Section: Pathology

Original Research Article

S(T)UMP(ED)!: DIAGNOSTIC DILEMMAS OF CELLULAR BASALOID NEOPLASMS IN SALIVARY GLAND

Jayakumar Niveditha[1], Chinthu P[2], Mercy Joyston[3]

[1]Assistant Professor, Department of Pathology, Madurai Medical College, Madurai, Tamil Nadu, India
[2]Assistant Professor, Department of Pathology, Government Medical College, Virudhunagar, Tamil Nadu, India
[3]Assistant Professor, Department of Pathology, Madurai Medical College, Madurai, Tamil Nadu, India

Received : *24/12/2024*
Received in revised form : *13/02/2025*
Accepted : *28/02/2025*

Keywords:
Milan IVB-SUMP, cellular basaloid neoplasms.

Corresponding Author:
Dr. Mercy Joyston,
Email: mercyswamidoss@gmail.com

DOI: 10.47009/jamp.2025.7.1.227

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (1); 1167-1171

Abstract

Background: After the introduction of Milan classification for salivary gland cytology, a standardized method of reporting has been adopted. The cellular basaloid neoplasms that feature in many categories of Milan, often pose diagnostic difficulties. Hence we have incorporated an algorithmic approach to sort it out, especially when we report in resource limited settings. The aim is to adopt the Milan system for salivary gland cytology in reporting cellular basaloid neoplasms. To follow an algorithm while diagnosing cellular basaloid neoplasms. **Materials and Methods:** This was a retrospective study conducted at a tertiary care hospital from January 2019-December 2020. The salivary gland FNA slides of 58 cases along with the available corresponding histopathological follow up, were collected. The smears had been fixed in alcohol and stained using Romanowsky stains. They were categorized using Milan system, of which Category IVB was selected. The characteristics of cellular basaloid neoplasms were analyzed, and risk of malignancy (ROM) was calculated. An algorithm was derived for a possible consensus. Statistical analysis used Spearman's Rho and Pearman's Coefficient correlation studies were done and p value was derived to determine the statistical significance of the study. **Result:** We found that salivary gland neoplasms were more common among middle aged males. Parotid gland was most commonly involved. The category IVB – SUMP was the commonest (32.8%) and ROM for SUMP was 36.8%. Cellular morphology, stroma and stroma-cell interface are the main entities to diagnose cellular basaloid neoplasms. **Conclusion:** By our simple approach to diagnose the cellular basaloid neoplasms, the need for ancillary tests and constant referrals can be averted. The turnaround time is also minimalized.

INTRODUCTION

The introduction of Milan classification has simplified and standardized the reporting of salivary gland cytology. The risk stratification of this six-tiered system serves as a communication tool between the clinician and pathologist. Each diagnostic category (I-VI) correlates with risk of malignancy (ROM) and patient management.

We aim to focus on cellular basaloid neoplasms as they are ambiguous and feature in many categories – benign, SUMP, suspicious for malignant and malignant. We also describe our experience in a limited resource setting, to classify salivary gland neoplasms using the Milan classification and bring to light the dilemmas we faced in categorizing cellular basaloid neoplasms

MATERIALS AND METHODS

Data Collection: A retrospective 2-year study (January 2019-December 2020) of 58 cases of salivary gland FNA specimens was done at a tertiary care center. Among these, 33 cases had histopathological follow-up. The lesions were examined by palpation. All FNAs were performed with 25-gauge needles with an average of 1 to 4 passes, depending on the size and complexity of the lesion. The first pass typically was to assess adequacy and additional passes were for additional smears, liquid-based cytology and/or cellblock preparation. Smears were alcohol-fixed and stained using Romanowsky stains.

Classification: The six diagnostic categories are: I – Non diagnostic (ND), II - non neoplastic (NN), III – Atypia of undetermined significance (AUS), IV -

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Neoplasm, V – Suspicious of malignancy (SM) and VI – Malignant(M). The diagnostic category IV is subdivided as A&B – neoplasm benign (NB) & salivary gland neoplasm of uncertain malignant potential (SUMP). The slides were independently evaluated by 2 pathologists into 7 categories. Discordant cases were reviewed by a third pathologist for final diagnosis.

