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Experience of Application of Milan System for Reporting Salivary Gland Cytopathology and Risk Stratification in a Tertiary Care Center in Northeast India

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Abstract: ***Introduction*: Fine needle aspiration cytology (FNAC) is a widely accepted tool for preoperative diagnosis and management of salivary gland tumors. Due to the wide range of heterogenicity of salivary gland lesions and cytomorphological overlap, the Milan system for reporting salivary gland cytology (MSRSGC) was introduced to improve communication between cytopathologist and clinician. *Materials and methods*: A retrospective study was done for the period from January 2021 to December 2022. The study included a total of 104 salivary gland swellings. Clinical data, FNAC specimens, histological and clinical follow - up of cases were done. All the lesions were categorized according to the Milan system for reporting salivary glandcytopathology (MSRSGC). *Results*: out of the total of 104 cases included in the study histological follow - up was done wherever possible. Distribution of cases into six different categories were ND, NN, AUS, NB, SUMP, SM, M with a ROM of 25%, 4%, 16%, 5%, 33%, 75%, and 100% for each category. *Conclusion*: MSRSGC a six - category scheme which places salivary gland FNAC into well - defined categories limiting the possibilities of false negative and false positive results.***

Keywords: Fine needle aspiration cytology, salivary gland, risk of malignancy, The Milan system

1. Introduction

Fine needle aspiration cytology (FNAC) is an excellent tool for pre - operative diagnosis and management of salivary gland lesions. It offers a minimally invasive, safe, cost effective, and accurate approach for classifying a significant subset of salivary gland nodules as benign, reducing unnecessary invasive surgical procedures in patients with benign illnesses. [1, 2]In addition, FNAC also helps to distinguishing between primary and metastatic lesions, particularly of head and neck cancers, thus aiding in treatment planning.[3]Salivary gland lesions (SGL) account for 3% to 6% of all head and neck tumors.4 Although FNAC is a sensitive and specific tool for the cytopathologist in salivary gland lesions, there are a few challenges for salivary gland FNAC diagnosis, such astumor diversity and heterogenicity, the morphological overlap between different malignant tumors, and between benign and malignant tumours.[5, 6, 7]Numerous studies have proposed the use of morphological pattern - based analysis to develop a risk stratification approach for classifying salivary gland neoplasm and providing risk of malignancy (ROM), as well as to guide further ancillary tests and management plans.[8, 9]These studies exhibit a wide range of ROM in several categories ranging from 6% to 100%, indicating a lack of a standard approach.[10] Numerous reporting formats, ranging from two tired schemes to six or even more, have been used.[11]

The various classifications made it difficult for the treating practitioner to interpret the report and decide on further care based on ROM, hence a consistent nomenclature for reporting salivary gland cytopathology was addressed. In order to bring uniformity to the reporting of salivary gland lesions The American Society of Cytopathology and International Academy of Cytology recently proposed a tiered international classification scheme called the “Milan System for Reporting Salivary Gland Cytopathology” (MSRSGC), providing a guide for clinical management according to ROM in different categories.[12]
The MSRSGC is a six - tier classification that provides each category with standardized terminology and ROM.

This study was conducted to classify various salivary gland cytological aspirates as per the Milan system, to ascertain the rate of malignancy and to determine the diagnostic accuracy by correlating with the histopathological diagnosis wherever available.

2. Materials and Methods

Study design: Retrospective study

Period of study: January 2021 to December 2022

Place of study: Department of Pathology Jorhat Medical College and Hospital

Salivary gland swellings both major and minor were aspirated through a direct percutaneous or intraoral route with a 22 or 23 - gauze needle with or without ultrasound guidance wherever needed. The slides were subsequently

stained with May - Grunwald - Giemsa stain, Hematoxylin &Eosin in all cases and with pap stain also.

The cytological features were evaluated and classified according to MSRSGC as follows -
Category 1 - Non diagnostic
Category 2 - Non neoplastic
Category 3 - Atypia of undetermined significance (AUS)
Category 4a - Neoplasm benign
Category 4b - Neoplasm - Salivary gland neoplasm of uncertain malignant potential (SUMP)
Category 5 - Suspicious for malignancy
Category 6 - Malignant
Histopathological data where available was retrieved as the histological diagnosis was considered the gold standard.

3. Results and Observations

- A total of 104 patients with a mean age of 45 years were included in the study. Among them 55 cases were of males and 49 were females.
- Male: Female ratio was 1.12.

