



CASE REPORT
CYSTIC LESIONS OF THE SALIVARY GLANDS
(Report of 3 cases)

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Abstract

At least one-third of cystic salivary gland lesions are neoplastic. Cystic lesion of the salivary gland requires only surgery, because regardless of the type and location, drug therapy is not possible with this diagnosis. If the cystic neoplasm is localized in a hard-to-reach place and if it is localized in the parotid gland, the surgical manipulation is performed from the outside, it is removed simultaneously with the parenchyma of the salivary gland. The FNA specimens from salivary gland cystic lesions can be no informative very often, because FNA of these lesions demonstrates hypocellular mucinous material contents, possibly with inflammatory cells and also scant epithelial cells. For example, the presence of mucin and admixed lymphocytes in cyst fluid can be demonstrated both in the benign inflammatory cysts and cystic neoplasms. A definitive diagnosis of cystic neoplasms of the salivary glands is possible only through histological examination of the neoplastic tissue. Prevention of cystic neoplasms of the salivary gland consists of preventing injuries and inflammations of the oral cavity, careful hygiene and regular visits to the dentist. This article presents cases of the salivary glands cystic neoplasms, which are the clinical interest.

Keywords: salivary glands cysts; maxillofacial surgery

INTRODUCTION

Diseases of the salivary glands account for up to 5% of all dental pathologies. From 3 to 5% of all neoplasms of the maxillofacial region are neoplasms of the salivary glands, among them the tumors of the parotid gland percentage is 92%¹.

Salivary gland cysts are pathological benign lesions most often are unicystic, less often polycystic. They are grouped based on their localization and histological structure.

There are two types of salivary gland cysts: the retention type (retention cyst of the minor salivary gland, formed when saliva is retained in the excretory duct) and the type of intratissue secretion, when the duct wall is injured, the saliva flows directly into the fibrous tissue surrounding the gland².

They differ by place of localization.

1. Cysts of small salivary glands (buccal,

labial, palatal, lingual, molar).

2. Cysts of large salivary glands.

- sublingual salivary gland (ranula)
- parotid salivary gland
- submandibular salivary gland

The cysts are filled with white or yellow mucous fluid from the inside, surrounded with fibrous capsule. More than half of all cases are cysts of small salivary glands, less often large ones are affected: sublingual, parotid, submandibular³.

Depending on the gland in which it formed, the symptoms of a salivary gland cyst can be distinguished. Salivary gland cysts themselves do not pose a danger to the patient, unlike complications that can develop in the absence of treatment. Penetration of pathogenic microorganisms into the lesion (most often, representatives of the opportunistic microflora of the oral cavity) leads to the development of an inflammatory process. In

general, the risk of malignancy is higher with smaller salivary glands than with larger salivary glands (for example, the parotid gland has a lower risk of malignancy than minor salivary glands).

In addition, a cyst can have got false or true nature. The former arise as a result of various types of soft tissue injuries, the latter - because of the occurrence of pathologies. In this case, a true cyst has an epithelial lining inside, a false cyst does not have one. Benign cystic lesions of soft tissues of the maxillofacial region do not represent a genetically homogeneous group. Cystic pathology can be caused by trauma or a tumor that compresses the channel and prevents the outflow of saliva⁴. As a result, the fluid stretches the glandular lobule or the salivary duct itself, and a cyst is formed at the site of the pathology.

Congenital types of pathology are formed because of a violation of embryonic development. Acquired cysts of the salivary glands, as a rule, are a consequence of blockage of the excretory duct. Predisposing factors are: inflammatory process (stomatitis, sialoadenitis); duct trauma; sialolithiasis (the excretory duct is blocked by a stone); lesion of a mucous plug in the duct. There are reports regarding the possible role of oncogenic viruses (Epstein-Barr, cytomegalovirus, herpes virus) in the development of salivary gland tumors⁵.

