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Utilizing the Milan System to analyse the lesions on the salivary glands and as a tool for risk identification

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Abstract
To classify and risk-group salivary swellings, the Milan approach of assessing salivary gland cytopathology is used. Salivary glands are significant pairs of exocrine glands that are distributed throughout the submucosa of the oral cavity and consist of three pairs of major pairs of glands and numerous smaller pairs of glands. Common salivary gland cancers may be diagnosed using well-defined cytological criteria according to the Milan method, however there are still some inconsistencies and challenges with diagnosis since many tumours are diverse and have cytomorphologic overlaps. The primary goal of the research is to analyse how well the Milan system of salivary gland cytopathology is being used as a tool for risk identification. Leishman stain is used on smears of tiny needle aspirations for salivary gland malignancies. eosin stains and hemotoxylin stains. Then came the physical examination, which focused on the lesion's size, the tumor's circumference, the existence of cystic alteration, and necrosis. Sections with a thickness of 2 to 3 mm were collected from all suspect regions. The material was handled routinely by an automated tissue processor. Sections of the tissue were stained with haematoxylin and eosin after being cut into paraffin blocks. Salivary gland lesions that weren't cancerous were identified using traditional criteria. The Milan technique of Repoting Salivary Gland Cytopathology was used to categorise the numerous salivary lesions, with results based on their cytomorphological characteristics. Ages 41 to 50 saw the highest percentage of cases (22.2%). The most frequent clinical manifestation was a clinically palpable enlargement that was often unilateral and well-circumscribed. The parotid gland was the most frequently impacted gland. Based on cytology, the lesions were divided into the following categories: (6.7%) non-diagnostic. Neoplastic-Salivary gland neoplasm of unclear malignant potential (8.9%).

Keywords: *Cytopathology, salivary gland, Milan system, cytological staining*

Introduction

Salivary glands are significant pairs of exocrine glands that are distributed throughout the submucosa of the oral cavity and consist of three pairs of major pairs of glands and numerous smaller pairs of glands. The parotid gland, submandibular gland, and sublingual gland make up the primary salivary glands.

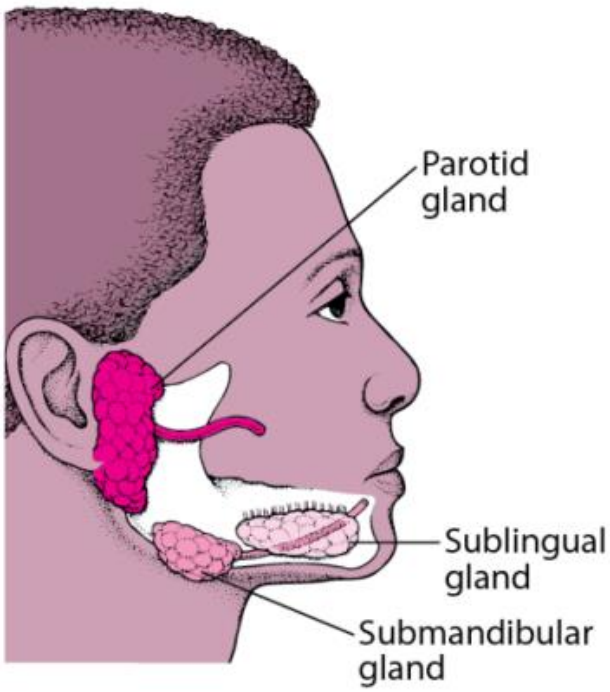


Figure 1: Salivary gland of oral cavity (Seethala et al., 2005)

The nasal cavity, larynx, and bronchi all have many glands with similar morphology, but none of them generate saliva (Seethala et al., 2005). Acinar cells, ductal epithelial cells, and a substantial amount of fibrovascular stroma make up their cytology. A comprehensive clinical examination backed by appropriate radiographic and cytological procedures is necessary for salivary gland lesions diagnosis. The examination of the salivary gland lesions by the spiration of fine needle has become quite popular among patients and doctors, making it a trustworthy and effective preoperative technique. Patients may endure it easily since it is inexpensive and produces little pain (Daneshbod et al., 2009). As a first-line inquiry, aspiration cytology of fine-needle has now surpassed core biopsies and the frozen section of salivary gland (Rossi et al., 2018). It offers the most benefit for distinguishing a neoplastic lesion from a non-neoplastic one and determining whether it is benign or malignant (Layfield et al., 2018). This difference is crucial because different diseases of the salivary gland have different therapeutic choices. Neoplastic disorders may need surgical excision, although non-neoplastic pathologies may be managed conservatively.

