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Original Research Article

Milan System for Reporting Salivary Gland Cytopathology with the Implication for Risk of Malignancy: An Experience in a Tertiary Care Hospital

Adhlakha B[1], Yadav P[2], Jigjini S[3], Swati[4]

[1]Assistant Professor, Department of Pathology, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh

[2]Senior Resident, University College of Medical Sciences, Delhi

[3]Professor, S. Nijalingappa Medical College & H. S. K. Hospital & Research Centre Bagalkot, Karnataka, India

[4]Senior Resident, University College of Medical Sciences, Delhi

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Corresponding author: Dr. Bhuvan Adhlakha

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Abstract

Introduction: Fine needle aspiration cytology (FNAC) of salivary gland lesions has diverse and overlapping cytological features making this a challenging work to give precise diagnosis. The Milan System for reporting salivary gland cytopathology (MSRSGC) helps standardize reporting systems across institutions, provides an intrinsic risk of malignancy (ROM) for each diagnostic category and guide the clinical management of patients. This study emphasises on validation of MSRSGC and evaluate its diagnostic utility.

Material and Methods: This was a retrospective study in which FNAC of salivary gland lesions done over a period of 3.5 years were retrieved. All cases were categorized according to MSRSGC and correlated with histopathological follow-up, wherever available. ROM was calculated for each MSRSGC category.

Results: A total of 90 cases were classified using the Milan system as non-diagnostic (0%), non-neoplastic (45.5%), atypia of undetermined significance (0%), benign neoplasm (38.8%), neoplasm of uncertain malignant potential (5.5%), suspicious for malignancy (2.2%), and malignancy (7.7%). Cytohistological correlation was done on 29 cases with discordance in 2/29 cases (6.8%). The risk of malignancy was zero for Category II, 5% for IVa, 33.5% for IVb, and 100% for both V and VI. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were 71.4%, 100%, 100%, 91.6%, and 93.1%, respectively.

Conclusion: MSRSGC provided a uniform system of reporting salivary gland cytomorphology, helps triage patients and thus facilitates individualized management. The present study confirms the validity and diagnostic utility of Milan system.

Keywords: FNAC, Cytology, Salivary Gland, malignancy

Introduction

Salivary gland lesions (SGL) represent 2-6.5% of all tumours of the head and neck region [1]. Salivary gland fine needle aspiration cytology (FNAC) has been an

accepted method worldwide for evaluating SGL preoperatively. Accurate diagnosis by the pathologist is required for proper management of these lesions. This would help clinician to plan the nature of lesion and extent of treatment. Biopsies from salivary gland have certain complications such as fistula formation, injury to facial nerve and tumor implantation [2]. Therefore, it necessitates the use of FNAC, which is a well-established diagnostic tool due to its safety, simplicity of procedure, minimum invasiveness, cost effective and acceptability by patients. It aids in providing information for preoperative strategy, material for ancillary studies (e.g., cell block, flow cytometry) and for microbiologic cultures [2,3].

FNAC of salivary gland tumors has shown to have high specificity in differentiating benign and malignant lesions (97%). While, FNAC falls flat in terms of sensitivity (80%) [4]. Cytological interpretations are challenging due to tumor heterogeneity and overlapping cytomorphological features. In addition, a variety of new salivary gland tumors have been recognized by the World Health Organization (WHO), making an accurate subtyping of lesions more difficult [5]. A descriptive cytological report without a definitive diagnosis often confuses the clinicians for further management. So, these diagnostic challenges mandate a unified stage to guide the correct surgical management and follow-up. Milan system for reporting salivary gland cytopathology (MSRSGC) has been introduced as a newer reporting system with the aim of providing a better communication between clinicians and cytopathologists.

The MSRSGC is a six-tier classification system, each with defined diagnostic criteria, explanatory notes, implied risk of malignancy (ROM) and clinical management strategy [6]. It comprises of six categories including [1-6].

