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Original Research Paper

Pathology

EVALUATION OF ACCURACY OF MILAN SYSTEM FOR REPORTING SALIVARY GLAND CYTOLOGY: AN EXPERIENCE WITH THE IMPLICATION FOR RISK OF MALIGNANCY.

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ABSTRACT

INTRODUCTION: Fine-needle aspiration cytology ((FNAC) is well-established technique for evaluation of salivary gland lesions, but because of the heterogenicity and morphological overlap between spectrum of lesion, there are few challenges in its wide use. Recently, "The Milan system for reporting salivary gland cytopathology" (MSRSGC) was introduced, providing guide for diagnosis and management according to the risk of malignancy (ROM) in different categories. The current study was conducted retrospectively to reclassify the salivary gland lesions from previous diagnosis and to evaluate the ROM in different categories.

MATERIAL AND METHODS: Clinical data, FNAC slides and Histological follow-up of cases were retrieved, cytological features were re-evaluated and cases were reclassified as follows: 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 of malignancy (SM); and Category 6: Malignant (M).

RESULT: Total 105 cases were evaluated cytologically, and histological follow-up was available in 69 cases. The distribution of cases into different categories was as follows: ND:6(5.71%), NN:36(34.28%), AUS:6(5.71%), NB:34(32.38%), SUMP:3 (2.86%), SM:3(2.86%), M:17(16.19%). Overall risk of malignancy (ROM) reported were 33.3%, 10%, 20%, 3.33%, 33.3%, 66.6% and 93.34% respectively for each category.

CONCLUSION: MSRSGC scheme provides standardization of reporting salivary gland lesions. MSRSGC is recently approved six category scheme, which places salivary gland FNAC into well-defined categories that guide for diagnosis and management according to the risk of malignancy (ROM) in different categories.

KEYWORDS : Fine-needle aspiration cytology, risk of malignancy, salivary gland lesion, the Milan system.

INTRODUCTION

The main purpose of fine-needle aspiration cytology (FNAC) in salivary gland lesions is to identify the lesion as salivary gland origin, classify them into benign or malignant, and further subtype them as low-grade or high-grade malignancy.[1] Hence, it helps to guide clinical management and surgical planning. The technique is minimally invasive, well-tolerated, and cost-effective.[2,3,4,5] The accuracy of FNA to differentiate benign lesions from malignant lesions has been observed to be as high as 81% to 100%.

However, the accuracy of FNA to provide a specific diagnosis has a wider range of 48% to 94%.[6,7,8,9,10,11] In an attempt to increase the accuracy of the test, several other methods were endeavored like pattern-based analysis by few authors.[12,13,14] Despite being an useful sensitive and specific tool in the armamentarium of cytopathologists, there are a few challenges for salivary gland FNAC diagnosis, such as diversity and heterogenicity of salivary gland tumors, morphological overlap between different malignant tumors, and even between benign and malignant tumors. To bring uniformity in reporting, international experts in salivary gland cytopathology proposed the Milan system in 2015, a risk-based stratification system, similar to that of the Bethesda system for reporting cervical and thyroid cytology.

Material And Method

This was a retrospective study done over a period of two years from June 1, 2019 to June 30, 2021 in the Department of Pathology at B.J. Medical College Ahmedabad. The study included cytology smears of patients who visited the cytology section of Pathology department for FNA of salivary gland lesions as a diagnostic workup during the above period. Thus, all FNAs of lesions involving major salivary glands, i.e. parotid, submandibular and submental glands as well as minor salivary glands were included. The cases with lost or damaged cytological materials were excluded from the study. The detailed clinical and radiological findings were noted from the records. As a routine practice in our department, in this study, all FNAs were already performed after taking informed consent from the patients. The lesions were aspirated using a 22-23 gauge needle via a direct percutaneous or transoral route by trained cytopathologists. A maximum of two passes were performed. If large swelling, aspirate was taken from multiple sites to avoid the diagnostic error. In the case of fluid aspiration, the fluid was centrifuged and smears were prepared from the sediment. Also, repeat aspirate was performed from any solid lesion remained after evacuating cystic contents. Aspirations were guided radiologically wherever solid cystic lesion was found. The material was spread on slide and 50% were fixed in 90% ethanol for hematoxylin and eosin (H and E) stain and Papanicolaou stain and 50% were air-dried for MGG stain.

The cytological features were evaluated, and then cases were reclassified according to MSRSGC as follows:

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 of malignancy (SM)
Category 6: Malignant (M).

All cytology smears were retrieved and reviewed by two cytopathologists and assigned to one of the six categories

after application of strict criteria given by MSRSGC.(12) The review was done blindly, independent of the histopathological diagnosis. All cases were evaluated in reference to the location of salivary gland involvement, age and sex of patient, and type of lesion. The cytological diagnoses were then correlated with clinical and histopathological follow-up, wherever available. Considering histopathology as a gold standard, the sensitivity, specificity, and diagnostic accuracy of FNA to detect malignant lesions were calculated. ROM was determined by dividing the number of malignant cases by a total number of histopathological follow-up available in the particular category.

RESULTS

The FNAC distribution of 105 cases according to age, sex, and site of involvement is shown in Table 1. Male were slightly more affected than female, 56 vs. 49 the ratio being 1.14:1. Largest number of cases were seen in age group 21 to 40 year (44.76%) followed by 41 to 60 year age group (28.57%). Parotid gland was involved in 59.05% cases followed by submandibular gland 27.62% with minor salivary gland involved in 13.33% of cases.

