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Pathology

STUDY OF SALIVARY GLAND SMEARS FOR REPORTING SALIVARY GLAND CYTOPATHOLOGY USING THE MILAN SYSTEM

Dr. Aishwarya Rao	Final year resident, Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India
Dr. Rajnish Kumar	Professor, Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India
Dr. Meenakshi Tyagi	Associate Professor, Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India
Dr. Anupam Varshney*	Professor & Head, Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India*Corresponding Author

ABSTRACT **Background:** Salivary gland lesions are rare and they account for 2-6% of all head and neck lesions. FNAC is an indispensable diagnostic method for pre-operative evaluation and appropriate therapeutic management. The Milan System for reporting Salivary Gland Cytopathology (MSRSGC) helps in enhancing overall effectiveness of reporting with better communication and improved patient care. **Material and Methods:** Sixty patients were studied prospectively over a period of one and half year. FNAC was done and smears were stained with May-Grunwald-Giemsa. Histopathological examination on routine H&E stain was done wherever biopsies were available. Results: All cases were analyzed and categorized according to the Milan system. The most common category was IVA followed by category II. Majority of the benign neoplasms were Pleomorphic adenoma, while Mucoepidermoid carcinoma was the most commonly diagnosed malignant neoplasm. In category II most common diagnosis was Sialadenosis. **Conclusion:** The Milan System is an efficient system that can improve the overall effectiveness of FNAC reporting of salivary gland lesions assisting in pre-operative management of the patients. FNAC has a high diagnostic accuracy, but the rate of characterization of specific type of tumours is lower due to variable cytomorphology, histopathology examination proved to be accurate for diagnosis in such cases.

KEYWORDS : MSRSGC; Salivary gland lesions; Pleomorphic adenoma; FNAC

INTRODUCTION

Salivary gland lesions comprise 2-6 percent of all head and neck lesions while salivary gland neoplasms form 3-10 percent of all head and neck neoplasms.[1,2] Salivary glands are usually not subjected to incisional or core needle biopsy, because of the possible risk of fistula formation and tumour seedling. [2]

FNAC is able to distinguish between neoplastic and non-neoplastic salivary gland lesions.[3]

The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) fosters better communication between clinicians in order to improve overall patient care. It consists of six diagnostic categories- Non-diagnostic (I), Non-neoplastic (II), Atypia of undetermined significance (III), Neoplasm (IV) is divided into Benign (IVA) and Salivary Gland Neoplasm of Uncertain Malignant Potential (IVB), Suspicious for malignancy (V) and Malignant (VI). Salivary gland FNA samples that are indefinite for a neoplastic condition are classified as Atypia of Undetermined Significance (AUS) in Milan system.[4]

MATERIAL AND METHODS

It is an eighteen months hospital based observational study which included 60 cases of salivary gland swellings, at the Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar.

INCLUSION CRITERIA- All the palpable salivary gland swellings falling within the specified period of time and USG/CT guided FNAC salivary gland swellings were included.

EXCLUSION CRITERIA- All uncooperative patients and patients having history of bleeding/ coagulative disorders.

Patients presenting with salivary gland swelling in Surgery and ENT department, advised for cytological examination were included in the study. Informed consent was taken and FNAC was performed. Smears were stained with May Grunwald Giemsa. The biopsy specimen were fixed in 10% buffered formalin and grossing followed by routine tissue processing was done. Histopathological diagnosis and cytohistological correlation was done. Risk of neoplasm/risk of malignancy along with statistical parameters as sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were calculated.

RESULTS

Sixty patients were included with salivary gland swellings but six cases were bilateral hence total number of cases studied were sixty six. Cytomorphological evaluation of these sixty six cases was done and reported using The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC). Out of sixty six cases, thirteen biopsies were received for histopathological examination.

Age of the patients in the present study was from 11 years to 80 years with mean age of 42 years. Most salivary gland cases were present in the third decade (20%).

Thirty five males (58.4%) and twenty five were females (41.6%) with male to female ratio of 1.4:1. The youngest patient was 11 years female and the oldest patient was 80 years male.

The major salivary glands were involved in 65 cases (98.5%) while the minor salivary gland comprised of only one case (1.5%) involving the lower lip which was reported in a 17 year old male patient. Among the major salivary glands, the parotid gland as 87.6% followed by submandibular gland as 12.3% was involved.

