UTILITY OF FNAC WITH CYTOMORPHOLOGICAL PITFALLS IN INTRAORAL LESIONS- A 6-YEAR EXPERIENCE AT A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

Intraoral region has a spectrum of distinct anatomical sites and there exists a wide variety of intraoral lesions. Fine Needle Aspiration Cytology (FNAC) is a simple tool and has gained importance, especially in cases with difficult intraoral accessibility and risk of bleeding obviating biopsy and thereby helping in the decision for surgical intervention.

Aim: This study was carried out to evaluate the diagnostic utility and pitfalls of FNAC in the intraoral lesions with histopathological correlation.

MATERIALS AND METHODS

This is a retrospective descriptive study and the data was collected retrospectively of intraoral lesions diagnosed on FNAC over a period of 6 years (July 2011 to June 2017) from the cytology records. The histopathology correlation was done wherever available.

RESULTS

Out of 102 cases, 82 (80.39%) were adequate for cytological study. Different sites involved were tongue, gingival region, buccal mucosa, floor of mouth, soft palate, hard palate, tonsil, oropharynx and parapharyngeal/ posterior pharyngeal wall. Of these 82 cases, 40 (48.78%) were neoplastic and 42 (51.22%) were non-neoplastic. Twenty-nine cases (72.5%) out of 40 neoplastic cases were diagnosed as benign and 11 cases (27.5%) as malignant. Cytological diagnosis was compared with the histopathology diagnosis. Histological correlation was found in 44 cases with concordance rate of 68.2% (30 of 44 cases). However, in 9 cases there was discordance with histological findings. In rest 5 cases, the histology report was descriptive without a definitive diagnosis. A single false positive case was of dense inflammation with squamous cells misinterpreted as squamous cell carcinoma on cytology.

CONCLUSION

FNAC was found to be useful in the diagnosis of variety of lesions in the oral cavity, though few cases can pose diagnostic difficulties. Cytological diagnosis can save many non-neoplastic cases from undergoing surgery or excision biopsy and helps identify the malignant cases for early management.

KEY WORDS

FNAC, Oral Lesions, Palate, Tongue, Histology.

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BACKGROUND

Fine Needle Aspiration Cytology (FNAC) is a well-established, simple and prompt diagnostic modality for lesions of head and neck, especially swellings in thyroid gland, salivary gland and lymph nodes.^[1-11] However, its use in intraoral lesions is limited.^[2-10] This may be because of the unapproachable lesion and non-compliance from the patient. FNAC can

provide an early probable diagnosis and help the clinicians in avoiding or choosing the surgical interventions wherever applicable.^[4-12] Here, we present a series of cases of intraoral lesions diagnosed on cytology in the past 6 years along with their histological correlation and the cytomorphological pitfalls.

MATERIALS AND METHODS

This is a retrospective descriptive study conducted at a tertiary care hospital over a period of 6 years (July 2011 to June 2017). The retrospective data of FNAC of a total 102 cases were obtained. In all cases, FNA was performed intra-orally with a 22-gauge needle attached to 5 mL disposable syringe. In cases of swelling in parapharyngeal region or posterior pharyngeal wall help from the ENT specialists were taken to perform the FNA. Subsequently, both air dried and wet fixed smears were prepared using Giemsa and Papanicolaou stains, respectively. Special stain like Ziehl-Neelsen stain was also done wherever required. Inadequate

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smears were those with only haemorrhagic material or only sparse benign squamous epithelial cells with blood.

A cytological diagnosis included non-neoplastic or neoplastic lesions (Benign/ Malignant) with further mentioning about the definitive cytological diagnosis. Otherwise, a descriptive report with inconclusive or suspicious findings were recorded. Histopathological correlation was done wherever available and considered as gold standard. Statistical analysis was done, and validity rate of cytological results were compared with histological diagnosis.

RESULTS

Out of 102 cases of intraoral FNAC, 82 cases were adequate for cytological evaluation. The rest 20 cases were inadequate for diagnosis and showed either only blood or sparse benign squamous epithelial cells. Among the total adequate cases (n=82), 48 (58.54%) were male and 34 (41.46%) were female. Male: female (M:F) ratio was 1.4: 1. The age of the patients ranged from 8 years to 95 years with a mean age of 45.2 years. The overall distribution of cases according to age revealed maximum number of cases in the age group of 31-50 years when combined together [Table 1].

FNAC was performed from different intraoral sites like tongue [Figure 1B and C], gingival region, buccal mucosa, floor of mouth, soft palate [Figure 1A], hard palate [Figure 1D], tonsil, oropharynx, parapharyngeal/ posterior pharyngeal wall. It was noted that most of the intraoral lesions were located in hard palate and tongue and maximum neoplastic lesions were encountered in hard palate [Table 2].

