GUIDELINES OF THE CANADIAN SOCIETY OF CYTOPATHOLOGY

The Milan System for Reporting Salivary Gland Cytopathology

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*The CSC endorses The Milan system for reporting salivary gland cytopathology (2018). The following document is a short summary of the highlights of the Milan system guidelines. Further details can be found in the original Atlas (Ref 1)

The Milan System for Reporting Salivary Gland Cytopathology is composed of 6 general diagnostic categories (summarized below). Each diagnostic category is associated with an implied risk of malignancy and recommendations for the clinical management (Table 1). The corresponding Milan System Atlas provides definitions and specific criteria for each of the 6 diagnostic categories, along with explanatory notes, tables, figures, and sample reports

Table 1. The Milan System for Reporting Salivary Gland Cytopathology.

Diagnostic Category	Risk of Malignancy	Usual Management
Non-Diagnostic	25%	Clinical and radiologic correlation/repeat FNA
Non-Neoplastic	10%	Clinical follow-up and radiologic correlation
Atypia of Undetermined Significance (AUS)	20%	Repeat FNA or surgery
Neoplasm		
a) Benign	<5%	Conservative surgery or clinical follow-up
b) Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP)	35%	Conservative surgery*
Suspicious for Malignancy	60%	Surgery*
Malignant	90%	Surgery* (extent dependent on type and grade of malignancy)

* intraoperative examination (frozen section) may be helpful to guide the extent of surgery

Nondiagnostic (ND)

Aspirates that have quantitatively and/or qualitatively insufficient diagnostic material to provide an informative interpretation are ND. At present, no set validated adequacy criteria have been established in the literature. Specimens can be ND for a variety of reasons: rare or absent interpretable lesional cells (<60), poor fixation, crush artifact, necrotic debris, excessive blood or other elements obscuring cellular detail. The ND category also includes "Benign (normal) salivary gland tissue" in the setting of a clinically or radiologically defined mass because it likely reflects sampling error (Fig. 1), as well as "Non mucinous cyst fluid with scant or no epithelial component". FNAs that should not be classified as ND include mucinous cyst contents, aspirates with atypia, and aspirates containing abundant acellular matrix material. Ideally, the ND category should be regularly monitored to ensure that it comprises <10% of samples.

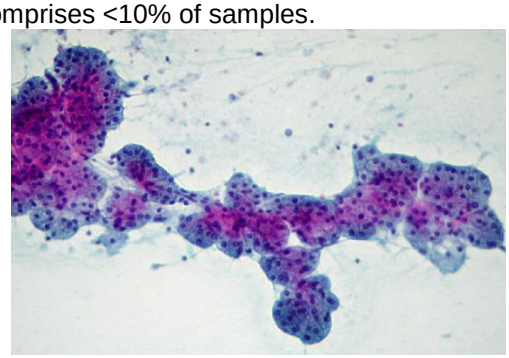

Figure 1. Non-Diagnostic. *This aspirate in a patient with a discrete mass consists only of non-neoplastic (normal) salivary gland acini, and is not considered representative of the lesion.*

Non-neoplastic (NN)

The NN category includes specimens lacking cytomorphologic evidence of a neoplastic process; consisting of benign acinar and/or ductal epithelium with an inflammatory component, metaplastic, or reactive changes (Fig. 2). It also includes specimens showing evidence of reactive lymphoid tissue since enlarged intra- and peri-parotid lymph nodes are a common non-neoplastic cause of a salivary gland mass; flow cytometry is recommended for these specimens. The major pitfall with salivary gland aspirates diagnosed as NN is the possibility of a false-negative diagnosis due to inadequate sampling. Therefore, careful clinical and radiologic correlation is recommended to avoid a false negative FNA result.

