Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

ORIGINAL ARTICLE

THE EFFICACY OF FINE NEEDLE ASPIRATION CYTOLOGY IN DIAGNOSING SALIVARY GLAND SWELLINGS: A 6-YEAR STUDY CORRELATING CYTOLOGICAL AND HISTOLOGICAL FINDINGS.

AJAY SINGH THAKUR [1], RUBY SAHU[2], ADITI DAS [3], CHANDRASHEKHAR INDORIA[4*], APURVA AGRAWAL [5]

[1] Associate professor, Department of Pathology, Shree Balaji Institute of medical sciences, Raipur, Chhattisgarh, India

[2] Assistant professor, Department of Pathology, Bharat Ratna Late Shree Atal Bihari Vajpayee Memorial Medical College, Rajnandgaon, Chhattisgarh, India

[3] Associate professor, Department of Pathology, Shree Balaji Institute of medical sciences, Raipur, Chhattisgarh, India

[4] Associate professor, Department of Pathology, Bharat Ratna Late Shree Atal Bihari Vajpayee Memorial Medical College, Rajnandgaon, Chhattisgarh, India

[5] Assistant professor, Department of Pathology, Shree Balaji Institute of medical sciences, Raipur, Chhattisgarh, India

Corresponding Author: Chandrashekhar Indoria[4]

Department of pathology, BRLSABVM GovernmentMedical College, Pendri, Rajnandgaon, Chattisgarh,India,491441

Mobile number--+918818967626,+919406355748

E-mail id—dr.csindoria@gmail.com

Abstract

Background: FNAC is a safe, reliable, cost-effective, and efficient method for initial screening of patients with salivary gland swellings.

Aims: The purpose of this study was to identify cytomorphological features and toevaluate the diagnostic efficacy of FNAC as a screening tool for salivary gland swellings.

Materials and Methods: A study included 195 cases of FNAC, with 62 cases being compared to histological diagnosis. Subsequently, discordant cases, including both false negatives and false positives, were retrospectively re-evaluated. Additionally, a thorough review of previous research on the factors that contribute to misdiagnosis was conducted.

Results: On cytology, 110 cases were neoplastic, of which 73 were benign and 37 were malignant. Histopathological correlation was available in 62 cases, 42 of which were benign and the remaining 11 were malignant**.** When suspected malignant and malignant group are all classified as cytologically positive, the sensitivity and specificity are 72.73% and 96.08% respectively. Overlapping cytological features, heterogeneity and unsampled areas were the primary factors contributing to false positive and false negative diagnosis.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

Conclusion: FNAC of salivary lesions is a precise, sensitive, and specific initial diagnostic procedure. However, the characterization of specific tumor types is limited due to variations in cytomorphology. False-negative diagnoses are mainly due to issues with the specimens obtained, while false-positive diagnoses are primarily caused by errors in interpretation. Cytopathologists should improve their skills and standards to avoid making false-positive diagnoses. In challenging cases, histologic examination may be used for accurate diagnosis.

Keyword: FNAC, salivary gland, misdiagnoses, false negative, false positive, efficacy.

Introduction

Diagnosing salivary gland pathology through fine needle aspiration cytology is challenging in cytopathology due to the diversity of salivary gland lesions, intratumoral heterogeneity, and morphological overlap[1,2,3,4] However, it is a widely accepted, cost-effective, and minimally invasive technique for the rapid cytological evaluation of salivary gland lesions. Various factors can cause nodular swelling or diffuse enlargement of salivary glands, including inflammation, cystic changes, and benign and malignant neoplasms. Salivary gland neoplasms account for 2-6% of all head and neck neoplasms[5]. FNAC (fine needle aspiration cytology) helps differentiate between benign and low-grade malignant neoplasms and high-grade malignant tumors [6,7].The Milan System for Reporting Salivary Gland Cytology has been introduced to address diagnostic challenges in the diagnosis and risk assessment of salivary gland lesions.[8,9]However, histopathology remains the gold standard for diagnosing salivary gland lesions. In view of the above consideration, the present study aims to assess the importance of cytological study of salivary gland masses and correlate it with histopathological examination to facilitate the diagnosis and treatment.

