DOI: 10.7860/NJLM/2020/44326:2395

Original Article

Pathology Section

Critical Analysis of Pitfalls in Cytological Diagnosis of Salivary Gland Lesions: Experience in a Tertiary Care Centre

NISHA THATTAMPARAMBIL GOPALAKRISHNAN[1], ANURADHA CALICUT KINI RAO[2], SNEHA ADITI[3], P SUPRIYA[4]

ABSTRACT

Introduction: Fine Needle Aspiration Cytology (FNAC) is an important diagnostic method which is used to evaluate and diagnose salivary gland pathologies. Diverse morphological patterns and overlapping features of benign and malignant lesions makes diagnosis a challenge. Application of classic cytological diagnostic criteria and awareness of pitfalls may help to improve performance characteristics of salivary gland FNAC. Accuracy depends on experience; an accurate diagnosis provides superior advantages to clinicians and then to the patients. This study discusses pitfalls in salivary gland FNACs of cases received at a tertiary care hospital.

Aim: To compare the preoperative FNAC findings with the histopathological diagnosis and assess causes of discordance and potential pitfalls of salivary gland lesions in cytology.

Materials and Methods: A retrospective study was conducted in the Department of Pathology, Yenepoya Medical College, Mangalore, Karnataka, India. All salivary gland FNAC smears received from January 2017 to June 2018 were reviewed. Discrepancies were evaluated by two pathologists, taking histopathological diagnosis as gold standard to establish the possible reason for discordance.

Results: In the present study, out of 54 cases of salivary gland FNAC, cyto-histological correlation was available in 22 cases, which formed the study group. Pleomorphic Adenoma (PA) was the commonest lesion in the study group. Out of 22 cases, 8 (36.4%) cases showed discordance. Discordance was seen mostly for Mucoepidermoid Carcinoma (MEC) (4/8), one case each of Salivary Duct Carcinoma (SDC), PA, basal cell adenocarcinoma and Acinic Cell Carcinoma (ACC). Discrepancies were mainly interpretation based.

Conclusion: FNAC is recommended as a very useful, quick, reliable and minimally invasive technique in preoperative diagnosis of salivary gland lesions. Inspite of high sensitivity, there are certain pitfalls due to the misleading diagnostic yields which should be kept in mind. Pitfalls could be due to sampling error, technically suboptimal slides, cystic lesions and misinterpretation of smears.

Keywords: Diagnostic challenge, Fine needle aspiration cytology, Salivary gland cytology

INTRODUCTION

Salivary glands lesions account for less than 3% of all head and neck tumours [1]. Salivary gland swellings could be of varied aetiologies, including benign/malignant tumours, inflammatory processes or cysts. Lesions mimicking salivary gland tumours can arise in lymph nodes, soft tissue, skin and in close proximity to the salivary gland [2]. Clinical examination of the salivary glands alone may not be accurate in distinguishing between enlarged lymph nodes, an inflammatory process or salivary gland tumours. In such cases, the clinical features when correlated with radiological findings on imaging can be of great utility in gleaning information regarding the physical aspects of the lesion and its site, besides defining the association with the adjacent salivary gland. However, imaging techniques alone are often insufficient in revealing the exact nature of the swelling [3]. Hence, a swelling in the region of any salivary gland poses a diagnostic challenge with regards to its site of origin, histological behaviour and tissue diagnosis. A careful history and clinical examination of the swelling, with specific consideration to the duration of disease is required [3].

FNAC is a simple, rapid, safe and an essential diagnostic method used to evaluate major and minor salivary gland lesions which is being increasingly used these days [1,4,5]. It helps in confirming inflammatory nature of lesion over neoplastic aetiology; in case of malignancies, FNAC helps to differentiate a primary tumour from metastasis and a carcinoma from a lymphoma [6]. Different studies reveal high sensitivity and specificity of FNAC with few diagnostic pitfalls. Prior reports indicate a sensitivity of 29% to 97% in detection of malignancy and a high specificity ranging from 84 to 100% [7].

