoma, SCC=Squamous cell carcinoma.

Table 4: Statistical analysis of neoplastic and non neoplastic lesions

	Specificity	Sensitivity	PPV	NPV	Accuracy
Nonneoplastic	89.65%	100%	50%	100%	90.6%
Benign tumour	88.9%	95.6%	95.6%	88.9%	93.75%
Malignant tumour	100%	50%	100%	89.65%	90.6%

PPV=Positive predictive value, NPV=Negative predictive value.

One hundred and nineteen cases (58.6%) were nonneoplastic and 84 cases (41.4%) were neoplastic.

i. Nonneoplastic Lesions

The site distribution for nonneoplastic lesions is 58% in parotid (69 out of 119 cases), 41.2% (49 out of 119 cases) in submandibular gland and 0.84% (1 out of 119) in minor salivary gland.

Sialadenitis was the most common lesion accounting 84.9% among the nonneoplastic lesions of which 68.9% were chronic sialadenitis and 16% were acute sialadenitis

Next commonest nonneoplastic lesion observed in the study is benign cystic lesions accounting 9.3% of non neoplastic lesions. Other nonneoplastic lesions observed are 2 cases of each lymph epithelial cyst, intraparotid lymphadenitis, one case each of necrotising sialometaplasia, sialadenitis. One case was unsatisfactory because of poor cellularity Table 1.

Six nonneoplastic lesions were subjected for histopathology, of which 3 cases were correlated with the remaining 3 being false positive Table 3. The statistical analysis of nonneoplastic lesions is as in Table 4.

ii. Neoplastic Lesions

The age of patients for benign tumours ranged from 17 years to 66 years with mean age of 37.85 years. Male to female ratio for benign tumour was 1:1.15. Benign tumours were more common (80.95%) than the malignant tumours (19.05%). Pleomorphic adenoma was the most common benign tumour accounting 72.6% of all tumours. Basal cell adenoma was the second most common benign

tumour constituting 4.76% of all tumours. Other benign tumours observed in the study are 2 cases of warthins tumour and a case of oncocytoma Table 2. Histopathological correlation for pleomorphic adenoma was available in 20 cases, of which 19 were correlated but 1 case was histologically confirmed as adenoid cystic carcinoma Table 3.

There were 16 cases (19.05%) of malignant salivary gland neoplasms in our study Table 2. Mucoepidermoid carcinoma was the most common malignant tumour constituting 5.95% of all tumours. Eighty percent of them occurred in parotid gland followed by submandibular gland. Among 16 cases, 3 were available for histopathological correlation. A case of cytologically diagnosed adenoid cystic carcinoma was confirmed histologically as adenoid cystic carcinoma Table 3. Among 2 cases of cytologically reported mucoepidermoid carcinoma one case was confirmed histopathologically and the other one as squamous cell carcinoma with 100% cytopathologic correlation Table 3. The statistical analysis of benign and malignant tumours is as in Table 4.

Discussion

FNAC is widely used, safe and less traumatic diagnostic procedure capable of providing important information to the treating physician [1]. Salivary gland lesions accounts for 3-10% of all head neck swellings [3,4]. Nonneoplastic lesions constituted 58.6% of all salivary gland aspirates in present study with predominantly sialadenitis and benign cystic lesions. In literature the prevalence ranges from 10% to 66% [1,5,6,7,8].

Of the 119 cases of nonneoplastic lesions, 6 cases were subjected for histopathology because of other differential diagnosis. The remaining nonneoplastic lesions were managed conservatively and responded to medical line of treatment. The cytohistopathologic correlation of these 6 nonneoplastic lesions is as shown in Table 3.

Out of 6 cases, 3 cases showed cytohistoconcordance with remaining 3 of false positive cases. This is because, an aspirate from hard palate cytologically diagnosed as necrotising sialometaplasia, on histopathology turned out to be pleomorphic adenoma. And then a case of cytologically diagnosed chronic sialadenitis and a benign cystic lesion on histopathology turned out to be mucoepidermoid carcinoma. In the present study cytologically reported case of necrotising sialometaplasia of minor salivary gland (hard palate) showed squamoid like epithelial cells against dense inflammatory background. Since the lesion was ulcerated the squamoid like epithelial cells against the dense inflammatory background were under diagnosed and the histopathologic diagnosis of pleomorphic adenoma of minor salivary gland was missed. Worry some squamous epithelial cell atypia can be found in a wide spectrum of salivary gland lesions causing diagnostic difficulties in FNAC [9].

Similarly an aspirate from a 21 year old female patient with preauricular swelling on cytology yielded fluid with cyst macrophages and cytologically diagnosed as benign cystic lesion. On histopathology it turned out to be low grade mucoepidermoid carcinoma. Low grade mucoepidermoid carcinoma is well recognised for its potential false negative diagnostic pitfall [10]. Low grade mucoepidermoid carcinoma accounts for about 80% of all mucoepidermoid carcinoma and is characterised by cystic growth pattern. Aspirates of low grade usually yields mucoid fluid and the smears are typically hypocellular having bland cytological features. Low grade mucoepidermoid has to be differentiated from warthins, benign salivary gland cyst, branchial cleft cyst, sialolithiasis [10].

