A retrospective six-year cytohistological correlation of fine-needle aspiration cytology with classification by the Milan system for reporting salivary gland cytopathology

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ABSTRACT

A retrospective six-year cytohistological correlation of fine-needle aspiration cytology with classification by the Milan system for reporting salivary gland cytopathology

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(Directed by Professor Soon Won Hong)

Salivary gland fine needle aspiration (FNA) is invaluable pre-operative technique for clinical management of salivary gland lesions. However, precise and definite diagnosis can be challenging due to intratumoral heterogeneity and overlapping features among diverse entities. There was no standard classification for salivary gland FNA lesions. As a result, there are various reporting styles for salivary gland FNA with equivocal terminology. This can lead to miscommunication between clinicians and pathologists. Recently new classification system named “The Milan System for Reporting Salivary Gland Cytopathology” (MSRSGC) was proposed. Our retrospective study aims to evaluate the accuracy of FNAs of salivary gland lesions according to the MSRSGC and determine their associated risk of neoplasm and malignancy. A retrospective slide review and classification of salivary gland FNAs over 6 years (2013-2018) were done. All samples were processed with alcohol fixed smears with Papanicolaou stain. FNAs were classified according to the MSRSGC as follows: non-diagnostic (ND), non-neoplastic (NN), atypia of undetermined significance (AUS), benign neoplasm (BN), salivary gland neoplasm of uncertain malignant potential (SUMP), suspicious for malignancy (SM), or malignant (M). The risk of neoplasm (RON) and malignancy (ROM) were calculated for all diagnostic categories. A total of 374 FNA cases (371 patients) were performed for 6 years and 150 FNA cases had clinical and surgical follow up

(40.1%). Among surgically treated cases, the distribution of each FNA's category were as follows; ND (13.3%), NN (5.3%), AUS (6.7%), BN (50.0%), SUMP (18.0%), SM (4.0%), and M (2.7%). The overall risk of neoplasm (RON) was 70.0% for the ND, 62.5% for NN, 90% for the AUS, 100% for BN, 96.3% for SUMP, 100% for SM and M. The overall risk of malignancy (ROM) was 35% for ND, 25% for NN, 50% for AUS, 4% for BN, 33.3% for SUMP, 83.3% for SM and 75% for M. Compared to the ROM recommended by MSRSGC, ND and NN were slightly higher, and there was a significant difference in AUS. BN were within the range, SUMP and M were slightly lower, and SM was higher. Newly proposed MSRSGC is a useful system for classifying salivary gland lesions according to their associated risk of malignancy. Adoption of MSRSGC could potentially stratify ROM and remove vagueness among clinician and surgeon.

Key words : salivary gland, fine needle aspiration, the milan system for reporting salivary gland cytopathology, risk of malignancy

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I. INTRODUCTION

Salivary gland fine needle aspiration (FNA) is well established, minimally invasive, cost-effective procedure with very rare complication.[1,2] FNA provides clue to clinical management such as distinguishing between a neoplastic and a non-neoplastic lesion, or benign or malignant and a sample for ancillary test.[3-7] Clinical management and surgery deeply depends on FNA together with clinical information and imaging studies. Therefore, it is very crucial to differentiate benign versus malignant lesions. However, intratumoral heterogeneity and overlapping cytologic features between salivary gland lesions makes accurate subtyping of neoplasm challenging.[8-11] Until recently there was no uniform reporting system for salivary gland lesions. Descriptive cytologic diagnosis without categorization can be confusing for clinicians who need more accurate information for their management plan.[9]

In an attempt to address these challenges, under supports of The American Society of Cytopathology and The International Academy of Cytology, an international group of pathologist and clinicians developed a tier-based classification system designated The Milan System for Reporting Salivary Gland Cytopathology (MRRSGC).[12-13] The goal of this classification was to standardize salivary gland reporting system and provide an outline for controlling clinical management. Like other similar reporting systems, such as the Bethesda System for reporting Thyroid Cytopathology, this classification provides clinically valuable framework for conceptualizing disease.[14] The MSRSGC is composed of seven categories as follows: non-diagnostic (ND), non-neoplastic (NN), atypia of undetermined significance (AUS), benign neoplasm (BN), salivary gland neoplasm of uncertain malignant potential (SUMP), suspicious for malignancy (SM), and malignant (M).