Most salivary gland lesions have well defined cytological features, making the diagnosis seem predictable; however, several factors can often lead to confusion, causing considerable difficulty in interpretation. In addition, some salivary gland malignancies cannot be diagnosed by cytomorphology alone; others can be distinguished from their benign counterparts only by the presence of capsular invasion, which is not appreciated in FNA smears [8]. At times, it is challenging to give a precise diagnosis of benign or malignant lesions on cytology, due to intralesional variabilities and overlapping cytomorphological features that can confound a cytologist [5]. Various factors can greatly impact the diagnosis, including inadequate cytological material aspirated, absence of specific pattern of architecture and considerable overlap of cytomorphological feature between different lesions in the salivary gland [9]. Sampling, observational or interpretational errors affect the final diagnosis rendered. Therefore, awareness of pitfalls and application of classic criteria will help to improve the performance characteristics of salivary gland FNAC in daily practice [10]. Thus, this study was aimed to compare the preoperative FNAC findings with their histopathological diagnosis and discuss the causes for discordance and identify the potential pitfalls of salivary gland lesions in cytology.

MATERIALS AND METHODS

A retrospective study was conducted between January 2017 and June 2018 to review FNAC findings of histopathologically diagnosed salivary gland lesions at Department of Pathology, Yenepoya Medical College, Mangalore, Karnataka, India. Discrepancies were evaluated, taking histopathological diagnosis as gold standard to

know the cause of discordance and potential diagnostic pitfalls. Ethical clearance was not required as it was a retrospective audit using diagnosed cytological and histopathological slides.

All the salivary gland FNACs which had histopathological diagnosis were identified during the study period. Slides were retrieved from the department. All the faded slides were restained using Papanicolaou (PAP) stain. The histopathological findings and clinical profiles including demographic data were obtained with the help of a histopathological request form and the Medical record department of the institute. Wherever available, the diagnostic information from FNAC was compared with that of histopathological findings to establish correlation of the results. When diagnosis differed between the two samples, the cases were reviewed by two pathologists, unaware of the prior diagnosis to establish possible underlying reasons for this discordance.

STATISTICAL ANALYSIS

Data was entered in excel sheet. Cytological features were compared with histopathological findings and a descriptive analysis was done for discordance.

RESULTS

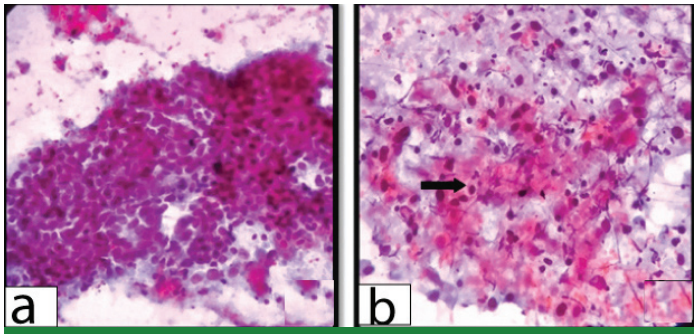
In the present study, out of 54 cases of salivary gland FNAC, cyto-histological correlation was available in 22 cases. Out of the total 54 cases, two cases were excluded due to sparse cellularity. The most common gland involved was Parotid gland. PA was the commonest lesion in the study. Out of 22 cases, 8 (36.4%) showed discordance. Discordance was seen mostly for MEC (4/8), one case each of SDC, PA, basal cell adenocarcinoma and ACC [Table/Fig-1].

Sl no	Age	Sex	Site	Cytologic diagnosis	Histopathologic diagnosis
1	72	Male	Submandibular	Metastatic squamous cell carcinoma	MEC- High grade
2	55	Female	Parotid	Pleomorphic adenoma	MEC- Intermediate grade
3	56	Male	Submandibular	Metastatic squamous cell carcinoma	MEC- High grade
4	55	Female	Parotid	Sialadenosis	Cellular pleomorphic adenoma
5	64	Female	Parotid	Pleomorphic adenoma	Basal cell adenocarcinoma
6	60	Male	Submandibular	Metastatic squamous cell carcinoma	Salivary duct carcinoma
7	42	Female	Parotid	Pleomorphic adenoma	MEC-Low grade
8	40	Male	Parotid	Cellular pleomorphic adenoma/ Monomorphic adenoma	Acinic cell carcinoma

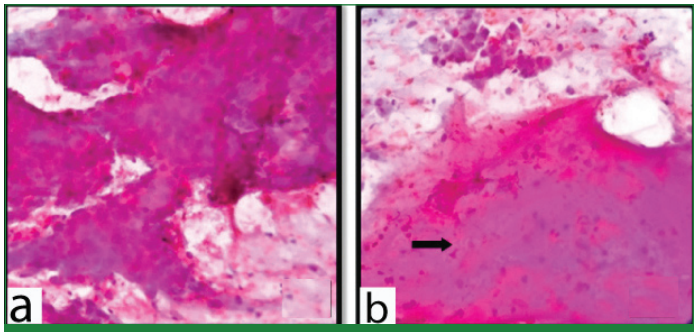
[Table/Fig-1]: Summary of discordant cases in present study.
MEC: Mucoepidermoid carcinoma