On cytological evaluation of the total 82 cases, 42 (51.22%) were non-neoplastic and 40 (48.78%) were neoplastic. The non-neoplastic category comprised of- 1) Cystic lesions like epidermal inclusion cyst (EIC), thyroglossal cyst and mucocele/ mucus retention cyst; 2) Inflammatory like non-specific acute and chronic inflammation/ abscess or granulomatous lesion; 3) Vascular lesions; 4) Parasitic infestation like cysticercosis. Non-specific inflammatory pathology was the most common non-neoplastic lesion (22 of 42; 52.38% of all non-neoplastic lesions) were noted in the study [Table 3]. An uncommon case of granulomatous lesion of tongue was also found [Figure 1B and 2C]. However, ancillary investigations ruled out tuberculosis and the patient responded to medical treatment.

The neoplastic category comprised of 29 (72.5%) benign lesions and 11 malignant cases (27.5%) and site wise distribution was recorded [Table 4]. Of all the benign neoplastic lesions, the most common was pleomorphic adenoma (18 of 29; 62.07%) followed by haemangioma (5 of 29; 17.2%), 2 cases each of Warthin's tumour and lipoma (6.9% each) and 1 case each of Schwannoma and inflammatory pseudotumour (3.4% each). The diagnosis of haemangioma was given on cytology in correlation with the radiological diagnosis of haemangioma; hence, aspiration of blood in such cases were not labelled as inadequate.

Among the total 11 malignant cases, squamous cell carcinoma was the most common malignancy (5 of 11; 45.45% cases of all malignant lesions) followed by adenoid cystic carcinoma (4 of 11; 36.36%) and 1 case each of low grade mucoepidermoid carcinoma and non-Hodgkin's lymphoma (9% each).

Histopathology was available in 44 of 102 cases (43.14%). In majority of the neoplastic cases, the histopathological findings were concordant with those of cytological diagnosis [Table 4]. Among non-neoplastic lesions, histology was available in 7 cases. A good correlation was noted in non-neoplastic lesions with histological concordance noted in six of the seven cases (85.71%). One case diagnosed on cytology as epidermal inclusion cyst was reported as squamous papilloma on histology [Figure 2D].

In neoplastic lesions, histological diagnosis was available in 42 cases [Table 4]. A positive concordance rate was noted in 34 of 42 cases (88.89%). The highest concordance was noted in the diagnosis of pleomorphic adenoma with 13 of the 14 cases (92.86%); however, one case showed low-grade mucoepidermoid carcinoma on histology which was reported as pleomorphic adenoma on cytology [Figure 2A]. 2 cases of haemangioma diagnosed on cytology had histological findings and only 1 case showed positive correlation. One case of Schwannoma diagnosed on cytology correlated on histology. In Schwannoma, loose clusters of spindle cells are noted with long slender nuclei.

Statistical analysis was done in both benign as well as malignant cases. After correlating the cytological results with histology findings in benign cases, the following results were obtained: - Sensitivity- 100%, Specificity- 83.33%, Positive predictive value- 88.24%, Negative predictive value- 100% and Positive likelihood ratio- 6. Validity rate of 92.59% was obtained in patients with benign lesions.

Among malignant lesions, all cases of adenoid cystic carcinoma (3 cases) and mucoepidermoid carcinoma (2 cases) had respective histological correlation. There were five cases of squamous cell carcinoma diagnosed on cytology. However, one case was reported falsely positive. The case was reviewed again, which showed dense inflammation and necrosis with few atypical squamous cells; morphology of which was not discernible along with bare nuclei in the background. The reactive atypia probably led to the misdiagnosis [Figure 2B].

There were five false negative cases, which were mainly attributed to sampling error and inadequacy of sample on cytology. These five cases were diagnosed as pleomorphic adenoma (3 cases), haemangioma (1 case) and squamous cell carcinoma (1 case) on histology. There were five cases which were either inadequate or given a descriptive diagnosis on cytology and these five cases were found to be inadequate on histology as well.

On applying the similar set of statistical analysis in malignant cases, the following results were obtained: - Sensitivity- 64.29% with Positive predictive value- 90%. An overall validity rate of 67% was obtained in malignant cases.