Table 1: Distribution of cases according to age, sex and site of involvement

	Parameter	No of cases
Age (years)	<30	18 (18.7%)
	31 - 50	58 (60.3%)
	51 - 70	22 (22.8%)
	71 - 80	04 (4.1. %)
	>81	02 (1.1%)
Sex	Male	55 (52.6%)
	Female	49 (47.4%)
Gland involved	Parotid	60 (62.4.7%)
	Submandibular	30 (31.2%)
	Minor salivary gland	14 (14.5%)

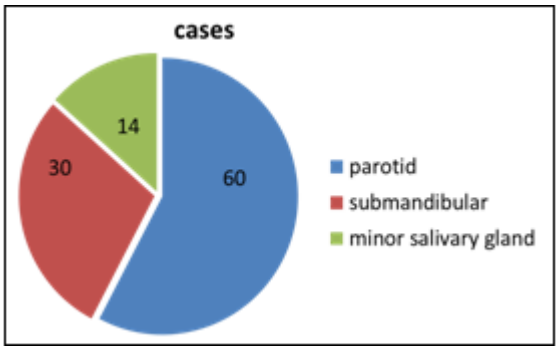

Table 2: The Milan System for Reporting Salivary Gland Cytopathology: Implied risk of malignancy and recommended clinical management

Diagnostic category	Risk of malignancy (%)	Management
1 Non - diagnostic	25	Clinical and radiologic correlation/repeat FNAC
2Non - neoplastic	10	Clinical follow up and radiological correlation
3 Atypia of undetermined significance (AUS)	20	Repeat FNAC or surgery
4a Neoplasm: Benign 4b Salivary gland neoplasm of uncertain malignant potential (SUMP)	<5 35	Surgery or clinical follow up Surgery
5Suspicious for malignancy - (SM)	60	Surgery
6Malignant	90	Surgery

Table 3: Categorization of FNAC cases according to the Milan system and correlation with histopathological findings

Milan category	Cat1	Cat2	Cat3	Cat4a	Cat4b	Cat5	Cat6	Total
No of cases	14 (14.5%)	30 (31.2%)	12 (12.4%)	20 (20.8%)	5 (5.2%)	7 (7.2%)	16 (16.6%)	104
No of cases with histological follow - up	4	7	6	18	3	4	9	51
Benign (non neoplastic)	2	6		1	1	0	0	
Benign (neoplastic)	1	1	5	16	1	1		
Malignant	1		1	1	1	3	9	
ROM	25%	4.1%	16%	5%	33%	75%	100%	

A total of 104 cases were studied according to age, sex and site of involvement. In this study Males were found to be slightly more affected than females. Out of the total of 104 cases, males were 55 (52.6%) and females were 49 (47.4%). Most of the cases were seen in the age group of 31 - 50 (60.3%) years followed by age group of 51 - 70 years (22.8%). Parotid gland was found to be most commonly involved in 60 (62.4 %) cases, followed by submandibular in 30 (31.2%) cases and minor salivary gland in 14 (14.5%) cases.

FNAC distribution of cases according to MSRSGC is shown in the table 3. It was found in the study that Non - neoplastic (NN) category 2 (31.2%) was the largest category, followed by category 4a (NB) (20.8%). M, AUS, ND, SM, SUMP constitute 16.6%, 12.4%, 14.5%, 7.2%, 5.2%.

In category 1 (ND) non - diagnostic out of a total of 14 cases we were able to follow up on only 4 cases. One case turns out to be adenoid cystic carcinoma on follow up. Risk of malignancy (ROM) was 25%.

A total of 30 cases were categorized in category 2 (NN). Histological follow - up was available in 7 cases. One case of benign tumor were reported which was misdiagnosed as chronic sialadenitis. Overall ROM was 4%.

In AUS category 3, out of a total of 12 cases histological follow - up was available in 6 cases.5 cases were classified as pleomorphic adenoma (PA) and 1 case was found to be adenoid cystic carcinoma. OverallROM was 16%.

We had a histological follow up of 18 cases out of a total of 20 cases in category 4a (NB).16 cases were diagnosed as

pleomorphic adenoma on FNAC which were concordant with histological follow up.1 case was classified as chronic sialadenitis and 1 case was found to be mucoepidermoid carcinoma. ROM was 5%.

In category 4b (SUMP) out of a total of 5 cases, 3cases were available for follow - up, 1 case was reclassified as chronic sialadenitis, 1 case as pleomorphic adenoma and 1 case was found to be adenoid cystic carcinoma. ROM was 35%.