The case 01 and case 03 [Table/Fig-2] were submandibular lesions. FNAC showed predominantly squamoid cells with dyskeratotic cells and eosinophilic material in the background and were diagnosed as metastatic Squamous Cell Carcinoma (SCC). On Histopathological Examination (HPE), predominance of diffuse sheets, cords, nests of squamoid cells with moderate pleomorphism was noted with few nests of Periodic Acid–Schiff (PAS) positive clear cells along with extensive areas of necrosis, hence, a final diagnosis of MEC- high grade was rendered.

The case 02 and case 07 [Table/Fig-3] showed cellular smears composed of epithelial and myoepithelial cells embedded in myxoid stromal matrix on FNAC and were diagnosed as PA. On histology, case 2 showed nests and sheets of tumour cells predominantly squamoid admixed with clear and intermediate cells and was diagnosed as MEC-intermediate grade. Case 7 showed variably sized glands lined by columnar and mucous cells; focally by intermediate cells in extensive mucin pools and a diagnosis of low grade MEC was offered.

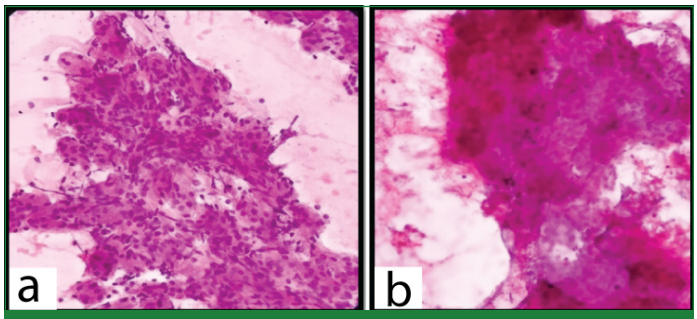


[Table/Fig-2]: FNAC showing: (a) predominantly squamoid cells; (b) background dyskeratotic cells and eosinophilic material marked with arrow; Diagnosed as metastatic SCC. (PAP, x100).



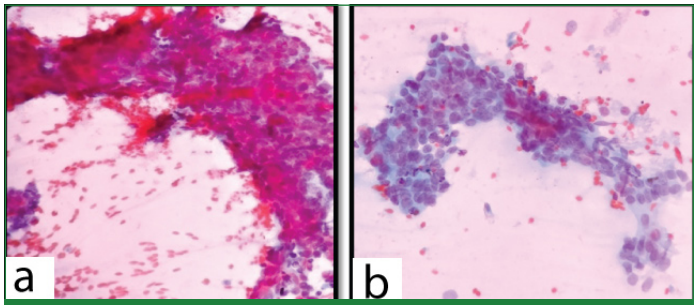
[Table/Fig-3]: Cellular smears composed of: (a) epithelial and myoepithelial cells; (b) embedded in myxoid stromal matrix (arrow); Diagnosed as pleomorphic adenoma (PAP, x100).

The case 4 [Table/Fig-4] on cytology showed, normal acinar epithelial cells in sheets, acini adherent to fibrovascular stroma with sparse inflammation in background and the diagnosis of sialadenosis was rendered. HPE however exhibited biphasic population of epithelial and myoepithelial cells with stroma showing myxoid and hyalinised areas and was diagnosed as PA.



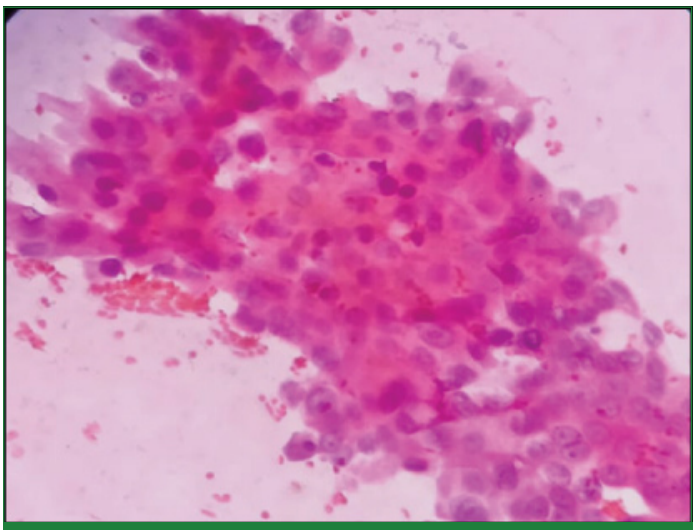
[Table/Fig-4]: FNAC showing: (a) normal acinar epithelial cells in sheets, acini; (b) adherent to fibrovascular stroma; with sparse inflammation in background; diagnosed as Sialadenosis (PAP, x100).