Material and method

Study subjects, sampling, technique and data acquisition

The current study, spanning six years, covering the period from January 2008 to January 2013. The study was conducted at the Department of Pathology, Pt. J.N.M. Medical College and its associated Dr. B.R.A.M.Hospital in Raipur, Chhattisgarh, India. The prospective study involved selecting cases from patients with salivary gland masses who were attending the ENT outpatient department and inpatient facilities. Ethical considerations were addressed by obtaining approval from the institutional ethics committee, and written consent was obtained from each patient. FNAs were conducted using palpation or ultrasound guidance, without on-site evaluation. The aspirates were prepared as direct smears. Smear made from the centrifuged deposit in the case of aspirated fluid. Staining of the wet fixed smears was done with Papanicolaou stain/ Haematoxylin and Eosin and air dried smears were stained with MGG (May Grunwald and Giemsa) stain. The cases were initially classified into benign lesions and malignant lesions (including those suspicious for malignancy as well). The final histopathological diagnosis was correlated with the FNAC findings to assess the precision of cytodiagnosis.

False negative and false positive diagnoses

Non-diagnostic cases were not included in the analyses. False-negative and false-positive diagnoses were defined as cases in which the results of the fine needle aspiration (FNA) did not

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

correspond with the findings of the final histological examination. A false-negative diagnosis is defined as a nodule that was initially determined to be benign lesion (non neoplastic and benign neoplastic lesion) through fine-needle aspiration cytology (FNAC), but it was discovered to be malignant lesion upon histological examination. Conversely, a false-positive diagnosis was described as a nodule with cytology indicating malignancy (suspicious for malignancy and malignant lesion) that was later found to be a nonneoplastic lesion or benign neoplasm upon histological analysis after surgery. All slides from the false-negative and false-positive FNAs were reexamined to determine the cause of misdiagnoses.

Statistical analysis

Statistical analysis was conducted to evaluate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy. IBM SPSS Statistics (version 19.0) was used for the analysis, and the chi-square test was employed for the primarily categorical variables. Cohen's kappa (κ) coefficient was utilized to assess the agreement between the FNA and pathology results. P value of <0.05 was considered statistically significant.

Result

During the period from January 2008 to January 2013, we conducted a comprehensive review of 195 cases of salivary gland fine-needle aspiration cytology (FNAC). The distribution of benign and malignant salivary gland lesions among the total 195 FNACs was as follows: 158(81%) and 37(19%), respectively. The patients' ages ranged from 1 to 65 years, with a mean age of 40.3 years. Non-neoplastic lesions accounted for 85 cases (43.5%), while 110 cases (56.4%) were neoplastic. Chronic sialadenitis was the most common lesion (95%, 81/85), followed by cystic lesions (4.7%, 4/85). Among the neoplastic lesions, 66.3% of cases (73/110) were benign, while 33.63% (37/110) were malignant. In benign tumors, pleomorphic adenoma accounted for the highest number of cases (89%, 65/73), followed by Warthin's tumor (4.1%, 3/73). In malignant lesions, 40.5% (15/37) of cases were diagnosed under the malignant neoplasm NOS category (cytologic diagnosis of malignancy was made without further tumor typing), followed by acinic cell carcinoma (21.6%, 8/37), mucoepidermoid carcinoma (16.2%, 6/37), adenoid cystic carcinoma (10.8%, 4/37), and adenocarcinoma (10.8%, 4/37). [Table-1].

In the present study, both cytology and histopathology were carried out in 62 cases. Out of these, 52 cases had benign salivary gland lesions, while 10 cases had malignant lesions. The FNA findings were correlated with the corresponding histological diagnosis. 92.3% of benign tumors were consistent with the histopathological diagnosis. In the malignant group, 80% of tumors showed concordance with histopathology. [Table-2,3]. Two cases initially diagnosed as pleomorphic adenoma on FNAC were later confirmed to be adenoid cystic carcinoma, and one case of pleomorphic adenoma was confirmed to be carcinoma ex pleomorphic adenoma on subsequent histopathology.One case of mucoepidermoid carcinoma on cytology was later confirmed to be pleomorphic adenoma. One case diagnosed as malignant tumour not otherwise specified on aspiration cytology was later confirmed to be basal cell adenoma.