Until now, few studies have demonstrated promise in its use for this system. In this study, we retrospectively applied the MSRSGC to categorize salivary gland FNAs for the past 6 years (2013-2018). The objective of this study was to evaluate the diagnostic accuracy within the framework of MSRSGC and evaluate this system as a tool for risk assessment.

II. MATERIALS AND METHODS

1. Research objective

A retrospective six-year search (January 2013 - December 2018) of the cytopathology database for salivary gland (All major and minor salivary gland) FNA specimens at Gangnam Severance Hospital, School of medicine, Yonsei University was performed. Clinical data regarding age, gender and location of lesion, type of tumor were collected from the medical records. The follow-up histopathological reports were gained wherever they were available

2. Fine needle aspiration procedure and method of slide preparation

The FNAs were performed using a direct percutaneous or transoral route with 23-gauged needle. Smears was fixed in 95% ethanol for Papanicolaou staining in the cytopathology laboratory.

3. Cytopathologic/histopathologic report & slide review according to diagnostic criteria

Cytopathology slides were reviewed by two different pathologists and each case was retrospectively assigned using The Milan system for Reporting Salivary Gland Cytopathology (MSRSGC). Additionally, classification rely on written diagnosis without evaluating cytopathology slides was performed. We also examined the distribution of histopathologic diagnosis. The histologic diagnosis of surgical specimens was categorized as non-neoplastic lesion, benign neoplasm, and low grade

malignant neoplasm and high grade malignant neoplasm.

4. Evaluation of risk of malignancy and risk of neoplasm

Cytohistologic correlation was performed to calculate the risk of malignancy (ROM) and risk of neoplasm (RON). The ROM is defined as the ratio of FNAs with malignant neoplasm follow up to the total number of FNAs with follow up. Similarly, the RON is defined as the ratio of FNAs with benign and malignant neoplasm follow up to the total number of FNAs with follow up.

5. Statistical analysis

Clinical parameters were offered with descriptive statistical methods (percentage and number). Cohen's kappa statistics was used to compare the agreement between the two methods (classification with slide review vs classification without slide review). The guideline of Landis and Koch was used to evaluate strength of agreement as follows: 0-0.20 for slight agreement; 0.21-0.40, fair agreement; 0. 0.41– 0.60, moderate agreement; 0.61–0.80, substantial agreement and 0.80–1.00, almost perfect agreement.[15] Statistical calculation was performed using SPSS ver. 21.0 (IBM Corp., Armonk, NY, USA). A p-value of < 0.05 was considered statistically significant.

III. RESULTS

1. Clinical manifestation

A retrospective investigation of salivary gland FNA over 6 years was performed,

and totally 374 cases were evaluated. The age of patients was variable from 10 to 102 years, and the mean age was 51 years. The female-to-male ratio was 1.2:1 with 205 females and 169 males. The most commonly involved salivary gland was parotid gland (77.5% or 290 of 374) followed by the submandibular gland (21.7% or 81 of 374), sublingual gland (0.5% or 2 of 374) and the minor salivary gland (0.3% or 1 of 631). The most common benign neoplasm was pleomorphic adenoma, comprising 58.0% of all cases. The most common malignant neoplasm was mucoepidermoid carcinoma, comprising 38.2% of all cases (Figure 1).