Category 5 (SM), out of a total of 7 cases 4 cases were available for follow - up.1 case was found to be pleomorphic adenoma and 3 case was concordant with diagnosis of malignancy. ROM was 75%.

Histological follow - up was available in 9 cases out of a total of 16 cases that was classified as malignant on FNAC in category 6 (M). out of the 9 cases 6 cases of adenoidcystic carcinoma, 2cases of mucoepidermoid carcinoma and 1 case of Carcinoma ex pleomorphic adenoma.

Pictures

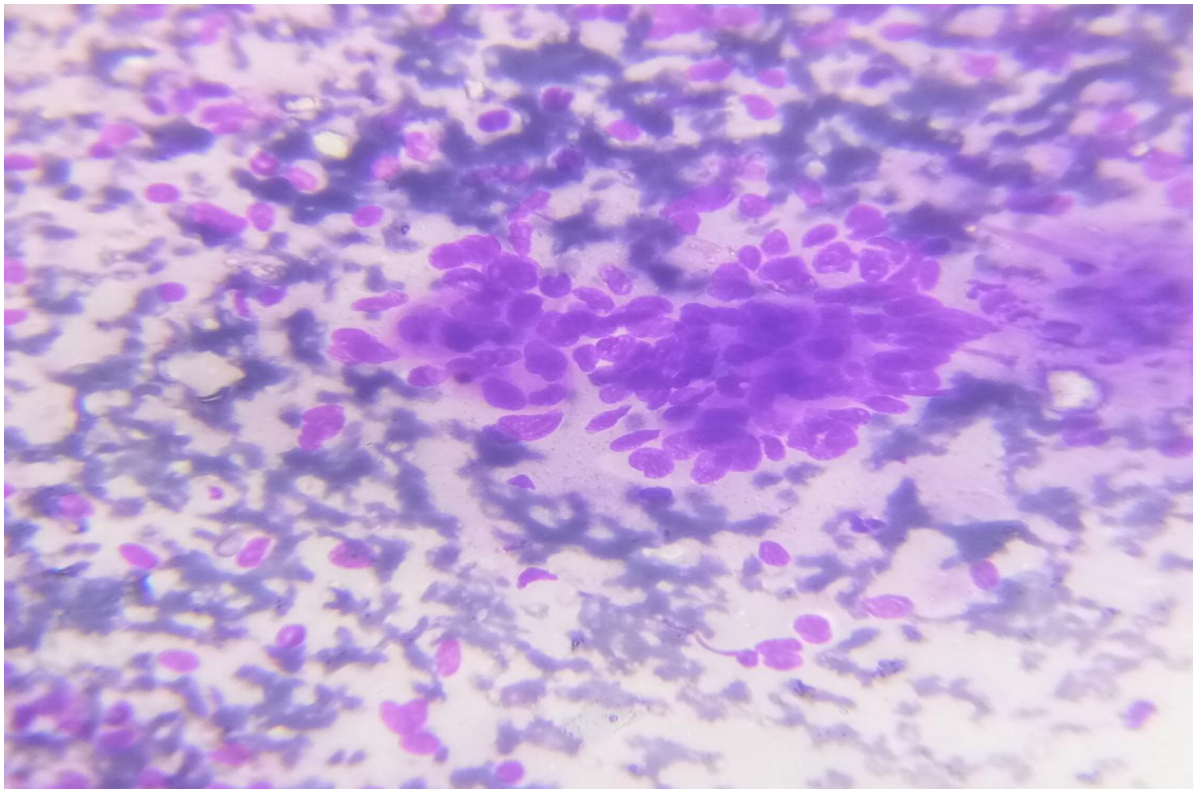

Figure 1 (a): cytology - AUS (40x)