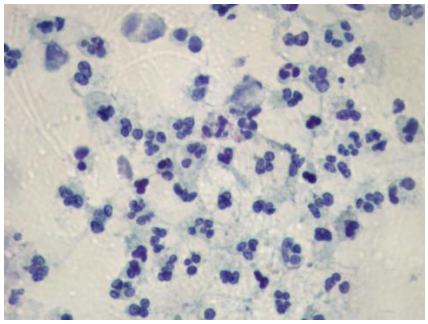

Figure 2. Non-Neoplastic*. This aspirate of acute sialadenitis shows abundant acute inflammation, but no neoplastic process.*

Atypia of undetermined significance (AUS)

The AUS category includes cases which are indeterminate for a neoplasm and often contain limited cellular and/or architectural atypia. It is a heterogeneous category that includes low cellularity samples that are suggestive but not diagnostic of a neoplasm (eg, scant population of basaloid, oncocytic, clear or spindle cells) and salivary gland lesions indefinite for a lympho-proliferative disorder. Mucinous cystic lesions with scant or absent epithelium (Fig. 3) are also included in the AUS category due to the possibility of low-grade mucoepidermoid carcinoma which is one of the most common cause of false-negative diagnosis. The AUS category is needed to accommodate a small subset of problematic FNA samples encountered in routine practice, but it should be used rarely (≤10% of all salivary gland FNA samples). The majority of samples classified as AUS will represent reactive atypia, or poorly sampled neoplasms on surgical follow-up. It is appropriate in most AUS cases to include a comment mentioning the reason for the AUS interpretation, along with the differential diagnosis and recommendations for the management (eg, repeat FNA with flow cytometry in case of lymphoid lesion).

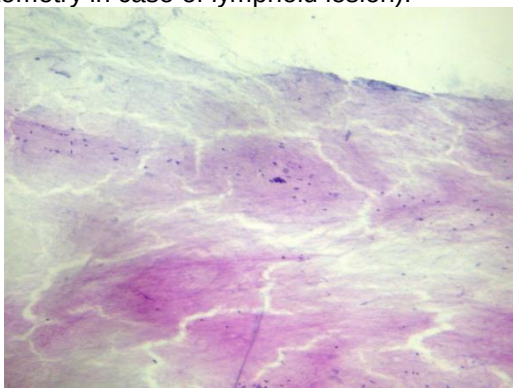

Figure 3. AUS. *This aspirate contains abundant mucin without epithelial cells. The differential diagnosis includes a benign mucinous cyst (mucocele); however, a low-grade muco-epidermoid carcinoma cannot be excluded.*

Neoplasm

The Neoplasm category includes two different subgroups:

1) Neoplasm-Benign

2) Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP).

Neoplasm-Benign

The Neoplasm-Benign category is reserved for cases of a benign neoplasm diagnosed based on the presence of conventional cytomorphologic criteria. Specific entities included in this category are classical examples of pleomorphic adenoma (Fig. 4),Warthin tumor, lipoma, and schwannoma.

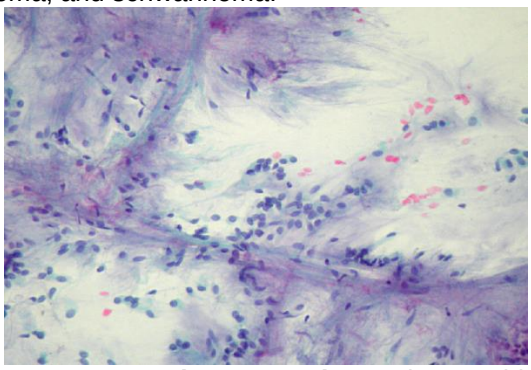

Figure 4. Neoplasm: Benign. *Pleomorphic adenoma showing classical cytologic features including abundant fibrillary matrix with embedded myoepithelial cells.*

Salivary gland neoplasm of undetermined malignant potential (SUMP)

SUMP encompasses FNA specimens that are diagnostic of a neoplasm but in which a diagnosis of a specific entity cannot be made, and importantly, a carcinoma cannot be entirely excluded. The most common pattern or diagnosis in this category are salivary gland tumors with basaloid features or “basal cell neoplasm” (Fig. 6) and oncocytic neoplasms. On surgical follow-up, a majority of these cases will include cellular pleomorphic adenoma, neoplasms with atypical features, and low-grade carcinomas (Fig. 5).

