



Research Journal of Pharmaceutical, Biological and Chemical Sciences

Fine Needle Aspiration Cytology of Salivary Gland-A Review of 90 Cases

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ABSTRACT

A mass in the salivary gland region often presents a diagnostic challenge. Present study is being conducted to study the spectrum of non-neoplastic and neoplastic lesions with respect to age, sex and site of occurrence by FNAC. A total of 90 FNACs were done, cytomorphological features were analyzed and lesions were categorized as: sialadenitis (41), non-neoplastic cysts (7), benign tumors (30), malignant tumors (7), mesenchymal lesion (1) and tumor-like lesions (4). Majority of patients were males in the age group of 21-30 years. In the present study, parotid gland (58 cases) was the commonest site involved. Pleomorphic adenoma (23 out of 30 benign tumors) and mucoepidermoid carcinoma (4 out of 7 malignant tumors) were commonest benign and malignant tumors respectively. Histopathological correlation was available for 30 cases and overall sensitivity, specificity and diagnostic accuracy were 95.65%, 71.43% and 90% respectively. Hence FNAC has high diagnostic accuracy and helps in early appropriate therapeutic management. This study documents that FNAC is an accurate, simple, rapid and inexpensive procedure which is well tolerated and harmless to the patient.

Keywords: Salivary gland lesions, FNAC, Sensitivity, Specificity, Diagnostic Accuracy.

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INTRODUCTION

Fine Needle Aspiration Cytology (FNAC) of suspected salivary gland lesions has an established role in preoperative diagnosis and management of patients [1]. Major and minor salivary glands are subjected to developmental, inflammatory, immunopathic, degenerative and neoplastic diseases. Thus, diseases of salivary gland form an important and yet an interesting group of lesions in respect to their diagnosis, treatment and prognosis.

Although salivary gland tumors account for 2-6.5% of all head and neck tumors, their superficial location, easy accessibility and high diagnostic accuracy makes FNAC a popular method for evaluating salivary gland tumors [2]. A review of the more recent reported series presented in 1994 found that diagnostic sensitivity varied between 81-100%, specificity was 94-100% and accuracy of tumor typing was 61-80% [3].

The mean age at presentation for malignant salivary neoplasms is 55 to 65 years while benign lesions typically develop at least a decade earlier, at a mean age of 45 years [4].

Between 64-80% of all primary epithelial tumors occur in parotid glands, 7-11% occur in the submandibular glands, less than 1% occur in the sublingual glands and 9-23% occur in the minor glands[5]. Malignant tumors comprise 15-20% of all parotid tumors, 37-43% of submandibular gland tumors and over 80% of minor salivary gland tumors [4]. The ratio of malignant to benign tumor is greatest (>2.3:1) in sublingual gland, tongue, floor of the mouth and retro-molar area.

Pleomorphic adenoma is the most common benign neoplasm, accounting to 52.04% of all tumors, 80% of which is seen in the parotid gland. Mucoepidermoid carcinoma is the most common malignant neoplasm, accounting to 4.06% of all tumors and it most commonly affects major salivary glands, especially the parotid gland (50% of mucoepidermoid carcinomas). Adenoid cystic carcinoma is the second most common malignant neoplasm, accounting to 1.63% of salivary gland tumors and is seen most commonly in minor salivary glands (50-70% of adenoid cystic carcinomas) [6].

FNAC plays a very important role in the management of salivary gland lesions as it allows for quick and precise diagnosis. The only well known and widely followed presurgical diagnostic procedure for diagnosis of salivary gland lesions today is FNAC as they are not subjected to incision or Tru-cut biopsy for the fear of fistula formation, facial nerve damage, seeding of tumor cells and hemorrhage. Also immunohistochemistry is unpopular because there is no reliable IHC marker for diagnosis and typing of tumors; high cost also limits its utility.

There is an ongoing controversy regarding the benefits of FNAC in evaluation of salivary gland lesions because there is a wrong assumption that management of any salivary gland tumor ends with tumor excision. But in this study we stress on accurate categorization of lesions into inflammatory and neoplastic, and if neoplastic into benign and malignant, because although surgery is the treatment for salivary gland tumors, extent of surgery depends on type

and aggressiveness of the tumor. For instance, superficial parotidectomy is sufficient for pleomorphic adenoma, but adenoid cystic carcinoma and high grade malignancies require a radical approach. The purpose of this study is to not only describe various patterns and spectrum of lesions with respect to age, sex and site of occurrence but also to document the utility of FNAC as a diagnostic procedure in appropriate and timely management of patients, and to stress the need for close collaboration and communication between clinician and cytopathologist to avoid committing blunders in patient management. This paper also attempts to show some of the pitfalls of FNAC especially in diagnosis of cystic lesions, and emphasizes on the need for having thorough knowledge about different lesions, their differential diagnosis and morphologic heterogeneity because, avoiding misdiagnosis is as essential and important as providing correct diagnosis. Accurate diagnosis depends on thorough clinical history, physical and radiological examination, close communication with clinician in addition to skills and knowledge of the cytopathologist.

