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Original Research Article

Application of Milan System in Cytopathology of Salivary Gland Lesions: A Retrospective Study

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Abstract:

Aim: Cytopathology of salivary gland lesions pose diagnostic challenges due to cytomorphological overlap and diversity. The Milan system for reporting salivary gland cytology (MSRSGC)is a flexible, risk stratification based reporting system that helps clinicians plan appropriate management. This study assesses the Milan System in a tertiary care centre.

Material and Methods: The FNA of salivary gland lesions over a period of 2 years were retrieved and placed in six diagnostic categories as per MSRSGC. Histopathology follow up slides were reviewed for available cases. The Risk of Malignancy for each category, sensitivity, specifity, diagnostic concordance, positive predictive value and negative predictive value were calculated.

Results: On reclassification of 191 cases based on MSRGC, there were 2, 107, 5, 50, 6, 2, 19 cases in Non-diagnostic, Non neoplastic, Atypia of undetermined significance, Classical Benign neoplasm, Salivary gland neoplasm of uncertain malignant potential, Suspicious for malignancy and Malignant categories respectively. Sensitivity was 72.2% and specificity 100%. Histological follow up was available for 28 of the 191 cases. (14.65%) with 85.71% histocytological concordance.

Conclusion: The results of this study are in line with MSRSGC. It helps standardise and stratify reports with risk of malignancy pre operatively for better patient care.

Keywords: FNA, Milan, Salivary Gland.

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Introduction

Salivary gland lesions are variegated with cytomorphological overlap posing a challenge to uniformity in reporting. These tumours are comparatively rare as it affects 0.4 – 13.5% per 100,000 people.[1,2] Cytopathology of salivary gland lesions is a cost effective method of evaluation as it is of low risk compared to incisional biopsy.

A new classification system was proposed by Authors like Griffith et al and Wang et al based on risk stratification similar to the Bethesda system in Thyroid cytology [3]. Table-1 The aim of the proposed classification system was also to help pathologist avoid pit falls due to identical cytological features [3] The reporting categories were proposed to be evidence based and targeted to optimal patient care. The Risk of Malignancy was calculated based on literature review [4]

Materials and Methods

The cytology slides of salivary gland lesions of 2 years were retrieved. The reports were reclassified into 6 diagnostic categories according to MSRSGC into Non diagnostic, Non neoplastic, Atypia of undetermined significance, Classical Benign neoplasm(BN), Salivary gland neoplasm of uncertain malignant potential(SUMP), Suspicious for malignancy(SM) and Malignant categories(M). Sensitivity, Specificity, Positive predictive value and Negative predictive value were calculated. The Risk of Malignancy (ROM) was calculated in different categories. The ROM is calculated for each category as the number of malignancies on histology divided by the total number of cases in histology a given category.

ROM= number of malignant cases in a category x 100. Total histopathology cases in same category

Results

This study had 191 cases over a period of 2 years which comprised 97 male and 83 female patients. Men in the age group of 50 to 60 years were commonly affected. Parotid lesions were the commonest followed by submandibular

involvement. Non neoplastic lesions (Milan Group-II) were the commonest with 107 (56%) cases. The neoplastic lesions included 50(27.2%) classical benign (Milan Group-III), 6(3.2%) SUMP (Milan Group-IV), 2(1%) SM (Milan Group-V) and 19 (10%) malignant cases (Milan Group-VI). Histology follow up was available for 28 out of the 191 cases.(25.1%). There was 85.7% histocytological concordance. The most common histopathological diagnosis was pleomorphic adenoma in the benign category and mucoepidermoid carcinoma in the malignant category. Parotid had the highest number of malignancies with 13 cases and submandibular gland had 4 cases. The cases that did not correlate were 3 in non-neoplastic cystic category(Milan Group-II) and 2 in the classical benign category. (Milan Group-IV). Histopathology of 13 cases in Suspicious for malignancy and Malignant group (Milan GroupV&VI) together was malignant. These include 4 metastatic deposits, 5 Mucoepidermoidcarcinoma, 1 Squamous Cell Carcinoma, 1 poorly differentiated tumor and 1 case of Malignant Oncocytoma. Table-2.