Risk of Malignancy Calculation: The ROM is defined as the ratio of FNAs with malignant follow-up to the total number of FNAs with follow-up for that category.

RESULTS

The analysis of the 58 FNAC cases showed the age group of 35-55 years were the most affected (36.2%). The male: female ratio was 1.07:1. The parotid gland was the commonest site of affliction (72.41%), followed by submandibular gland (24.13%). Table (1) summarizes the percentage of cases in each category and their histopathological follow-up. According to Milan classification – SUMP (IV B) was the largest category (32.8%), followed by NB (IV A) 29.3%.

Cytological features of cellular basaloid neoplasms:

The 19 cases diagnosed as Milan IV B commonly presented as firm swellings of the salivary gland with hemorrhagic aspirates Table (2). The patients had a median age of 43.7 years. The commonest site was parotid with a gender predilection for males. All diagnosed SUMP category tumors were cellular basaloid neoplasms. They had several sheets of ductal epithelial cells and myoepithelial cells. Acinar cells were found albeit uncommonly. A significant finding was the absence of fibrillary stroma in all the cases. Stroma when present was either amorphous or hyaline. The background was predominantly hemorrhagic.

The histopathological follow up for all the 19 cases of SUMP yielded – pleomorphic adenoma (10), basal cell adenoma (2), basal cell adenocarcinoma (1), mucoepidermoid carcinoma (4) and adenoid cystic carcinoma(2). The ROM for SUMP was 36.8%.

Table 1: Distribution of cases as per Milan classification & HPE diagnosis.

MSRSGC category	No of cases (58)	HPE cases (39)	Benign	Malignant	ROM (%)
Non-diagnostic- I	2(3.5%)	2	1	1	50
Non neoplastic –II	15(25.9%)	5	4	1	20
Atypia of undetermined Significance -III	1(1.8%)	nil	nil	nil	nil
Neoplasm benign-IV A	17(29.3%)	9	8	1	11.1
Neoplasm of uncertain malignant potential-IVB	19(32.8%)	19	12	7	36.8
Suspicious of malignancy-V	2(3.5%)	2	nil	2	100
Malignant-VI	2(3.5%)	2	nil	2	100

Table 2: Cytomorphology of cellular basaloid neoplasm in Milan IV B (N=19)

Variable	Mean/n	Frequency (%)
AGE (in years)	43.7	
GENDER		
Male	12	63.1
Female	7	36.9
SITE		
Parotid	13	68.4
Submandibular gland	5	26.3
Cheek	1	5.3
GROSS		
Solid	17	89.5
Cystic	2	10.5
CELLULARITY		
Scanty	2	10.5
Moderate	11	57.9
High	6	31.6
COHESIVENESS		
Cohesive	13	68.4
Loosely cohesive	2	10.5
Dyscohesive	4	21.1
Acinar cell present	5	41.6
Myoepithelial cell present	6	50
STROMA		
Absent	12	63.2
Myxoid	5	26.3
Hyaline	2	10.5
BACKGROUND		
Eosinophilic	8	42.1
Haemorrhagic	10	52.6
Clear	1	5.3
DUCTAL CELLS		
Monotonous basaloid	13	68.4
Mild atypia	4	21.05

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Occasional squamoid	1	5.3
Occasional Oncocytic	1	5.3
HPE DIAGNOSIS		
Pleomorphic adenoma	10	52.6
ADCC	2	10.5
MEC	4	21.05
BSA	2	10.5
BCAC	1	5.3

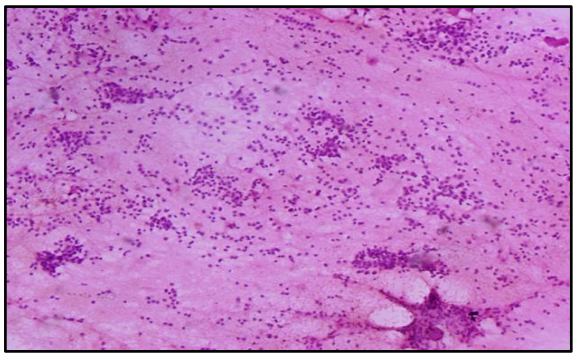

Figure 1: 10X, H & E stain- Cellular pleomorphic adenoma lacking fibrillary matrix