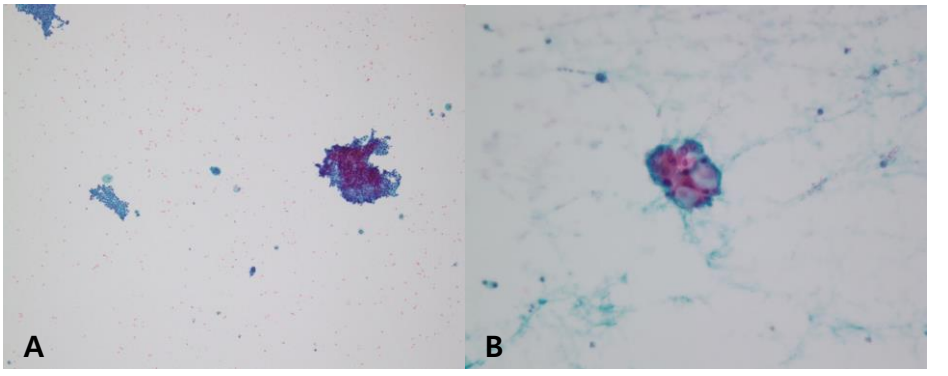

Figure 1 (A) Fine-needle aspiration reveals the cytomorphologic appearance of the mucoepidermoid carcinoma with admixed of mucus cells, intermediate cells and epidermoid cells with mild nuclear atypia; cystic background (Papanicolaou stain), (B) Mucus-producing cells (Papanicolaou stain).

2. Cytohistologic correlation according to cytopathology slide review

According to the MSRSGC categorization, 83 cases were assigned to the non-diagnostic category (22.2%), 64 cases to the non-neoplastic category (17.1%), 27

cases to the atypia of undetermined significance category (7.2%), 132 cases to the benign neoplasm category (35.3%), 47 cases to salivary gland neoplasm of uncertain malignant potential category (12.6%), 7 cases to suspicious for malignancy category (1.9%), and 14 cases to malignant category (3.7%). (Table 1 and 2) Of all cases, 3 cases (0.8%) had repeat FNA. The reason for repeat FNA was due to non-diagnostic category, leading to a repeat FNA to get a management-based diagnosis.

The preoperative cytological diagnosis and histological follow up are listed in Table 1 and Table 2. Of the 374 cases, 150 (40.1%) had corresponding histological follow-up. 20 cases were assigned to the non-diagnostic category (13.3%), 8 cases to the non-neoplastic category (5.3%), 10 cases to the atypia of undetermined significance category (6.7%), 75 cases to the benign neoplasm category (50.0%), 27 cases to salivary gland of uncertain malignant potential category (18.0%), 6 cases to suspicious for malignancy category (4.0%), and 4 cases to malignant category (2.7%)

The risk of neoplasm (RON) was 70.0% for non-diagnostic, 62.5% for non-neoplastic, 90.0% for atypia of undetermined significance, 100% for benign, 96.3% for salivary gland neoplasm of uncertain malignant potential, 100% for suspicious for malignancy, and 100% for malignant The risk of malignancy (ROM) was 35.0% for non-diagnostic, 25.0% for non-neoplastic, 50.0% for atypia of undetermined significance, 4.0% for benign, 33.3% for salivary gland neoplasm of uncertain malignant potential, 83.3% for suspicious for malignancy, and 75.0% for malignant

Table 1 Histologic diagnosis according to cytologic slide review

Cytology	Histology Non-neoplastic	Benign neoplasm	Malignant (low)	Malignant (high)
I. Non-diagnostic	4 Lymphoepithelial cyst 1 Chronic sialadenitis 1 Fibrocalcific nodule	3 WT 1 PA 1 Lipoma 1 Basal cell adenoma 1 Hemangioma	2 ACC 2 EMC 1 MEC	1 Carcinoma ex PA 1 MEC
II. Non-neoplastic	1 Epidermal cyst 1 Ig-G4 related disease 1 Reactive lymph node	3 WT	1 MEC	1 DLBCL
III. Atypia of Undetermined Significance (AUS)	1 Ig-G4 related disease	1 PA 1 WT 1 Myoepithelioma 1 Lipoma	2 MEC	1 Squamous cell carcinoma 1 Metastatic carcinoma 1 DLBCL
IV-A. Benign		48 PA 22 WT 1 Oncocytoma 1 Basal cell adenoma	2 MEC 1 EMC	
IV-B. Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP)	1 Reactive lymph node	9 PA 5 WT 1 Myoepithelioma 1 Oncocytoma 1 Basa cell adenoma	4 MEC 2 EMC	2 AdCC 1 DLBCL
V. Suspicious for Malignancy (SM)		1 PA	3 ACC 2 MEC	
VI. Malignant		1 Atypical PA	1 ACC	1 Adenocarcinoma, NOS 1 Metastatic malignant melanoma

