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Original Research Article

SPECTRUM OF SALIVARY GLAND FNAC AND CATEGORIZATION IN MILAN SYSTEM OF REPORTING: A RETROSPECTIVE STUDY

Asttha Kapoor[1], Pinki Pandey[2], Alka Yadav[3], Alok Dixit[4], Udbhav Tewari[5]

[1]*Senior Resident, Department of Pathology, U.P.U.M.S, Saifai, Etawah, Uttar Pradesh, India.*
[2]*Professor and Head, Department of Pathology, U.P.U.M.S, Saifai, Etawah, Uttar Pradesh, India.*
[3]*Assistant Professor, Department of Pathology, U.P.U.M.S, Saifai, Etawah, Uttar Pradesh, India.*
[4]*Professor and Head, Department of Pharmacology, U.P.U.M.S, Saifai, Etawah, Uttar Pradesh, India.*
[5]*Senior Resident, Department of Psychiatry, U.P.U.M.S, Saifai, Etawah, Uttar Pradesh, India*

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Corresponding Author:
Dr. Udbhav Tewari,
Senior Resident, Department of Psychiatry, U.P.U.M.S, Saifai, Etawah, Uttar Pradesh, India.
Email: udtewari@gmail.com

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ABSTRACT

Background: Fine needle aspiration cytology (FNAC) for salivary gland lesions is a cost effective technique in categorizing and differentiating benign versus malignant lesions. To surmount this, an international group of pathologists have proposed a management-oriented, 6 tiered classification for reporting salivary gland FNA specimens, "The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)". Six percent of head and neck malignancies are salivary gland neoplasms. In the United States, the overall incidence of salivary gland neoplasms is roughly 5.5 cases per 100,000 people, of which 0.9 % are malignant neoplasms.

Materials and Methods: All cases of salivary gland FNA with available surgical follow-up, in the period from 2017 to 2020 were retrieved, cytological features were re-evaluated and reclassified according to MSRGC Category 1: Non-diagnostic(ND); Category 2: Non-neoplastic (NN); Category 3: Atypia of undetermined significance (AUS);Category 4a: Neoplasm: benign(NB); Category 4b:Neoplasm: salivary gland neoplasm of uncertain malignant potential (SUMP); Category 5:Suspicious for malignancy (SM);Category 6: Malignant(M).

Results: Total 110 cases were evaluated cytologically, and histopathology was available for 59 cases Distribution of the specimens according to the Milan System was as follows: 7.27% (ND), 33.63% (NN), 4.54% (AUS),30% (NB), 3.63% (SUMP), 4.54% (SM), and 16.36% (M).Overall ROM reported were 25%,8.3%,20%,4.75%,33.3%,75%,92.8%., respectively for each category. Overall, sensitivity was 82.21%, specificity was 96.32%, positive predictive value 91.71%, and negative predictive value was 90.17%.

Conclusion: The Milan System proved to be a useful method to categorize salivary gland FNAC into well-defined categories and to predict the risk of malignancy in the sample studied.

Keywords: Salivary gland lesions, The Milan system, 6-tiered classification, Fine needle aspiration cytology, Risk of malignancy.

INTRODUCTION

Fine-needle aspiration cytology (FNAC) of salivary gland is a popular method for the diagnosis and management of salivary gland tumors due to their superficial nature and easy accessibility for the procedure. It is a less invasive, safe and cost-effective technique that is extremely useful in identifying a substantial subset of salivary gland lesions as benign and thus reduces unnecessary surgical procedure in patients with benign diseases. In addition, it guides the further management strategy.[1-3]

The cytomorphological features associated with common salivary gland lesions are well-documented; however, diagnostic accuracy can be compromised

due to certain overlapping patterns and interpretative pitfalls.[2]

Fine needle aspiration cytology (FNAC) of salivary gland lesions shows high sensitivity (86% to 100%) and specificity (90% to 100%) in differentiating a neoplastic from a non-neoplastic lesion as well as benign and malignant lesions.[4-6] The struggle for salivary gland FNAC diagnosis, such as heterogeneousness of salivary gland tumors and morphological overlap amongst malignant entities as well as between benign and malignant lesions, limits its value in diagnosing specific neoplastic entities especially those with well-differentiated morphology.[7-9]

The other shortcoming is the terminology used in reporting of salivary gland cases which varied from 2 tiered to 6 tiered systems or even more.[10,11] Various terminology such as atypical, suspicious, and malignant have been used whereas, some have used histological categories to diagnose a case.[12,13]

