

# Aspiration and Brushing Cytology in tumors and tumor-like conditions of the tongue: A Study of 27 Cases

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## SUMMARY

**Background.** Lesions of the tongue have a broad differential diagnosis ranging from benign idiopathic processes to infections, cancers, and infiltrative disorders. An important thing to remember is that most tongue lesions will resolve spontaneously or with simple therapy within a week, if not, they should be biopsied or evaluated further for a definitive diagnosis of a potentially serious disorder. Some tongue lesions may be clues to other underlying illnesses which require further evaluation. Tongue lesions are traditionally evaluated by surgical biopsy. Most of them, however, are easily accessible by fine-needle aspiration (FNA) or brushing.

**Study design.** Fifteen males and twelve females aged from 15 to 72 were examined in our institution over a period of 15 years and 27 lesions, were evaluated by fine-needle aspiration cytology (FNAC) or brushing cytology.

**Results.** The lesions were located at the mobile aspect of the tongue. 10 malignant tumors were diagnosed: 9 cases of squamous cell carcinoma (SCC), and 1 non-Hodgkin lymphoma (NHL). In addition, 13 benign tumors (7 cases of papillomas / fibromas, 3 cases of hemangiomas, 2 cases lymphangiomas, and 1 case of lipoma), and 4 nonneoplastic benign conditions (3 traumatic ulcers and 1 hematoma) were found. There were no false-positive diagnoses. There were no clinical complications resulting from FNA or brushing.

**Conclusion.** Cytologic examination is rapid, safe, accurate, inexpensive, and patient-friendly for establishing preoperative diagnosis in tumors and tumor-like conditions of the tongue, and we recommend this method as the first diagnostic step in the evaluation of these lesions.

**Keywords:** fine-needle aspiration cytology, brushing cytology, tongue tumors, malignant tumors, benign tumors.

## INTRODUCTION

Although cytology is used increasingly in the evaluation of lesions of the neck and head region (1-3), there is limited experience concerning the aspiration of intraoral masses, particularly of the tongue (4-8).

Preoperative diagnosis is of utmost importance and the anatomy of the area, with its great variety of heterogeneous groups of benign and malignant tumors and tumor-like conditions, makes this task difficult. Despite the revolutionary advances in radiologic diagnostic techniques with three-dimensional computerized tomography (3D-CT scan), magnetic resonance imaging, positron emission tomography, and color ultrasonography, a biopsy is mandatory before vital anatomic elements of the face are sacrificed in the attempt to control the disease.

Open biopsies for histologic diagnosis in some cases carries a surgical risk or are contraindicated in others (vascular tumors).

Fine-needle aspiration cytology (FNAC) is an alternative diagnostic method that in recent years has gained wide acceptance in many medical and surgical specialties. Although the method has been in existence for 150 years, its usefulness, safety, and

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diagnostic accuracy have been demonstrated repeatedly only during the last 20 years.

In the field of oral and maxillofacial surgery, preoperative diagnosis by FNAC offers several advantages (19). It can be used to diagnose a mass in the area, differentiate benign from malignant tumors, confirm a suspected malignancy, determine the extent of malignant disease, evaluate metastasis in suspected or enlarged lymph nodes, diagnose multiple tumors, verify recurrence of a previously treated neoplasm, document malignancy for patients with non operable disease, identify microorganisms, and obtain material for culture from infectious masses and tumor-like conditions. The cooperation between the surgeon and the cytopathologist is of paramount importance to obtain and evaluate the material needed for a safe and accurate diagnosis.

Complications from the procedure are rare and, especially for the head and neck area, there are no contraindications for its use. The only reported complication is needle tract seeding but contemporary technique applied by experienced clinicians make this risk negligible (20).

The diagnostic accuracy of the method varies from 90–97% depending on the anatomic site of aspiration. There are many factors affecting the accuracy of FNAC, with experience in performing the procedure being the most important. Failure to obtain a representative sample is the prime cause of an erroneous diagnosis. This could be the result of needle positioning outside the target tissue or to central necrosis, hemorrhage, or cystic change in the tumor.