Table 1: The Fnac Distribution Of 105 Cases According To Age, Sex, And Site Of Involvement.

Parameters		No. of cases
A)	Sex : Male	56
	Female	49
B)	Age : </= 20 years	14 (13.3%)
	21-40 years	47 (44.76%)
	41-60 years	30 (28.57%)
	61-80 years	11 ((10.47%)
	>80 years	3 (2.86%)
C)	Site : Parotid gland	62(59.05%)
	Submandibular gland	29(27.62%)
	Minor salivary gland	14(13.33%)

The FNAC distribution of cases according to MSRSGC is shown in Table 2. NN category was the largest category 34.28% followed by NB category 32.38%. ND, AUS, SUMP, SM and M constitute 5.71%, 5.71%, 2.86%, 2.86% and 16.19% respectively.

Table 2 : Distribution Of Cases According To Msrsgc.

Category	1 (ND)	2 (NN)	3 (AUS)	4a (NB)	4b (SUMP)	5 (SM)	6 (M)
No. of cases	6 (5.71 %)	36 (34.2 8%)	6 (5.71 %)	34 (32.3 8%)	3 (2.86%)	3 (2.86 %)	17 (16.1 9%)
No.of cases with histopathological follow up	3	10	5	30	3	3	15
Non neoplastic	0	7	2	1	1	0	0
Benign neoplasm(NB)	2	2	2	28	1	1	1
Malignant	1	1	1	1	1	2	14
Risk of malignancy (ROM)	33.3 %	10%	20%	3.33 %	33.3%	66.6 %	93.34 %

DISCUSSION

FNAC is a safe, accurate, and cost-effective method for evaluation of salivary gland swelling and can help in management of the patient by providing nature of the lesion.[2]

MSRSGC is a newer system for reporting salivary gland lesions according to risk stratification with an objective to provide a better communication between clinicians and cytopathologists so as to improve overall patient management. It is an evidence based six tiered system, which provides ROM and clinical management strategies for each category.[6,11,15] It classified FNAC into six categories; ND, NN, AUS, NB, SUMP, SM, and malignant with ROM of 25%, 10%, 20%, 5%, 35%, 60%, and 90% for each category.[16] The present study had also categorized salivary gland FNAC into six categories according to MSRSGC, and overall, ROM reported was 33.3%, 10%, 20%, 3.33%, 33.3%, 66.6% and 93.34%, respectively for each category, and results are comparable to that provided in MSRGSC.

In category 1 ((ND) out of 6, follow up was available in only 3 cases, and out of these 1 case turned out to be Acinic cell carcinoma on histological follow up; overall, ROM for this category reported was 33.3%.

In category 2 ((NN) out of 36, follow up was available in only 10 cases, and out of these 2 cases of benign tumor were reported, which were wrongly diagnosed as category 2 (NN)- Chronic Sialadenitis, and 1 case of Mucoepidermoid Carcinoma (MEC) was reported on histopathology, which was wrongly diagnosed as category 2 (NN)- Granulomatous Sialadenitis on FNAC. Overall, ROM reported for this category was 10%.

Histological follow up of 5 out of 6 cases were available in category 3(AUS). Two cases were reclassified as chronic Sialadenitis, 2 cases as Pleomorphic Adenoma and 1 case was reclassified as Adenoid cystic carcinoma. Overall, ROM for this category was 20%.

Category 4a (NB) had histological follow up of 30 cases out of 34 cases. One case of Warthin's tumor on FNAC was reclassified as chronic Sialadenitis on histological follow up. 1 case of Pleomorphic Adenoma turned out to be Mucoepidermoid carcinoma(MEC) on histological follow up. Overall, ROM for this category reported was 3.33%.

Category 4b (SUMP) cases were those, where a specific neoplastic entity cannot be made, and out of 3 cases 1 case was reclassified as Chronic Sialadenitis, 1 case as Pleomorphic Adenoma and 1 case as Adenoid cystic carcinoma. Overall, ROM for this category reported was 33.3%.

On histological follow up of 3 cases of category 5 (SM), 1 case turned out to be Warthin's tumor, 1 case reclassified as Mucoepidermoid Carcinoma(MEC) and 1 case as Acinic cell carcinoma. Overall, ROM for this category reported was 66.6%.

Histological follow up of 15 out of 17 cases were available for category 6 (M). Only One case of Pleomorphic adenoma was misdiagnosed as epithelial myoepithelial carcinoma reported on FNAC. Overall, ROM for this category reported was 93.34%.

The risk of malignancy (ROM) for individual Milan category in various studies is shown in table 3.

Table 3 : The Risk Of Malignancy (rom) For Individual Milan Category In Various Studies

Author	Year	Non diagnostic (%)	Non neoplastic (%)	Atypia (%)	Benign (%)	SUMP (%)	Suspicious for malignancy (%)	Malignancy (%)
Viswanathan et al[17]	2018	6.7	7.1	5	38.9	34.2	92.6	92.3
Pujani et al[18]	2018	0	10	50	2.5	50	100	100
Layfield et al[19]	2018	12	5	19	5	40	60	93
Farahani et al[20]	2018	17	8	34	4	42	58	91
Present Study	2021	33.3	10	20	3.33	33.3	66.6	93.34

CONCLUSION

Reporting of salivary gland lesions according to MSRSGC, provides standardization of reporting salivary gland lesions. MSRSGC is a recently proposed six category scheme which places salivary gland FNAC into well defined categories that guide for diagnosis and management according to the risk of malignancy (ROM) in different categories.

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