Table 1: The Milan Categories with Clinical Management Strategies

	Categories	**Clinical management**	**Likelihood of malignancy**
I	Non diagnostic	Repeat FNAC with USG is recommended for this category	25%
II	Non neoplastic	Radiologic correlation and close clinical follow up is needed to ensure that specimen is representative of the lesion.	02%
III	Atypia of undetermined significance	Repeat FNA or conservative surgical resection	20%
IV	Neoplasm a) Classical Benign neoplasm with established cytologic criteria(BN) b) Salivary gland neoplasm of uncertain malignant potential (SUMP)	 Conservative surgery or clinical follow up only. Conservative surgery with negative margins	 Less than 05% 35%
V	Suspicious for malignancy(SM)	Surgery	60%
VI	Malignant(M)	Low grade limited surgery Preservation of Facial Nerve High grade – Radical surgeries with major nerves and neck dissection. Ancillary tests like IHC is needed	90%

Table 2: Classification based on Milan Reporting System with estimated ROM

Category	**No. of cases in cytology/%**	**HP follow up of available cases**	**Concordant/Discordant diagnosis on HP**	**Risk of Malignancy**
1	2/1	0	0/0	-
2	107/56	17	14/3	5.8%
3	5/2.6	1	1/0	100%
4a	50/26.2	15	13/2	13.3%
4b	6/3.2	2	2/0	100%
5	2/1	2	2/0	100%
6	19/10	11	11/0	100%

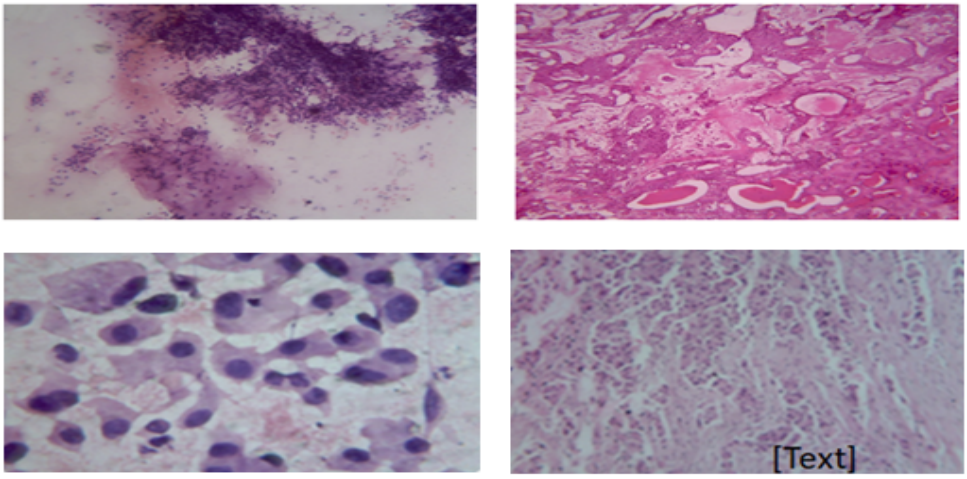

Figure 1: FNA with corresponding Histopathological photograph of pleomorphic adenoma and malignant oncocytoma

Discussion

Cytology of salivary gland lesions has been documented to be an effective diagnostic tool in optimizing surgical intervention and follow up in patient care. Of the 191 salivary gland aspirates, 54% were that of male patients. 58.2% were parotid lesions and the rest were submandibular lesions. Parotid gland was most commonly involved in most other studies with involvement of 61% to 93% [2,3,5-10].

The 191 cases were re-classified according to MSRSGC into 6 diagnostic categories. Maximum of 107(56%) cases was in non-neoplastic category. (NN) Other studies have also stated high number of cases in this group.[2] Histopathology follow up was available in 17 cases in this category.(Fig:1) 3 of the 7 cases reported as infected cystic lesions were confirmed to be monomorphic adenoma, basal cell adenoma and low grade mucoepidermoid carcinoma in histology. Cystic lesions of salivary gland can be malignant or benign. Pleomorphic adaenoma in benign category and malignancies like mucoepidermoid carcinoma and acinic cell carcinoma can be cystic.

Atypia of undetermined significance (AUS) in a newly introduced entity in reporting of salivary gland lesions. Our study had 5 cases (2.6%) in this group. One case had HP follow up and was diagnosed to be Acinic cell Carcinoma. FNA and histology concordance of Acinic Cell Carcinoma is 83-91% (11) in other studies.