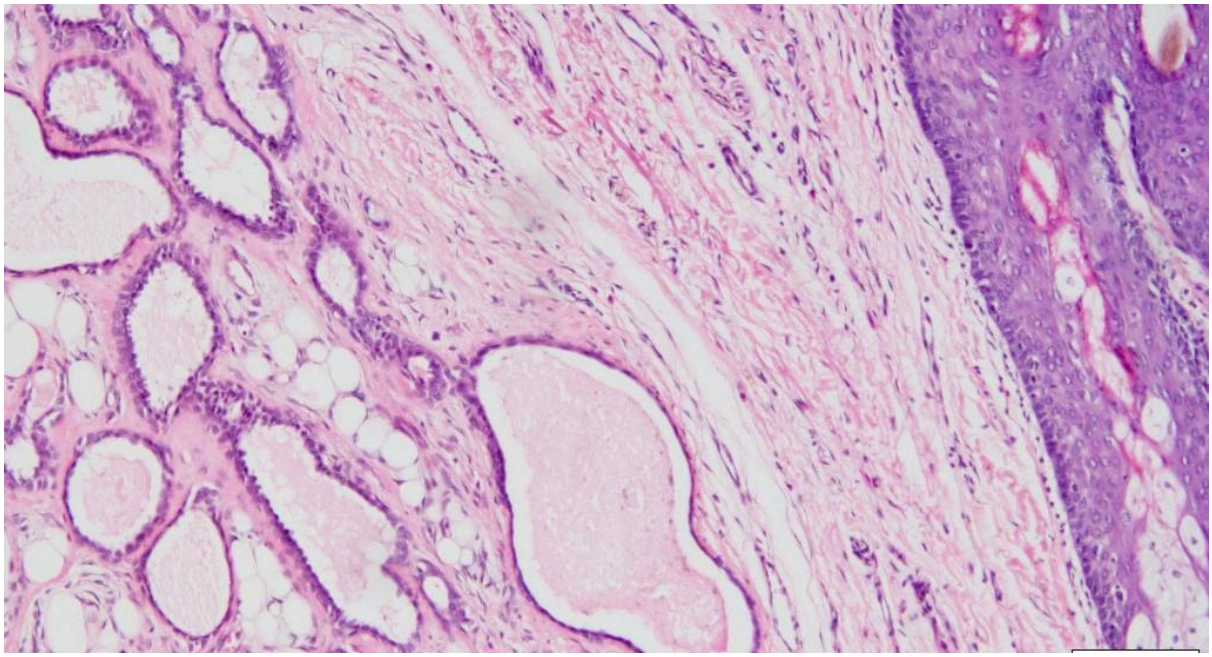

Figure 1 (b): Histopathology Concordant – Pleomorphic Adenoma (40x)

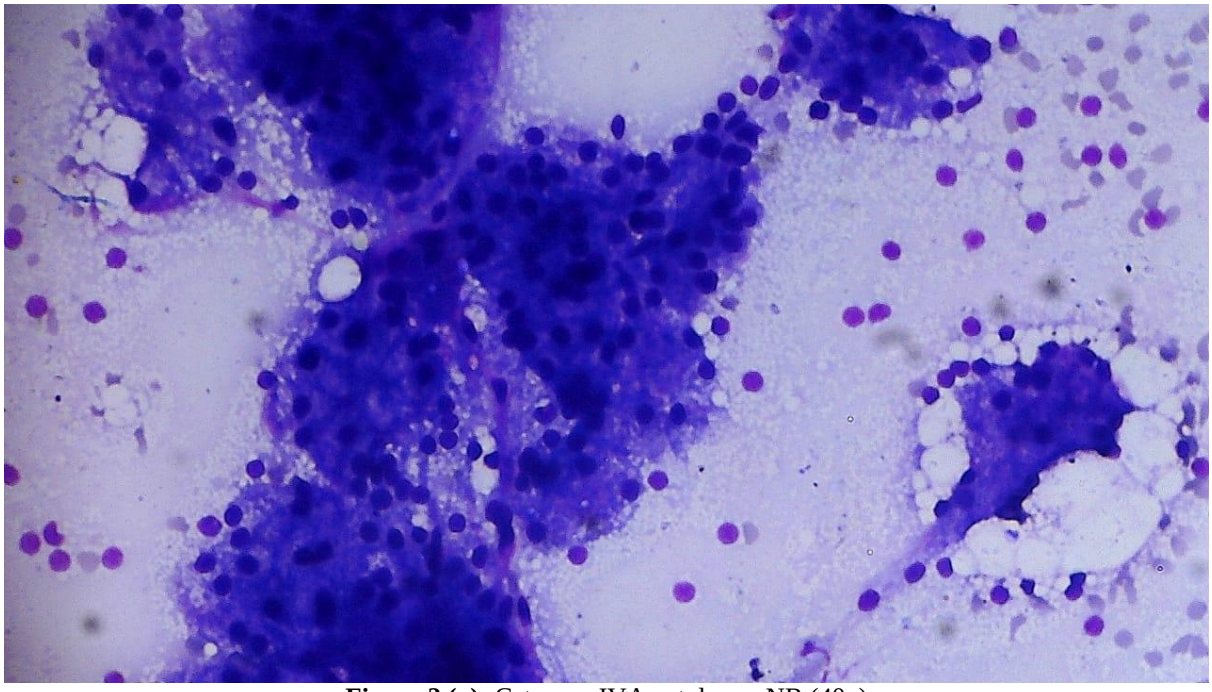

Figure 2 (a): Category IVA cytology –NB (40x)