The case 05 [Table/Fig-5] on cytology showed monomorphous population of ductal epithelial cells admixed with spindled and plasmacytoid myoepithelial cells in a background of fibromyxoid stroma and was diagnosed as PA. On histology, small tumour cells in nests, islands, acinar and cribriform pattern with focal palisading in a fibrous stroma was noted and diagnosed as basal cell adenocarcinoma.



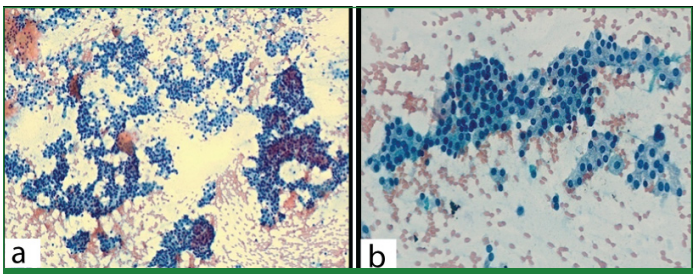
[Table/Fig-5]: (a,b) Monomorphous ductal epithelial cells admixed with spindled and plasmacytoid myoepithelial cells in a background of fibromyxoid stroma; Diagnosed as pleomorphic adenoma (PAP, x100).

The case 06 [Table/Fig-6] showed sheets of tumour cells having oncocytic appearance with vesicular nuclei in a necrotic background on cytology and a differential diagnosis of SCC/MEC high grade was rendered on cytology. Histology showed oncocytic tumour cells in nests, expanded ducts with central comedo necrosis diagnostic of SDC.



[Table/Fig-6]: Sheets of tumour cells having oncocytic appearance with vesicular nuclei in a necrotic background. Differential diagnosis: Squamous carcinoma/MEC high grade (PAP, 40x).

The case 8 [Table/Fig-7] showed cellular smears with predominantly epithelial cells in poorly cohesive sheets, clusters, groups and scattered singly. Cells are round-oval with ovoid nuclei, bland finely granular chromatin and moderate cytoplasm. Few myoepithelial cells were seen. Background showed scant myxoid stroma, hyaline material and haemorrhage and was diagnosed as Cellular PA/ Monomorphic adenoma. On histology, lobules, island of basophilic acinic tumour cells were seen, diagnostic of ACC.



[Table/Fig-7]: FNAC smears displaying: (a) cellular smears with predominantly epithelial cells in poorly cohesive sheets, clusters, groups and scattered singly; (b) Cells were round-oval with ovoid nuclei, bland finely granular chromatin and moderate cytoplasm; Diagnosed as Cellular pleomorphic adenoma/ Monomorphic adenoma. (PAP, x100)

DISCUSSION

FNAC of salivary gland lesions are routinely practiced, useful, quick, reliable, minimally invasive and less traumatic diagnostic modality in use; however, various challenges in interpretation are encountered during pathology practices [4,11]. The overall accuracy has been reported to be 87% to 100% in distinguishing benign from malignant lesions [5]. FNAC of salivary lesions is challenging due to heterogenous and overlapping cytological features that account for the indeterminate or "suspicious" diagnosis. False positive and false negative diagnosis account for problems and pitfalls in cytologic interpretation [11].

Parotid gland was the most commonly involved gland in present study, next being submandibular gland. Similar observations were made by Gao N et al., and Ashraf A et al., in their studies [12,13].

Majority of malignant salivary gland tumours, clinically behave in a manner similar to benign tumours. Hence, the primary challenge of FNAC is to differentiate benign lesions from malignant lesions, followed by subtyping the lesions. Thus, all suspected salivary gland lesions should be assessed by a step by step approach. The first aim is to decide whether the lesion is of salivary gland origin or not. Second step is to identify the cells and their morphology, then to classify them into non-neoplastic and neoplastic categories; then further categorise into benign or malignant [4,8]. Some diagnostic problems do occur in differentiating benign from malignant lesions and are the cause for diagnostic pitfalls [8]. To overcome the pitfalls and increase the accuracy of FNAC, several modifications were attempted such as pattern-based analysis. Similar to the Bethesda system for reporting cervical and thyroid cytology, the International experts in salivary gland cytopathology proposed the Milan system in 2015, which is a risk-based stratification system; that brings uniformity among cytopathologists, in reporting across the world [14,15].