In response to these issues, an international consortium of experts, under the guidance of the American Society of Cytopathology and the International Academy of Cytology, proposed a 6 tiered and evidence based reporting system in 2015 now recognized as the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC). This system helps to standardize the terminology which facilitates communication and optimizes management by providing risk of malignancy (ROM) for each category.[14,15]

The system categorizes salivary gland fine-needle aspiration (FNA) findings into six distinct groups: Category I- Nondiagnostic, Category II- Nonneoplastic, Category III- Atypia of Undetermined Significance (AUS), Category IVa - Benign Neoplasm, Category IVb - Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP), Category V - Suspicious for Malignancy (SFM), and Category VI - Malignant. Each category is linked to an evidence-based estimated risk of malignancy (ROM) and is accompanied by corresponding clinical or surgical management recommendations.

In this study, we reclassified salivary gland lesions based on the MSRSGC's second edition to investigate cytohistological concordance and risk stratification by calculating ROM for each category.

MATERIALS AND METHODS

Study design and sample collection: In this retrospective observational study clinical data and FNAC specimen of 110 cases of salivary gland FNA were retrieved. The study was conducted in Department of Pathology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah from the period between 2017 to 2020.

Inclusion and exclusion criteria

All the patients attending FNAC and presenting with salivary gland swelling were included. Other neck swellings such as lymph node were not included in the study.

Procedure: Patient was prepared by cleaning and disinfecting the region. FNAC was performed using a 21-23 gauge needle. The sample obtained by a minimum of two needle passes were spread on two or three slides, thin smears were prepared. The slides were stained with H&E (haematoxylin and eosin) and MGG(May Grunwald-Geimsa Stain).

All the FNA smears were re-evaluated and reclassified using MSRSGC categories by experienced pathologist, blinded to the earlier diagnosis.

Among 110 samples of cytology, histopathology was available for 59 cases which were compared and ROM was calculated thereafter. Histopathological diagnosis was utilized as the reference standard to evaluate the diagnostic accuracy of fine needle aspiration (FNA) cytology. Subsequently, a cytohistopathological correlation was performed. All discordant cases underwent a thorough re-evaluation of their cytology smears to identify potential reasons for diagnostic discrepancies. For cases with available histological follow-up, the risk of malignancy (ROM) was determined for each of the six diagnostic categories, and concordance rates were calculated accordingly. This study was ethically approved by Ethical board of the Institution.

Statistical analysis: Data was collected and entered in Microsoft excel sheet. Confidentiality of each participant was maintained throughout the study. Descriptive summary was presented (age, gender, gland involved) using frequency and percentage.

RESULTS

The cases included in our study were categorized according to sociodemographic parameters and site of involvement. Of the total cases 59 were male and 51 were female. Maximum number of patients were seen in age group 21 to 40 years (39.09%) followed by 41 to 60 years (30.90%). Parotid gland was involved in majority of patients 64 (58.18%) followed by submandibular gland 38 (34.54%) [Table 1]. All cases were reclassified into six categories based on the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC). The distribution of FNA cases across these MSRSGC categories, along with their respective concordance rates and risk of malignancy (ROM), is presented in [Table 2]. [Table 3] provides a detailed account of the FNA diagnoses and their cytohistopathological correlation as per the Milan system categories.

Histopathological follow-up was available in 59 cases. In category 1 (ND) histopathology was available for 4 out of 8 cases, of these, 1 case turned out to be adenoid cystic carcinoma on histopathology. In category 2 (NN), a total of 37 cases were reported with available histological follow up of 12. In this category 2 cases were wrongly diagnosed on cytology. 1 case was wrongly diagnosed as category

2 (NN)- chronic sialadenitis which was reported as benign tumor on histopathology, and 1 case of mucoepidermoid carcinoma which was wrongly diagnosed as category 2 (NN) - granulomatous sialadenitis on cytology.

In category 3(AUS), follow up was available in 1 of total 5 cases which was reclassified as Adenoid cystic carcinoma on histopathology. Follow-up of 21 out of 33 cases was available in Category 4a. Out of 19 cases which were diagnosed as Pleomorphic adenoma on cytology, 17 were in concordance on histological follow-up, and 2 cases were wrongly diagnosed on cytology and were categorised into malignant category on histopathology as Adenoid cystic carcinoma and mucoepidermoid carcinoma.

Category 4b case were those, where a specific neoplastic entity cannot be made, and out of 3 cases, 1 case was reclassified as granulomatous sialadenitis, 1 case as Pleomorphic adenoma, and and 1 as Mucoepidermoid carcinoma. Category 5 had histological follow-up of 4 cases, all of them showed concordance with diagnosis of malignancy.