METHODOLOGY

In this present study, FNAC procedure was performed on 90 patients who presented with salivary gland mass to the surgical outpatient clinic from November 2008 to May 2010. Aspiration was performed on all patients at the department of pathology after taking thorough clinical history and examination by cytopathologist in each case. After taking the informed consent, patient was made to take a suitable position on bed. In each case aspiration was done with a 24-22 gauge needle attached to a 10-20 ml disposable syringe. Fine needle sampling without aspiration, recommended by Zajdela was adopted for aspiration of solid tumors. This procedure is based on the observation that capillary pressure in a fine needle is sufficient to keep the scrapped cells inside the lumen. Although yield is much lesser than with aspiration, it is sufficient in majority of cases to diagnose solid tumors. This procedure also allows for better assessment of tumor consistency while aspirating the lesion. Procedure was repeated in cases where the aspiration was acellular or inconclusive. In cases of fluid aspiration from cystic lesions, slides are made from uncentrifuged as well as from centrifuged material. In all cases, aspiration was performed at multiple sites and in different directions as salivary gland lesions are known for their heterogeneity. For Papanicolaou, H and E staining, slides are immediately fixed in Carnoy's fixative/95% ethanol and rest of the slides was air dried for MGG staining. Special stains like PAS stain were performed as and when required. After assessing the adequacy of material, slides were analyzed by the cytopathologist and lesions were categorized into non-neoplastic and neoplastic. In addition to categorizing the neoplastic lesions into benign and malignant tumors, an attempt was made in each case to establish a precise diagnosis and to type all tumors. Final diagnosis was arrived at taking not more than 15 minutes for whole procedure in most of the cases. Close collaboration with clinician in cases when aspiration is performed by the surgeon allows for quick and accurate diagnosis which is beneficial both to the patient and surgeon.

FNAC results were compared with histopathology in 30 cases who underwent surgery. Sensitivity, specificity and diagnostic accuracy were calculated with the help of statistical data.

RESULTS

Following observations were made from the aspiration conducted on 90 cases.

Age distribution in salivary gland lesions

Age of the patients ranged from 18 months to 85 years and maximum number of lesions were seen in the age group 21-30 years (26.67%), followed by 41-50 years (18.89%) and 51-60 years (13.33%).

Gender distribution in salivary gland lesions

In the present study, a male predilection was seen. Among the 90 cases studied, 59 cases (65.56%) were males and 31 cases (34.44%) were females and male to female ratio was 1.9:1.

Site distribution pattern

Parotid gland (58 cases) was the commonest site involved, followed by submandibular gland, sublingual gland and minor salivary glands in 27 cases, 2 cases and 3 cases respectively. In 3 cases bilateral parotid glands were involved, a case of sialadenosis, benign acinar hyperplasia and benign lymphoepithelial cyst.

Categories of salivary gland lesions on FNAC

Among the total number of 90 cases, 41 cases were sialadenitis, 30 were benign tumors, 7 were non-neoplastic cysts and malignant tumors each, 4 were tumor-like lesions and 1 was a case of mesenchymal lesion.

Cytological types, site and percentage of salivary gland tumors

Pleomorphic adenoma was the most common benign tumor in parotid gland constituting 54.04% (20 out of 37) of all tumors. In most sites, pleomorphic adenoma was the predominant benign tumor and most of them were present in parotid gland, 86.96% (20 out of 23 cases).

Mucoepidermoid carcinoma was the most common malignant tumor of parotid gland constituting 10.81% (4 out of 37) of all tumors and all of them (100%) were present in parotid gland in the present study.

Comparison of cytological diagnosis and histopathology

The initial cytological diagnosis was compared with the gold standard, histopathological diagnosis in 30 cases (Table 1).