Age Group (In Years)	Number of Cases (%)
0-10	02 (2.43)
11-20	04 (4.90)
21-30	06 (7.31)
31-40	23 (28.05)
41-50	29 (35.37)
51-60	08 (9.75)
>60	10 (12.2)

Table 1. Age-Wise distribution of Intraoral Lesions (n= 82)

Sl. No.	Site	Total No. of Cases (%), n=82	Number of Neoplastic Lesions on Cytology (n=40)
1.	Tongue	24 (29.27)	04
2.	Gingival/ Gum region	02 (2.44)	02
3.	Buccal mucosa	10 (12.20)	02
4.	Floor of mouth	06 (7.31)	01
5.	Soft palate	07 (8.54)	03
6.	Hard palate	25 (30.49)	22
7.	Tonsil	04 (4.88)	02
8.	Oropharynx	01 (1.22)	01
9.	Parapharyngeal/ Posterior pharyngeal wall	03 (3.66)	03

Table 2. Site-Wise distribution of Intraoral Lesions (n= 82)

Sl. No.	Lesions	No. of Cases
1.	Cystic Lesions:	
	a. Epidermal inclusion cyst	3
	b. Thyroglossal cyst	2
	c. Mucocele/ Mucus retention cyst	5
2.	Vascular Lesions:	
	a. Haematoma	8
3.	Inflammatory Lesions:	
	a. Acute and chronic inflammation/ abscess	22
	b. Granulomatous lesion	1
	c. Parasitic infestation	1

Table 3. Cytological Diagnosis of Non-Neoplastic Lesions (n= 42)

Cytological Diagnosis	Histological Correlation
Benign	
a. Pleomorphic adenoma (n= 14)	13
b. Haemangioma (n= 2)	01
c. Schwannoma (n= 1)	01
Malignant	
a. Adenoid cystic carcinoma (n= 3)	3
b. Low-grade mucoepidermoid carcinoma (n= 2)	2
c. Squamous cell carcinoma (n= 5)	4

Table 4. Cytological Diagnosis of Neoplastic Lesions with Histologic Correlation (n= 27)

DISCUSSION

Intraoral lesions comprise a wide variety of pathologic lesions with distribution at many distinct anatomical sites.^[2-12] The aetiology of intraoral lesions is not exactly known. However, allergic reaction, dietary habits, betel nut chewing, tobacco use and vitamin deficiency have been noted as underlying causes in many cases. The prevalence rate of intraoral lesions varies from 0.2 - 0.6% with male preponderance.^[4-7]

Though biopsy is used commonly to diagnose these intraoral lesions, but it requires anaesthesia and pose problems in diagnosing the transmucosal lesions. FNAC is frequently used in diagnosis of lesions of head and neck region, but its role in evaluation of intraoral lesions is limited.^[4-10] This is due to the inaccessibility of the intraoral lesions and poor patient's compliance. Other factors which decrease the sensitivity and specificity of FNAC are small size and deeper location of lesions which make it difficult to fix these lesions during FNAC.

However, FNAC can still help in the preliminary evaluation of these lesions and help the clinicians in avoiding unnecessary surgical intervention in many non-neoplastic cases as noted in the present study. There are studies in the literature presenting the role of FNAC in the diagnosis of these intraoral lesions.^[2-20] The present study attempts to highlight the reliability and pitfalls of FNAC in differentiating the non-neoplastic and neoplastic conditions.

Singhal et al^[5] and Gupta et al^[6] included 55 and 157 cases of intraoral lesions in their studies respectively with inadequacy noted in 10% and 07% respectively. However, inadequacy was seen in 19% cases in the present study. The overall frequency of malignant intraoral lesions is varying in the literature ranging from 20% to 70%, whereas it was 30% in our study^[5-9] [Table 5].

The age of the patients in our study ranged from 8 years to 95 years with a mean age of 45.2 years and preponderance of cases in adult. A wide range of age in patients was noted in other studies as well.^[2-15]

In the present study, most intraoral lesions encountered were in hard palate and tongue. Sakarwal et al^[10] reported majority of lesions from the buccal mucosa. Few other studies also showed different regions like pharynx/ oropharynx, mandible and palate as common sites of aspiration.^[5-20]

Among the non-neoplastic cases, non-specific inflammation was noted as the most common lesion and few studies including those by Singh et al^[11] and Sakarwal et al^[10] also noted similar findings. A solitary case of granulomatous lesion of tongue was also noted in the present study; however, specific aetiology could not be established. It is uncommon to find such lesion on the tongue.

A positive correlation was noted in 24 of 27 cases (88.89%) of neoplastic lesion with highest concordance noted in the diagnosis of pleomorphic adenoma. Abrari et al^[12] also reported similar findings.

FNA of pleomorphic adenoma yields thick mucoid to myxoid material, which sometimes become difficult to spread. Cytology reveals ductal epithelial cells, myoepithelial cells and chondromyxoid matrix material. Some cases may show predominantly matrix material with scanty cells or the reverse with abundant myoepithelial and ductal cells; thereby, posing diagnostic difficulties. In our series also, one case of pleomorphic adenoma diagnosed on cytology ultimately came out as mucoepidermoid on histology. This may be due to the interpretation of matrix material as mucus along with presence of squamous metaplastic cells.