Histopathological follow-up of 14 cases was available in Category 6. Only 1 case was misdiagnosed as malignant on cytology, which was reported as Pleomorphic Adenoma on histological follow-up. 8 cases of Mucoepidermoid carcinoma, 4 cases of Adenoid cystic carcinoma,1 case of carcinoma ex pleomorphic adenoma. Overall ROM reported were 25%,8.3%, 20%, 4.75%, 33.3%, 75%, 92.8%, for category 1,2,3,4a,4b,5 and 6 respectively. Overall, sensitivity was 82.21%, specificity was 96.32%, positive predictive value 91.71%, and negative predictive value was 90.17%.

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

Parameters	Number of cases
Sex	
Male	59(53.63%)
Female	51(46.36%)
Age	
<20	20(18.18%)
21-40	43(39.09%)
41-60	34(30.90%)
61-80	10(9.09%)
>80	03(2.72%)
Gland involved	
Parotid gland	64(58.18%)
Submandibular gland	38(34.54%)
Minor salivary gland	8(7.27%)

Table 2: Distribution of cases according to the The Milan System and their respective risk of malignancy.

Cytology Category	No. of Cases (110)	No. of cases with histological follow-up (59)	Benign: Non neoplastic	Benign: Neoplastic	Malignant	Risk of malignancy	ROM (%)
Cat I	8	4	2	1	1	1/4	25%
Cat II	37	12	9	2	1	1/12	8.3%
Cat III	5	1	0	0	1	1/5	20%
Cat IVa	33	21	1	19	1	1/21	4.75%
Cat IVb	4	3	1	1	1	1/3	33%
Cat V	5	4	0	1	3	3/4	75%
Cat VI	18	14	0	1	13	13/14	92.8%

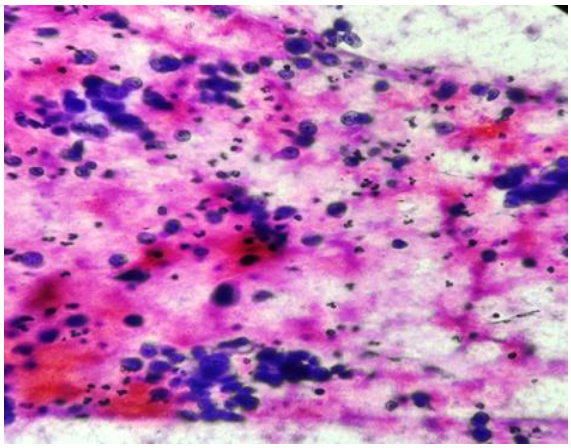

Figure 1: Bland epithelial cells with pleomorphism embedded in myxoid matrix. (Haematoxylin and eosin X400)

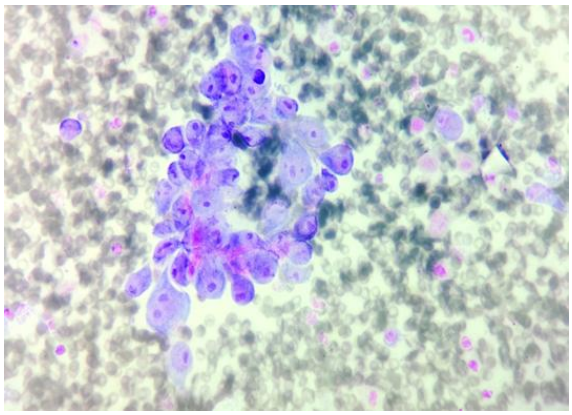

Figure 2: Atypical cells with a high nuclear cytoplasmic ratio admixed in a myxoid FNA diagnoses and their cytohistopathological correlation as per the Milan system categories.

DISCUSSION

MSRSGC is a system for reporting salivary gland cytopathology which categorises lesion according to risk stratification. The usage of uniform terminology and categories aids in better communication between clinicians and pathologists which improves management of patients.[12,16,17] Our study had also categorized salivary gland lesion according to risk stratification and overall ROM is comparable to that provided in MSRGSC.

Category 1(ND) cases are those cases where material aspirated in insufficient for final diagnosis. Follow up was available in 4 out of 8 cases, of these, 1 case turned out to be adenoid cystic carcinoma on histopathology with cystic changes. This may be the possible reason of misdiagnosis as cystic areas on FNAC might have yielded acellular material.

