Minor salivary glands tumors of oral cavity

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- Lingual minor glands:
  - Anterior: mixed
  - Middle: serous
  - Posterior: mucous
- Buccal: mixed
- Palatine: mucous
- Labial: mixed

Introduction

Q/ What are the salivary glands and what it's function and what types of minor salivary glands ?

Human salivary glands are : group of compound exocrine glands that produce saliva, an important fluid required for lubrication, immunity, mastication, deglutition, taste, speech, etc.

Salivary glands consist of a series of branched ducts which terminate in a spherical or tubular endpieces or acini; a correlation can be made to a bunch of grapes, with the stems analogous to the ducts and the grapes indicating the secretory endpieces. Serous and mucous cells are the two main types of secretory cells found in salivary gland and divided into two main groups:

The major salivary glands include the paired parotid, submandibular, and sublingual glands.

Additionally, the mucosa of the upper aerodigestive tract is lined by hundreds of small, minor salivary glands. The connective tissue forms a capsule around the gland and extends into it, dividing groups of secretory units and ducts into lobes and lobules. Blood vessels, lymphatic vessels and nerves that supply the gland, are present within the capsule.

The salivary glands are compound glands as they have more than one tubule entering the main duct, and the architectural arrangement is tubuloacinar, where acini are secretory units. These secretory units are merocrine as they release only the secretion of the cell from the secreting units.

Myoepithelial cells are contractile cells associated with the secretory endpieces and intercalated ducts of the salivary gland.

Minor salivary glands

Minor salivary glands are placed below the epithelium in almost all parts of the oral cavity .

These glands comprise numerous small groups of secretory units opening via short ducts directly into the mouth. They lack a distinct capsule, instead mixing with the connective tissue of the submucosa or muscle fibers of the tongue or cheeks [2] .

1- ***Labial and buccal glands : presented on the lips and cheeks and comprise of mucous tubules with serous demilunes [1, 2] .***
2- ***Glossopalatine glands : located to the region of the isthmus in the glossopalatine fold but may extend from the posterior extension of the sublingual gland to the glands of the soft palate [1, 2] .***
3- ***Palatine glands : located in the glandular aggregates present in the lamina propria of the posterolateral aspect of the hard palate and in the submucosa of the soft palate and uvula [1, 2] .***

4- Lingual glands : It's the glands of the tongue and can be divided into various groups [1, 2] .

A) The anterior lingual glands (glands of Blandin and Nuhn) are present near the apex of the tongue. The ducts open on the ventral surface of the tongue near the lingual frenulum.

B) The posterior lingual mucous glands are present lateral and posterior to vallate papillae and in association with lingual tonsil .

The ducts of these glands open on the dorsal surface of the tongue .

C) The posterior lingual serous glands (von Ebner's glands) are located between the muscle fibers of the tongue below the vallate papillae, and the ducts open into the trough of circumvallate papillae and at the rudimentary folate papillae on the sides of the tongue

Minor salivary gland tumors definition & epidemiology & types

Salivary gland neoplasms are a distinct group of lesions with varying morphology, which present challenges in their diagnosis and treatment.[3-8] Minor salivary gland neoplasms represent less than 25% of intraoral salivary neoplasms. They have distinct characteristics, especially regarding frequency, distribution, and clinical aspects.

Studies that evaluate the epidemiology of minor salivary gland neoplasms are important. These tumors are often malignant, in particular when compared to neoplasms of major salivary glands. In addition, differences between race and geographic location are also observed.[9-14]

Neoplasms of the minor salivary glands are a heterogeneous group of tumors. Epidemiological studies are important to understand their frequency and clinical aspects. Investigations in different populations are essential to observe geographic and racial variations of these unusual tumors.[3,14,15,16].

Malignant neoplasm is more prevalent, and mucoepidermoid carcinoma (45.9%) is the most observed histological type, followed by pleomorphic adenoma (24.4%) and polymorphous low-grade adenocarcinoma (13.5%). Most patients are female (70.2%), with a ratio of 2.3:1

The benign tumors have two peaks in prevalence regarding age: 21 to 30 years and 71 to 80 years. The malignant tumors showed peak prevalence between 71 and 80 years. In general, most patients were aged over 70 years.

neoplasms of minor salivary glands were observed mainly in the palate (67.6%) and the retromolar region (15.4%).