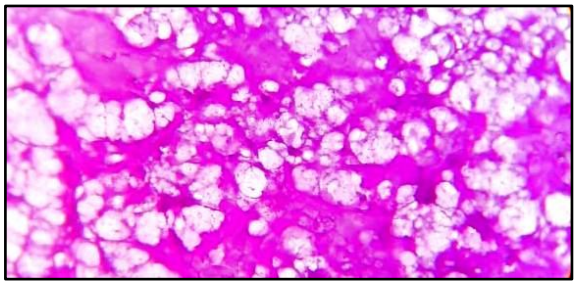

Figure 2: 40X, H & E stain- Pink hyaline matrix in pleomorphic adenoma

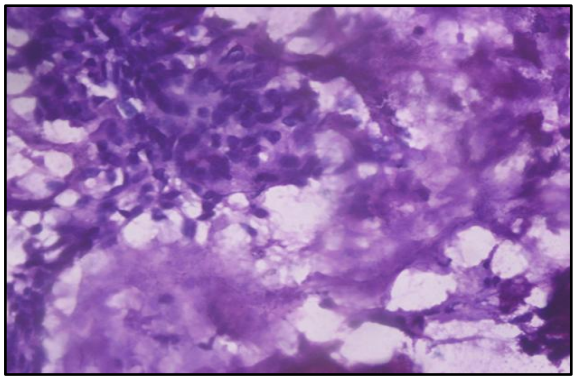

Figure 3: 40X, H & E stain – Sharp cell- stromal interface in Adenoid cystic carcinoma

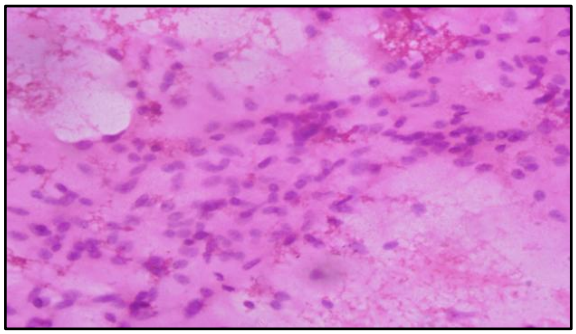

Figure 4: 10X, H & E stain - Pink stroma in mucoepidermoid carcinoma

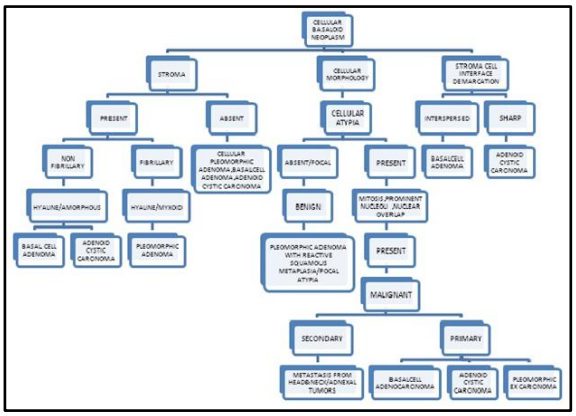

Figure 5: Algorithmic approach to cellular baaloid neoplasms of salivary gland cytology