PA, Pleomorphic adenoma; WT, Warthin tumor; MEC, Mucoepidermoid carcinoma; EMC, Epithelial myoepithelial carcinoma; AdCC, Adenoid cystic carcinoma; ACC, Acinic cell carcinoma; DLBCL, Diffuse large B cell lymphoma

Table 2 Histological follow-up and risk stratification of salivary gland lesions on fine needle aspiration cytology using MSRSGC (with slide review)

		ND	NN	AUS	BN	SUMP	SM	M
Cytologic diagnosis	Total n = 374 (100%)	83 (22.2%)	64 (17.1%)	27 (7.2%)	132 (35.3%)	47 (12.6%)	7 (1.9%)	14 (3.7%)
Surgical follow up	Total n = 150 (100%)	20 (13.3%)	8 (5.3%)	10 (6.7%)	75 (50.0%)	27 (18.0%)	6 (4.0%)	4 (2.7%)

	Non-neoplastic n = 11 (7.3%)	6	3	1	0	1	0	0
	Benign neoplasm n = 105 (70.0%)	7	3	4	72	17	1	1
	Malignant (low) n = 23 (15.4%)	5	1	2	3	6	5	1
	Malignant (high) n = 11 (7.3%)	2	1	3	0	3	0	2
Risk of neoplasm		70.0%	62.5%	90.0%	100.0%	96.3%	100.0%	100.0%
Risk of malignancy		35.0%	25.0%	50.0%	4.0%	33.3%	83.3%	75.0%
Proposed ROM		25.0%	10.0%	20.0%	<5%	35.0%	60.0%	90.0%

ND, non-diagnostic; NN, non-neoplastic; AUS, atypia of undetermined significance; BN, benign neoplasm; SUMP, salivary gland neoplasm of uncertain malignant potential; SM, suspicious for malignancy

3. Cytohistologic correlation according to descriptive report without slide review

According to the MSRSGC categorization, 81 cases were assigned to the non-diagnostic category (21.6%), 64 cases to the non-neoplastic category (17.1%), 25 cases to the atypia of undetermined significance category (6.7%), 135 cases to the benign neoplasm category (36.1%), 48 cases to salivary gland neoplasm of uncertain malignant potential category (12.8%), 7 cases to suspicious for malignancy category (1.9%), and 14 cases to malignant category (3.7%).

The preoperative cytological diagnosis and histological follow up are listed in

Table 3. Of the 374 cases, 150 (40.1%) had corresponding histological follow-up. 18 cases were assigned to the non-diagnostic category (12.0%), 8 cases to the non-neoplastic category (5.3%), 8 cases to the atypia of undetermined significance category (5.3%), 78 cases to the benign neoplasm category (52.0%), 28 cases to salivary gland of uncertain malignant potential category (18.7%), 6 cases to suspicious for malignancy category (4.0%), and 4 cases to malignant category (2.7%)

The risk of neoplasm (RON) was 66.7% for non-diagnostic, 62.5% for non-neoplastic, 87.5% for atypia of undetermined significance, 100% for benign, 96.4% for salivary gland neoplasm of uncertain malignant potential, 100% for suspicious for malignancy, and 100% for malignant The risk of malignancy (ROM) was 33.3% for non-diagnostic, 25.0% for non-neoplastic, 50.0% for atypia of undetermined significance, 6.4% for benign, 32.1% for salivary gland neoplasm of uncertain malignant potential, 83.3% for suspicious for malignancy, and 75.0% for malignant

Table 3 Histological follow-up and risk stratification of salivary gland lesions on fine needle aspiration cytology using MSRSGC (reclassification based on report of diagnosis without slide review)

		ND	NN	AUS	BN	SUMP	SM	M
Cytologic diagnosis	Total n = 374 (100%)	81(21.7%)	64(17.1%)	25(6.7%)	135(36.1%)	48(12.8%)	7(1.9%)	14(3.7%)
Surgical follow-up	Total n = 150 (100%)	18(12.0%)	8(5.3%)	8(5.3%)	78(52.0%)	28(18.7%)	6(4.0%)	4(2.7%)
	Non-neoplastic n = 11 (7.3%)	6	3	1	0	1	0	0