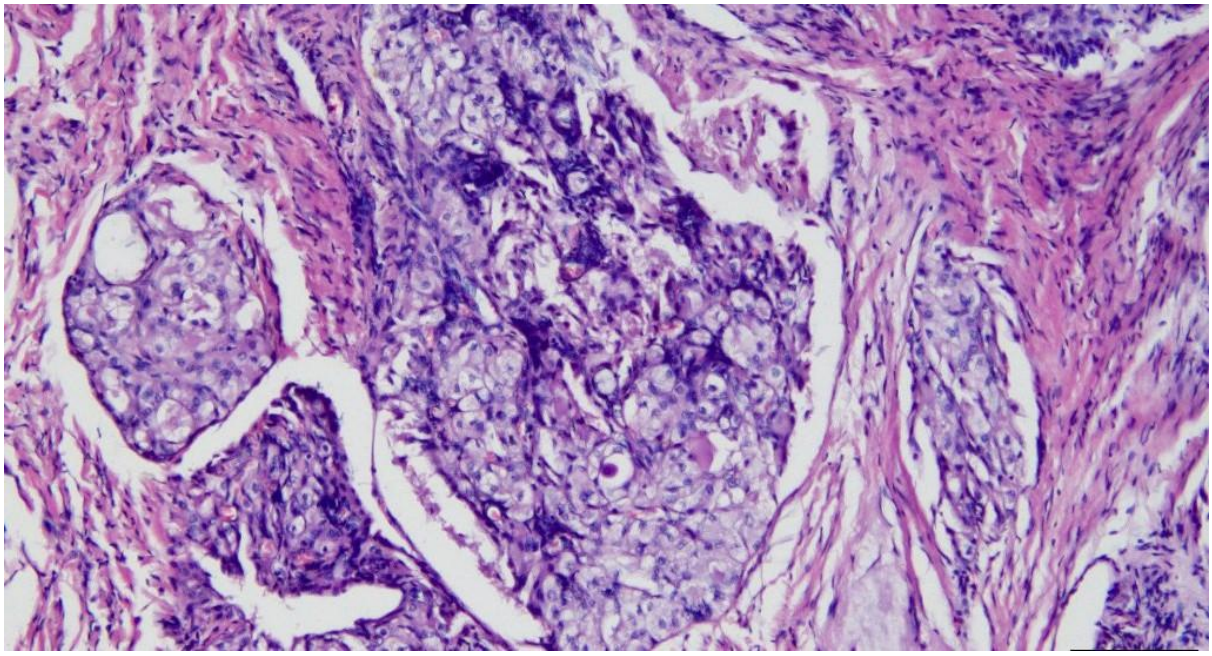

Figure 2 (b): Histopathology Concordant – Mucoepidermoid Carcinoma (40x)