- non-diagnostic (ND) (category I)
- non-neoplastic (NN) (category II)
- atypia of undetermined significance (AUS) (category III)
- benign neoplasm (BN) (category IVa)
- salivary gland neoplasm of uncertain malignant potential (SUMP) (category IVb)
- suspicious for malignancy (SFM) (category V)
- malignancy (M) (category VI)

The current study was conducted retrospectively to reclassify the SGL according to MSRSGC, determine the diagnostic accuracy by cyto-histological correlation wherever available and to ascertain the ROM for each category.

Material and Methods

It was a retrospective study undertaken in the Department of Pathology at the tertiary care institute over a period of 3.5 years. FNA smear of 90 patients having salivary gland lesions were retrieved and reviewed. Each case was reclassified into one of the six categories after application of strict criteria given by MSRSGC. These cases were evaluated in reference to the age and sex of patient, site and side of the lesion. The review was done blindly, independent of the histopathological diagnosis.

The histology reports were compared wherever available and ROM was calculated for each category. ROM was determined by dividing the number of malignant cases by a total number of cases on histopathology follow-up in that particular category. Considering histopathology as a gold standard, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy (DA) of FNA were calculated.

Results

Out of total 90 patients, the age ranged from 4 to 90 years with mean age of 37 years. The male (44.4%) to female (55.5%) ratio was 0.8:1. Parotid gland (57.8%; N = 52) was involved in the majority of cases while the submandibular gland was affected in 42.2% (N = 38) of cases. Left and right sided lesion was seen in 52.2% (N = 47) and 44.4% (N = 40) cases whereas only 3.3% (N = 3) cases had lesions bilaterally.

The cytology for these cases were reviewed and categorized according to the MSRSGC into six categories. The majority of the cases belonged to category II (45.5%; N = 41) followed by category IVa (38.8%; N = 35). There were 5.5% (N = 5), 2.2% (N = 2) and 7.7% (N = 7) cases labelled under category IVb, V and VI respectively, while no cases were found for category I and III. (table) In nonneoplastic, benign and malignancy categories, the most common lesion was chronic sialadenitis (N = 28), pleomorphic adenoma (N = 31), and mucoepidermoid carcinoma (MEC) (N = 5), respectively (Table 1)

Table 1: Cytohistological correlation in each category and their risk of malignancies. (N = 90)

Milan Category	Number Of Cases	Diagnosis	Hp Avail-Able	Hp Diagnosis	Rom
Nondiagnostic I	0	-	-	-	-
NonneoplasticII	41(45.5%)	Acute sialadenitis –13	- 0	-	0%
		Chronicsialadenitis–28	- 01	- Sialadenitis – 01	
AUS III	0	-	-	-	-
Benign neoplasm IVa	35 (38.8%)	Pleomorphic adenoma – 31	- 19	Pleomorphic adenoma – 18 Adenoid cystic carcinoma* – 01	05%
		Warthin's tumor – 04	- 01	Warthin's tumor – 01	
Uncertain malignant potential IVb	05 (5.5%)	Cellular basaloid neoplasm – 03	- 02	Basal cell adenoma – 01 Adenoid cystic carcinoma* – 01	33.5%
		Abundance of oncocytic cells – 02	- 01	Warthin's tumor – 01	
Suspicious for malignancy V	02 (2.2%)	Suspicious for mucoepidermoid carcinoma – 01	- 01	Mucoepidermoid carcinoma – 01	100%
		Suspicious for acinic cell carcinoma – 01	- 01	Acinic cell carcinoma – 01	
Malignancy VI	07 (7.7%)	Mucoepidermoid carcinoma – 05	- 02	Mucoepidermoid carcinoma – 02	100%
		Acinic cell carcinoma – 02	- 01	Acinic cell carcinoma – 01	

(HP- histopathology, ROM- risk of malignancy, AUS- atypia of undetermined significance)
'*'= disconcordant cases

Histological follow-up was available for 29 cases, of which 2 cases (2.2%) showed discordance on correlation with cytology. This may be attributed to the morphological diversity of the lesion. In category II, only one case of chronic sialadenitis could be followed on histology, which was diagnosed as sialadenitis. The ROM was 0% for category II.