As in the case of neoplasms of other localizations, the etiologic role of gene mutations, hormonal factors, adverse environmental influences (excessive ultraviolet radiation, frequent X-ray examinations of the head and neck area, previous radioactive iodine therapy for hyperthyroidism, etc.), smoking (smoking causes one type of benign tumor - Warthin's tumor) is considered. An opinion is expressed about possible alimentary risk factors (high cholesterol content in food, lack of vitamins, fresh vegetables and fruits in the diet, etc.). At least one-third of cystic salivary gland lesions are neoplastic (Warthin tumor, sebaceous adenoma, sebaceous lymphadenoma, intraductal papilloma, pleomorphic adenoma, mucoepidermoid carcinoma, acinic cell carcinoma, cystadenoma, cystadenocarcinoma, secretory carcinoma, any neoplasm (e.g., lymphoma) with cystic degeneration, metastatic carcinoma to intraglandular node). Non-neoplastic cystic salivary gland lesions include obstructive sialadenopathy (mucus retention cyst, mucocele), lymphoepithelial cyst, sclerosing polycystic adenosis, polycystic (dysgenetic) disease, epidermoid cyst, first branchial arch anomalies, hydatid cyst. Salivary gland cysts can typically be identified by ultrasound. However, occasionally, benign or malignant tumors (e.g., lymphoma, metastases) can be misinterpreted as a

simple cyst, pseudocysts can be hard to discern, and paradoxically certain cystic lesions can present as solid lesions on ultrasound^{6,7}. Cysts of the salivary glands are recognized on the basis of the clinical picture, instrumental and laboratory studies. In addition, additional methods allow differential diagnosis of cystic formations with salivary gland tumors.

Fine needle aspiration (FNA) is a common diagnostic tool used in the initial evaluation of parotid masses^{10,11}.

Employing FNA early on in the diagnostic work-up of patients can help avoid unnecessary surgery¹².

Presents treatment 3 cases of the salivary glands cystic neoplasms, which are the clinical interest.

Case reports.

In cases 1 and 2, the patients are with a preliminary diagnosis of a neoplasm in the left postmandibular region. The complaints and clinical symptoms in both cases were the same, according to the patients, they considered themselves sick for about a year. They noticed a swelling in the postmandibular region, which gradually increased, which was not painful. They did not mention other diseases during their lifetime.

A preliminary diagnosis was made already at the stage of external examination of the patient's face and oral cavity, during which a characteristic lesion in the projection of the gland was found.

Palpation allowed to verify the absence of pain, local increase in temperature, tissue edema and other signs of the inflammatory process. In palpation the cystic lesions had a spherical shape with an elastic structure. The skin above the cyst localization site did not change color or structure. The gland affected by the cyst did not show signs of fluctuation and did not cause painful sensations, it was mobile. The lesion of the parotid salivary gland was accompanied by swelling of the tissues in the ear area, facial asymmetry. The color and appearance of the skin were not changed. The facial nerves were not involved in the tumor process. To understand the actual size of the cystic lesions, patients were sent for magnetic resonance imaging, which was performed by contrast, during which clearly defined cystic lesions were detected, and the cervical lymph nodes were not enlarged.

An examination was performed according to the A-scheme: complete blood count (blood group, coagulogram, Rh), biochemical (glucose, creatinine, total-bound-free bilirubin), albumin, chest X-ray, ECG, ultrasound, general urine examination. Based on the clinical laboratory and instrumental examinations performed, the cystic lesion diagnosis was confirmed.

Case 1.

Men, 61 years old. In the left postmandibular region revealed a 3*3*1.5 cm voluminous mass with clear borders in the left parotid salivary gland (Figure 1).