	Benign neoplasm n = 105 (70.0%)	6	3	3	73	18	1	1
	Malignant (low) n = 23 (15.4%)	5	2	1	4	5	5	1
	Malignant (high) n = 11 (7.3%)	1	0	3	1	4	0	2
Risk of neoplasm		66.7%	62.5%	87.5%	100.0%	96.4%	100.0%	100.0%
Risk of malignancy		33.3%	25.0%	50.0%	6.4%	32.1%	83.3%	75.0%
Proposed ROM		25.0%	10.0%	20.0%	<5%	35.0%	60.0%	90.0%

ND, non-diagnostic; NN, non-neoplastic; AUS, atypia of undetermined significance; BN, benign neoplasm; SUMP, salivary gland neoplasm of uncertain malignant potential; SM, suspicious for malignancy

4. Evaluation of agreement between two different methods of classification

Compare reclassification based on slide review with reclassification based on report of diagnosis without slide review, the overall kappa value was 0.922 which is almost perfect agreement on the Landis and Koch scales

Table 4 Evaluation of agreement between two different methods of classification

		Reclassification based on report of diagnosis without slide review							kappa	p-value
		ND	NN	AUS	BN	SUMP	SM	M		
Reclassification based on slide review	ND	17	1	0	0	2	0	0		
	NN	0	6	0	2	0	0	0	0.922	<0.001
	AUS	1	1	8	0	0	0	0		
	BN	0	0	0	75	0	0	0		

SUMP	0	0	0	1	26	0	0
SM	0	0	0	0	0	6	0
M	0	0	0	0	0	0	4

ND, non-diagnostic; NN, non-neoplastic; AUS, atypia of undetermined significance; BN, benign neoplasm; SUMP, salivary gland neoplasm of uncertain malignant potential; SM, suspicious for malignancy

5. False positive and false negative cases

Discrepancy between FNA and histological diagnoses was observed in ten cases (Table 4, 5). In the non-neoplastic FNA group (8 cases), three (37.5%) cases were diagnosed as Warthin tumor, one as a mucoepidermoid carcinoma (12.5%) and one was diagnosed as diffuse large B-cell lymphoma (12.5%). Among cases classified as benign neoplasm on FNA (75 cases), three cases (4.0%) were reported to be malignant on resection and included two cases of mucoepidermoid carcinoma and one case of epithelial myoepithelial carcinoma. Among cases classified as salivary gland neoplasm of uncertain malignant potential (27 cases), one cases (3.7%) was diagnosed as reactive lymph node (paracortical hyperplasia). Finally, of cases called malignant on FNA, one of four (25.0%) was diagnosed as pleomorphic adenoma on histological follow-up. The diagnostic accuracy was 96.9% (281/290 cases) for parotid gland, 97.5% (79/81 cases) for submandibular gland, 100% (2/2 cases) for sublingual gland and 100% (1/1 case) for minor gland. The overall diagnostic accuracy was 97.8% (366/374 cases)

Table 5 Characterization of the False-Negative (non-neoplastic and neoplastic lesion) cases

No.	Laterality	Site	Original diagnosis	MSRSGC	Histological diagnosis
1	Right	Parotid	Cellular smear showing diffusely scattered histiocytes with acute and chronic inflammatory cells, favor benign cystic lesion	Cat II	Mucoepidermoid carcinoma, low grade
2	Right	Parotid	Numerous lymphocytes and a few oncocytic epithelial cells	Cat II	Diffuse large B-cell lymphoma
3	Right	Submandibular	Suggestive of pleomorphic adenoma	Cat IV-A	Mucoepidermoid carcinoma, low grade
4	Left	Submandibular	A few bland-looking oncocytic epithelial clusters in lymphocytic background, favor Warthin's tumor	Cat IV-A	Mucoepidermoid carcinoma, low grade
5	Left	Parotid	Trabeculae and cords of basaloid cells with myoepithelial cells	Cat IV-A	Epithelial myoepithelial carcinoma
6	Left	Parotid	Spindle cells, ductal cells and rare acinar cells.	Cat II	Warthin tumor
7	Left	Parotid	Many blend-looking acini and some ductal cells	Cat II	Warthin tumor
8	Right	Parotid	Mainly acute inflammatory cells suggestive of abscess	Cat II	Warthin tumor