In category IVa, histological follow up consisted of 20 cases. One of the case was disconcordant which was diagnosed as pleomorphic adenoma (PA) on cytology but on histological follow-up diagnosis of adenoid cystic carcinoma (AdCC) was made (Table 1). Remaining 19 cases were concordant including 18 cases of pleomorphic adenoma (PA) and 1 case of warthin's tumor. The ROM was 5% for category IVa.

Category IVb consisted of 3 cases on follow up, one case showed scattered basaloid cell clusters on cytology but was diagnosed as AdCC on histology. Remaining 2 cases in this category were benign with diagnosis of basal cell adenoma and warthin's tumor (1 case each) (Table 2). The ROM was 33.3%.

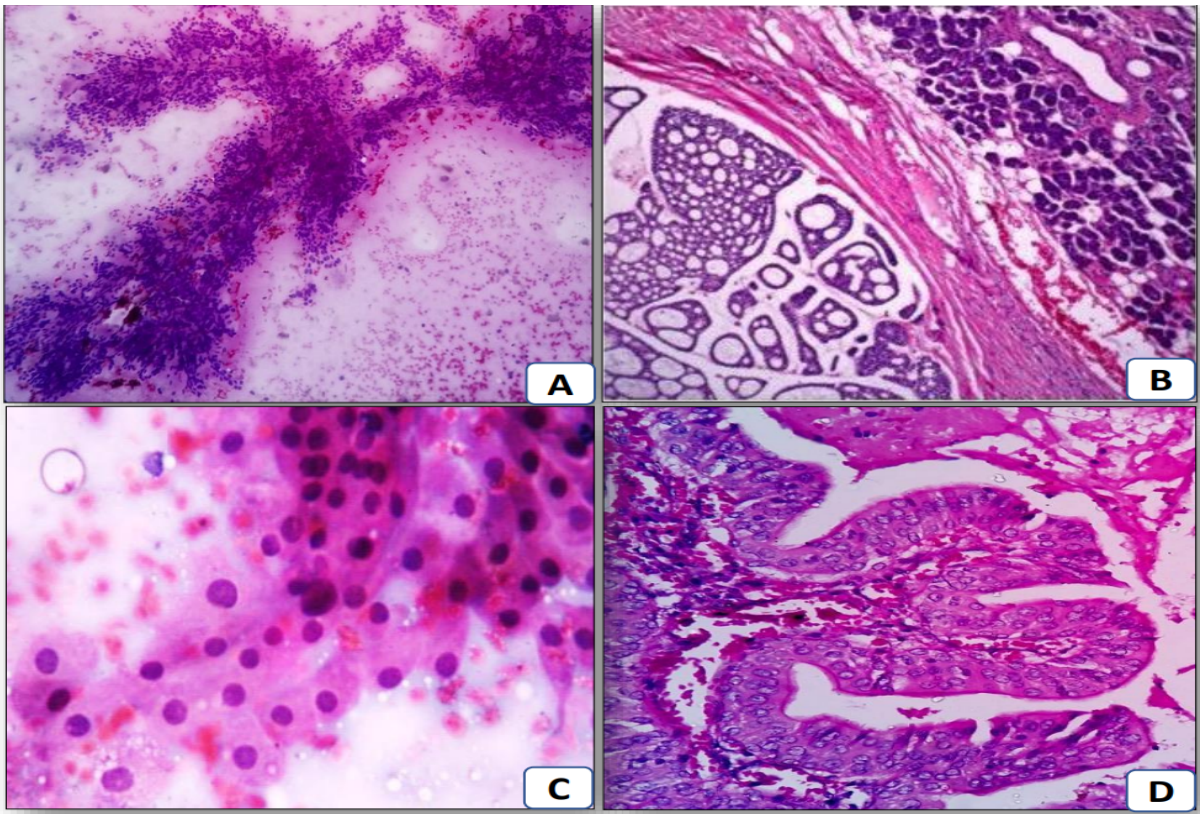

Figure 1: A and B- FNAC smear of cellular basaloid neoplasm and its corresponding HP showing cribriform pattern of adenoid cystic carcinoma along with normal salivary gland tissue (100x, MGG and H&E respectively); C and D- FNAC smear showing abundance of oncocytes and its corresponding HP showing Warthin's tumor (400x, MGG and H&E respectively).