DISCUSSION

The use of salivary FNA in triaging patients for surgery and extent of excision is exemplary.[1] An analysis of various systematic reviews and Meta analytic studies revealed a low sensitivity despite a high specificity for the diagnosis of malignancies in salivary FNA.[2,3] This is because of the cellular basaloid neoplasms (Milan IVB) with deceptively bland monotonous cells, causing significant cytomorphological overlap. As basaloid cells have high nuclear cytoplasmic ratio, malignancies primary to salivary gland and metastases are impossible to distinguish, let alone cellular benign neoplasms. The treatment for a low-grade malignancy is conservative excision whereas a high-grade tumor requires radical neck dissection.[4] This further exemplifies the need for an accurate diagnosis to avoid grave implications. Therefore, a pattern-based approach seems plausible. Hence, we took it upon us as a challenge to categorize cellular basaloid neoplasms in an algorithmic manner. It features cellular benign tumors, basaloid tumors, oncocytic/oncocytoid tumors, clear cell tumors and low-grade malignant neoplasms. The efficiency of diagnosis of a SUMP category tumor relies on the adequacy of smear, experience of the pathologist, intratumoral heterogeneity, type of stain used and minimizing of artifacts. The neoplasms commonly encountered are pleomorphic adenoma, basal cell adenoma, canicular adenoma and sclerosing polycystic adenosis. Basaloid adnexal tumors of head and neck are close differentials. Adenoid cystic carcinoma, basal cell adenocarcinoma, epithelial myoepithelial carcinoma, polymorphous adenocarcinoma, carcinomas ex pleomorphic adenoma, metastatic squamous cell carcinomas and extension of basal cell carcinoma of skin are the malignant counterparts.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

The entities that can be taken into account when examining a basaloid neoplasm are: stromal quality, cytoarchitecture of the matrix, cell stromal interface, cohesion of cell clusters, cytonuclear grade, nucleus shape, nuclear membrane irregularity, nucleoli, overlapping of nuclei, chromatin and mitosis.

Diagnostic dilemmas faced by us:

Cellular pleomorphic adenoma [Figure 1] Lack of the classical fibrillary stroma, presence of hyaline or amorphous stroma [Figure 2] and presence of hyaline globules & squamoid cells.

Basal cell adenoma-Presence of extracellular matrix and presence of tumor cells surrounding hyaline globules

Adenoid cystic carcinoma– Cohesive, deceptively bland and lack of matrix material.

Clues that denote benignity of the neoplasm: Presence of myoepithelial cells embedded in matrix, cytoarchitecture of the matrix –presence at periphery of cells, palisading ribbons, interdigitating tumor cells, cell stromal interface not sharply demarcated, Nuclear cytoplasmic ratio maintained and fine granular chromatin of basaloid cells

In our experience, pleomorphic adenoma was the commonest among cellular basaloid neoplasms (52.6%). In cases which are myoepithelial predominant, myoepithelioma is a close differential. Regarding basal cell adenoma and adenoid cystic carcinoma, the cell stromal interface was a helpful feature in making a diagnosis [Figure 3].[6]

Adenoid cystic carcinoma had a sharply demarcated interface compared to interspersed stromal cell interface in basal cell adenoma. Presence of mitoses and denser hyaline globules also favour adenoid cystic carcinoma.[7]

The diagnosis of mucoepidermoid carcinoma usually is straightforward. If at all, it is diagnosed as SUMP, it comes under the oncocytic/squamoid subtype. The conditions where MEC can be a dilemma in basaloid SUMP are the stroma when pink can be misconstrued as hyaline matrix. [Figure 4]

The presence of epithelial cell clusters with basaloid cells that turned out to be reactive squamous metaplasia in pleomorphic adenoma.[8]

Basal cell adenocarcinoma, a rare tumor, is also a diagnostic dilemma in basaloid SUMP. The features one must keep in mind in cytology of BCAC are dual cellularity as presence of spindle shaped stromal cells is common and closely packed, rosette like morphology.[9]

We have tried to incorporate various studies,[10-13] into a single algorithm [Figure 5] to help referral centres with minimal possible follow-up. Hang et al (2018),[10] has subtyped SUMP into 3 groups: oncocytic/squamoid, basaloid and myoepithelial. Hang et al (2022),[14] has modified it by subclassifying SUMP as: Oncocytic/oncocytoid, basaloid, SUMP NOS.

Therefore, when encountered with a cellular basaloid neoplasm, we can take into account three entities – cellular morphology, stroma and stroma-cell interface. Depending on the presence of cellular atypia, stromal nature and pattern of cell stromal interface, we further rule out possibilities to arrive at the diagnosis. When ancillary techniques are unavailable in a periphery set up, we can easily provide a meaningful differential diagnosis.