Due to these issues, a tiered categorization was required, which guarantees consistency in reporting and gives doctors useful data. During their meeting in Milan, Italy, the International Academy of Cytology (IAC) and American Society of Cytopathology (ASC) gathered a group of dignitaries to create a common reporting mechanism for the SG FNA. Methodology was to deliver a uniform method of reporting the findings rather than alter any of the well accepted criteria for identifying salivary gland abnormalities (Rossi et al., 2018).

The (MSRSCG) Milan SystemforreportingSalivaryGland Cytopathology, the most current effort at a standardised, worldwide system of reporting for the categorization of salivary gland lesions, is the product of this and is a tiered reporting system. This classification approach is consisting of six diagnostic categories, as shown in Table 1.

Table 1: The Milan System categorization for detecting salivary gland cytopathology (MSRSCG) (Rossi, 2018)

Category	Salivary gland lesions
1	Non-diagnostic

2	Benign non-neoplastic
3	Atypia of undetermined significance
4a	Benign neoplasm
4b	Salivary gland neoplasm of uncertain malignant potential
5	Suspicious for malignancy (SFM)
6	Malignant

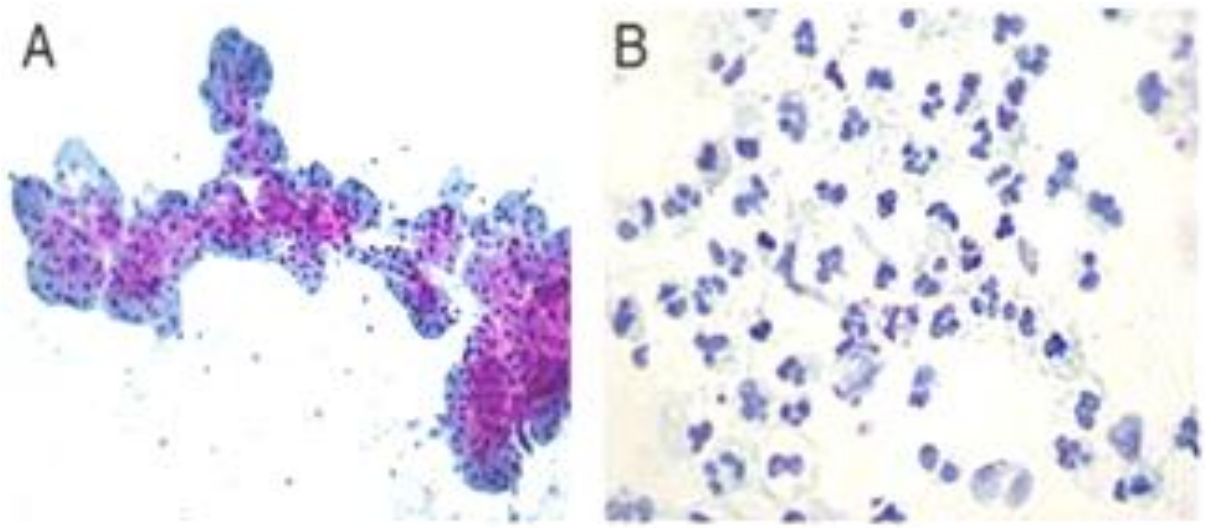
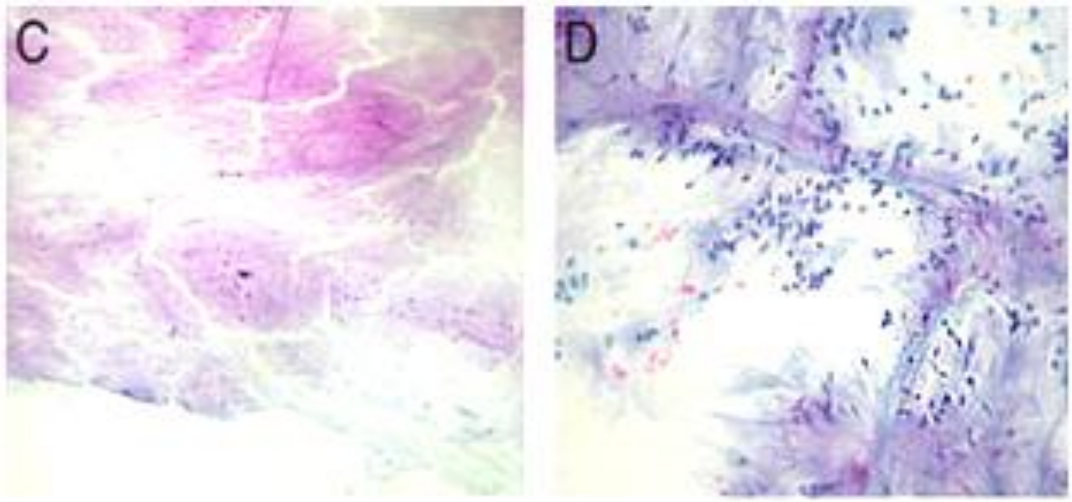
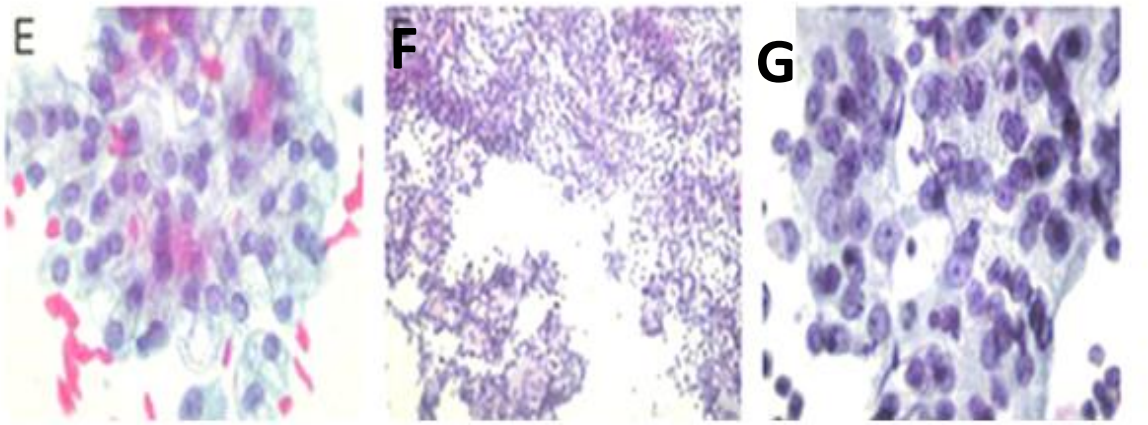


Figure 2:These are instances of salivary gland fine-needle extracts with specific Milan System for Monitoring Salivary Gland Cytopathology classifications(Rossi, 2018). (A) The nondiagnostic category (B) The non-neoplastic category



(C) Atypia of uncertain significance (D) Neoplasm-benign



(E) Neoplasms (neoplasm-salivary gland neoplasm of uncertain malignant potential [SUMP]) (F) suspicious for malignancy. (G) Malignant.

In the current investigation,the objective of the study is to divide Salivary gland cytology into non-diagnostic and potentially malignant salivary gland neoplasms and to identify the cells as malignant or non-malignant by using staining methods.