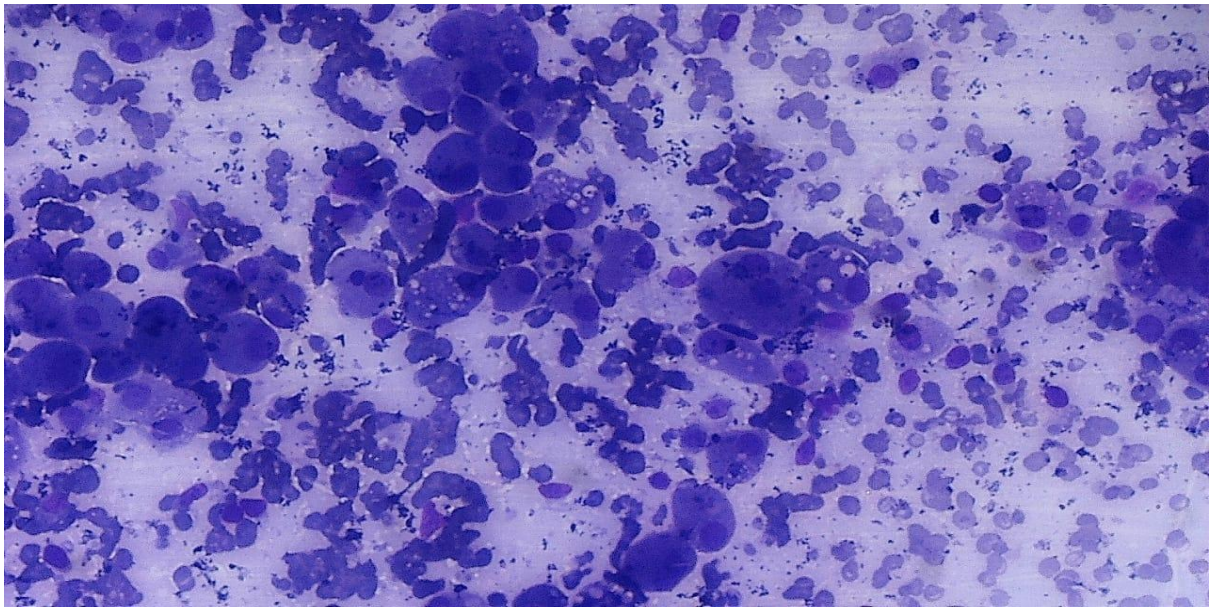

Figure 3 (a): Category IV b cytology–SUMP

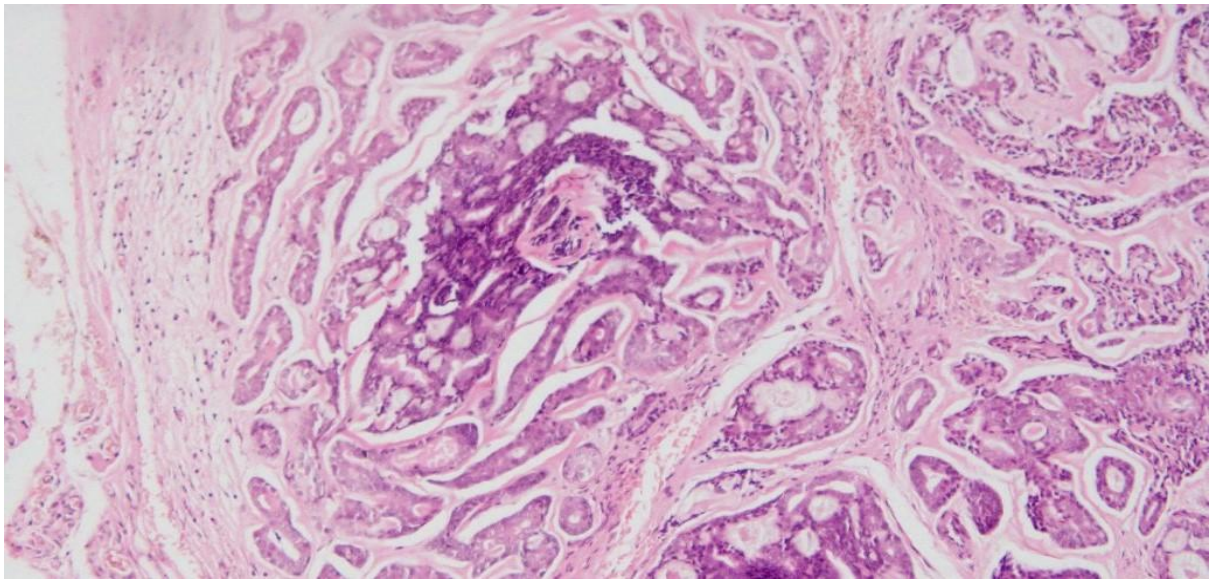

Figure 3 (b): Histopathology Concordant - Adenoidcystic carcinoma (40x)