Common benign and malignant pathologies identified in a large study of minor salivary glands tumors are listed next in order of most frequent to lleast[17] :

Benign

Pleomorphic adenoma

Basal cell adenoma

Cystadenoma

Myoepithelioma

Oncocytoma

Sialadenoma papilliferum

Malignant

Mucoepidermoid carcinoma

Adenoid cystic carcinoma

PLGA

Adenocarcinoma not specified

Basal cell adenocarcinoma

Clear cell carcinoma

Salivary ductal carcinoma

Carcinoma ex pleomorphic adenoma

Mucinous adenocarcinoma

Sebaceous carcinoma

RISK fACTORS FOR SALIVARY GLAND tumors INCLUDE

- old age

- Tobacco use

- Alcohol use

- History of radiation to the head and neck

- History of any cancer

- Human immunodeficiency virus (HIV) infection

Protective factors may be related to diet. [18,19,20] Vitamin C and fiber from fruit and vege-

table sources have been found to lower the risk of salivary gland cancer. Diets high in

cholesterol are associated with increased risk. [19]

PRESENTATION

Patients typically present with asymptomatic, painless swelling or mass. Patients presenting later in their disease course may have pain . It must be borne in mind that pain at presentation is a red flag for a perineural invasion associated with malignant tumors

or malignant conversion in a benign tumor. In patients who do present with symptomatic masses, their symptoms tend to be related to mass effect or infiltration of adjacent structures. Minor salivary gland tumors of the sinonasal cavity can present with

epistaxis or nasal obstruction. In the oropharynx and larynx, masses may result in

dysphagia, dysphonia, or dyspnea.

Physical examination may reveal a submucosal

Mass with adherent mucosa with or without overlying ulceration (Fig. 1).[18,21,22].

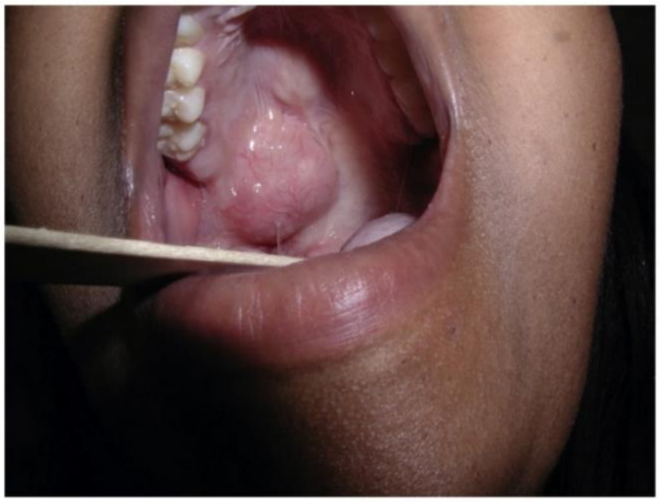

Fig. 1. Patient with enlarging hard palatal mass found to be adenoid cystic carcinoma.

Physical examination ***: Patients with salivary gland lesions require a thorough head and neck evaluation. Cranial nerve function is carefully noted and documented. Careful attention is given to findings that may indicate malignancy, such as the following [23] :***

- ***Rapid growth***
- ***Fixation to adjacent structures***
- ***Associated cervical adenopathy***
- ***Pain***
- ***Paresthesias***
- ***Ulceration***
- ***Cranial nerve involvement***

The differential diagnosis for this presentation includes acute necrotizing sialometaplasia, mucocele, and mucus retention cysts. [24,25]

Acute Necrotizing Sialometaplasia

This is a benign lesion most commonly seen on the palate. The lesion presents as a painful mass that eventually ulcerate . In the early stage,

these lesions can look similar to basal cell carcinomas or other neoplasms with rolled edges over a central ulceration. As this disease process progresses, the lesion mucosalizes and heals over aperiod of several weeks. However, most tumors are often biopsied and/or surgically excised before this stage because of their concerning clinical presentation and appearance. On pathologic evaluation, the squamous metaplasia can appear similar to mucoepidermoid carcinoma.

Mucocele

Mucoceles present as a painless or painful oral submucosal mass. They typically occur after trauma that results in injury to the salivary duct and are characterized by submucosal accumulation of saliva with surrounding inflammation and granulation tissue without a true epithelial capsule.