Materials and method

The research conducted at Delhi Institute of Medical Sciences' pathology department

The Delhi Institute of Medical Sciences' Cytology OPD is where total 45 patients with clinically palpable swellings present for the current investigation. The time period of the study is 6months to 1 year. Throughout the whole treatment, aseptic measures were performed and informed consent was acquired. In every instance, a thorough history is followed by a clinical examination. Wherever possible, information from radiological investigations and other relevant sources was retrieved. A thorough local examination was documented. The Fine needle aspiration cytology (FNAC) was carried out using a disposable plastic syringe with a 10ml capacity and a 21G needle attached. There was a maximum of two passes made. To reduce sample error in bigger swellings, aspiration was performed from several locations. After the cyst had completely been evacuated from cystic lesions, FNAC was performed on the solid region that remained. For each example, alcohol fixed (90 percent ethanol) and air-dried smears were created. On smears that had been air dried, Leishman stain was applied, and on smears that had been fixed with alcohol, H&E stain was applied. Where necessary, papanicolaustain was performed on smears fixed in 90% ethanol. Staining of the cytosmears was recorded, and all cases were categorised into two groups in accordance with MSRSGC's suggestion (Non-diagnostic, Neoplasm). Wherever possible, corresponding histopathology samples were obtained. After receiving the sample, the patient's credentials were checked. After that, the sample was maintained for 24 hours in a 10% Neutral Buffered Formalin solution to facilitate fixation. Then came the physical examination, which focused on the lesion's size, the tumor's circumference, the existence of cystic alteration, and necrosis. Sections with a thickness of 2 to 3 mm were collected from all suspect regions. The material was handled routinely by an automated tissue processor. Sections of the tissue were stained with haematoxylin and eosin after being cut into paraffin blocks. Salivary gland lesions that weren't cancerous were identified using traditional criteria. Tumors were identified using the WHO categorization system for salivary gland tumours.

STATISTICAL ANALYSIS: Quantitative information was reported using numbers and percentages once the observation findings were processed using the software SPSS was employed for the statistical analysis.Means (±standard deviation) are presented for all values. One-way analysis of variance (ANOVA) was used to analyse the data. The *p* value of <0.001 was considered to be significant.

Results and Discussion

To classify and risk-stratify salivary swellings, the Milan method of reporting salivary gland cytopathology was put into place. The Milan method has clear-cut cytological criteria for diagnosing common salivary gland cancers, although there are still differences and challenges with diagnosis since many tumours are diverse and have cytomorphologic overlap. We conducted this research with the intention of demonstrating the competency of the Milan system since there aren't many studies in our nation that do so.

As per the Milan approach of reporting the salivary gland cytopathology, which is based on the cytomorphological characteristics of FNAC smears, the various salivary lesions were categorised. Additionally, demographic data, clinical data, and radiological findings were gathered whenever feasible.

AGE DISTRIBUTION OF THE SALIVARYGLANDLESIONS(N = 45)