Table 1- Comparison of FNAC with histopathological study

Cytological diagnosis	Histopathological diagnosis									Total
	Normal salivary gland	Chronic sialadenitis	Benign lymphoepithelial cyst	Pleomorphic adenoma	Basal cell adenoma	Warthin's tumour	Mucoepidermoid carcinoma	Adenoid cystic carcinoma	Carcinoma ex pleomorphic adenoma	
Chronic sialadenitis	0	2	0	0	0	0	2	0	0	4
Sialadenosis	1	0	0	0	0	0	0	0	0	1
Benign lymphoepithelial cyst	0	1	1	0	0	0	0	0	0	2
Pleomorphic adenoma	0	0	0	12	1	0	0	0	0	13
Warthin's tumour	0	0	0	0	0	4	0	0	0	4
Mucoepidermoid carcinoma	0	0	0	0	0	0	3	0	0	3
Adenoid cystic carcinoma	0	0	0	0	0	0	0	2	0	2
Carcinoma ex pleomorphic adenoma	0	0	0	0	0	0	0	0	1	1
Total	1	3	1	12	1	4	5	2	1	30

The parameters reflecting the diagnostic accuracy of FNAC in salivary gland tumors are as follows: sensitivity – 95.65%, specificity – 71.43%, positive predictive value – 91.67%, negative predictive value – 83.33%, percentage of false negative – 4.35%, percentage of false positive – 28.57% and diagnostic accuracy – 90%. In our present study, diagnostic accuracy and sensitivity were similar to other studies but specificity was less compared to other studies (Table 2).

Table 2- Comparison of diagnostic accuracy, sensitivity and specificity of FNAC in the diagnosis of salivary gland tumors with other studies

Sl. No.	Authors	Diagnostic Accuracy (%)	Sensitivity (%)	Specificity (%)
1	Cristallini EG ^[8] (1985-1995)	97.90	97.60	98.45
2	O'Dwyer ^[9] (1986)	90.00	73	94.00
3	Jayaram ^[10] (1989)	87.70	80.9	94.30
4	Shintani ^[11] (1997)	93.00	88.9	94.10
5	Present study (2008-10)	90.00	95.65	71.43

DISCUSSION

Salivary gland neoplasm accounts for 2 to 6.5% of all neoplasms of the head and neck[1].64-80% of all primary epithelial tumors occur in the parotid glands, 7-11% occur in the

submandibular glands, <1% occur in the sublingual glands and 9-23% occur in the minor salivary glands[1].15-30% of tumors in the parotid glands are malignant in contrast to about 40% in the submandibular glands, 50% in the minor salivary glands and 70-90% in the sublingual glands.

These tumors usually occur in adults with a female predominance, but Warthin's tumor are more common in males. Mean age at presentation for malignant salivary gland neoplasm is 55 to 65 years while benign lesions typically develop at least a decade earlier.

A mass in the salivary gland region often presents a diagnostic challenge. It is very difficult to differentiate between benign and malignant tumors just by their clinical presentation. A high grade malignant tumor can remain localized for a long time, whereas a completely benign tumor can widely metastasize, like pleomorphic adenoma. Even some of the inflammatory lesions may masquerade as malignancy; for instance, chronic sialadenitis of submandibular gland may produce a stony hard mass, Kuttner's tumor. In this study histopathological correlation was available in 4 cases of chronic sialadenitis. Out of 4 cases, 2 cases were diagnosed as mucoepidermoid carcinoma. On reviewing the smears from latter cases it was found that one of them showed squamoid cells which were misinterpreted as squamous metaplasia of ductal epithelial cells (Figure 1). The smears also comprised mucin secreting cells which contained PAS positive substance (Inset of Figure 1). This illustration makes clear that all salivary gland masses should be subjected to FNAC without which definite diagnosis cannot be offered only by considering clinical criteria.

Salivary gland tumors can occur in many locations including mucosa of aero- digestive tract and breast. Although any tumor of salivary gland can occur in any location, some tumors have predilection for certain sites. For instance, pleomorphic adenoma is the most common tumor in all locations, but it has a predilection for major salivary glands, especially parotid gland. Although adenoid cystic carcinoma can occur in major salivary glands, it is more common in minor salivary glands. Occurrence of myoepithelioma is restricted to parotid gland.