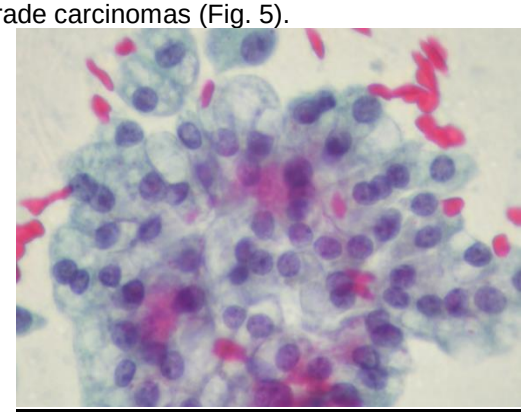

Figure 5. Neoplasm: SUMP. *FNA of a cellular neoplasm with clear cell features The histologic follow-up of this case was acinic cell carcinoma.*

Suspicious for malignancy (SM)

SM is for aspirates which show features that are highly suggestive of malignancy but are not unequivocal for malignancy, because of insufficient quantitative and/or qualitative features (Fig. 6). Many, but not all, specimens in this category will be high-grade carcinomas.

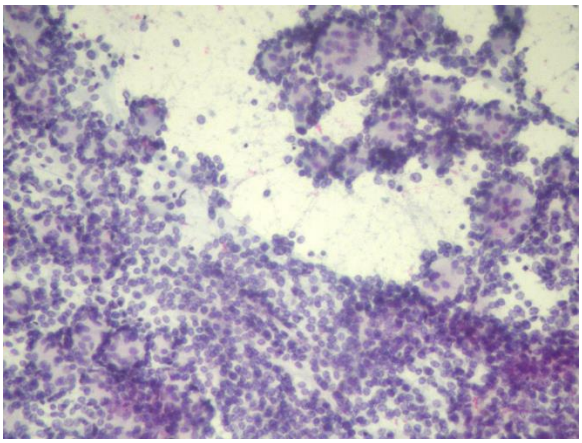

Figure 6. SM. *Adenoid cystic carcinoma. This FNA shows basaloid tumor cells associated with poorly formed hyaline globules. Depending upon the cellularity and amount of matrix combined with clinical findings, the diagnosis of cases such as this can range from "SUMP-basaloid neoplasm" to "suspicious for adenoid cystic carcinoma" to frankly Malignant. Ancillary studies can be helpful in such cases.*

Malignant

The Malignant category is for aspirates in which the cytomorphologic features are diagnostic of malignancy. When possible, it is recommended to subclassify specimens into low- and high-grade cancers because the management for high-grade salivary gland carcinomas may include radical surgical resection, sacrifice of major nerves, and lymph node dissection. In addition, it is important to indicate whether the cancer is primary or secondary.

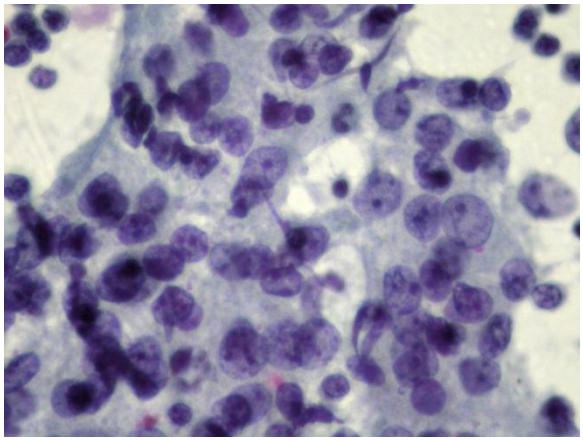

Figure 7. Malignant. *This aspirate of a high-grade carcinoma, not otherwise specified contains groups high-grade malignant cells. Clinico-radiological correlation as well as ancillary studies can be used to exclude the possibility of metastasis.*

Ancillary studies for salivary gland FNA

Ancillary testing, including immunohisto-chemistry, FISH and molecular testing for specific translocations associated with a subset of salivary gland tumors, should be considered only for cases in which the results would alter clinical management or at least modify diagnostic category/clinical risk within the Milan system framework (Figs. 6 and 7).

References: 1- *Faquin WC, Rossi ED, editors. The Milan system for reporting salivary gland cytopathology. Cham: Springer; 2018.*