Category IV was the most common category comprising of 39/66 cases (59%), out of which 36/39 cases (92.3%) were categorised as IVA and 3/39 cases (7.7%) were IVB. Category II comprising of 19/66 cases (28.9%). The indeterminate categories comprising of category III, category IVB and category V constituted 1/66 case (1.5%), 3/66 cases (4.5%), and 1/66 cases (1.5%) respectively. None of the case was in category I as repeat FNAC/USG-guided FNAC was carried out in these cases and categorized from category II to VI, based on cytomorphological features.

Parotid gland involvement was most commonly seen in category IVA, 36/57 cases (63.1%). Submandibular gland comprised of 5/8 cases (62.5%) in category II. Minor salivary gland was only involved in category III comprising of only one case.

Maximum size of the lesion was 7cm x 3 cm which was in category VI diagnosed as mucoepidermoid carcinoma, while minimum size was 0.8 x 0.5 cm in category II diagnosed as sialadenosis.

Majority of the cases (90%) were predominantly unilateral with

maximum cases in category IVA and rest 10% were bilateral. In bilateral cases, diagnosis were same on both sides.

Mostly the lesions were mobile with 89.3% cases and 20% cases had a history of smoking

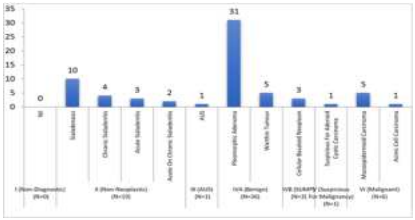


Figure 1: Bar diagram showing various cytological diagnosis under MSRSGC categories (N=66)

Table 1: Cytohistopathological correlation of different MSRSGC categories (N=13)

S.No.	Cytological Category according to MSRSGC	No. of Cases (N=13)	Cytological Diagnosis	Histopathological Diagnosis	RON (%)	ROM (%)
1	III	1	AUS	Mucocele	-	00
2	IVA (N=7)	5	Pleomorphic adenoma	Pleomorphic adenoma	100	00
		2	Warthin tumour	Warthin tumour	100	00
3	IVB	1	Cellular basaloid neoplasm	Adenoid cystic carcinoma	100	100
4	V	1	Suspicious for adenoid cystic carcinoma	Adenoid cystic carcinoma	100	100
5	VI (N=3)	2	Mucoepidermoid carcinoma	Mucoepidermoid carcinoma	100	100
		1	Acinic cell carcinoma	Acinic cell carcinoma	100	100

Table 2: Calculation of statistical parameters of salivary gland lesions cases

Statistical Parameter (N= No. of cases)	MSRSGC Category	FNAC Findings – Cytological diagnosis (No. of cases)	Histopathological Diagnosis (No. of cases)
True Positive (3)	VI	Mucoepidermoid carcinoma (2)	Mucoepidermoid carcinoma (2)
		Acinic cell carcinoma (1)	Acinic cell carcinoma (1)
True Negative (8)	III	AUS (01)	Mucocele (1)
	IVA	Pleomorphic adenoma (5)	Pleomorphic adenoma (5)
		Warthin tumour (2)	Warthin tumour (2)
False Negative (2)	IVB	Cellular basaloid neoplasm (1)	Adenoid cystic carcinoma
	V	Suspicious for adenoid cystic carcinoma	Adenoid cystic carcinoma

All the cytology smears were categorized into different groups and the histopathological diagnosis results were correlated and consistent in 11/13 cases (84.6%). We evaluated the validity of MSRSGC in terms of sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy, and values were 60%, 100%, 100%, 80% and 84.61% respectively (Table 2). Category V was taken as non-malignant and counted as False Negative. Since no false positive case was recorded hence specificity and positive predictive value were 100%.

Figure 2: Photomicrograph of cytological smears: (a) Sialadenosis (MGG, 100X), (b) Acute sialadenitis (MGG, 40X), (c) AUS (mucinous cystic content) (MGG, 100X), (d) Pleomorphic adenoma (MGG, 100X), (e) Warthin tumour (MGG, 100X), (f) Cellular basaloid neoplasm (MGG, 100X), (g) Suspicious for adenoid cystic carcinoma (MGG, 400X), (h) Mucoepidermoid carcinoma (MGG, 400X), (i) Acinic cell carcinoma (MGG, 100X)