Pitfalls in diagnosis may be due to sampling problems including false negative diagnosis in cystic tumours like PA, Warthins Tumour (WT), low grade MEC and ACC; small size of lesion, regenerative epithelial hyperplasia and squamous metaplasia in sialadenitis or WT. Other sources of errors could be due to cases of PA showing increased cellularity and focal atypia in epithelial cells; cytological overlap may be noted in some tumours, like hyaline stromal globules a feature considered to be diagnostic of ACC can be seen in other tumours. Thus, a diagnostic approach based on specific cytologic criteria is needed to avoid misinterpretation of FNAC smears [8]. Since, the cytodiagnosis of salivary gland lesions is challenging due to its complexity of cytological features, Miller proposed a five group cytodiagnostic approach for salivary gland lesions as follows: 1) myxoid-hyaline;

Sl no	Type of lesion	Differential diagnosis to be kept in mind
1	Myxoid hyaline	**Salivary gland tumour** 1. Benign mixed tumours 2. Adenoid cystic carcinoma 3. Carcinoma Ex Benign mixed tumour (PA) 4. Polymorphous low grade adenocarcinoma **Non-salivary gland tumours** 1. Schwannoma 2. Myxoma 3. Myxoid lipoma 4. Myxoid neurofibroma
2	Basaloid	1. Basal cell adenoma 2. Basal cell carcinoma 3. Solid variant of Adenoid cystic carcinoma 4. Polymorphous low-grade adenocarcinoma 5. Small cell undifferentiated carcinoma
3	Oncocytoid	**Intraglandular oncocytic lesions:** 1. Warthin's tumour 2. Oncocytoma 3. Acinic cell carcinoma **Extraglandular oncocytic lesions:** 1. Paraganglioma 2. Carcinoid 3. Granular-cell tumour 4. Rhabdoid tumours 5. Renal cell carcinoma 6. Melanoma 7. Medullary carcinoma 8. Hurthle cell carcinoma 9. Hepatocellular carcinoma
4	Lymphoid	1. Chronic sialadenitis 2. Benign lymphoepithelial lesions 3. Intra-/ peri-salivary gland lymph nodes 4. Warthin's tumour 5. Lymphoepithelial carcinoma 6. Metastasis to intra-/ peri-parotid lymph node
5	Squamoid lesions	**Non-neoplastic lesions** 1. Retention cyst/mucoceles **Benign congenital cysts extrinsic to salivary glands** 1. Branchial cleft cysts 2. Thyroglossal duct cysts 3. Thymic cysts 4. Dermoid/epidermal inclusion cysts **Malignant cystic lesions** 1. Squamous cell carcinoma

[Table/Fig-8]: Miller's five group approach in salivary gland cytodiagnosis [4,16].

2) basaloid; 3) oncocytoid; 4) lymphoid; and 5) squamoid lesions. Differential diagnosis of the lesion based on these morphologies is given in [Table/Fig-8] [4,16].

MEC is the most common malignant tumour of major salivary glands that posed a major diagnostic challenge in present study. The challenge pertains to cytodiagnosis and cytological typing. Various studies state that false-negative diagnosis usually occur due to fluid causing dilution of tumour cells, inflammatory cells and debris obscuring the tumour cells [8]. Two out of four cases were erroneously diagnosed as PA and another two cases as Metastatic SCC on FNAC. On FNAC, the intermediate cell population of MEC closely resembled myoepithelial cells of PA. The stranded stroma, crushed nuclei and exudate plasma mimicked myxoid stroma of PA which caused erroneous diagnosis in present cases. A definitive diagnosis of MEC in FNAC smears requires the co-existence of cells showing squamous differentiation and mucin-secreting cells [17]. But, detection of intracellular mucin is the key feature. Special stains like Periodic Acid–Schiff–Diastase (PAS-D) and mucicarmine may help in confirming the mucinous material [5]. In a study by Kotwal M et al., three out of four cases were misdiagnosed as PA [18]. Two of the cases of MEC in the present study were misdiagnosed as Metastatic SCC since only squamous cells were aspirated on FNAC; however, there was no change in the mode of treatment. In these cases, the study observed that more extensive sampling of the lesion and rendering a diagnosis of malignant lesion with a list of differential diagnosis would have been a better option rather than rendering a direct final report [5].