The speciality of salivary gland tumors is that, more than one tumor can assume similar morphology, for instance basement membrane material in the form of hyaline globules can be present in adenoid cystic carcinoma, a frankly malignant tumor; polymorphous low grade adenocarcinoma, an intermediate grade tumor; and basal cell adenoma (Inset of Figure 2), a benign tumor. But adenoid cystic carcinoma has predilection for minor salivary gland, polymorphous low grade adenocarcinoma also occurs in minor salivary glands especially in hard palate, and basal cell adenoma has predilection for parotid gland. Thus while diagnosing salivary gland tumors it is very important to take into account the site of tumor occurrence in addition to cellularity of the smears, nuclear atypia and cellular arrangement among others for definite tumor typing.

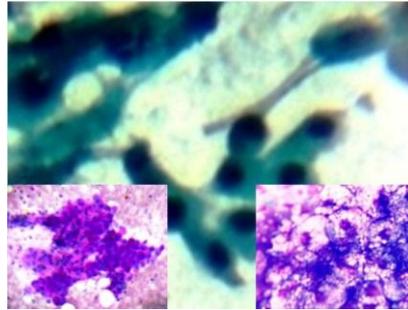


Figure 1: Epidermoid cells of mucoepidermoid carcinoma (Papanicolaou stain, x400) Inset- a) PAS positive intracytoplasmic mucin present in mucin producing cells in mucoepidermoid carcinoma (PAS stain, x100) b) Mucous producing cells of mucoepidermoid carcinoma with abundant vacuolated cytoplasm (MGG, x400) Figure 2: Tight cohesive clusters of basaloid cells in basal cell adenoma which was misdiagnosed as cellular pleomorphic adenoma in cytology (H&E, x400) Inset- Basal cell adenoma showing hyaline globule surrounded by basaloid cells (MGG stain, x400)

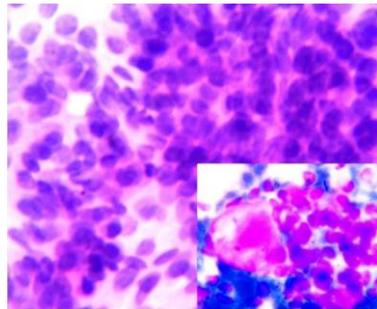


Figure 2: Tight cohesive clusters of basaloid cells in basal cell adenoma which was misdiagnosed as cellular pleomorphic adenoma in cytology (H&E, x400) Inset- Basal cell adenoma showing hyaline globule surrounded by basaloid cells (MGG stain, x400)

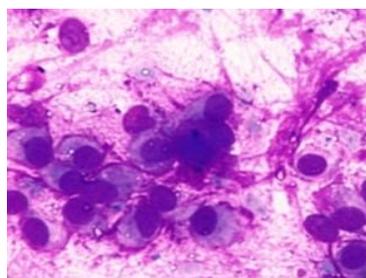


Figure 3: Plasmacytoid hyaline-cells seen in pleomorphic adenoma (MGG stain, x400)

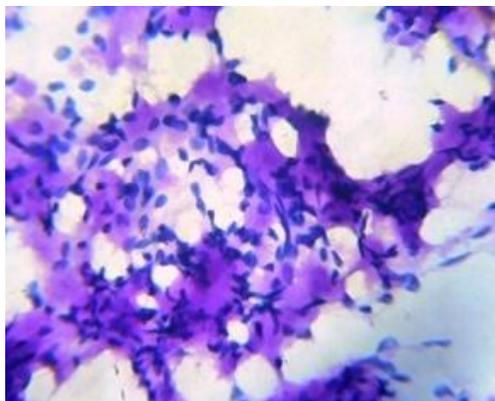


Figure 4: Cribriform arrangement of bland cells against the characteristic basement membrane material in adenoid cystic carcinoma (H&E, x100)

In this study we encountered 3 patients who presented with bilateral parotid enlargement. One of them was a female child, 10 years old. She had bilateral parotid enlargement since birth. Smears studied from the aspirate were moderately cellular and showed acinar epithelial cells, normal to slightly increased in size with micro architecture as that of normal gland. The final cytological diagnosis given was bilateral sialadenosis. In another case a middle aged man was diagnosed to be having bilateral benign acinar hyperplasia of parotids. The smears consisted predominantly of normal looking acinar cells, interspersed between them were occasional ductal epithelial cells. This emphasizes the importance of correlation between clinical history (age as in this case) and cytological findings as there were very minor cytological differences between the two cases. In another case, an AIDS patient presented with bilateral parotid mass. Smears made from centrifuged deposit of aspirated fluid showed mononuclear cells and few epithelial cell clusters. Since we knew the clinical history, diagnosis of lymphoepithelial cyst was made.