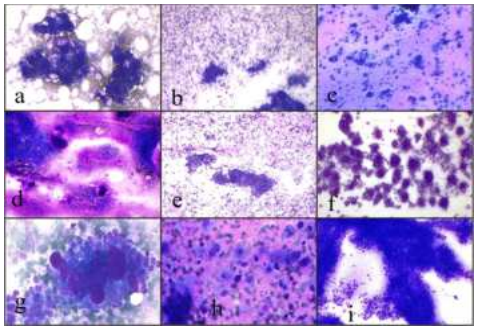
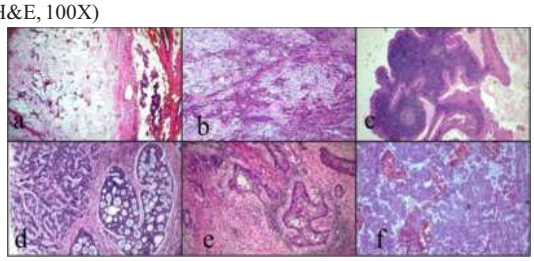


Figure 3: Photomicrograph of H&E stained sections: (a) Mucocele (H&E, 100X), (b) Pleomorphic adenoma (H&E, 100X), (c) Warthin tumour (H&E, 40X), (d) Adenoid cystic carcinoma (H&E, 100X), (e) Mucoepidermoid carcinoma (H&E, 100X), (f) Acinic cell carcinoma (H&E, 100X)



DISCUSSION

Mean age reported in the present study was 42 years, while Gupta C et al [5] , Bharti JN et al [6] , and Viswanathan K et al [7] showed mean age of 42.9 years, 39 years and 60.3 years respectively.

Thirty five males (58.4%) and 25 females (41.6%) with male to female ratio of 1.4:1 were in the current study. The oldest patient was an 80-year-old male, while the youngest was an 11-year-old female. In category IVA, mainly pleomorphic adenoma and all four cases of warthin tumour comprised of exclusively male patients. On the basis of study of Sandhu VK et al[8], pleomorphic adenoma was more frequent in females in contrast to warthin tumour which occurred only in males. Work of Singh S et al [9], Pahwa S et al[10] showed a male predominance similar to the present study. This was discordant with studies of Viswanathan K et al [7] , Gupta C et al [5] , and Aruna S et al [11] where majority of the patients were female.

In the present study majority of the salivary gland lesions were situated in the parotid gland followed by submandibular gland. Minor salivary gland involving the lower lip comprised of only one case. In the studies of Singh S et al [9], Legaspi et al[12] majority cases were in parotid gland while in Das DK et al[13] it was in the submandibular gland.

In the current study size of the lesions ranged from 0.8 x 0.5 cm to 7 x 3 cm and greatest dimension was taken into consideration which was similar in findings of Rossi ED et al[14] where the mean size ranged from 2.25 to 2.73 cm, the lesions ranged in size from 0.4 cm to 6 cm in greatest dimension. [15] In the studies by Viswanathan K et al[7] size of the lesions ranged from 0.2 cm to 10.5 cm, with an average size of 2.2 cm.

In the present study category IV was the most common category comprising of 39 cases (59.1%), out of which 36 (54.6%) were categorised as IVA. This was followed by category II comprising of 19 cases (28.9%). The indeterminate categories i.e. category III had 1 case (1.5%), category IVB comprised of 3 cases (4.5%), and category V had 1 (1.5%) case. Gautam D et al[16] , Singh S et al[9] , and Pahwa S et al[10] also showed majority cases were in category IVA followed by category II, and inconsistent with the findings in the study done by Cablao NP et al[17] and Maleki Z et al[18] wherein category II comprised of majority of cases. In a study done by Cablao NP et al[17] , least number of cases were found in category III, V and VI. Singh S et al[9] placed only one case was in category V which was in concurrence with our study. This was inconsistent with the findings of Maleki Z et al[18] where category III