Another frequently observed difficulty in interpretation of salivary gland lesions on FNAC include expected cytomorphological variations of PA [8]. Multiple sampling from different sites of the tumour is important to overcome this pitfall due to the variability of morphology in different parts of the same tumour [15]. The diagnosis of PA is usually straight forward when there is a good mixture of both epithelial and stromal components. Diagnostic problems arise when there is a marked overgrowth of one of the components. In cases where there is predominance of stromal material, it can be mistaken for mucus, which is seen in benign cyst or low grade MEC. Predominance of myoepithelial cells can be mistaken for myoepithelioma or spindle cell soft tissue tumour. Other possible misdiagnosis includes epithelial cell predominant smears being misdiagnosed as ACC or other epithelial neoplasms depending on cell type; the presence of a mixture of glandular, squamous and mucinous cells, may be mistaken for MEC [19]. Diagnostic problems can also arise, if there is presence of hyaline globules or bizarre cells [20].

While studying histopathological features in PA that could most likely be a forerunner of malignancy, researchers noted that abundant hyalinisation and the presence of moderate mitotic activity were the most likely indicators of development of malignancy, as compared to their absence in PA. The clinical indicator for the same was sudden rapid growth in a tumour present since a long duration [8].

In present study, one case of PA was misdiagnosed as sialadenosis on FNA, as only acinar and benign ductal epithelial cells were present. The myxoid stroma was very scant. It could be due to sampling error. This highlights the importance of multiple sampling especially in small sized lesion.

One case of basal cell adenocarcinoma was misinterpreted as PA on FNAC. Smears being highly cellular with monomorphous ductal epithelial cells and scant stromal component with scattered myoepithelial like cells in the background were mistaken for a cellular PA. Biopsy however, showed classical histopathological findings of basal cell adenocarcinoma. This misinterpretation occurred as basaloid nature of cells and peripheral palisading of nuclei, due to which atypia was seen to be focal and hence, overlooked on cytology.

One case of SDC was misdiagnosed as metastatic SCC. SDC are difficult to diagnose specifically on FNAC. SDC should be included in differential diagnosis in FNACs of a cystic lesion with papillary or cribriform architectural pattern and presence of eosinophilic cells. Eccentric nuclei showing intranuclear inclusions are considered characteristic cytologic finding in SDC [21]. This was not appreciated in this case and oncocytic cells were mistaken for squamoid cells and hence, misinterpreted as high grade MEC.

One case of ACC was misdiagnosed as cellular PA or monomorphic adenoma because of scant stroma, no pleomorphism, very few bare nuclei and loosely cohesive intermediate sized epithelial cells. Retrospective analysis of FNAC smears showed resemblance of normal salivary smears with monolayered sheets, small groups of acinar cells with abundant granular, vacuolated, clear cytoplasm with eccentric, uniform, round nuclei, absence of well-formed ducts and acini and bare nuclei in clean background. ACC is the most likely low grade malignant salivary gland neoplasm to be misdiagnosed as benign and is difficult to recognise on cytology due to innocuous nature of acinar cells [22]. It also lacks the hallmark morphologic features of malignancy such as necrosis, cellular pleomorphism, and high mitotic activity [23]. Monotonous acinar cellularity of a well differentiated ACC resembles hyperplastic or normal salivary gland, but latter is intermingled with adipose tissue and ductal epithelial cells. ACC have predominance of acinar cells