Klijanienko et al [11] reviewed 50 cases of mucoepidermoid carcinoma and suggested that FNAC is an accurate technique for diagnosing high or intermediate grade tumours but unsatisfactory in detecting low grade tumours. Clinical follow up of cystic salivary gland lesions is essential if a specific diagnosis cannot be made [12].

In present study a case of cytologically diagnosed chronic sialadenitis on histopathology turned out to be mucoepidermoid carcinoma. This case was missed cytologically because of predominant inflammatory background with very few neoplastic cells. Usually long standing cases of chronic sialadenitis are known for over diagnosis as neoplastic lesion or even malignancy mainly low grade mucoepidermoid. This may be due to

regenerative ductal epithelium in chronic sialadenitis may undergo squamous metaplasia and may appear atypical with mucous like material from dilated ducts [12].

In the present study out of total 84 neoplastic lesions, 80.95% were benign tumours and 19.05% were malignant. This is similar to other studies [1,7,8,13]. Salivary gland tumours were commonly seen in parotid gland followed by submandibular and minor salivary glands. Similar observations were seen in other studies [6,14,15]. Among the benign tumours, pleomorphic adenoma was commonest (72.6%) as observed in other studies [1,6,15,16].

Out of 20 cytologically diagnosed cases of pleomorphic adenoma, 19 were correlated histologically with 95% of cytohistologic agreement. Thus the accuracy of diagnosing benign neoplasm cytologically is 93.75% Table 4. This is in agreement with other studies [5,15,16]. In present study a case of pleomorphic adenoma on histopathology turned out to be adenoid cystic carcinoma. Similar observation was seen in other study [16]. The distinction of pleomorphic adenoma from well differentiated adenoid cystic carcinoma is clinically important. Hyaline stromal globules resembling those characteristic of adenoid cystic carcinoma or a beaded hyaline stroma sometimes also occur in pleomorphic adenoma [17,18]. A well defined cytoplasm, no or few stripped nuclei and a bland finely granular nuclear chromatin favor pleomorphic adenoma. Scanty cytoplasm, a high N/C ratio, naked nuclei, nuclear molding and nuclear hyperchromatism and coarseness favor adenoid cystic carcinoma [12].

Next to pleomorphic adenoma, the commonest benign tumour in study is basal cell adenoma accounting 4.76% of all tumours. All were in females and in parotid gland. The cytohistopathologic correlation was 100%. Similar observation was seen in other study [5]. Other benign tumours observed in the study are 2 cases of warthins tumour and a case of oncocytoma which were not available for histopathological correlation.

Mucoepidermoid carcinoma was the commonest malignant tumour observed in present study accounting 5.95% of malignant salivary gland tumours. Mucoepidermoid carcinoma comprise 5-10% of all the salivary gland tumours and 9/10th of these tumours occur in parotid gland [19]. In present study of the 5 mucoepidermoid carcinomas, 2 were available for histopathology correlation, wherein one is correlated, and the other one on histopathology turned out to be squamous cell carcinoma. Generally, the diagnosis is most difficult in low grade mucoepidermoid carcinoma which are mistakenly reported as benign cystic lesion as it observed in present study. Smears of high grade mucoepidermoid carcinoma contain malignant squamous epithelial cells. Mucin secreting cells can be difficult to find and it may be difficult or impossible to distinguish primary

high grade mucoepidermoid carcinoma from metastatic squamous cell carcinoma, although obvious keratinisation identified cytologically effectively excludes mucoepidermoid carcinoma [12].

Adenoid cystic carcinoma is the next common malignant salivary tumour accounting 2.38% of the tumours. Among 2 cases of adenoid cystic carcinoma, only one was available for histopathology correlation and showed cytohistologic concordance.

For malignant salivary gland tumours the rate of false negative diagnosis on cytology reported in literature ranges from 0% to 37% [8]. The false negative rate in our study was 50% due to 2 cases of mucoepidermoid carcinoma reported as benign cystic lesion and chronic sialadenitis and a case of adenoid cystic carcinoma cytologically wrongly reported as pleomorphic adenoma. The false positive rate has been reported to be low with greater accuracy and less sampling error in FNAC. This rate ranges from 0% to 10% in the published literature [20]. In our study it was 0%.

Considering histologic diagnosis as the gold standard the sensitivity and specificity for diagnosis of malignant tumours was 50% and 100% whereas it was 92.8% and 93.9% in Jain R et al [1]. The positive predictive value of FNAC for malignant diagnosis was 100% and negative predictive value 89.65%, whereas in Jain R et al [1] it was 81.2% and 98.4%. Another study reported sensitivity for diagnosis of malignant lesions as 77.77%, specificity of 98.78% and positive predictive value of 93.33% [8]. Further statistical analysis showed a good cytohistologic agreement with kappa value of 0.64 which is similar to Jain R et al [1].

The inadequate sampling rate in present study is 0.5%. The inadequacy rate in literature ranges from 5-10% [1,13,21,22]. A recent study evaluated the utility of repeat FNAC in cytological diagnosis of salivary gland tumours and found the sensitivity and specificity of repeat FNAC similar to the initial procedure [21].

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