The results of the assessment comparing the findings of fine-needle aspiration cytology (FNAC) with the final histopathology results of the patients are presented in [Table 4]. Upon inspection of

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

the aforementioned table, a significant correlation was identified between the two measurements (κ: 0.713, p<0.001). The test sensitivity was found to be 72.73%, while the specificity was determined to be 96.08%. Based on the results of the FNAC test, the positive predictive value (PPV) for malignancy was 76.63%, while the negative predictive value (NPV) for benign cases was 95.24%.

Table 01. Demographic and clinical data of the study patients

Characterstics			**n or mean**
Age	Total number of lesion (n=195)		40.3
FNAC cases (n=195)	Non neoplastic lesion		85
	Neoplastic lesion	Benign	73
		Malignant	37
FNAC cases (n=195)	Benign lesion (n=158)	Sialadenitis	81
		Pleomorphic adenoma	65
		Warthins tumour	03
		Benign cystic lesion	04
		Sialadenosis	02
		Retention cyst	01
		Oncocytoma	01
		Myoepithelioma	01
	Malignant neoplastic lesion (n=37)	Malignant tumour without typing	15
		Acinic cell carcinoma	08
		Mucoepidermoid carcinoma	06
		Adenoid cystic carcinoma	04
		Adenocarcinoma	04
Histopathological confirmed cases (n=62)	Non neoplastic lesion (n=09)	Sialadenitis	08
		Benign cystic lesion	01
	Benign neoplastic lesion (n=42)	Pleomorphic adenoma	39
		Warthins tumour	02
		Basal cell adenoma	01
	Malignant neoplastic lesion (n=11)	Adenoid cystic carcinoma	05
		Acinic cell carcinoma	01

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

		Mucoepidermoid carcinoma	03
		Carcinoma ex-pleomorphic adenoma	01
		Adenocarcinoma	01

Table 02. Comparative analysis of cytological and histological diagnosis of benign salivary gland lesions

S. No	Cytological Diagnosis	No. of cases	Histopathological Diagnosis		
			Concordance	Discordance	
1	Sialadenitis	09	08(88.9%)	01(01 Pleomarphic adenoma)	
	Benign cystic lesions	01	01(100%)		
2	Pleomorphic adenoma	40	37 (92.8%)	03 (Ca ex pleomorphic adenoma 01, Adenoid cystic carcinoma 02) –	False Negative
3	Warthin tumours	02	02(100%)		
	Total	**52**	**48(92.3%)**	**04 (7.6%)**	

Table 03. Comparative analysis of cytological and histological diagnosis of malignant salivary gland lesions

S. No	Cytological Diagnosis	No. of cases	Histopathological Diagnosis		
			Concordance	Discordance	
1	Acinic cell carcinoma	01	01(100%)		
2	Adenoid cystic carcinoma	03	03(100%)		
3	Mucoepidermoid carcinoma	04	03(75%)	01(Pleomorphic adenoma)	False positive
5	Suspicious for malignancy	02	01(50%)	01(Basal cell adenoma)	False positive
	Total	**10**	**08 (80%)**	**02(20%)**	

Table 04. Conformity of the FNAC and histopathology results of the study patients

PPV, positive predictive value; NPV, negative predictive value; FNR, false-negative rate; FPR, false-positive rate.

Variables		Histopathological diagnosis		
		Malignant lesion	Benign lesion	
		n	n	**Total**
Cytological diagnosis	**Malignant lesion**	08	02	10

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

	Benign lesion	03	49	52
Total		11	51	62
Statistical Statistical analysis Result		Sensitivity		72.73%
		Specificity		96.08%
		Accuracy		91.94%
		PPV		76.60%
		NPV		95.23 %
		Cohen's Kappa		0.7135
		p value		< .00001

Discussion

Fine-needle aspiration (FNA) serves as an uncomplicated, secure, cost-efficient, and precise diagnostic method for the initial assessment of patients with salivary nodules. [10] The primary objective of FNA is to identify neoplastic nodules that require surgical removal while avoiding unnecessary surgery for nonneoplastic lesions. However, fine-needle aspiration cytology (FNAC) of salivary gland lesions often presents a diagnostic challenge because different pathological processes display diverse and somewhat overlapping cytologic features. In cases of uncertainty, a histologic examination of the resected specimen provides an accurate diagnosis. [10,11].