The cytologic examination of brushing material can be considered as a rapid screening technique and may be used as an adjunct to biopsy. Patient anxiety can be relieved by providing an instant diagnosis followed by discussion of treatment options. Surgery can be avoided if the lesion proves to be non-neoplastic, or delayed for convenience if it is benign. A diagnosis of malignancy allows preoperative staging and planning of the extent of surgery.

The evaluation of material adequacy must be based not only on the microscopic features of the sample, but also on the clinical and anatomic data of the tumor. Expertly prepared smears, proper fixation, and staining techniques are also sine qua non for optimal diagnostic results. Cytology is a useful tool for differentiating inflammatory and infectious lesions from those that are neoplastic. In many cases cytology is also helpful in determining whether a tumor is malignant or benign. Cytology does however have its limitations and these should be recognized. Problems may arise when an inflammatory response results



**Fig. 1.** A gynecologic cytobrush used to perform the brushings

in secondary dysplastic changes which can mimic those normally associated with neoplasia. It is also worth noting that with poorly differentiated tumors, cytological examination may not identify the tissue of origin. Cytology, therefore, should not be regarded as a substitute for histopathological examination of biopsy specimens. Histology is more likely to provide a definite diagnosis and, since biopsies preserve tissue architecture, grading and classification of the tumor is usually possible.

The tongue consists of striated muscular tissue admixed with fat and divided into symmetrical halves by a septum of fibrous tissue. It is covered by stratified squamous epithelium except at the root. Minor salivary glands, as well as vessels, nerves, and lymphoid aggregates, are part of tongue tissue. Because of its complex anatomy, lesions of the tongue show a wide spectrum of benign and malignant conditions. Although squamous cell carcinoma (SCC) is the most frequently occurring type of malignancy of the tongue (9), one can expect a variety of benign and malignant tumors originating from such different entities as salivary glands (10), mesenchymal structures (11), and lymphoid tissue (12). In addition, some inflammatory conditions or systemic disorders may present as tongue lesions (5-12). Evaluation of tongue lesions usually requires morphologic examination, and cytology can play an important role in the preliminary assessment or give a definitive diagnosis.

## MATERIALS AND METHODS

Over a 15-year period (1991-2006), 27 patients had undergone cytologic examination of previously undiagnosed tongue lesions at the Department of Oral and Maxillofacial Surgery, University Hospital, Alexandroupolis, Greece.

Cytological and histological slides, as well as the necessary medical records and radiograms of the 27 cases, were reviewed.



**Fig. 2.** Squamous cell carcinoma arising in the tongue. Brushing cytology. Papanikolaou stain  $\times 500$ .

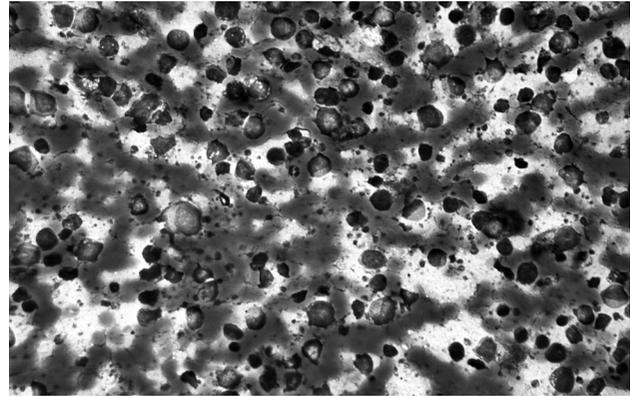
The aspirations were performed using a Cameco (Taby, Sweden) syringe pistol with a 20-ml disposable plastic syringe and needles with 0.4–0.7-mm outer diameter. A gynecologic cytobrush (Fig. 1) was used to perform the brushings. Aspirates and brushings were prepared as air-dried smears or fixed in 95% ethanol. May-Grunwald-Giemsa (MGG) and hematoxylin-eosin (H&E) stains were applied, respectively. Histological sections for routine evaluation were stained with H&E. In addition, immunohistochemical staining was performed. A three-step peroxidase or alkaline phosphatase antialkaline phosphatase immunostaining was used according to a protocol described previously (13,14). The following antibodies were used: Cytokeratins (CK) [pan-CK, CK CAM 5.2, and CK AE1/AE3], anti-kappa, anti-lambda, CD45 (leukocyte common antigen-LCA), CD3, CD10, CD20, Bcl-2, and EBV latent membrane protein.