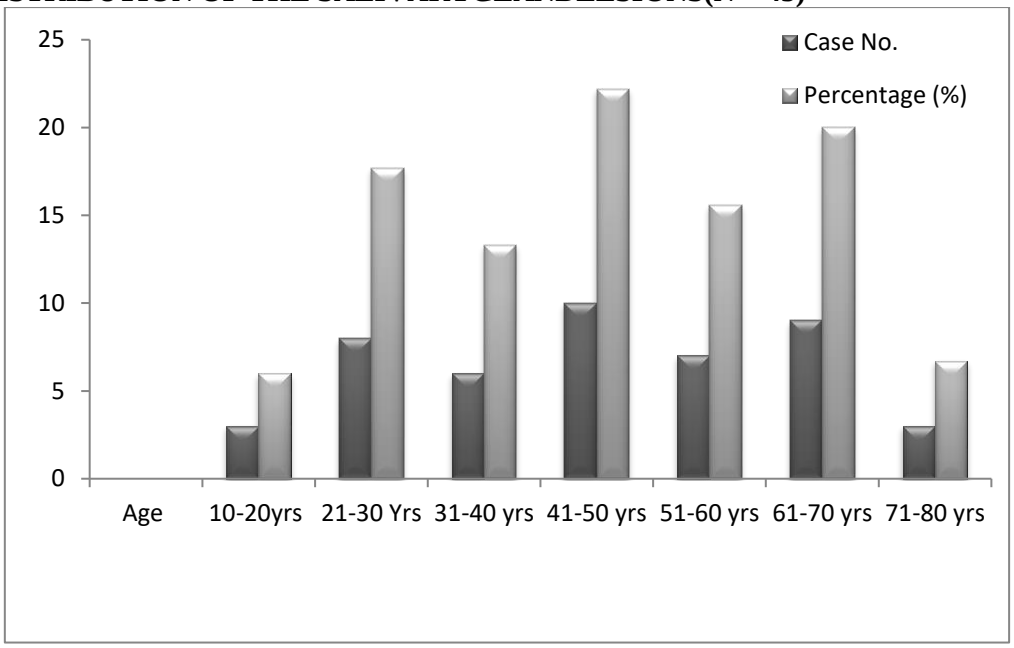


Figure 3:Age distribution of Salivary Gland lesions

The number of patients and their age distribution are shown in Figure 3. Patients varied in age from 13 to 77, with the age group 41 to 50 having the greatest percentage of patients (21.2%). The average age was 46.40. The majority of cases (22.2%) in the current research belonged to the 41–50 age range. However, most studies, including Kala et al. (2019), found that the age range of 21 to 40 years accounted for no more than 46.1% of cases.

GENDER WISE DISTRIBUTION OF SALIVARY GLANDLESIONS(N = 45)

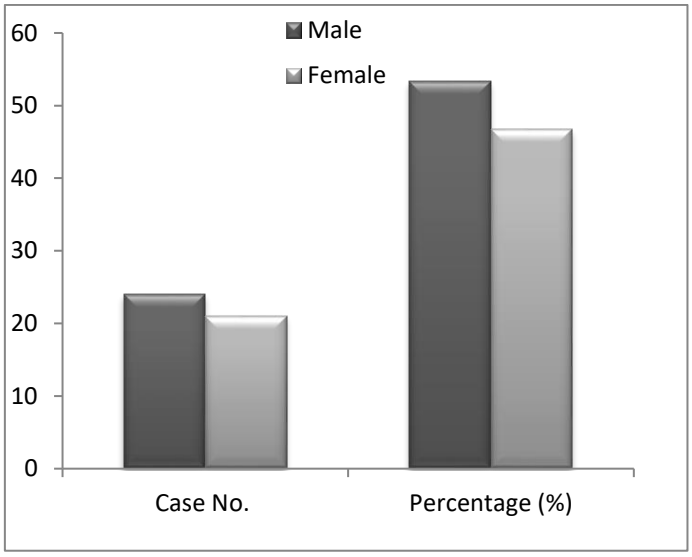


Figure 4: Gender distribution of Salivary Gland lesions

Male patients made up 53.3% (24 cases) of the total patients, while female patients made up 46.7% (21 cases) of the cases. 1.1:1 was the M:F ratio. Gender distribution among the patients is shown in Figure 4. The majority of the research (Gaikwad et al., 2020; Mishra et al., 2019) revealed a prevalence of female participants. However, the lot of salivary gland lesions were discovered in individuals who were male in our research. This matched Das et al. 2004's research and Mullen et al. 2020's, which reported M:F ratios of 1.28:1 and 1.19:1 respectively.

SITE OF INVOLVEMENT OF SALIVARY GLAND LESIONS(N = 4 5)