Table 6 Characterization of the False-Positive (non-neoplastic and neoplastic lesion) cases

No.	Laterality	Site	Original diagnosis	MSRSGC	Histological diagnosis
1	Right	Parotid	Positive for malignancy	Cat VI	Pleomorphic adenoma
2	Right	Parotid	Cellular smear showing many atypical lymphocytes with enlarged nuclei and no epithelial cells	Cat IV-B	Reactive lymph node

IV. DISCUSSION

Compare to classification with slide review method, there was no significant difference in the classification based on descriptive diagnosis without slide review.

(Table 2, 3 and 4). As for the ROM, there were no differences for NN, AUS, SM, M categories between two methods. The ROM of ND and SUMP was slightly decreased as 33.3%, 32.1% respectively. The ROM of BN was increased as 6.4% above the expected ROM of less than 5%. The main reason for the discrepancy was mainly due to inadequate interpretation of slides and confusing descriptive diagnosis that can lead to miscommunication between surgeon and pathologists.

The majority of salivary gland FNAs with surgical follow-up were benign (105 cases; 70.0%), like with other studies.[14,16-18] The diagnosis rate of ND was 22.2% at our institution, with a 70% of RON and 35% of ROM. The frequency of ND diagnosis was higher than 10% set by the MSRSGC. According to MSRSGC recommendations, specimens were considered non-diagnostic if only insufficient quantitative and/or qualitative elements are contained such as rare or absent cells, non-mucinous cyst, inadequately prepared slides with artifact, and the exclusive non-neoplastic (normal) salivary gland in suspicion of a clinically/radiologically defined mass.

The ROM of ND in our study was high compared to other studies.[14, 16-20] Many factors are involved in non-diagnostic specimen, including the aspiration technique, character of lesion, method of processing specimen, and artifacts from the slide preparation.[21] Quality control through monitoring these factors and feedback between doctors can lower the diagnostic rate of the ND category, thereby contributing to ROM reduction. Also clinico-radiologic correlation is mandatory to avoid misdiagnosis as non-diagnostic specimen. Normally, a small number of cells would

be an inadequate specimen in the general case, but suspicious for malignancy category are possible if clinically suspected malignancy and the cells themselves show high grade.[21]

Table 7 Comparison of risk of malignancy (ROM) with other studies

	ND	NN	AUS	BN	SUMP	SM	M
Our study	35.0	25.0	50.0	4.0	33.3	83.3	75.0
Rosai et al.[17]	17.0	16.0	53.0	6*		79.0	100
Song et al.[14]	17.8	14.3	30.6	2.2	46.6	78.9	98.8
Viswanathan et al.[16]	6.7	7.1	38.9	5.0	34.2	92.9	92.3
Thiryayi et al.[19]	8.5	1.6	0	1.9	26.7	100	100
Rophilla et al.[18]	0	17.4	100	7.3	50.0	-	96.0
Park et al.[20]	19.5	6.9	0	2.4	26.2	83.3	100
Expected ROM	25.0	10.0	20.0	<5	35.0	60.0	90.0

ND, non-diagnostic; NN, non-neoplastic; AUS, atypia of undetermined significance; BN, benign neoplasm; SUMP, salivary gland neoplasm of uncertain malignant potential; SM, suspicious for malignancy
* case of BN and SUMP categories are calculated together in this study