Figure 1. The patient with parotid gland cystic lesion, external view of the patient

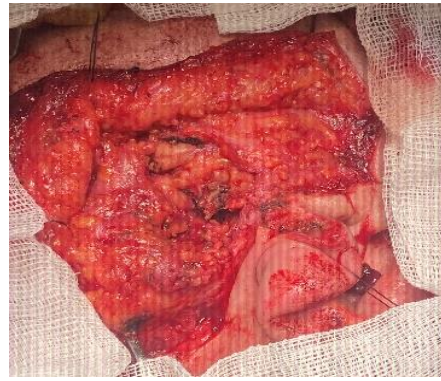


Figure 3. Intraoperative view of the exposed tumor

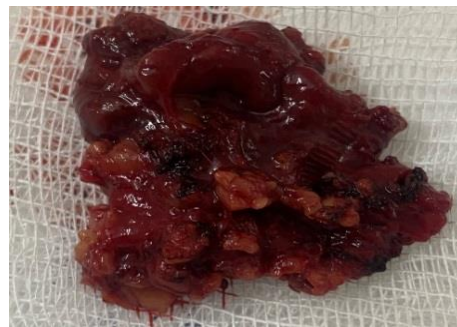


Figure 4. Removed tumor



Figure 5. View of the postsurgical wound



Figure 2. a,b MRI picture of the cystic lesion in 2 projections.



Figure 2. b MRI picture of the cystic lesion in 2 projections.



Figure 6. Gross appearance of the removed tumor

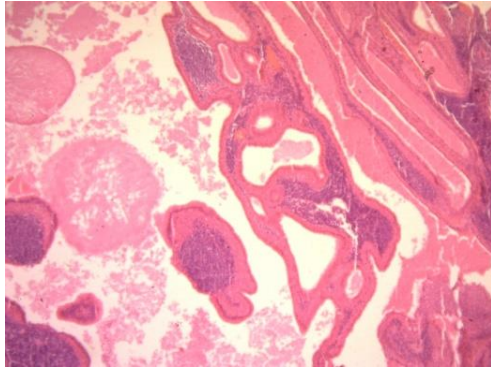


Figure 7. Microscopical picture of the removed tumor (Warthin tumor). Stained with hematoxylin-eosin, x 100.

Case 2.

Men, 69 years old. In the left postmandibular region revealed a 4.5*3*2 cm voluminous mass with clear borders in the left parotid salivary gland, (Figure 8).



Figure 8. The patient with parotid gland cystic lesion, external view of the patient

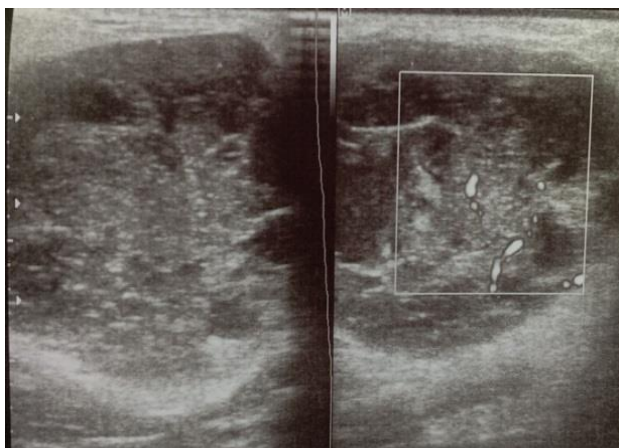


Figure 9. MRI picture of the cystic lesion

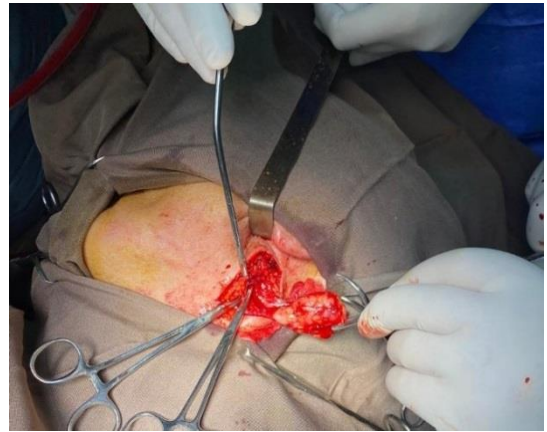


Figure 10. Intraoperative view of the exposed tumor



Figure 11. Intraoperative view of the exposed tumor



Figure 12. Removed tumor



Figure 13. View of the postsurgical wound



Figure 14. Gross appearance of the removed tumor.