Salivary glands are subjected to wide variety of lesions including mesenchymal lesions. In this study we encountered a 14 year old male child who presented with left parotid mass. Repeated aspirations yielded only hemorrhage and smears consisted of occasional spindle shaped cells. The diagnosis of hemangioma of parotid was made, based on the USG diagnosis of vascular tumor. This case illustrates that salivary gland can be an unusual site for the most common tumor or tumor-like lesions and also emphasizes on the importance of radiological examination in the diagnosis of such lesions.

The mass may contain cystic component which makes the diagnosis very difficult[11]. In interpreting the cystic lesions, particular attention has to be given to the epithelial cells lining the cyst wall[12,13]. We also encountered similar challenge in our study. We documented 7 cystic lesions; out of which 4 were benign lymphoepithelial cysts and 3 were mucocoeles. Histological correlation was available for 2 cases of benign lymphoepithelial cysts, one of which turned out to be chronic sialadenitis with cystic change. The tumors which are known to undergo cystic degeneration are Warthin's tumor, mucoepidermoid carcinoma and adenoid cystic carcinoma. These can be misdiagnosed as inflammatory lesion or as benign

lymphoepithelial cyst. When Warthin's tumor undergoes cystic change obtaining diagnostic material may be difficult. Both oncocytic and lymphoid tissue may be sparse, absent or obscured by mucoid debris. If the overall smear pattern suggests Warthin's tumor but the cells show some atypia and lack a distinctly oxyphil cytoplasm, the alternative of a mucoepidermoid tumor should be considered. Mucoepidermoid carcinoma is prone for false negative diagnosis for the same reason. Hence it is necessary to subject cystic lesions to multiple aspirations in different directions.

Another important pitfall of FNAC is inadequate aspiration which makes assessment of lesions difficult due to poor cellularity or quality of the smears. FNAC is a blind procedure and like any limit biopsy; FNAC samples derive cells from a small area. This is a disadvantage because salivary gland tumors are known for morphological heterogeneity. Myoepithelial cells of pleomorphic adenoma can assume different forms like spindle shaped cells, squamoid cells, hyaline-plasmacytoid cells (Figure 3) etc. In this study, a parotid mass which was diagnosed as cellular pleomorphic adenoma (Figure 2) cytologically, turned out to be basal cell adenoma on histopathological examination. Since both are benign tumors, ethically it does not make a difference as both are managed by superficial parotidectomy. But this is not the case when it comes to matter of differentiating between pleomorphic adenoma and adenoid cystic carcinoma. Pleomorphic adenoma can contain abundant basement membrane material and adenoid cystic carcinoma can appear as benign as pleomorphic adenoma (Figure 4). Despite the inherent inaccuracies the rate of inadequate samples can be minimized by improved technique and experience [14].

One of the percepts of salivary gland FNAC is to offer correct diagnosis and to differentiate between non-neoplastic and neoplastic lesions on one hand and benign and malignant tumors on other hand. Whereas the non-neoplastic lesions and benign tumors are cured by superficial parotidectomy, high grade malignant tumors and adenoid cystic carcinoma requires a radical approach. Pre-operative diagnosis reduces the short and long term morbidity caused by facial nerve damage and or Frey's syndrome and also FNAC offers an opportunity for tumor typing to take surgical decisions in patients who are considered to be poor surgical risk. FNAC also allows for planning the extent of surgical procedure so that informed consent regarding the possible risk of permanent facial nerve damage can be taken well in advance to the procedure. Also cases of fistula formation and seeding of tumor cells by the needle, which are known complications following Tru-cut biopsy have not been reported following FNAC [15].

In the present study all the aspirations were done in the outpatient clinic by the cytopathologist after thorough clinical examination. Aspirations performed and immediately reported by the cytopathologist in the outpatient clinic offers several advantages. Both surgeon and pathologist can examine the patient and discuss the suspected diagnosis, and provision of an immediate diagnosis allows for early therapeutic planning. FNAC of the salivary gland tumors is an accurate, simple, rapid, inexpensive procedure well tolerated and harmless to the patient.[3] FNAC of salivary gland tumors is advantageous to both the patient and the clinician because of its immediate results, accuracy, lack of complications and economy.

CONCLUSION

Accuracy in cytological diagnosis is as valuable as a correct clinical diagnosis. The appropriate management of patients completely depends on close cooperation, communication and combined intelligence of surgeon and cytopathologist. Apart from the difficulties in diagnosis of certain salivary gland tumors and cystic lesions, FNAC plays a very valuable role in the diagnosis of salivary gland lesions.

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