Category V consisted of two cases as suspicious of MEC and acinic cell carcinoma (ACC) (1 case each) with concordant histology. Category VI consisted of 3 cases on follow up, MEC (2 cases) and ACC (1 case) with concordant histology. The ROM for both these categories was 100%

(Figure 1). In this study, the sensitivity, specificity, PPV, NPV, and diagnostic accuracy of FNAC in diagnosing salivary gland lesions using Milan system was found to be 71.4%, 100%, 100%, 91.6%, and 93.1%, respectively (Table 2)

Table 2: Comparison of statistical data of present study with MSRSGC and other studies.

Studies	HP follow-up cases	Disconcordant cases	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	DA (%)
MSRSGC [6]	-	-	86-100	90-100	-	-	-
Rohilla *et al* [12]	94/631 (14.8%)	11/94 (11.7%)	79.4	98.3	-	-	91.4
Karuna *et al* [15]	76/105 (72.3%)	14/76 (18.4%)	85	98.1	94.4	96.6	94.5
Kala *et al* [9]	172/293 (58.7%)	8/172 (4.6%)	83.3	98.3	95.7	92.8	-
Amita *et al* [10]	64/131 (48.8%)	6/64 (9.3%)	89.4	100	100	95.7	-
Jha *et al* [11]	102/292 (34.9%)	17/102 (16.6%)	64.2	97.01	90	86.6	87.3
Pahwa *et al* [14]	76/256 (29.6%)	8/76 (10.5%)	75	98.5	-	-	-
Present study	29/90 (32.2%)	2/29 (6.8%)	71.4	100	100	91.6	93.1

(HP- histopathology, PPV- positive predictive value, NPV- negative predictive value, DA- diagnostic accuracy)

Discussion

Salivary gland cytology is diagnostically challenging owing to the heterogeneity and overlapping cyto-morphological features of these lesions. MSRSGC has provided the diagnostic category for salivary gland lesion cytology, where each category has defined management plan and ROM, gathering wide acceptance among clinicians [6].

In our study, there was a slight female preponderance with male to female ratio of 0.8:1, similar to other studies [7,8]. The mean age group was from 3rd to 4th decade, similar to various studies from India [8-11]. Parotid gland (57.8%) was mostly affected in our study followed by submandibular gland (42.2%), identical to most of the studies in literature [12-14]. On categorization according to the MSRSGC, we found majority of the cases belong to category II (45.5%) followed by category IVa (38.8%), VI (7.7%), IVb (5.5%) and V (2.2%), which correlates well with the studies conducted by Amita *et al* [10]. and Jha *et al* [11].There were no cases categorized as category I and III in our study. In nonneoplastic, benign and malignancy categories, the most common lesion was chronic sialadenitis (68.2%), pleomorphic adenoma (88.5%), and MEC (71.4%), respectively (Table 1). Predominance of these lesions is in concordance with various previous studies [10-12].

On histological follow up ROM for each category in our study was in concordance with the actual ROM of the MSRSGC and various other studies (Table 3) [6-15].

Table 3: Comparison of category-wise Risk of Malignancy (ROM) of present study with MSRSGC and other studies.