comprised of 19.7% cases. In the present study among benign neoplasms, pleomorphic adenoma was the most frequently encountered lesion with higher incidence of occurrence in parotid gland which was similar to the study of Singh Nanda KD et al[19] and Cohen EG et al[20] . In the non-neoplastic category of our study maximum cases were of sialadenosis followed by chronic sialadenitis, which was discordant with the study by Aruna S et al[11] , where maximum cases reported were of sialadenitis followed by sialadenosis. Study of Singh S et al[9] showed that after histopathological follow up the concordant and discordant cases were noted. Out of the seven cases in the non-neoplastic group, five had concordant diagnoses; of the discordant cases, one had a diagnosis of pleomorphic adenoma and the other of mucoepidermoid carcinoma. One case of category V was identified as carcinoma ex pleomorphic adenoma during histological follow-up. On the basis of study by Singh S et al [9], histological follow up was available for in 46.6% cases in which three instances of category III were found to have mucocele in investigation but on histological follow-up revealed discrepancies and the cases were diagnosed as pleomorphic adenoma, myoepithelioma, and adenoid carcinoma. According to Singh S et al, adenoid cystic carcinoma and polymorphous low-grade adenocarcinoma were among the discordant diagnoses in category IVA, although all of the cases in our investigation that had histological follow-up were in agreement with their cytological results. In category IVB, pleomorphic adenoma, myoepithelial carcinoma, and adenoid cystic carcinoma were found on histological follow-up but in the present study, a cellular basaloid neoplasm turned out to be adenoid cystic carcinoma on histopathology. Histopathologically, one case in the study that was suspected for adenoid cystic carcinoma turned out to be adenoid cystic carcinoma upon histological follow-up. In category V, the diagnosis was carcinoma ex pleomorphic adenoma. In category V, the final diagnosis of pleomorphic adenoma was given to two out of ten patients that were found to be discordant on histological follow-up; in contrast, in the current study, the cytological diagnosis of both mucoepidermoid carcinoma and acinic cell carcinoma were in concordance. For category III, no neoplastic case was reported so RON could not be estimated, whereas was found to be 100% in all the other categories (Table 1). According to the study conducted by Singh S et al [9] overall RON was found to be least in category II (28.57%), non-diagnostic followed by category I, non-diagnostic (33.33%) while for rest other categories it was 100%. In our study risk of malignany was 100% for category IVB, V and VI, while 0% for category III and IVA. As no case was available for category I, and no biopsy was available for category II, therefore risk of malignancy could not be evaluated.

According to Faquin and Rossi, MSRSGC [21] ROM with range for category I, II, III, IVA, IVB, V and VI were 15% (0-50%), 11% (0-100), 30% (0-100), <3% (0100%), 35% (0-100%), 83% (50-100%) and 98% (80-100%) respectively. In the study conducted by Pahwa S et al[10] histological follow up was available, all of which were concordant, hence the ROM was 0% for category IVA which was consistent with the findings of our study. On the basis of study of Cablao NP et al[17] , Rohilla M et al[22], Mukundapai M et al[23], Wang Z et al[24] , ROM for malignant category was 100%, 96%, 96.72% and 97.7% respectively. ROM for category IVB was also comparable to the study of Legaspi CM et al[12]. One case of cellular basaloid neoplasm in our study on histopathological follow-up was diagnosed as adenoid cystic carcinoma. Similarly in the study of Legaspi CM et al[12] two cases of SUMP turned out to be adenoid cystic carcinoma and another two were basal cell adenoma. For malignant category, all cases had cytohistologic correlation, and the ROM was at par with study done by Legaspi CM et al[12]. The projected ROM in our study for the indeterminate categories (AUS, SUMP, and suspicious for malignancy) was 0% for AUS since no malignant case was recorded after follow up, for category IVB and V as one case from each category turned out to be malignant with ROM of 100% (Table 1). In contrast to the study by Viswanathan K et al [7] as very few samples were available in category III, IVB and V.

Table 3: Various statistical parameters of salivary gland lesions

Authors	Study year	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Present study	2024	60.00	100.00	100.00	80.00	84.61
Cablao NP et al [17]	2022	71.6	90.9	88.3	76.9	-
Wang Z et al [24]	2022	99.2	74.8	-	-	-
Pahwa S et al [10]	2022	75	98.5	85.7	97.1	-
Legaspi CM et al [12]	2022	69.20	87.30	52.90	93.20	-
Singh S et al [9]	2020	80	89.80	-	-	87.50
Bharti JN et al [6]	2020	36.3	94.4	66.6	82.9	80

CONCLUSION

The Milan System for Reporting Salivary Gland Cytopathology helps the surgeons in the management of salivary gland lesions. Variations and pitfalls in cytological diagnosis of indeterminate salivary gland swellings, refined criteria to place each cytological smear into defined diagnostic category will be helpful. The histopathological examination is the gold standard for diagnosing indeterminate cases of salivary gland swellings. There were limitations in the present study with relation to sample size which should be larger. Every institution should audit their frequencies and malignancy rates to serve as a quality indicator during patient care.

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