Mucus Retention Cyst

These also present as a painless oral mass and result from an obstruction of a salivary duct resulting in mucoid salivary accumulation. Unlike mucoceles, mucus retention cysts they have a capsule lined by ductal epithelium. They more commonly affect the major salivary glands.

OTHER LESS COMMON PATHOLOGIES INCLUDE

Lymphoepithelial cysts (see most commonly in HIV patients).

Metastatic cutaneous malignancy, especially melanoma .

Benign masses, including epidermoid cysts, fibromas, and bony tori of themandible or hard palate.

Diagnosis

Laboratory Studies

A complete blood count (CBC) with differential may be elevated in cases with an underlying inflammatory process. This possibility must be excluded before definitive surgical intervention is initiated. For patients undergoing fine-needle aspiration (FNA), determination of

prothrombin time (PT)/international normalized ratio (INR) may be indicated to assess for baseline coagulopathy.

Imaging Studies

Controversy exists regarding the routine use of imaging for small lesions of the minor salivary glands because radiographic imaging typically does not alter the management of these lesions.

Nevertheless, computed tomography (CT), magnetic resonance imaging (MRI), or both may be useful for suspected tumors of the parapharyngeal space. MRI and CT are also optimal for delineating the complete extent of the tumor and assessing for regional lymphadenopathy. In addition, these imaging modalities are useful for evaluating the possibility of invasion into surrounding tissues and facilitating the planning of definitive surgical resection.

Computed tomography

When bony erosion is a concern (eg, in palatal minor salivary gland tumors), CT may be required to assess the extent of locoregional involvement, which will play a role in planning for definitive resection as well as subsequent reconstruction. Similarly, CT is indicated for minor salivary gland neoplasms involving the paranasal sinuses to delineate the extent of the tumor and differentiate tumor from obstructive inflammatory changes.

Magnetic resonance imaging

MRI (see the image below) is superior in soft-tissue differentiation and is particularly helpful in assessing tumor extent, marrow infiltration, and perineural spread. It can also detect signal changes and extracapsular spread within regional lymph nodes while simultaneously avoiding exposure to ionizing radiation. The disadvantages of MRI include its relatively high cost in comparison

with CT, its susceptibility to motion artifact, and its poor cortical bone delineation. [26].

Ultrasonography

Minor salivary gland lesions in the mucosa of oral cavity, pharynx and tracheobronchial tree are not easily accessible or visualized via conventional ultrasonography (US). Accordingly, US is rarely employed in the management of minor salivary gland lesions.

Other Tests

Fine-needle aspiration cytology

FNA cytology was first developed as a diagnostic tool at the Memorial Sloan-Kettering Cancer Center in the 1930s. However, it is only in the past two decades that it has become a widely applied technique in the management of salivary gland tumors. [27] In general, the histopathology of salivary gland tumors is extremely varied and complex; therefore, correct cytologic typing of a primary salivary gland neoplasm can be difficult to perform. [28]

The utility of FNA was established by Eneroth and others, who advocated its routine use and reported accuracy rates in the range of 74-90%. [29] Although the procedure is somewhat operator-dependent, it is generally regarded as safe, simple to perform, relatively inexpensive, and low in morbidity. When a needle of appropriate size is used, the risk of seeding of the needle tract is negligible (0.003% and 0.009%). [30] Open biopsy is rarely performed, because of the risk of tumor spillage, associated infection, and tumor recurrence. [31]

The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC), implemented in 2018, is an evidence-based standardized reporting system for salivary gland FNA that aids in the determination of malignancy risk. [32]

Core needle biopsy

Currently, core needle biopsy (CNB) is not commonly employed in the management of salivary neoplasms, because of the risk of tumor spillage. The overall risk of tumor seeding with CNB is estimated to be in the range of 0-22%.[33] Factors implicated include needle size, use of a single vs coaxial needle, and tumor-related factors. There may, however, be a role for CNB in cases where prior FNA was nondiagnostic. Thus, surgeons must exercise discretion when considering CNB in the management of these lesions.