Studies	I (%)	II (%)	III (%)	IVa (%)	IVb (%)	V (%)	VI (%)
MSRSGC [6]	25	10	20	<5	35	60	90
Rohilla *et al* [12]	0	17.4	100	7.3	50	-	96
Karuna *et al* [15]	0	0	50	2.4	33.3	100	93.3
Kala *et al* [9]	25	5	20	4.4	33.3	85.7	97.5
Amita *et al* [10]	-	6.2	100	0	25	100	100
Jha *et al* [11]	42.8	30.7	100	10.1	0	71.4	100
Pahwa *et al* [14]	14.2	9	50	0	0	-	83.3
Present study	-	0	-	5	33.5	100	100

There were in total 41 cases in nonneoplastic category (II), out of which only 1 case could be followed up on histopathology, diagnosed as sialadenitis. Hence the ROM in our study was 0%, similar to MSRSGC and various other studies [6,9,10,15]. However, according to many other studies, there is a wide range of ROM from 0-20% [11,12]. MSRSGC believes that this overestimation of ROM may be due to selection bias for surgery in non-neoplastic cases.

There were 35 cases belonging to benign neoplasm category (IVa), with histological follow up of 20 cases. 1 case as false negative was seen, with cytological diagnosis of pleomorphic adenoma, and upon histology was diagnosed as AdCC. Rohilla *et al*. [12] found two cases of MEC and one case of oncocytic carcinoma as false negative in category IVa. In the present study, the ROM for this category was 5%, similar to MSRSGC and various other studies [6,9,12,15]

In our study, there were 5 cases of SUMP category (IVb). Three cases were labelled as cellular basaloid neoplasm and 02 cases showed abundance of oncocytic cells. The differential diagnoses for cellular basaloid neoplasm with hyaline matrix include basal cell adenoma/carcinoma, adenoid cystic carcinoma, epithelial-myoepithelial carcinoma, or polymorphous low-grade adenocarcinoma [6]. This is why, histological evaluation is essential to differentiate benign from malignant entities. Histology for 02 out of 03 cases of cellular basaloid neoplasm was available. One case was diagnosed as basal cell adenoma (BCA) while the other case was diagnosed as AdCC. The differential diagnosis for oncocytic cell as predominant cell type includes few benign conditions such as oncocytosis, warthins tumor and oncocytoma; along with few malignant conditions such as oncocytic carcinoma, mucoepidermoid carcinoma, secretory carcinoma, acinic cell carcinoma, including the high-grade tumors like salivary duct carcinoma. These differentials also include possibility of high-grade tumors, thence necessitate need for histology [6]. Histology of only 01 case of oncocytic morphology was available, which was diagnosed as warthin's tumor. The ROM in our study was 33.5% for category IVb, which was in concordance with MSRSGC recommended ROM for SUMP (35%) [6]. It varies from 0-100% in different studies, Indian data ranging from 33.33% to 50% [9,10,12,15]. This wide and varied range is potentially due to the low number of cases in the SUMP category.

Two cases were considered for suspicious of malignancy category (V) in our study. Histological follow up confirm these cases as MEC and ACC. Thus, ROM was 100% for category V, in concordance with various studies [9,10,15]. However, MSRSGC recommended that it should be around 60% [6].

Seven cases were cytologically diagnosed as malignant (category VI) including 05 cases of MEC and 02 cases of ACC. Histological follow up for 3 cases was available, confirming the diagnosis as MEC (02 cases) and ACC (01 case). The ROM was 100% for category VI, similar to findings in various studies [9-11,15]. Whereas, MSRSGC recommends it to be around 90% (Table 3) [6].

Sensitivity and specificity to differentiate benign and malignant lesions, in our study was 71.4% and 100%. PPV, NPV, and diagnostic accuracy was found to be 100%, 91.6%, and 93.1%, respectively. Comparable results have been reported in literature (Table 2) [9-12,14,15].

The major limitation of our study was the smaller sample size. However, the study with larger sample size may throw better light to validate MSRSGC.

This study was undertaken to classify the salivary gland lesions based on MSRSGC, and to calculate their ROM for specific categories, sensitivity, specificity and diagnostic accuracy, in order to validate MSRSGC. Our data show consistent results with MSRSGC and various other studies, thus recommend the MSRSGC for the standardization of salivary gland FNA reporting and planning the therapeutic approach in patients.

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