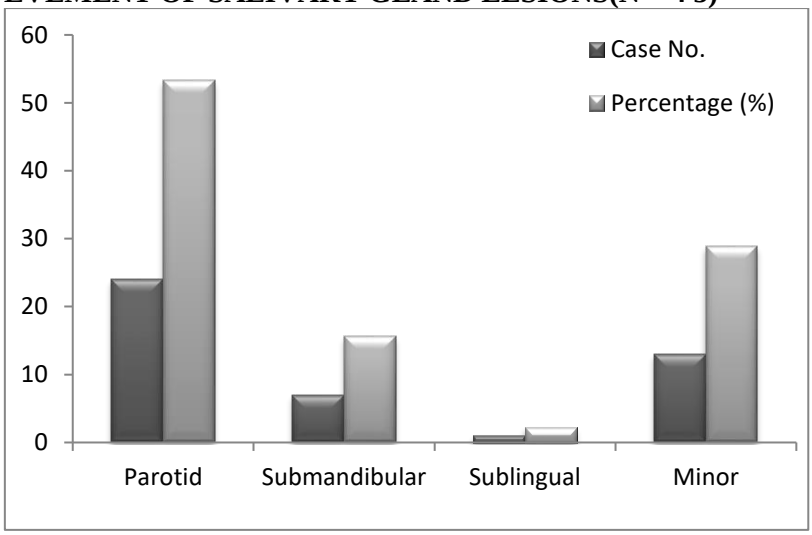


Figure 5: Sites of salivary gland with case numbers and percentage

The locations of the salivary glands and the number of instances is shown in Figure 5. In 32 (71.1%) of the 45 instances, the main salivary glands were at fault, while the minor glands were at fault in 13 (28.1%) of the cases. Among the primary salivary glands, Parotid gland (53.3%) was the one that was mostly affected, then by submandibular gland (15.6%) and the sublingual gland (2.2%).

Cytohistopathology categories

Non-Diagnostic

Table2: Cytopathological diagnosis of non-diagnostic salivary gland

Cytology Diagnosis	Case No.	Histopathological diagnosis

Poorly preserved Sample	1	Basal cell adenoma
Insufficient Cellularity	1	Warthin tumor
Inflammatory lesion	1	Warthin Tumor

A cytology smear from the salivary gland is deemed sufficient if it contains at least 60 lesion cells. The other two cases (66.66%) were grouped under this category because of an abundance of inflammatory cells with non-mucinous fluid and poor slide preservation, while one case (33.33%) lacked sufficient material for evaluation. Both of these cases were identified as Warthin tumours on histopathologic examination, while the other case was identified as a Basal cell adenoma. For this group, the likelihood of cancer was 0%. Three cases (6.7%) were classified as Category I in the current study due to low cellularity, an abundance of inflammatory cells that obscured cellular morphology, and non-mucinous cyst fluid alone. Our findings were compared to those of study by Kala et al. (2019), which found 6.1% of cases to be non-diagnostic. Figure 6, as well as Table 2, display the slides for this non-diagnostic category.

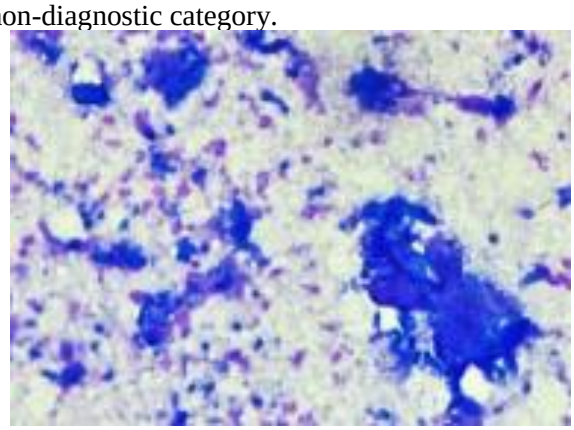


Figure 6: Cytopathology smear of Non diagnostic patient with inflammatory cells

Diagnostic

Table 3: Cytopathological diagnosis of neoplasm salivary gland

Cytology Diagnosis	Case No.	Histopathological diagnosis
Salivary gland of uncertain malignant potential	1	Warthin Tumor
	2	Cellular pleomorphic adenoma 25
	1	Carcinoma ex pleomorphic adenoma

The cytopathological diagnosis of a salivary gland tumour is described in Table 3 and Figure 7. Following histological analysis, it was determined that there were two instances of Warthin tumours and one case of basal cell adenoma. Low cellularity of slides, as found by Thiryayi et al., might be the source of this discrepancy (2018). Additionally, non-mucinous cyst fluid with significant mixed inflammatory cells but no epithelial component could not be classified as any particular entity in cytology, underdiagnosing a case of Warthin's tumour with a biopsy showing it.