Salivary gland neoplasms can occur in any age group. In the present study, the lesions were observed in individuals aged 1 to 65 years, with a mean age of 40.3 years, and the majority of cases occurring in the fourth decade of life. These results align with the research conducted by Khandekar et al.[12] and Kakoty et al. [13], whereas in studies by Koirala et al. [14] and Anita Omhare et al. [15], the majority of the cases were seen in the third decade.

The present study showed that chronic sialadenitis was the most common non-neoplastic lesion, accounting for 95% of cases, followed by cystic lesions. This finding was similar to other studies that also identified chronic sialadenitis as the most common non-neoplastic lesion [16, 17, 18]. Among the neoplastic lesions, 66.3% of salivary gland tumors were benign and 33.7% were malignant. This is similar to previous reports.[19-21]. Among the neoplastic lesions, pleomorphic adenoma was the most common, accounting for 89%, followed by Warthin's tumors (4.1%). Similar results were seen in studies conducted by Upasana P et al., Gandhi S et al., Singh A et al., and Khandekar et al. (16, 17, 18, 22, 23). However, Jain C et al. found that 20% of the cases involved pleomorphic adenoma, while 1.42% each involved basal cell adenoma and oncocytoma in their study. [16].

On cytology of pleomorphic adenoma reveals a biphasic pattern composed of epithelial/myoepithelial cells and fibro-myxochondroid stroma. The components may be arranged in a wide spectrum of microscopic appearances with the potential for errors in cytological interpretation. It can be a source of confusion with tumors such as basal cell adenoma, adenoid cystic carcinoma, and mucoepidermoid carcinoma - low grade on cytology. In the present series, 37 cases were correctly identified on cytology. One case proved to be

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

carcinoma ex-pleomorphic adenoma and two cases were later confirmed to be adenoid cystic carcinoma ,on subsequent histopathology. Thus, the cyto-histological correlation for pleomorphic adenoma was 92.8%. Differentiating between adenoid cystic carcinoma and PA can sometimes be the most challenging [24-27] Both of these tumors may present as pseudo-columnar tumors and pseudo-trabecular structures, leading to misdiagnosis. Moreover, artificial alterations, such as the distortion of the transparent adenoid cystic carcinoma sphere into a rectangular shape (caused by the traumatic impact of suction and sliding procedures), can mimic the trabecular appearance of the gelatinous matrix component of PA, potentially resulting in a misdiagnosis. In this study, 2 cases of adenoid cystic carcinoma (ACC) were initially misdiagnosed as pleomorphic adenoma (PA). We conducted a thorough analysis of the underlying causes and identified several potential issues: (1) In cases where the tumor is small and the cytologic sampling technology is inadequate, the most diagnostically significant components of the tumor may not be observable. (2) Pleomorphic adenoma (PA) is prevalent benign tumors of the salivary gland that share similar cellular morphology with adenoid cystic carcinoma (ACC). Consequently, ACC may coexist within the same mass as pleomorphic adenoma and exhibit comparable morphological features in cytologic smears. (3)While the morphological differentiation of tumor cells may be well-defined, the heterogeneity is minimal, making it challenging to distinguish from a benign tumor. (4) Inaccurate interpretation of the cytologic smears, lack of diagnostic expertise, and misidentification of diagnostically important cells can result in errors. Carcinoma ex pleomorphic adenoma (Ca ex PA) is an uncommon condition that presents challenges in its cytological diagnosis.[28,29] Studies have indicated that fine needle aspiration cytology (FNAC) has demonstrated a low sensitivity in detecting Ca ex PA, with reported rates as low as 29%. As a result, distinguishing this condition from benign pleomorphic adenoma can be very difficult.[30,31]. According to Klijanienko et al.[32], carcinoma ex-pleomorphic adenoma has the highest false negative rate (35.3%) out of all malignant salivary gland tumors. Careful clinicocytologic correlation and representative, meticulous sampling is mandatory.