Case Number	Histopathologic diagnosis	Classic cytological features	Pitfalls in FNAC Diagnosis in Present Study
1,3	MEC- High grade	Co-existence of cells showing squamous differentiation and mucin secreting cells. Obviously malignant squamous epithelial cells [17].	Malignant: Metastatic SCC. Predominantly squamoid cells on FNAC with dyskeratotic cells and eosinophilic material in background.
2,7	MEC- Low and Intermediate grade	Low cellularity; dirty background of mucus and debris; Various cell types predominantly intermediate cells, some mucous cells and infrequently squamous cells [4].	Benign: Pleomorphic adenoma. Intermediate cell population of MEC closely resembled myoepithelial cells of PA; Stranded stroma, crushed nuclei and exudated plasma mimicked myxoid stroma of PA.
4	Cellular pleomorphic adenoma	Variable cellularity; mainly spindle shaped myoepithelial cells in single, in poorly cohesive clusters, sheets; embedded in thick, sticky, fibrillary chondromyxoid stromal matrix [4].	Benign: Sialadenosis Only acinar and benign ductal epithelial cells present. The myxoid stroma was very scant. Due to sampling error.
5	Basal cell adenocarcinoma	Numerous small basaloid cells in singles, multilayered clusters; occasional peripheral palisading; scanty cytoplasm and rounded nuclei; scanty inconspicuous stroma [4].	Benign: Pleomorphic adenoma Highly cellular with monomorphous ductal epithelial cells and scant stromal component with scattered myoepithelial like cells in the background.
6	Salivary duct carcinoma	Malignant epithelial cells in singles and clusters; cells have abundant cytoplasm, squamoid, sometimes oncocytic like; no stromal component; background necrotic debris; [4] intranuclear inclusions and nuclear eccentricity of cells [21].	Malignant: Metastatic SCC Oncocytic cells were misinterpreted for squamoid cells; intranuclear inclusions and nuclear eccentricity as characteristic cytologic finding was not appreciated.
8	Acinic cell carcinoma	Acinar cells in clusters; abundant, fragile, finely vacuolated cytoplasm; rounded medium sized nuclei with mild to moderate anisokaryosis and bland chromatin; clean background without ductal cells or stroma [4].	Benign: Cellular pleomorphic adenoma/ Monomorphic adenoma. Resemblance of normal salivary smears with monolayered sheets, scant stroma, no pleomorphism, very few myoepithelial cells, intermediate sized epithelial cells lead to an interpretational error.

[Table/Fig-9]: Summary of diagnostic pitfalls in FNAC in present study.

with presence of azurophilic granules, absence of ductal cells and plenty of bare nuclei in the background. A College of American pathologist interlaboratory control program revealed that 49% were called benign on cytology. Lack of familiarity with cytological features may lead to diagnostic difficulty and pitfalls [24], summary of which is shown [Table/Fig-9].

Limitation(s)

Limitation of this study was the sample size; many of the FNAC cases did not have histological correlation and hence, could not be included in the study. This severely restricted the number and type of salivary gland lesions that could be analysed for discordance in this study.

CONCLUSION(S)

FNAC is recommended as a preliminary investigation, in conjunction with thorough clinical history, physical examination and radiological findings to render a correct diagnosis in salivary gland lesions. Furthermore, an adequate and representative sample is essential for proper cytological evaluation and to reduce errors in diagnosis. A cautious approach towards salivary gland lesions is highly recommended keeping in mind the cytological overlaps and pitfalls in salivary glands FNAC. Pitfalls could be due to uncertainty of site, sampling error, cystic lesions, lack of architectural patterns and overlapping cytological features leading to misinterpretation of smears. In smears where a definitive cytological diagnosis is not possible, listing of the differential diagnosis or re-aspiration in scant smears is advisable.