Squamous Cell Carcinoma (SCC) was the most common malignant lesion and its frequency in our study was 45%. On reviewing the literature, there was variation in frequency of intraoral SCC.^[18-25] A solitary case of non-Hodgkin's lymphoma noted in the current study was tonsillar in origin. A study by Deng et al^[13] found metastatic lesions in the intraoral region. However, no such case was noted in the present study.

Positive histological correlation was noted in all cases of adenoid cystic carcinoma and mucoepidermoid carcinoma and four out of the five squamous cell carcinoma cases. Adenoid cystic carcinoma reveals hyaline globules; however, no myoepithelial cells are embedded in this matrix. Tumour cells are seen in sheets and dispersed. Cells are monomorphic with scanty cytoplasm, high N: C ratio. Necrosis is usually not seen. Mostly the diagnosis is straight forward; however,

problem arises in solid variant which lacks hyaline globules. In such cases, differentiating the basal cell adenoma and polymorphous low-grade adenocarcinoma becomes difficult. Secondly, mucoepidermoid carcinoma shows predominantly three types of cells: Squamous cells, Intermediate cells and Mucus secreting cells. Background is dirty with mucus and debris. Diagnosis of high-grade mucoepidermoid carcinoma is easier as compared to low-grade, as it may often be mistaken as retention cyst, Warthin's tumour, cystic pleomorphic adenoma or metastatic squamous cell carcinoma with cystic changes.

One case diagnosed as SCC on cytology showed only reactive squamous epithelium on histology. A false positive diagnosis was due to scant representative material along with areas of inflammation, foci of necrosis and atypia on cytology.

Gupta et al^[6] also reported a false-positive case due to inflammatory atypia misinterpreted as SCC on cytology. This emphasises the fact that a diagnosis of SCC in the presence of inflammation should be offered with extreme caution.

There were five false negative cases in the present study, which were mainly attributed to sampling error and inadequacy of sample on cytology. Gupta et al^[6] reported eight false-negative cases of which 6 were due to sampling error, highlighting the fact that sampling of intraoral lesions on FNAC poses problems and can lead to false negative results. The sampling difficulty in some cases was further substantiated by the fact that the five cases which were given a descriptive diagnosis on cytology were found to be inadequate on histology as well. These cases qualify for the need of repeat FNAC or biopsy. In the present series, 88.90% cases had concordant histological correlation [Table 5].^[5-9]

Study Reviewed	Number of Cases	Inadequacy (%)	Histological Correlation (%)	Frequency of Malignant Intraoral Lesions (%)
Gilani et al, ^[7] 2012	40	13.1	96.80	77
Mondal et al, ^[8] 2009	54	3.7	97.00	18.2
Gandhi et al, ^[9] 2011	98	11	90.00	28.0
Gupta et al, ^[6] 2012	157	07	87.70	60.0
Singhal et al, ^[5] 2015	55	10	94.12	50.0
Present Study, 2017	102	19	81.00	30.0

Table 5. Comparative Data of Intraoral FNAC with different Studies^[5-9]

It is a well-known fact that FNAC is considered as a simple and rapid diagnostic modality for preliminary examination of intraoral lesions. It helps in diagnosing a wide spectrum of lesions in this region. Non-neoplastic lesions can be managed conservatively and an early intervention can be made in malignant cases.^[25-32] Sampling error, especially due to patient compliance and unapproachable location attributes to the false negative cases.^[20-32] The present study highlights the importance of FNAC in differentiating the non-neoplastic and neoplastic intraoral lesions, thereby guiding further clinical management.

Figure 1 A-D. A- Swelling over Soft Palate; B- Diffuse Swelling on Ventral Surface of Tongue; C- Swelling at posterior one-third of the Tongue; D- Large Swelling noted on Hard Palate

Figure 2 A-D. A- Cellular Smear showing Clusters of Epithelial Cells with areas of Myxoid Matrix [Giemsa, 200X]; B- Smear showing Epithelial Cells Cluster with Atypia and Focal Keratinous Debris [Giemsa, 400X]; C- Smears from Tongue Swelling revealing Acute and Chronic Inflammatory Cells along with Epithelioid Cell Granuloma [Pap, 200X]; D- Smear showing many benign Mature Squamous Cells in a Haemorrhagic Background [Pap, 400X]

CONCLUSION

FNAC was found to be useful in the diagnosis of variety of lesions in the oral cavity, though few cases can pose diagnostic difficulties. Cytological diagnosis can save many non-neoplastic cases from undergoing surgery or excision biopsy and helps in identifying the malignant cases for early management.

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