Various authors have reported that the incidence of malignant tumors ranged from 15% to 32% [33,34]. In the present study, it accounted for 33.6%, while Nguansangiam et al. found a lower incidence of malignant neoplasms. Among malignant salivary gland lesions, the most common malignancy was malignant neoplasm not otherwise specified. This diagnosis was based on cytologic evidence of malignancy without further tumor typing, highlighting the limitations of FNAC in characterizing specific tumor types due to variations in cytomorphology. Acinic cell carcinoma was the second most common type of cancer in the current study, accounting for 21.6% of cases. Gandhi et al. and Singh et al. obtained comparable results. [17, 22]. Published literature indicates a false-positive rate ranging from 1% to 20%. [35]. In our study, the false-positive rate was 20%, attributed to two instances, where cytology suggestive of mucoepidermoid carcinoma (MEC) but histopathology revealed pleomorphic adenoma. Upon reevaluation of the cytology smears, it was discovered that the round to ovoid ductal epithelial cells were mistaken for intermediate cells, and chondromyxoid stroma of pleomorphic adenoma

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

was misinterpreted as the thick mucoid background. Diagnosis of low-grade MEC by FNA can be challenging due to spatial heterogeneity and multiple histologic components. Therefore, adequate sampling of various components within the tumor is essential to arrive at correct diagnosis [36]. Another case of suspected malignant tumour in cytology diagnosed to be basal cell adenoma on subsequent histopathology. The smears showed homogenous material along with three-dimensional clusters, acini, or sheets of basaloid cells with variable cohesion, and were reported as a suspected malignant tumor. The membranous subtype of basal cell carcinoma is a well-established mimic of adenoid cystic carcinoma in cytology.[37]

FNAC as a screening modality for malignancy

In our study, we found that fine-needle aspiration cytology (FNAC) demonstrated a sensitivity of 72.73% and a specificity of 96.08% in detecting malignant lesions when compared to histologic diagnosis, as shown in Table 4. The positive predictive value for a malignant diagnosis using FNAC was 76.6%, and the negative predictive value was 95.23%. These results indicate that FNAC has a higher specificity (96%) than sensitivity (72.73%) in distinguishing malignant from benign disease, with an overall diagnostic accuracy of 92%. Furthermore, statistical analysis revealed a strong agreement between cytological and histological findings, with a kappa value of 0.7135. These findings suggest that FNAC can effectively predict the presence of malignancy, contingent upon the prevalence of malignancy. The literature review demonstrated considerable variability in the sensitivity and specificity of fine needle aspiration cytology for diagnosing salivary gland swelling across different populations and settings [38-40]. For instance, Zerpa et al. conducted a study on 93 cases of parotid gland tumors and reported a sensitivity of 57% and a specificity of 95% [41]. In contrast, Pastore et al. found a sensitivity of 83% and a specificity of 93% in their evaluation of 357 cases of salivary gland lesions [42]. Similarly, Jaein et al. observed a sensitivity of 92.8% and a specificity of 93.9% in their study involving 80 cases of salivary gland swellings, including 14 cases of malignant salivary gland neoplasms [43]. Kim et al. reported a diagnostic accuracy of 92% for FNAC in distinguishing malignant from benign salivary gland tumors [44]. Fakhry et al identified common false positive results, such as Warthin’s tumor and pleomorphic adenoma, and noted false negative diagnoses in cases of lymphomas and mucoepidermoid carcinomas. [45].

Our study has some limitations, with the most significant being its retrospective nature and the fact that it was conducted at a single center. Furthermore, the sample size was very limited; this led to the exclusion of numerous FNAC cases that lacked histopathology reports. Secondly, because patients had to travel long distances and faced financial constraints, no follow-up data were available. Thirdly, we did not conduct immunocytochemistry or molecular analysis in cytologic or histologic samples. Certain researchers have applied these techniques to cytologic specimens and have reported favorable results.[46-50].Despite these limitations, this research represents an investigation to examine the association between FNAC and their corresponding

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

histopathology in the context of diagnosing salivary cancers. Additionally, it assesses the accuracy rate, sensitivity, specificity, positive predictive value, negative predictive value, false negative rate, and false positive rate of fine needle aspiration cytology (FNA) as a diagnostic tool for salivary gland nodules.