CONCLUSION

MILAN IV B-SUMP category is a broad challenging entity with a significant ROM. A definitive diagnosis requires a host of ancillary techniques. In its absence, an elaborate differential diagnosis, often perplexing to the treating clinician is provided. Referrals to tertiary care centres, repeat FNAC, application of a panel of immunohistochemistry markers like p63, p40, PLAG1, calponin, S100 etc. and loss to follow up are practical difficulties faced by them. Hence, our algorithmic approach simplifies the technique for the pathologist, helping them to provide a meaningful differential diagnosis. The need for additional tests and constant referral to higher centres is abated. The reduction in turnaround time is a major beneficial factor to the patient and clinician alike.

REFERENCES

1. Pranab Dey, Fine Needle Aspiration Cytology Interpretation and diagnostic difficulties, 2nd edition, New Delhi: Jaypee Brothers medical publishers; 2015.70p.
2. MacCallum PL, Lampe HB, Cramer H, Matthews TW. Fine-needle aspiration cytology of lymphoid lesions of the salivary gland: a review of 35 cases. J Otolaryngol 1996; 25(5):300-4.
3. Hara H, Oyama T, Saku T. Fine needle aspiration cytology of basal cell adenoma of the salivary gland. Acta cytol 2007; 51(5): 685-91.
4. Stanley MW, Horwitz CA, Rollins SD, Powers CN, Bardales RH, Korourain S, Stern SJ. Basal cell (monomorphic) and minimally pleomorphic adenomas of the salivary glands. Distinction from the solid (anaplastic) type of adenoid cystic carcinoma in fine needle aspiration. Am J Clin Pathol 1996; 106(1): 35-41.
5. Salivary gland neoplasms with basaloid features in the era of the Milan system for reporting salivary gland cytology: Classification and interobserver agreement Lester J. Layfield MD, Magda Esebua MD, Liron Pantanowitz MD, MHA, Zahra Maleki MD, FCAP, MIAC, Maryna Vazmitsel MD, Zubair Baloch MD, PhD et al
6. Singh A, Sharma R, Nema SK. Basal cell adenoma mimicking adenoid cystic carcinoma on FNAC - A case report. Int J Med Rev. 2014; 2:166–8.
7. Jurczyk M, Peevey JF, Vande Haar MA, Lin X. Pitfalls of fine-needle aspiration cytology of parotid membranous basal cell adenoma-A review of pitfalls in FNA cytology of salivary gland neoplasms with basaloid cell features. Diagn Cytopathol. 2015 May;43(5):432-7
8. Jo HJ, Ahn HJ, Jung S, Yoon HK. Diagnostic difficulties in fine needle aspiration of benign salivary glandular lesions. Korean J Pathol. 2012 Dec;46(6):569-75.
9. Ishida M, Okano K, Sandoh K, Ebisu Y, Fujisawa T, Iwai H, Tsuta K. Cytological features of basal cell adenocarcinoma of the salivary glands. Diagn Cytopathol. 2019 Jul;47(7):733-737
10. Hang, J.-F., Alruwaii, F., Zeng, B.-R., Lai, C.-R. And Wu, H.H. (2018), Subtyping salivary gland neoplasm of uncertain malignant potential based on cell type demonstrates differential risk of malignancy. Cancer Cytopathology, 126: 924-933.
11. Faquin WC, Rossi ED, Baloch Z, et al. The Milan System for Reporting Salivary Gland Cytopathology. 1st ed. Springer International Publishing AG; 2018.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

12. Griffith CC, Pai RK, Schneider F, et al. Salivary gland tumor fine-needle aspiration cytology: a proposal for a risk stratification classification. Am J Clin Pathol. 2015; 143: 839-853.
13. Griffith CC, Schmitt AC, Pantanowitz L, Monaco SE. A pattern-based risk-stratification scheme for salivary gland cytology: a multi-institutional, interobserver variability study to determine applicability. Cancer Cytopathol. 2017; 125: 776- 785.
14. Hang J.F., Lee J., Nga M., Higuchi K., Hirata Y., Wu H. et al(2022), Multi-institutional validation of a modified scheme for subcategorizing salivary gland neoplasm of uncertain malignant potential (SUMP). Cancer Cytopathol, 130: 511-522.

ISSN (O): 2687-5365; ISSN (P): 2753-6556