2 cases reported as Pleomorphic Adenoma in Classical Benign group (BN) in cytology turned out to be carcinoma ex pleomorphic adenoma and low grade mucoepidermoid carcinoma on histology. This is a known pitfall in salivary gland cytology. (12) The cyto histological concordance of pleomorphic adenoma is 75% in this study. In many studies it is found to be high. [13,14,15]. 2 cases that had histology follow up in SUMP category were Mucoepidermoid Carcinoma on histology with cyto histological concordance of 100%. In study by Maleki et al.,cyto histological concordance was 83.3% for this group.[16] All the 11 cases that had histopathology follow up in Suspicious for malignancy and Malignancy category (Milan Group V&VI) turned out malignant with cyto histological correlation of 100%. In other comparative studies, it was 79.95% and 88% respectively.[17,18]

The ROM for non-neoplastic lesions according to MSRGC should be around 2%. We had HP correlation in 15 cases out of 56 cases with ROM of 5.8%. The ROM for this category in other studies varied between 100% and 53% in other studies. [2,6].The ROM is 100 for AUS category and 18.1 for benign neoplasms which is more than that cited in literature [9] which varies between 73.08% to 0.00% among instituitions. [9] The ROM for SUMP, Suspicious for malignancy and Malignant groups was 100%. Literature cites ROM in the range of 0-100%, 0-100% and 57-100% respectively for these categories. [3,6,7] The Sensitivity, Specificity, PPV, NPV were 66.6% and 100%, 100% and 72.2% respectively. Various other studies show varying Sensitivity between 62% to 97.6% and specificity from 94.3% to 100%, in salivary gland cytology (19-24). PPV and NPV vary between 88.8-92.9% and 91.8-97.5% in literature. [6,25,26]

The false negative rate was 17.8%.The range of false negative cases is 0-37% in literature. [26] With the introduction of the terms AUS and SUMP in MSRGC ,the non-malignant cystic/paucicellular lesions and cellular neoplasms that could not be defined as benign or malignant could be appropriately categorized so that false negative rate decreases.

Conclusion

The newly introduced Milan system of salivary gland cytology will lead to a uniform and internationally standardised reporting format of salivary gland FNA. Due to risk stratified categories, cases in groups with higher risk of malignancy can be monitored and treated surgically if indicated.

References:

1. Z. Tian, L. Li, L. Wang, Y. Hu, and J. Li, "Salivary gland neoplasms in oral and maxillofacial regions: a 23-year retrospective study of 6982 cases in an eastern Chinese population," International Journal of Oral and Maxillofacial Surgery, vol. 39, no. 3, pp. 235–242, 2010.
2. Rohilla, M., Singh, P., Rajwanshi, A., Gupta, N., Srinivasan, R., Dey, P. and Vashishta, R. K. (2017), Three-year cytohistological correlation of salivary gland FNA cytology at a tertiary center with the application of the Milan system for risk stratification. Cancer Cytopathology, 125: 767-775.
3. Griffith CC, Pai RK, Schneider F, Duvvuri U, Ferris RL, Johnson JT, et al. Salivary Gland Tumor Fine-Needle Aspiration Cytology: A Proposal for a Risk Stratification Classification. American Journal of Clinical Pathology. 2015; 143(6):839–53.
4. American Society of Cytopathology. The Milan System for ReportingSalivary Gland Cytopathology.http://www.cytopathology.org/the-milansystem-for-reporting-salivary-gland-cytopathology/.
5. Rossi, E. D., Wong, L. Q., Bizzarro, T., Petrone, G., Mule, A., Fadda, G. and Baloch, Z. M. (2016), The impact of FNAC in the management of salivary gland lesions: Institutional experiences leading to a risk-based classification scheme. Cancer Cytopathology, 124: 388-396. doi:10.1002/cncy.21710
6. Rossi ED, Faquin WC, Baloch Z, et al. The Milan System for Reporting Salivary Gland Cytopathology: analysis and suggestions of initial survey [published online ahead of print July 14, 2017]. Cancer. doi: 10.1002/cncy. 21898.
7. Schmidt RL, Hall BJ, Wilson AR, et al. A systematic review and meta-analysis of the diagnostic accuracy of fine-needle aspiration cytology for parotid gland lesions. Am J ClinPathol. 2011;136:45–59.
8. Ali NS, Akhtar S, Junaid M, Awan S, Aftab K. Diagnostic Accuracy of Fine Needle Aspiration Cytology in Parotid Lesions. ISRN Surgery. 2011; 2011:1–5.
9. Wang H, Malik A, Maleki Z, Rossi ED, Ping B, Chandra A, et al. "Atypical" salivary gland fine needle aspiration: Risk of malignancy and interinstitutional variability. Diagnostic Cytopathology. 2017; 45(12):1088–94.
10. Wei S, Layfield LJ, LiVolsi VA, Montone KT, Baloch ZW. Reporting of fine needle aspiration (FNA) specimens of salivary gland lesions: A comprehensive review.Diagnostic Cytopathology.2017; 45:820–827.
11. Klijanienko, J. and Vielh, P. (1997), Fine-needle sampling of salivary gland lesions V: Cytology of 22 cases of acinic cell carcinoma with histologic correlation. Diagn. Cytopathol., 17: 347-352.
12. Hussain N, Krishnani C, Gahine R, Sudarshan V. Pleomorphic adenoma: A diagnostic pitfall in the diagnosis of salivary gland lesions on FNAC: Case reports with review of the literature. CytoJournal. 2010; 7(1):17.
13. Mihashi H, Kawahara A, Kage M, Kojiro M, Nakashima T, Umeno H, et al. Comparison of preoperative fine-needle aspiration cytology diagnosis and histopathological diagnosis of salivary gland tumors. Kurume Med J. 2006; 53:23–7.
14. Rajwanshi A, Gupta K, Gupta N, Shukla R, Srinivasan R, Nijhawan R, et al. Fine-needle aspiration cytology of salivary glands: Diagnostic pitfalls – Revisited. DiagnCytopathol. 2006; 34:580–4.
15. Jayaram G, Verma AK, Sood N, Khurana N. Fine needle aspiration cytology of salivary gland lesions. Journal of oral pathology & medicine. 1994 Jul 1; 23(6):256-61.
16. Maleki, Z, Miller, JA, Arab, SE, Fadda, G, Bo, P, Wise, O, Rossi, ED, Jhala, N, Ashish, C, Ali, SZ & Wang, H 2017, '"Suspicious" salivary gland FNA: Risk of malignancy and interinstitutional variability' Cancer Cytopathology. DOI: 10.1002/cncy.21939.
17. .Colella G, Cannavale R, Flamminio F, et al. Fine-needle aspiration cytology of salivary gland lesions: a systematic review. J Oral Maxillofac Surg. 2010; 68:2146–2153.
18. Postema RJ, van Velthuysen ML, van den Brekel MW, Balm AJ, Peterse JL. Accuracy of fine-needle aspiration cytology of salivary gland lesions in the netherlands cancer institute. Head & neck. 2004 May 1; 26(5):418-24.
19. Kocjan G, Nayagam M, Harris M. Fine needle aspiration cytology of salivary gland lesions: Advantages and pitfalls. Cytopathology. 1990; 1:269–75.
20. Qizilbash AH, Sianos J, Young JE, Archibald SD. Fine needle aspiration biopsy cytology of major salivary glands. ActaCytol. 1985; 29:503–12.
21. Zurrida S, Alasio L, Tradati N, Bartoli C, Chiesa F, Pilotti S. Fine-needle aspiration of parotid masses. Cancer. 1993; 72:2306–11.
22. Jayaram G, Verma AK, Sood N, Khurana N. Fine needle aspiration cytology of salivary

gland lesions. J Oral Pathol Med. 1994; 23:256–61.
23. Chakrabarti S, Bera M, Bhattacharya PK, Chakrabarty D, Manna AK, Pathak S, et al. Study of salivary gland lesions with fine needle aspiration cytology and histopothology along with immunohistochemistry. J Indian Med Assoc. 2010; 108:833–6.
24. Nguansangiam S, Jesdapatarakul S, Dhanarak N, Sosrisakorn K. Accuracy of fine needle aspiration cytology of salivary gland lesions: routine diagnostic experience in Bangkok, Thailand. Asian Pac J Cancer Prev. 2012 Sep; 13(4):1583-8.
25. Tahoun N, Ezzat N. Diagnostic accuracy and pitfalls of preoperative fine needle aspiration cytology in salivary gland lesions. Journal of the Egyptian National Cancer Institute. 2008 Dec; 20(4):358-68.
26. Ashraf A, Shaikh AS, Kamal F, Sarfraz R, Bukhari MH. Diagnostic reliability of FNAC for salivary gland swellings: A comparative study. Diagn Cytopathol. 2010; 38:499–504.