Figure 16. The patient with sublingual gland cystic lesion.

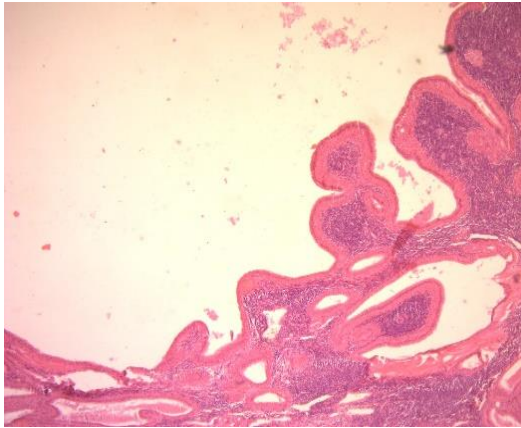


Figure 15. Microscopical picture of the removed tumor (Warthin tumor). Stained with hematoxylin-eosin, x 100.

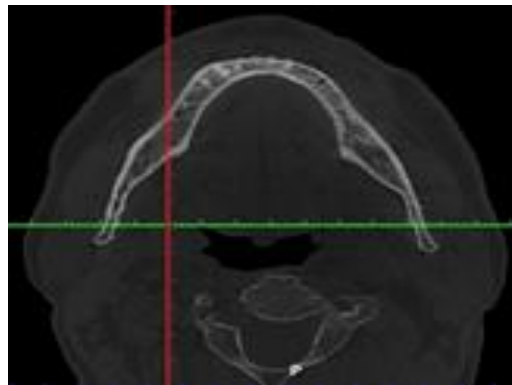


Figure 17. CT picture of the cystic lesion.

Case 3.

M, 62 years old was admitted to the maxillofacial surgery department. The patient was complaining of swelling and mild pain in the sublingual region. He considers himself ill for about 8 months. The patient's mouth opened normally. Mild swelling is observed in the left maxillo-lingual sulcus, the mucous membrane is slightly red, palpation is mildly painful (fig 16). Palpation in the maxillo-lingual sulcus area reveals a mildly painful lesion with sizes approximately 4 x 1.5 cm thick. CT of the lower jaw examination did not reveal any bone changes (fig.17). Based on the performed examinations, a neoplasm of the left maxillo-lingual sulcus was diagnosed. The tumor was removed under general anesthesia and sent for histological examination (fig18,19,20,21,22). The patient spent 4 days in the hospital. The surgery and the postoperative period went smoothly, without complications. During this time, the patient received antibiotics and analgetic drugs.



Figure 18. Intraoperative view of the exposed tumor.



Figure 19. Removed tumor

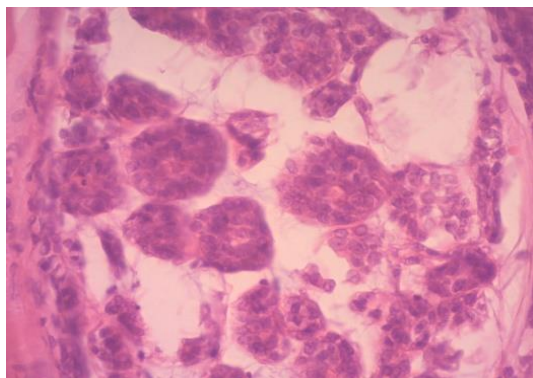


Figure 20. Microscopical pictures of the removed tumor (Sclerosing polycystic adenoma)