Conclusion

The results of our study have shown that fine-needle aspiration cytology (FNAC) of salivary lesions demonstrates a significant level of accuracy, sensitivity, and specificity, allowing for appropriate initial diagnostic intervention. Although the ability to characterize specific tumor types is limited due to variations in cytomorphology. False-negative diagnoses were mainly attributed to issues with the specimens obtained, while false-positive diagnoses were primarily caused by errors in interpretation. Cytopathologists should improve their skills and standards to avoid making false-positive diagnoses. Moreover, Fine Needle Aspiration Cytology (FNAC) is a safe, reliable, cost-effective, and efficient method that should be used as the primary investigative tool for salivary lesions.

References

1 .Schindler S, Nayar R, Dutra J, Bedrossian CW. Diagnostic challenges in aspiration cytology of the salivary glands. SeminDiagnPathol 2001; 18: 124–46.PubMed

2. Ashraf A, Shaikh AS, Kamal F, Sarfraz R, Bukhari MH. Diagnostic reliability of FNAC for salivary gland swellings: a comparative study. DiagnCytopathol 2010; 38: 499–504.ArticlePubMed

3 .Jain R, Gupta R, Kudesia M, Singh S. Fine needle aspiration cytology in diagnosis of salivary gland lesions: a study with histologic comparison. Cytojournal 2013; 10: 5.PubMedPMC

4. Colella G, Cannavale R, Flamminio F, Foschini MP. Fine-needle aspiration cytology of salivary gland lesions: a systematic review. J Oral MaxillofacSurg 2010; 68: 2146–53.ArticlePubMed

5.Eveson JW, Cawson RA. Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. *J Pathol.* 1985;146:51–8.

6.Christopher C Griffith Reetesh K Pai Frank Schneider UmamaheswarDuvvuri Robert L Ferris Jonas T Johnson Raja R Seethala Salivary Gland Tumor Fine-Needle Aspiration Cytology: A Proposal for a Risk Stratification ClassificationAm J ClinPathol2015 ,1436839 -853.

7. R L Schmidt B J Hall A R Wilson A systematic review and meta-analysis of the diagnostic accuracy of fine-needle aspiration cytology for parotid gland lesionsAm J ClinPathol 201113645-59.

8. Rossi ED, Faquin WC. The Milan system for reporting salivary gland cytopathology (MSRSGC): an international effort toward improved patient care-when the roots might be inspired by Leonardo da Vinci. *Cancer Cytopathol*. 2018;126(9):756-766. doi: 10.1002/cncy.22040 [PubMed] [CrossRef] [Google Scholar] [Ref list]

9. Fine needle aspiration cytology in diagnosis of salivary gland lesions: A study with histologic comparison,jain et al, Cytojournal. 2013; 10: 5.

10.Akhter J, Hirachand S, Lakhey M.. Role of FNAC in the diagnosis of salivary gland swellings. *Kathmandu Univ Med J (KUMJ)* 2008;6:204–208.

11. Mairembam P, Jay A, Beale T, et al. Salivary gland FNA cytology: role as a triage tool and an approach to pitfalls in cytomorphology. *Cytopathology.* 2016; **27**: 91-96.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