Basaloid and oncocytoid kinds of lesions were created from salivary gland lesions that were classified as having an unclear malignant potential. Two cytosmears had monomorphic basaloid cells with little nuclear atypia connected to fibrillary stroma. Basaloid cells predominated in one smear, while the stroma was heterogeneous. Another cytosmear had a thin stroma and included basaloid cells as well as oncocytic cells. One of the three instances in our investigation had reactive lymph node hyperplasia, as shown by a biopsy. This discovery was similar to that made in a study by Wu et al.

(2019), who noted that reactive lymph nodes might have the larger cells, which may cause a cytology diagnosis of a neoplasm to be made incorrectly, it was a pleomorphic adenoma. Seven of these instances were also categorised by Layfield J. et al. (2018) using the Milan method in their research.

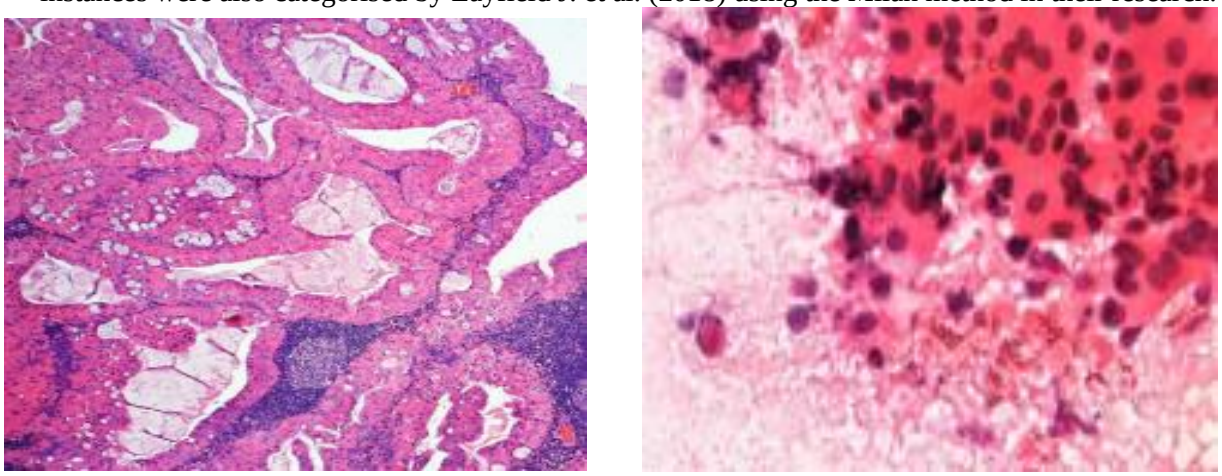


Fig 7. Cytopathology smear of warthintumor and salivary gland of uncertain malignant potential

One instance was identified as a carcinoma-ex pleomorphic adenoma on histological follow-up. The sections included pleomorphic myoepithelial cells, chondromyxoid stroma, and extremely pleomorphic cells grouped in nests, cribriform pattern, and acinar pattern. Additionally, comedonecrosis was seen. One case was identified as a Warthin tumor, which contained nests and clusters of oncocytic cells in addition to reactive inflammatory cells. This finding may have limited the ability to diagnose the cytosmears in that case. Two examples of salivary glands that were cytologically classified upon biopsy were found to be cellular pleomorphic adenomas. In this example, a diagnostic conundrum might have resulted from a lack of stroma in smears. This category's cancer risk was estimated as 25.0%.

Conclusion

The Milan technique of Reporting Salivary Gland Cytopathology was used to categorise the different salivary lesions based on their cytomorphological characteristics. Ages 41 to 50 saw the highest percentage of cases (22.2%). The median age of the patients was 40.30 years, with the youngest 13 years old and oldest about 77 years old. The most frequent clinical manifestation was a clinically palpable swelling that was often unilateral and well-circumscribed. The parotid gland was the most frequently impacted gland. Based on cytology, the lesions were divided into these categories: (6.7%) non-diagnostic. Neoplastic-Salivary gland neoplasm of unclear malignant potential (8.9%).

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