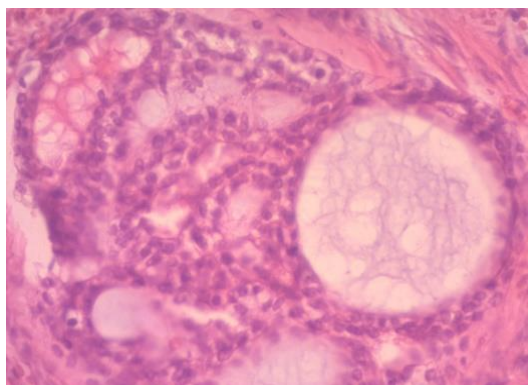


Figure 21. Stained with hematoxylin-eosin, x 100.



Figure 22. View of the postsurgical wound

Surgical operation

Both patients (cases 1 and 2) underwent surgery under general anesthesia for removing the tumor. The operation was a subtotal resection of the left parotid salivary gland with preservation of the branches of the facial nerve, followed by sending the removed lesion of the parotid salivary gland for a planned histological examination.

The surgical and postoperative course went smoothly, without complications. The patients spent 1 day in the hospital and were gone out with improvement.

In case 3 the patient surgery was planned to remove the tumor under general nasotracheal

anesthesia. The patient was warned about the possible complications associated with the surgery. The tumor was removed completely with sublingual gland, which was totally replaced with the tumor. The wound healed by primary intention.

Morphological study

The materials for morphological studies were the samples of lesion tissues. According to the standard histological scheme, the pieces of the tissue were fixed in 10% neutral formalin, dehydrated and embedded in paraffin. A series of sections 4 μ m in thickness were stained with hematoxylin–eosin for a general assessment of the condition of the examined tissues. Histological micropreparations were studied with a ZEISS Primo Star trinocular microscope (ZEISS Microscopy, Jena, Germany) under 100, 400- and 1000-times magnification. Microphotographs were taken with a ZEISS Axiocam ERc 5 s (Carl ZEISS Microscopy, Jena, Germany).

Results

Grossly, in the first and second cases, macroscopically, cystic neoplasms were clearly delimited and represented single, unilocular lesions filled with yellowish mucous fluid. Solid areas and multiple cysts with papillary projections are apparent on the cut surface.

Microscopically, varying proportions of papillary cystic structures lined by bilayered oncocytic epithelial cells and surrounded by a lymphoid stroma including germinal centers. Epithelial component is comprised of inner columnar and outer cuboidal cells.

Limited foci of squamous, mucous, ciliated and sebaceous cells can be present. Histopathological diagnosis: Warthin tumor of the left parotid gland.

In third case, grossly the lesion was well delimited, pale, firm, with sizes 4x1,5 cm.

Microscopically, it was circumscribed with preservation of lobular architecture, composed of irregularly distributed bilayered ducts and acini within a sclerotic stroma. Ducts range from small tubules to ectatic spaces; may contain secretory material or foamy macrophages.

Ductal cells were vacuolated, foamy, apocrine and mucous appearances.

Hyperplastic ductal epithelium is forming solid, microcystic and cribriform structures in some places. Small eosinophilic globules of basement membrane-like material was revealed in some cribriform areas. Histopathological diagnosis: Sclerosing polycystic adenoma.

Discussion

The diagnosis and treatment of cystic lesions of the salivary glands have been widely discussed in the pathology literature.

The latest World Health Organization 2017 Classification of Head and Neck Tumours includes a new chapter on tumors and tumor-like lesions of the neck and lymph nodes.¹³⁻¹⁵

Tumor-like lesions include a variety of cystic lesions of the parotid gland. Cystic lesions of the parotid gland can be divided into three groups: non-neoplastic cysts, benign tumors with macrocystic change, and malignant tumors with macrocystic change. It is important to distinguish these lesions from one another because treatment and patient management differ among the three groups.