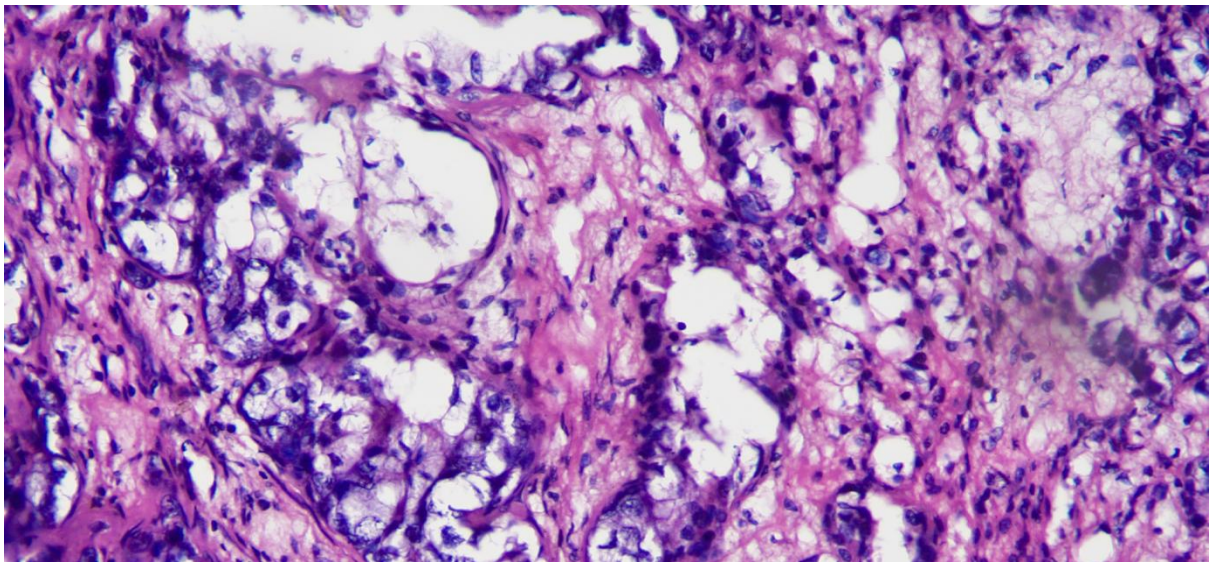

Figure 4: Histology image of carcinoma ex pleomorphic adenoma (40x)

4. Discussion

Fine - needle aspiration cytology (FNAC) is now widely used as a first line diagnostic tool in the detection of salivary gland lesions.1[3]It can aid in the treatment of the lesion by providing thenature of the lesion.1[4]MSRSGC is a modern salivary gland lesion reporting system designed to improve communication between doctors andcytopathologists and thus help in overall patient management. It is an six - tiered evidence based approach that provides ROM and treatment options for each category.1[5] Six categories are ND, NN, AUS, NB, SUMP, SM, M with a ROM of 25%, 10%, 20%, 5%, 35%, 60% and 90% for each category. In the present study we had also categorized the salivary gland FNA into six categories according to MSRSGC and overall ROM reported was 25%, 41%, 16%, 5%, 33%, 75% and 100% for each category.

Category 1 (ND) cases were non - diagnostic salivary gland aspirates providing inadequate diagnostic material for an informative interpretation. Out of the total of 14 cases, 4 cases were available for follow up.2 cases were reclassified as chronic sialadenitis, the misdiagnosis might be due to the presence of inflammatory cells and loss of acini, 1 case was misdiagnosed as Warthintumorwhich might be due to the presence of necrotic debris.1 case was diagnosed as adenoid cystic carcinoma where cystic change along with ductal and myoepithelial cells were present.

Category 2 (NN) - we had a total of 7 casesfor follow up out of a total of 30 cases.1 case was wrongly classified as chronic sialadenitis which later was found to be a case of pleomorphic adenoma. The misdiagnosis could be due to a lack of usual fibrillary character of the stroma and mimics thick mucin.

Category 3 (AUS) - Out of a total of 12 cases histological follow up was available in 6 cases.5 cases were of pleomorphic adenoma which was placed in this category due to high cellularity mild atypia and presence of scanty matrix.1 case was of adenoid cystic carcinoma which was categorized under AUS and might be due to the presence of basaloid cells with atypical features.

Category4a (NB) - Histological follow up was available in 18 cases out of a total of 20 cases.16 case was of pleomorphic adenoma, 1 case of chronic sialadenitis and 1 case was found to be of mucoepidermoid carcinoma which might have been missed due to the presence of mucoid background and the absence of malignant epithelial component.
Category4b (SUMP) - out of the total 5 cases, 3 cases were available for follow up 1case was reclassified as chronic sialadenitis, 1 case of pleomorphic adenoma and 1 case was found to be of adenoid cystic carcinoma the misinterpretation could be due to the presence of basaloid cells with mixed stroma.

Category 5 (SM) - Out of the total 7cases, 4 cases were available for follow up, 1 case was found to be that of pleomorphic adenoma and the rest 3 cases were concordant with the diagnosis of malignancy.

Category6 (M) - A total of 16 cases were in this category and 9 cases were available for follow up. All 9 cases were found to be concordant where 6 cases were of adenoid cysticcarcinoma, 2 cases of mucoepidermoid carcinoma and 1 case was of carcinoma ex pleomorphic adenoma.