12. Khandekar MM, Kavatkar AN, Patankar SA, Bagwan IB, Puranik SC, Deshmukh SD. FNAC of salivary gland lesions with histopathological correlation. Indian J Otolaryngol Head Neck Surg 2006;58:246-8.
13. Kakoty S, Baruah TD, Babu CP. FNAC and Histopathological correlation of salivary gland lesions: An observational study. Int Surg J 2017;4:2148-52.
14. Koirala S, Sayami G, PantAD. Correlation of FNAC and histopathology in diagnosis of salivary gland lesions. J Pathol Nepal 2014;4:654-7.
15. Omhare A, Singh SK, Nigam JS, Sharma A. Cytohistopathological study of salivary gland lesions in bundelkhand region, uttar pradesh, India. Patholog Res Int 2014;2014:804265
16.Jain, C. (2013). Fine needle aspiration cytology of salivary gland lesions: a study of 70 cases. *Int J Med Pharm Sci*, *3*(07).
17.Gandhi, S. H., Purohit, T. M., Purohit, M. B., Jethwani, D., &Vidja, M. (2013). FNAC Diagnosis of salivary gland lesions with histopathological correlation. *NJIRM*, *4*(3), 70-7.
18. Upasana, P., Ina, S., &Hansa, G. (2015). A cytological and histological comparative study of salivary gland lesions at tertiary health care centre. *Int J Biomed Adv Res*, *6*(6), 470-4.
19. Mihashi H, Kawahara A, Kage M, Kojiro M, Nakashima T, Umeno H, et al. Comparison of preoperative fine-needle aspiration cytology diagnosis and histopathological diagnosis of salivary gland tumors. *Kurume Med J.* 2006;**53**:23–7. [PubMed: 17043392]
20.Rajwanshi A, Gupta K, Gupta N, Shukla R, Srinivasan R, Nijhawan R, et al. Fine-needle aspiration cytology of salivary glands: Diagnostic pitfalls – Revisited. *Diagn Cytopathol.* 2006;**34**:580–4. [PubMed: 16850487]
21. 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**:499–504. [PubMed: 19950398]
22.Singh, A., Haritwal, A., &Murali, B. M. (2011). Correlation between cytology and histopathology of the salivary glam. *The Australasian medical journal*, *4*(2), 66.
23. Khandekar, M. M., Kavatkar, A. N., Patankar, S. A., Bagwan, I. B., Puranik, S. C., &Deshmukh, S. D. (2006). FNAC of salivary gland lesions with histopathological correlation. *Indian Journal of Otolaryngology and Head and Neck Surgery*, *58*(3), 246-248.
24. Kapatia G, Dey P, Saikia UN. Artificial neural network model to distinguish pleomorphic adenoma from adenoid cystic carcinoma on fine needle aspiration cytology. Cytopathology. 2020;31:445–50.
25.Andreasen S, Melchior LC, Kiss K, Bishop JA, Hgdall E, Grauslund M. The prkd1 E710D hotspot mutation is highly specific in separating polymorphous adenocarcinoma of the palate from adenoid cystic carcinoma and pleomorphic adenoma on fna. Cancer Cytopathol. 2018;126:275–81.
26. Dimitrijevic MV, Boricic IV, Tomanović NR, Dimitrijevic AM.Bjelogrlić GM, Djurkovic PM., Clinicopathological Analysis of 907 Major and Minor Salivary Gland Tumors. Craniofac Surg J. (2022)33:e507-e509. Doi.
27. Wan, Y., Long, C., Liu, Y. *et al.* Value of cytopathology in the diagnosis of adenoid cystic carcinoma and an analysis of misdiagnoses. *BMC Surg* **23**, 52 (2023).
28. Antony J, Gopalan V, Smith RA, Lam AK. Carcinoma ex pleomorphic adenoma: A comprehensive review of clinical, pathological and molecular data. Head Neck Pathol 2012;6:1–9.
29. Singh, Kanika & Agarwal, Charu & Pujani, Mukta & Verma, Pragya & Chauhan, Varsha. (2017). Carcinoma ex pleomorphic adenoma: A diagnostic challenge on cytology: CARCINOMA EX PLEOMORPHIC ADENOMA. Diagnostic Cytopathology. 45. 10.1002/dc.23704.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