The ROM for the NN and BN categories in our study were 25% and 4% respectively. The RON was 62.5% and 100% individually. The ROM for NN category was higher than proposed ROM of 10% by MSRSGC whereas ROM for BN

was within the proposed ROM of 5%. In comparison with other studies, The ROM for NN category ranged from 1.6% to 17.4% and for BN category, 1.9% to 7.3% (Table 6) False-negative FNAs affected the ROM in two categories. [14,15-20] In our study, low grade mucoepidermoid carcinoma, and diffuse large B-cell lymphoma contributed to the increase in ROM in the NN category in comparison to Rossi et al., Viswanathan et al. and Song et al., in which B-cell lymphomas predominantly attributed false-negative diagnoses.[14, 16-17] The increase in ROM in our BN category was attributed to 2 case of low grade mucoepidermoid carcinoma, and 1 case of epithelial myoepithelial carcinoma which shows similar distribution compare to Rossi et al.[17] In the study of Song et al., the increase in ROM in the BN category was contributed by 3 cases of carcinoma ex pleomorphic adenoma and 1 case of adenoid cystic carcinoma.[14]

According to MSRSGC's goals, the AUS category should not exceed 10% of the total. In current study, 7% of the salivary gland FNAs were classified as AUS in keeping with recommendation. The ROM for the AUS category was 50%, higher than 20% of the MSRSGC. In comparison with other studies, The ROM was variable in literature from 0% to 100%. Various entities were included in this category, with mucoepidermoid carcinoma being the most common

The RON and ROM for the SUMP category in our study was 96.3% and 33.3% with Warthin tumor and low grade mucoepidermoid carcinoma being the most common benign and malignant diagnoses respectively. This ROM was similar from MSRSGC target rate and slightly lower than other studies (Song et al. and

Viswanathan et al. was 46.6% and 34.2%).[14,16]

For SM category, the RON and ROM was 100% and 83.3% respectively. The reported ROM in this category varies from institution to institution, ranging from 78.9% to 100% (Table 6). [14, 16-20] This was probably due to different institutional practices and experience of pathologists. Marked atypia of cells with inadequate samples, Focal marked atypical cells with sparse cells, equivocal features admixed with benign and malignant cells were assigned to the SM category

The RON and ROM for M category were 100% and 75% respectively. ROM of malignancy was lower compared to the MSRSGC and other published studies.[14, 16-20] In M category, totally 3 cases (1 case of acinic cell carcinoma, 1 adenocarcinoma NOS, 1 metastatic malignant melanoma) were included without predominant tumor type. However squamous cell carcinoma was the most common malignant tumor in M category in Rossi et al., Song et al., and Viswanathan et al. [14, 16-18] Compared with other studies, the limited sample size (4 cases) may have affected lower ROM and tumor types. [14, 16-20] For the particular case of false positive, the cytology specimen showed several clusters composed of marked atypical cells without necrosis in the degenerated background. However, in resected specimens, except for cytologic atypia, none of the features were indicating malignancy. Atypical pleomorphic adenoma was given with the recommendation of close follow up. Rohilla et al. reported similar false positive case.[18]

In this study, there were 8 false negative cases and 2 false positive case. (Table 4, and 5). Contributed factors were sampling errors, inadequate technique, vagueness in

interpretation and underestimation of low grade malignant tumors. Among the false negative cases, low grade mucoepidermoid carcinoma and Warthin tumor were the most common entity. In particular, MECs with cystic changes are difficult to diagnose due to failure to gain optimal material.[22-23] It should be noted that only limited cases of MEC contain all three types of cells (mucous, intermediate and squamous cells).[24] (Figure 1)

In one study, modification for the MSRSGC to improve the surgical relevance was proposed. Mazzola et al. modified the MSRSGC by combining cat III (atypia of undetermined significance) and cat IV-B (salivary gland neoplasm of uncertain malignant potential) into new category named salivary lesion of uncertain malignant potential (SLUMP). [25] The researchers noted that both cat III and cat IV-B show high malignancy rates, eventually surgical excision is performed. So it is desirable to combine them together in terms of clinical relevance.[25] In addition, new category called hematologic malignant neoplasm was created for early consultation to hematologist avoiding needless surgical treatment.[25]

As for slide review, when two pathologists assigned FNA slides through this system, the assignment was consistent with the exception of a few cases, indicating that the system has an advantage over previous description diagnosis in terms of reproducibility.

Limitation of this current study lies in its retrospective design. However, as well as many other institutions including ours, MSRSGC has not yet been adopted. Therefore, the most of studies investigating MSRSGC have been retrospective studies.