Comparison of risk of malignancy (ROM) with other studies

Authors	ND (%)	NN (%)	AUS (%)	NB (%)	SUMP (%)	SM (%)	M (%)
Kala C, et al[21]	25	5	20	4	33	85	97
JhaS et la[21]	42	26	100	10	0	71	100
Farahani et al[18]	17	8	34	4	42	58	91
Current study	25	4	16	5	33	75	100

MSRSGC is a recent six - category scheme to classify salivary gland smears. It will undoubtedly meet the needs of cytopathologists and treating clinicians because in addition to risk stratification and providing ROM this six - tiered system places the salivary gland FNAC into well - defined categories limiting the possibilities of false positive and false negative results. Limitations of this study are the small number of sample size, lesser number of histological follow up and retrospective nature of the study.

References

[1] 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.
[2] Schindler S, Nayar R, Dutra J, Bedrossian CW. Diagnostic challenges in aspiration cytology of the salivary glands. SeminDiagnPathol 2001; 18: 124-46.
[3] Pusztaszeri MP, Faquin WC. Update in salivary gland cytopathology: Recent molecular advances and diagnostic applications SeminDiagnPathol 2015; 32: 264-74.
[4] Artur CV, Felipe N, Luise M, et al. Clinicopathological analysis of salivary gland tumors over a 15-year period Bio Reprod 2016; 30: 1-2.
[5] Ahn S, Kim Y, Oh YL. Fine needle aspiration cytology of benign salivary gland tumors with myoepithelial cell participation: An institutional experience of 575 cases. ActaCytol 2013; 57: 567-74.
[6] Novoa E, Gurtler N, Arnoux A, Kraft M. Diagnostic value of core needle biopsy and fine needle aspiration in salivary gland lesions. Head Neck 2016; 38: E346-52
[7] Layfield LJ, Tan P, Glasgow BJ. Fine-needle aspiration of salivary gland lesions. Comparison with frozen sections and histologic findings. Arch Pathos Lab Med 1987; 111: 346-53

[8] Griffith CC, Schmitt AC, Little JL, Magliocca KR. New developmentsin salivary gland pathology: Clinically useful ancillary testing and new potentially targetable molecular alterations. Arch Pathos Lab Med 2017; 141: 381-95
[9] Rossi ED, Wong LQ, Bizzarro T, Petrone G, Mule A, Fadda G, et al. The impact of FNAC in the management of salivary gland lesions: Institutional experiences leading to a risk-based classification scheme. CancerCytopathol 2016; 124: 388-96
[10] Malik A, Maleki Z, Zhao HQ, Rossi ED, Bo P, Chandra A, etal. Inter-institutional variability of "atypical" salivary gland fine needle aspiration: A multi-institutional study [abstract]. Lab Invest2017; 97: 107A. Abstract 411
[11] Wang H, Fundakowski C, Khurana JS, Jhala N. Fine-needle aspiration biopsy of salivary gland lesions. Arch Pathos Lab Med 2015; 139: 1491-7
[12] Rossi ED, Faquin WC, Baloch Z, Barkan GA, Foschini MP, Pusztaszeri M, et al. The Milan system for reporting salivary gland cytopathology: Analysis and suggestions of initial survey. Cancer Cytopathol2017; 125: 757-66.
[13] Liu CC, Jethwa AR, Khariwala SS, et al. Sensitivity, specificity and posttest probability of parotid fine needle aspiration: a systematic review and metaanalysis. Otolaryngol Head Neck Surg 2016; 154 (1): 9
[14] Mairembam P, Jay A, Beale T, Morley S, Vaz F, Kalavrezos N, et al. Salivary gland FNA cytology: Role as a triage tool and an approach to pitfalls in cytomorphology. Cytopathology 2016; 27: 91-6.
[15] Kala C, Kala S, Khan L. Milan system for reporting salivary gland cytopathology: An experience with the implication for risk of malignancy. Journal of cytology.2019 Jul; 36 (3): 160.
[16] Farahani SJ, Baloch Z. Retrospective assessment of the effectiveness of the Milan system for reporting salivary gland cytology: a systematic review and meta-analysis of published literature. Diagnostic cytopathology.2019 Feb; 47 (2): 67 - 87.
[17] Jha S, Mitra S, Purkait S, Adhya AK. The Milan System for Reporting Salivary Gland Cytopathology: assessment of cytohistological concordance and risk of malignancy. ActaCytologica.2021; 65 (1): 27 - 39.