Cystic lesions as a group account for about 5% of all salivary gland tumors, most are unilateral, and nearly 50% mimic benign salivary neoplasms and require surgical resection and histopathologic examination. Bilateral or multiglandular salivary gland involvement is occasionally seen, and may indicate systemic pathologic processes such as Sjogren's syndrome, cystic fibrosis, and human immunodeficiency virus (HIV).

Parotid duct cysts are part of a larger group of parotid cysts (Table 1), and represent 10% of all salivary gland cysts. Most parotid cysts are detected in the fifth to seventh decades of life, and prevalence rates are similar in men and women.¹⁶

Table 1

Classification of parotid cysts (modified from Pieterse²)

I- Cystic tumours	
1. Benign	
a.	Warthin's tumour
b.	Pleomorphic adenoma
c.	Cystadenoma
d.	Lymphangioma
2. Malignant	
a.	Low-grade mucoepidermoid carcinoma
b.	Adenoid cystic carcinoma
c.	Metastatic squamous cell carcinoma
d.	Lymphoma
II- Non-neoplastic cysts	
1. Epithelial - unilocular or multilocular	
	- with lymphoid tissue (may be associated with HIV infection) or without lymphoid tissue
a.	Epidermoid
b.	Epidermoid with sebaceous glands
c.	Ductal
d.	Branchial
e.	Multiple
f.	Traumatic
g.	Associated with cholesteatoma of mastoid air cells
2. Non-epithelial	
a.	Tuberculosis
b.	Abscess
c.	Parasitic
d.	Gas in glassblowers and musicians
e.	Traumatic

Parotid gland cysts can be congenital or acquired. Congenital cysts are thought to result from a malformation of the embryonal duct system or from defects of the first branchial pouch and cleft.¹⁷ Congenital parotid cysts are referred to as branchial cleft cysts or lymphoepithelial cysts.

Although they are congenital, such cysts may not manifest until adulthood. Cysts in the parotid gland represent a small percentage of benign parotid masses. They usually arise within the gland from salivary or non-salivary parotid tissue, and may be congenital or acquired. Some, however, may arise from surrounding structures.

Unless the cyst is superficial and therefore readily amenable to proper examination, it usually escapes a definite diagnosis even with the help of sialography or more sophisticated procedures. Exploration is eventually resorted to for diagnosis and treatment. That is why the surgeon should be ready to perform extensive surgery if the findings at exploration necessitate it.

One-third of cystic salivary gland lesions are neoplastic¹⁸.

The clinical diagnosis is frequently a mass that is considered to be solid.

Salivary gland cysts can typically be identified by ultrasound.¹⁹

However, occasionally, benign or malignant tumors (e.g., lymphoma, metastases) can be misinterpreted as a simple cyst, pseudocysts can be hard to discern, and paradoxically certain cystic lesions can present as solid lesions on ultrasound.²⁰

In such a scenario, the fluid should be aspirated and sent for cytology, which may reveal the nature and diagnosis of the swelling.

Radiologically benign cysts (e.g., mucous retention cysts, lymphoepithelial cysts, cysts of the first branchial cleft, ranulas, parotid cysts, and pseudocysts) have similar intensity on computed tomography and MRI.

Salivary gland cytopathology is one of the most challenging areas of diagnostic cytology. Salivary Gland Cytopathology will use a simplified algorithmic approach based upon differential diagnostic groups to cover practical aspects of diagnosing common as well as challenging salivary gland lesions.²¹

In order to provide a practical classification system an improve communication between cytopathologists and clinical teams, the first edition of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was released in February 2018 and further updated in July 2023^{22,23}.

The MSRSGC comprises six diagnostic categories: non-diagnostic, non-neoplastic, atypia of undetermined significant (AUS), neoplasm (A. benign; B. salivary gland neoplasm of uncertain malignant potential, SUMP), suspicious for malignancy and malignancy

Table 2. illustrates how various cystic salivary gland lesions are handled according to the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC).