With publication of MSRSGC and as MSRSGC is becoming widely used among pathologists, more prospective data will become available.

In summary, the ROM for each category in our study according to the Milan system did not show a significant difference from the recommended value. It is thought that the newly proposed system may help in prognostic and patient management.

V. CONCLUSION

The FNA is a reliable diagnostic tool in the preoperative evaluation of salivary gland lesion and MSRSGC can prove to be an effective scheme for reporting and management of these lesions. As the criteria for MSRSGC become well defined and established, reproducibility of diagnosis can be maximized.

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ABSTRACT(IN KOREAN)

The milan system for reporting salivary gland cytopathology 적용을 통한 세침 흡인 세포검사의 재분류 및 임상적 유용성 측정

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박지현

침샘의 세침 흡인 세포검사는 최소 침습적, 비용 대비 효율적인 검사로서 종양성/비종양성 병변 혹은 양성/악성 종양을 감별하거나 부가적인 분자검사를 위한 견본으로서 침샘 병변의 수술 전 진단에 있어서 유용한 방법으로 정립되어 있다. 하지만 침샘에서 기원하는 대부분의 종양들은 세포형태학적 특징을 공유하는 경우가 많으며 하나의 종양 안에서도 다양한 특징들을 보이는 경우가 많아 세침 흡인 세포검사를 통해 정확한 진단하는 것은 어렵다. 현재까지 단일화된 분류체계는 없는 상황으로 The American society of cytopathology와 The International Academy of Cytology의 주관 하에 전세계의 병리의사와 외과의사들이 모여 표준화된 분류체계를 만들었으며 이를 The Milan system for Reporting Salivary Gland Cytopathology (MSRSGC)이라 명명하였다.

새로 만들어진 The Milan system for Reporting Salivary Gland Cytopathology (MSRSGC)이 이전과 비교하였을 때 수술 전 진단 분류체계로서 효용성이 있는지 비교하고자 지난 6년 동안 강남세브란스병원에서 시행된 침샘 세침 흡인 세포검사 슬라이드들을 다시 검토하였다. 그 중 수술 검체를 통해 조직 진단이 이루어진 증례들을 취합하여 각 항목 별로 risk of neoplasm, risk of malignancy를 측정하였

다. 총 6년 (2013년 ~ 2018년) 동안 진행된 침샘 세침 흡인 세포검사에 대하여 후향적 연구를 실시하였다. MSRSGC에 따라 다음과 같은 항목으로 분류되었다. Non-diagnostic (ND), non-neoplastic (NN), atypia of undetermined significance (AUS), benign neoplasm (BN), salivary gland neoplasm of uncertain malignant potential (SUMP), suspicious for malignancy (SM), or malignant (M). 각 항목에서 대하여 risk of neoplasm (RON) and malignancy (ROM)를 계산 하였다.

374건 (371명)의 세침흡인 세포검사가 시행되었었으며 그 중 150건 (40.1%)은 수술을 통하여 조직 진단이 이루어졌다. 150건의 세침 흡인 세포검사들은 각 카테고리 별로 ND (13.3%), NN (5.3%), AUS (6.7%), BN (50.0%), SUMP (18.0%), SM (4.0%), 그리고 M (2.7%)의 분포를 보였다. Risk of neoplasm (RON)은 ND: 70.0%, ND: 62.5%, AUS: 100%, BN: 100%, SUMP: 96.3%, SM과 M: 100%로 나타났다. Risk of malignancy (ROM)은 ND: 35%, ND: 25%, AUS: 50%, BN: 4%, SUMP: 33.3%, SM: 83.3%, 그리고 M: 75%로 나타났다. 위의 결과는 MSRSGC에서 제시하는 이상적인 ROM과 큰 차이를 보이지 않았으며, 유용한 것으로 나타났다. 표준화된 새로운 분류체계를 통하여 임상의사와 병리의사 간의 의사소통에도 도움이 될 것이며, 각 분류 항목의 ROM을 토대로 환자 치료 방향 수립에도 큰 도움이 될 것으로 생각된다.

핵심되는 말 : 침샘, 세포흡인 세포검사, the milan system for reporting salivary gland cytopathology, risk of malignancy