12 out of a total of 37 cases had histological follow up in category 2 (NN). 1 case was wrongly diagnosed as category 2 (NN)- chronic sialadenitis which was reported as benign tumor on histopathology, and 1 case of mucoepidermoid carcinoma which was wrongly diagnosed as category 2 (NN) - granulomatous sialadenitis on cytology. The presence of cystic macrophages and formation of foreign body granuloma due to mucin might be the reason for the same.

Category 3 comprises of those cases where neoplastic entity can not be excluded, out of 5 cases follow up was available only in 1 case which was diagnosed as Adenoid cystic carcinoma on histopathology. Presence of occasional atypical cells may be the possible explanation for categorization into AUS on cytology.

Out of 33 cases histopathology was available for 21 cases in Category 4a. Maximum number of cases in this category were of Pleomorphic Adenoma i.e.19 cases. Of these 17 were in concordance on histopathology, and 2 cases were misinterpreted on cytology. These 2 cases were re-categorised on histopathology as Adenoid cystic carcinoma and mucoepidermoid carcinoma which were falsely diagnosed as PA on cytology. In these 2 cases presence of occasional hyaline globules surrounded by micro acini of basaloid cells and abundance of mucoid background devoid of malignant epithelial component may be the reason of false diagnosis.

Category 4b comprises of those cases where cytology features suggest diagnosis of neoplastic lesion but distinction between benign and malignant entity in is not definite. Three cases were reclassified: one as mucoepidermoid cancer, one as pleomorphic adenoma, and one as granulomatous sialadenitis. Case that was determined to be MEC had bland epithelial cells and occasionally goblet cells with the myxoid matrix. [Figure 1] Thus, the case was categorized as SUMP in FNAC as a result of these findings.

When cytological characteristics are indicative of a neoplastic process but are unable to reliably differentiate between a benign and malignant tumor, the FNAC specimen is the only one used to diagnose SUMP.[14] Four cases from Category 5's histological follow-up demonstrated concordance with the diagnosis of malignancy.

The SM category includes those FNAC specimens that do not meet all the requirements for a specific malignancy diagnosis, but whose overall cytomorphological traits are indicative of malignancy.[14] Cytologists have been using the SM category for a long time, and clinicians are also familiar with it.[2,10,18,19] The Milan system's intermediate diagnostic categories are represented by the designations AUS, SUMP, and SM.[15]

The majority of FNAC cases in our study that were categorized as SM lacked a definitive diagnosis of malignant lesion. A case that was first identified as SM using FNAC analysis showed admixed basaloid cells with prominent squamous metaplasia and no myxoid or hyaline stroma; however, upon histological examination, the case was reclassified as PA with squamous metaplasia. When cytomorphological characteristics are diagnostic of malignancy,only then the salivary gland aspirates are designated as malignant.[14]

In category 6 (14/18) histopathology was available. Only 1 case was misinterpreted as Mucoepidermoid carcinoma on cytology, which was reclassified as Pleomorphic Adenoma on histological follow-up. Out of 8 cases of Mucoepidermoid carcinoma 4,1 case were diagnosed as Adenoid cystic carcinoma, and carcinoma ex pleomorphic adenoma respectively. False diagnosis may result from the existence of singly dispersed atypical cells with a high nuclear cytoplasmic ratio amidst a myxoid background. [Figure 2]

FNAC is a reliable, accurate, and reasonably priced way to assess salivary gland swelling. By identifying the type of lesion, it can also aid in the patient's care. 19, 20, 21 FNAC has a high sensitivity of 97%–98% in identifying benign from malignant neoplasms.3, 22, 23 In addition, FNAC is a helpful tool in determining the treatment plan by distinguishing primary from metastatic lesions, particularly in head and neck cancers.[24]

By using FNAC to diagnose malignant lesion with MSRSGC , overall results showed that the positive predictive value was 91.71%, the negative predictive value was 90.17%, the sensitivity was 82.21%, and the specificity was 96.32%. The values for the diagnosis of salivary gland lesions are on par with or even better than several studies that used the traditional method.[16]

In addition to offering ROM and risk stratification, the recently developed six-category MSRSGC scheme for classifying salivary gland smears will undoubtedly meet the needs of cytopathologists and treating clinicians because it offers a tiered system that classifies salivary gland FNAC into clearly defined categories, thereby reducing the likelihood of false positive and false negative cases.

This study's limitations include its retrospective design, limited sample size, and low number of histological follow-ups. For the study's potential use, more research with a sizable sample size and the suggested management plan are needed.

CONCLUSION

The Milan System proved to be a useful method to categorize salivary gland FNAC into well-defined categories and to predict the risk of malignancy in the sample studied. It provides a better communication between clinicians and cytopathologists so as to improve overall patient management.

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