Table 2. The Milan System for reporting salivary gland cytopathology for cystic lesions

Diagnostic category	Example of cystic salivary gland lesion
Non-diagnostic	Cystic non-mucinous fluid only
Non-neoplastic	Inflammatory cyst with amylase crystalloids
Atypia of undetermined significance	Histiocytes ± scant epithelial cells in a background of abundant mucin (cannot exclude low-grade mucoepidermoid carcinoma)
Benign neoplasm	Warthin tumor, or cystic pleomorphic adenoma
Salivary gland neoplasm of uncertain malignant potential (SUMP)	Cellular oncocytic/oncocytoid neoplasm with cystic background (differential includes Warthin tumor or oncocytic cystadenoma)
Suspicious for malignancy	Atypical cells in a mucinous background, suspicious for low-grade mucoepidermoid carcinoma
Malignant	Keratinizing squamous cell carcinoma

Acellular aspirates from cystic non-mucinous lesions are classified as nondiagnostic (cystic fluid only) while hypocellular samples with mucinous material are classified as atypia of undetermined significance (AUS). However, these two diagnostic categories should only be used after all cyst contents have been processed and examined.

The Milan System for reporting salivary gland cytopathology provides useful criteria for acellular aspirates derived from cystic non-mucinous lesions (i.e., classified as non-diagnostic) and those containing mucinous material but with only scant epithelial cells (i.e. classified as atypia of undetermined significance). Evaluation of the literature regarding salivary gland cysts is challenging given the change in terminology for several of these cystic entities.

Also, further studies are required to determine the feasibility of employing newer ancillary studies to evaluate hypocellular cyst samples.

A definitive diagnosis of cystic neoplasms of the salivary glands is possible only through histological examination of the neoplastic tissue^{24,25}

Most neoplastic parotid cysts develop in benign tumours, usually Warthin’s type. Any cartilage or lymphoid tissue that is detected in the walls of a parotid cyst during histopathological examination is presumed to be of branchial origin,

and should alert the surgeon to the possibility of associated sinuses and fistulae.

Only a limited number of articles have reported cytopathology studies of cystic salivary gland lesions^{26,27}.

Nevertheless, FNA remains a useful procedure early on in the diagnostic work-up of patients with cystic salivary gland lesions since it can help reduce the number of patients requiring surgery²⁸⁻³⁰.

The FNA specimens from salivary gland cystic lesions can be no informative very often, because FNA of these lesions demonstrates hypocellular mucinous material contents, possibly with inflammatory cells and also scant degenerated cuboidal, oncocytic or squamoid epithelial cells^{31,32}. For example, the presence of mucin and admixed lymphocytes in cyst fluid can be demonstrated both in the benign inflammatory cysts associated with chronic sialadenitis, sialolithiasis with duct ectasia and in Warthin tumor moreover, the clinicians should be informed that by FNA a low-grade mucoepidermoid cannot be excluded.

The diagnostic value of FNA can be increased if, after drainage of cyst fluid, any residual solid components are also sampled. FNA may yield mucoid (mucin) or non-mucoid (e.g., serous) material³⁴⁻³⁶. For this reason aspirates of cystic salivary gland lesions are typically divided into “mucinous” and “non-mucinous types”.

Mucin (mucicarmine-positive) may be viscous and resemble thick colloid-like material. Non-mucinous cyst contents are generally more watery, proteinaceous and may contain scattered acute and/or chronic inflammatory cells (e.g., lymphocytes, macrophages) and debris. Crystals may sometimes also be identified Some Warthin tumors can have squamous metaplasia which may contain atypical squamous cells, making it possible to misdiagnose them as squamous cell carcinoma. There may infrequently also be mucinous metaplasia, which raises the consideration of a MEC.