REFERENCES

[1] Singh A, Haritwal A, Murali BM. Correlation between cytology and histopathology of the salivary gland. Australas Med J. 2011;4(2):66.
[2] Chan MK, McGuire LJ. Cytodiagnosis of lesions presenting as salivary gland swellings: A report of seven cases. Diagn Cytopathol. 1992;8:439-43.
[3] Zurrida S, Alasio L, Tradati N, Bartoli C, Chiesa F, Pilotti S. Fine- needle aspiration of parotid masses. Cancer. 1993;72:2306-11.
[4] Rajendra Santhosh AB, Bakki SR, Mantapuri S. A review of research on cytological approach in salivary gland masses. Indian J Dental Res. 2018;29:93-106.
[5] Ul-Aan N, Tanwani AK. Pitfalls in salivary gland fine-needle aspiration cytology. Int J of Pathol. 2009;7(2):61-65.
[6] Arul P, Akshatha C, Masilamani S, Jonathan S. Diagnosis of salivary gland lesions by fine needle aspiration cytology and its histopathological correlation in a tertiary care center of southern India. J Clin Diagn Res. 2015;9(6):EC07-EC10.
[7] Inancli HM, Kanmaz MA, Ural A, Dilek GB. Fine needle aspiration biopsy: In the diagnosis of salivary gland neoplasms compared with histopathology. Indian J Otolaryngol Head Neck Surg. 2013;65(1):121-25.
[8] Ameli F, Baharoom A, Md Isa N, Noor Akmal S. Diagnostic challenges in fine needle aspiration cytology of salivary gland lesions. Malays J Pathol. 2015;37(1):11-18.
[9] Supreetha MS, Hemalatha A, Bhaskaran A. Salivary gland tumours: Features not to be missed on cytology. A study of five cases. IP J Diagn Pathol Oncol. 2019;4(1):50-53.
[10] Lü BJ, Zhu J, Gao L, Xie L, Xu JY, Lai MD. Diagnostic accuracy and pitfalls in fine needle aspiration cytology of salivary glands: A study of 113 cases. Zhonghua Bing Li Xue Za Zhi. 2005;34(11):706-10.
[11] Saldanha CS, Fernandes H, Fazalbhoy Z, Jayaprakash CS, Sumanth D, Kini R. Diagnostic accuracy and pitfalls in fine needle aspiration cytology of salivary gland lesions. Ann Pathol Lab Med. 2017;4(3):A274-78.
[12] Gao N, Li Y, Li LJ, Wen YM. Clinical analysis of head and neck cancer cases in south-west China 1953–2002. J Int Med Res. 2009;37(1):189-97.
[13] Ashraf A, Shaikh AS, Kamal F, Sarfraz R, Bukhari MH. Diagnostic reliability of FNAC for salivary gland swellings: A comparative study. Diagn Cytopathol. 2010;38(7):499-504.
[14] Zubair B, Andrew SF, Nora K, Bruce MW. The Milan System for Reporting Salivary Gland Cytopathology. In: William CF, Esther DR, editors. The Milan System for Reporting Salivary Gland Cytopathology. 1st ed. American Society of Cytopathology. Springer International Publishing AG; 2018. p. 2-4.
[15] Amita K, Rakshitha HB, Singh A, Shankar SV. Evaluation of accuracy of Milan system for reporting salivary gland cytology: Review of morphology and diagnostic challenges in each category. J Cytol. 2020;37(1):18-25.
[16] Miller TR. FNA of salivary gland: Problems and pitfalls. San Francisco: Director of Cytology, University of California; 2006.CAP.org document.
[17] Orell SR, Sterret GF, Whitaker D, editors. Fine Needle Aspiration Cytology, 5th ed. Edinburgh: Churchill Livingstone-Elsevier; Philadelphia.2012:62-63.
[18] Kotwal M, Gaikwad S, Patil R, Munshi M, Bobhate S. FNAC of salivary gland-A useful tool in preoperative diagnosis or a cytopathogist's riddle? J Cytol. 2007;24(2):85.
[19] Verma K, Kapila K. Role of fine needle aspiration cytology in diagnosis of pleomorphic adenomas. Cytopathology. 2002;13(2):121-27.
[20] Takeda Y. An immunohistochemical study of bizarre neoplastic cells in pleomorphic adenoma: Its cytological nature and proliferative activity. Pathol Int. 1999;49(11):993-99.
[21] Khurana KK, Pitman MB, Powers CN, Korourian S, Bardales RH, Stanley MW. Diagnostic pitfalls of aspiration cytology of salivary duct carcinoma. Cancer. 1997;81(6):373-78.
[22] Prieto-Rodríguez M, Artés-Martínez MJ, NavarroHervás M, Camañas-Sanz A, Vera-Sempere FJ. Cytological characteristics of acinic cell carcinoma (ACC) diagnosed by fine-needle aspiration biopsy (FNAB). A study of four cases. Med Oral Pathol Oral Cir Bucal. 2005;10(2):103-08.
[23] Al-Zaher N, Obeid A, Al-Salam S, Al-Kayyali BS. Acinic cell carcinoma of the salivary glands: A literature review. Hematol Oncol Stem Cell Ther. 2009;2(1):259-64.
[24] Sharma A, Ahuja S, Diwaker P, Wadhava N, Arora VK. Acinic cell carcinoma of the parotid gland: A diagnostic dilemma on cytology. Malaysn J Pathol. 2019;41(2):191-94.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Pathology, Yenepoya Medical College, Yenepoya Deemed to be University, Mangalore, Karnataka, India.
2. Professor, Department of Pathology, Yenepoya Medical College, Yenepoya Deemed to be University, Mangalore, Karnataka, India.
3. Postgraduate Student, Department of Pathology, Yenepoya Medical College, Yenepoya Deemed to be University, Mangalore, Karnataka, India.
4. Assistant Professor, Department of Pathology, Yenepoya Medical College, Yenepoya Deemed to be University, Mangalore, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Anuradha Calicut Kini Rao,
Department of Pathology, Yenepoya Medical College, Deralakatte, Mangalore-575018, Karnataka, India.
E-mail: rao.anuradhack@yahoo.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Mar 13, 2020
- Manual Googling: May 27, 2020
- iThenticate Software: Jun 10, 2020 (16%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Mar 12, 2020**
Date of Peer Review: **Apr 30, 2020**
Date of Acceptance: **May 28, 2020**
Date of Publishing: **Jul 01, 2020**