Immunohistochemical diagnostics

Immunohistochemical diagnostics have specific applications and may facilitate the delineation of different cell components. Various diagnostic markers can be utilized to make an accurate diagnosis. For example, Ki-67 can differentiate between benign basal cell adenomas and malignant basal cell adenocarcinomas, and PLAG1 is specific for pleomorphic adenomas. [34] PLAG1 and HMGA1 have been found to be increased in benign tumors and can aid in differentiating benign from malignant. [35] Although these markers are helpful for characterizing tumors, they are not essential for diagnosis.

Differential Diagnoses

Amyloidosis

Cheilitis Glandularis

Mucocele and Ranula

Mumps

Necrotizing Sialometaplasia

Sarcoidosis

Sjogren Syndrome

Treatment

1-Surgery

Minor salivary gland tumours may arise anywhere in the head and neck. Local surgical excision is always the recommended treatment. In general, the treatment of these tumours follows the pattern adopted for squamous cell carcinomas arising in the upper aerodigestive tract and a margin of resection greater than 1 cm can be considered adequate for the majority of these tumours [36] A low rate of cervical lymph nodes metastases has been reported [37] .Therefore, there is probably little benefit from elective neck dissection for patients with small and low-grade tumours of the minor salivary glands. Difference in surgical planning and treatment may be encountered in case of adenoid cystic carcinoma which represents the most common malignant tumour of minor salivary glands. This locally aggressive neoplasm shows an extensive perineural spread and a tendency to give skip metastases along nerves. Subperiosteal bone invasion and extent into fat spaces are other characteristics that should be carefully considered before surgery. The behaviour of this histotype supports the high rate of inadequate surgical margins ranging from 27 % to 64 % [38]. Based on these data the surgical approach for adenoid cystic carcinoma of the minor salivary glands should be more aggressive. According to lopes [36] the tumour should be widely resected with clear margins of 2–3 cm including adjacent bone when suspected for superiosteal infiltration. Intraoperative extensive use of frozen section is recommended. Post-operative radiotherapy should always be considered.

Transcervical approach

Larger tumors of the parapharyngeal space may necessitate a more complex surgical approach; intraoral resection typically is not recommended in such cases.

Often, in the treatment of benign lesions arising from the minor salivary glands, an attempt is made to avoid a mandibulotomy.

However, in patients with tumors located in the superior aspect of the parapharyngeal space that are approaching the eustachian tube and skull base, a mandibulotomy may be necessary in order to provide optimal surgical access . [39]

Transoral robotic surgery

Applications of minimally invasive transoral robotic surgery (TORS) to head and neck surgery have increased. There are case series of patients safely undergoing TORS for certain benign minor salivary tumors of the parapharyngeal space. TORS allows access to the parapharyngeal space and allows precise tumor dissection, avoiding the need for an external approach and thereby improving cosmetic outcomes for patients. [40]

Complications of surgery

Complications associated with definitive excision and reconstruction of palatal minor salivary gland tumors (both benign and malignant) include the following [41] :

Eustachian tube dysfunction

Flap loss

Trismus

Velopharyngeal insufficiency

Wound dehiscence.

Complications associated with definitive transcervical excision of parapharyngeal minor salivary gland tumors include the following [42]

Facial nerve paralysis

First bite syndrome

Frey syndrome

Hemorrhage

Infection

Complications associated with TORS include the following [43] :

Bleeding

Dysphagia

Aspiration-related infections

Local pain

2-Unresectable/inoperable locoregional disease

In cases of unresectable/inoperable loco-regional disease definitive radiotherapy is recommended. Photons or particle radiotherapy can be employed. Long-term loco-regional control rates with photons are lower than 50 % and 20 % for adenoid cystic carcinoma and non-adenoid cystic carcinoma, respectively. Most of the data on particle therapy derive from patients with adenoid cystic carcinoma. Although neutrons obtained a significant improvement in 2-year loco-regional control over photons (67 % vs. 17 %), they are not routinely employed due to the high rate of late severe toxicities and a doubtful benefit over photons in terms of therapeutic index as well as the lack of direct comparison with modern photons RT such as IMRT. Carbon ions seem to have more biological advantages over protons; however, both these particles were able to obtain a better 5-year local-control (66–68 %) and overall survival over photons alone, supporting their use in advanced adenoid cystic carcinomas [44]. Carbon ions can also be used as a sequential boost to achieve improvement of local control, PFS and OS via dose-escalation [45].

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