If FNA findings show only necrotic debris they should be reported as non-diagnostic with a comment that this finding raises the possibility of a neoplastic process. Given that aspirates with only scant epithelial cells and mucinous cyst contents may represent a low-grade MEC, they are considered to be indefinite for a neoplasm, and hence best classified as AUS. If abundant inflammatory cells are present (e.g., abscess material, granulomatous inflammation), even without an epithelial component, such cases should be interpreted as adequate and non-neoplastic.

Other salivary gland cysts that belong to this non-neoplastic category are the benign inflammatory

cysts associated with chronic sialadenitis, duct obstruction (sialolithiasis) and duct ectasia.

Ultrasound is considered a very valuable, reliable and useful method in the differential diagnosis of neoplastic lesions of the salivary glands, however, ultrasound does not allow for the correct assessment of lesions located in hard-to-reach places (for example, in the deep lobe of the parotid gland, behind the bones), and is ineffective for the differential diagnosis of small lesions³⁷⁻⁴¹.

Surgical treatment of the maxillofacial region's cystic lesions is difficult for patients to bear on a psycho-emotional level, because one of the main external criteria for the beauty of a person is the face, which, forms the first impression and creates a decent self-esteem of the individual in society⁴².

Regardless of the type and location, drug therapy is impossible with this diagnosis. Cystic lesion of the salivary gland requires surgery. If the cystic neoplasm is localized in a hard-to-reach place and if localized in the parotid gland, surgical manipulation is performed extraorally, it is removed simultaneously with the parenchyma of the salivary gland, since in most cases it atrophies under the pressure of a large tumor⁴³⁻⁴⁴.

However, it is necessary to try as much as possible to do this operation carefully, preserving the facial nerve. Since this is associated with the risk of damage to the facial nerve, the operation requires careful visual control, since damage to the facial nerve leads to paralysis of the facial muscles and deformation of the face for life, the development of postoperative salivary fistulas⁴⁵. Prevention of cystic neoplasms of the salivary gland consists in preventing injuries and inflammations of the oral cavity, careful hygiene and regular visits to the dentist. Early diagnosis and initiation of appropriate therapy is of the most importance for effective treatment, as well as for long-term prognosis, especially in cancer.

Surgical treatment of salivary gland pathologies applies to all types of lesions, both neoplastic and non-neoplastic⁴⁶⁻⁵⁰.

Prevention of cystic neoplasms of the salivary gland consists of preventing injuries and inflammations of the oral cavity, careful hygiene and regular visits to the dentist.

This article presents cases of the salivary glands cystic neoplasms, which are the clinical interest.

In the presented clinical cases, based on clinical, laboratory and instrumental studies, the diagnosis of

the cyst was confirmed and surgical treatment was performed. The operation and postoperative period went smoothly, without complications.

All cystic lesions were retrospectively evaluated with respect to preoperative diagnostic examinations and histopathological confirmed diagnosis. Cystic components in surgical specimens were also evaluated histopathologically. The relationships with magnetic resonance imaging (MRI) findings and histopathological confirmed diagnosis were studied.

Our cases is consistent with previous reports that describe cystic lesions with well-defined margins and no solid components as indicative of non-neoplastic cysts on MRI. In conjunction with the typical MRI characteristics, served to reinforce the diagnosis of an epidermoid cyst rather than a cystic degeneration of a benign tumour.

This cases contributes valuable insights into the management of gland lesions and reinforces the necessity for careful diagnostic and surgical planning in cases of cystic formations.

To prevent such problems, it is important to consult a doctor, undergo the necessary diagnostics and eliminate the pathology.

Conclusion

Cystic parotid gland lesions are difficult to diagnose correctly before surgery, but the evaluation of cystic components by MRI and histopathology is helpful in differentiating between benign and malignant tumors. Surgical treatment of salivary gland cystic lesions and neoplasms may prevent further malignant transformation.

Declarations

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the University ethics committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

The work was not funded.

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