30. Rao S, Sundaram S, Duvuru P. Carcinoma ex pleomorphic adenoma: A rare sight on cytology. Sri Ramachandra J Med 2011;4:45–47
31. Bahrami A, Dalton JD, Shivakumar B, Krane JF. PLAG1 alteration in carcinoma ex pleomorphic adenoma: Immunohistochemical and fluorescence in situ hybridization studies of 22 cases. Head Neck Pathol 2012;6:328–335. Sep;
32. Klijanienko J, El-Naggar AK, Vielh P. Fine-needle sampling findings in 26 carcinoma ex pleomorphic adenomas: diagnostic pitfalls and clinical considerations. *Diagn Cytopathol.* 1999;21:163–166. doi: 10.1002/(SICI)1097-0339(199909)21:3<163::AID-DC3>3.0.CO;2-2.
33. R. S. Cajulis, S. T. Gokaslan, G. H. Yu, and D. Frias-Hidvegi,"Fine needle aspiration biopsy of the salivary glands: a five year experience with emphasis on diagnostic pitfalls," *ActaCytologica*, vol. 41, no. 5, pp. 1412–1420, 1997.
34. P. Boccato, G. Altavilla, and S. Blandamura, "Fine needle aspiration biopsy of salivary gland lesions: a reappraisal ofPathology Research International pitfalls and problems," *ActaCytologica*, vol. 42, no. 4, pp. 888–898, 1998.
35. Daneshbod Y, Daneshbod K, Khademi B. Diagnostic difficulties in the interpretation of fine needle aspirate samples in salivary lesions: Diagnostic pitfalls revisited. *Acta Cytol.* 2009;**53**:53–70. [PubMed: 19248555]
36. J. Klijanienko and P. Vielh, "Fine-needle sampling of salivary gland lesions IV.: review of 50 cases of mucoepidermoid carcinoma with histologic correlation," Diagnostic Cytopathology, vol. 17, no. 2, pp. 92–98, 1997.
37. Pal S, Mondal PK, Sharma A, Sikder M. Fine Needle Aspiration Cytology of Basal Cell Adenoma of Parotid Simulating Adenoid Cystic Carcinoma. J Cytol. 2018 Jan-Mar;35(1):55-57. doi: 10.4103/JOC.JOC_46_16. PMID: 29403173; PMCID: PMC5795731.
38. Murai N, Taniguchi Z, Takahashi Y, Kuboshima F, Tateya I. A study of salivary gland aspiration cytology reporting: guideline validity. Nihon Jibiinkoka Gakkai Kaiho. 2011;114(7):615–9.
39. Piccioni LO, Fabiano B, Gemma M, Sarandria D, Bussi M. Fine needle aspiration cytology in the diagnosis of parotid lesions. Acta Otorhinolaryngol Ital. 2011;31(1):1–4.
40. Singh A, Haritwal A, Murali B. Correlation between cytology and histopathology of th salivary gland. Australas Med J. 2011;4(2):66–71.
41. Zerpa Zerpa V, Cuesta Gonzales MT, Agostini Porras G, Marcano Acuna M, EstellesFerriol E, Dalmau GJ. Diagnostic accuracy of fine needle aspiration cytology in parotid tumors. Acta Otorrinolaringol Esp. 2014;65(3):157–61.
42. Pastore A, Borin M, Malagutti N, Di Laora A, Becati D, Delazer AL, et al. Preopertive assisment of salivary gland neoplasm with fine needle aspiration cytology and echography: a retrospective analysis of 357 cases. Int J Immunopathol Pharmacol. 2013;26(4):965–71.
43. Jain R, Gupta R, Kudesia M, Sing S. Fine needle aspiration cytology in the diagnosis of salivary gland lesions: a study with histologic comparison. Cytojournal. 2013;10:5.
44. Kim BY, Hyeon J, Ryu G, Choi N, Baek CH, Ko YH, et al. Diagnostic accuracy of fine needle aspiration cytology for high grade salivary gland tumors. Ann Surg Oncol. 2013;20(7):2380–7.
45. Fakhry N, Antonini F, Michel J, Penicaud M, Mancini J, Lagier A, et al. Fine needle aspiration cytology in the management of parotid masses: evaluation of 249 patient. Eur Ann Otorhinolaryngol Head Neck Dis. 2012;129(3):131–5.
46. Rotellini M, Palomba A, Baroni G, Franchi A. Diagnostic utility of PLAG1 immunohistochemical determination in salivary gland tumors. *Appl Immunohistochem Mol Morphol*. 2014; **22**: 390–394.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

47. West RB, Kong C, Clarke N, et al. MYB expression and translocation in adenoid cystic carcinoma and other salivary gland tumors with clinicopathological correlation. *Am J Surg Pathol*. 2011; **35**: 92–99.
48. Stenman G. Fusion oncogenes in salivary gland tumors: molecular and clinical consequences. *Head Neck Pathol*. 2013; **7**: 12–19.
49. Weinreb I, Piscuoglio S, Martellotto LG, et al. Hotspot activating PRKD1 somatic mutations in polymorphous low-grade adenocarcinoma of the salivary glands. *Nat Genet*. 2014; **46**: 1166–1169
50. Pusztaszeri M, Faquin WC. Update in salivary gland cytopathology: recent molecular advances and diagnostic applications. *Semin Diagn Pathol*. 2014; **2570**: 115–114.