There were no clinical complications resulting from the FNA. The series included 15 men and 12 women ranging in age from 15–72 years. Patients were divided into five groups: group 1: SCC; group 2: NHL; group 3: benign tumors; and group 4: non-neoplastic lesions.

#### **Group 1 (9 cases)**

Approximately 90% of cancers in the oral cavity are SCC. After the lips, the tongue is the most frequently involved site, with approximately two thirds of cases arising from the mobile anterior part, and one third from the base and root of the tongue (9). SCC of the tongue is more common in men than women, with a majority of cases occurring between age 40–80 years.

The patients were 6 men and 3 women, with ages ranging from 27–68 years. Five tumors were localized on the mobile two thirds and four on the posterior one third of the tongue. Cytological specimens were, quite cellular, with clusters and dissociated malignant cells showing marked nuclear



**Fig. 3.** Non Hodgkin Lymphoma arising in the tongue. Aspiration cytology. May Grunwald Giemsa stain  $\times 500$ .

pleomorphism (Fig. 2). Varying degrees of keratinization were observed.

#### **Group 2 (1 case)**

Intraoral lymphoma is usually a manifestation of systemic disease. Primary oral lymphomas are uncommon (12, 15). The patient with NHL included in this study, was male (60 year old). The tongue lesion was the first manifestation of lymphoma. Follow-up magnetic resonance imaging of the abdomen and chest revealed no enlarged lymph nodes. There was no peripheral lymphadenopathy and bone marrow biopsy was negative for lymphoma. The tumor was located in the base of the tongue and covered by intact mucosal epithelium. Smears contained a mixture of small and medium-sized lymphocytes, some of them with a plasmacytic appearance (Fig. 3). Large immunoblasts were seen occasionally. The lesion was measured  $2 \times 2 \times 1.5$  cm. Histologically the cells were large and resembled immunoblasts. They had scant amphophilic cytoplasm, vacuolated nuclei, coarse chromatin, and conspicuous nucleoli. Mitoses were numerous with scattered single-cell necrosis. Tangible-body macrophages were readily noticeable. The neoplastic cells were positive for leukocyte common antigen (Dako) and demonstrated a B-cell phenotype (CD20 positive) (Dako). There was also a positive reaction of tumor cells with CD10 and Bcl-2 (Dako). Immunostains demonstrated reactivity of the tumor cells for kappa but not lambda light chain (Dako). Focally, the kappa-positive tumor cells were arranged in follicles, displacing the kappa-containing plasma cells. The findings were consistent with large B-cell lymphoma, focally follicular. Immunohistochemical staining for EBV latent membrane protein was negative.

#### **Group 3 (13 cases)**

**Papillomas/fibromas.** Papillomas are the most common epithelial neoplasms within the oral cavity,

with predominant sites on the lips and tongue (18).

The clinical appearance is of an exophytic, occasionally pedunculated growth. In our patients the yield from the smears of papillomas was not characteristic but served to rule out malignancy. The smears contained benign squamous cells with an admixture of some fibroblasts and inflammatory cells. Fibromas are also very common benign lesions within the oral cavity. The majority of fibromas develop as a result of mechanical irritation (irritation fibroma), and only a small number of fibromas represent “true” benign neoplasm (18).

Cytological smears from fibromas are similar to those obtained from benign reactive or inflammatory conditions of the tongue. In fibromas included in this study, the smears were cell-poor and consisted only of scattered fibroblasts, mature squamous cells, and inflammatory cells. FNAC in this situation could rule out malignancy but could not give a specific cytologic diagnosis.

**Hemangiomas.** The lips, buccal mucosa, and tongue are the most common sites for hemangioma within the oral cavity (16). Their size and distribution may vary, and multicentric or deep penetrating hemangiomas are not unusual. In rare cases the tumor may cause macroglossia. Hemangioma of the tongue seems to be more a clinical, radiological, or histological rather than a cytological diagnosis (17). In our study, the diagnosis was benign (2 cases) or unsatisfactory (2 cases), and in the others FNA was suggestive of hemangioma, not because of any characteristic microscopic picture only, but because of the clinical appearance, radiologic findings, and extremely bloody smears. Blood entering the syringe under arterial pressure may suggest a tumor of vascular origin.

**Lymphangioma.** Lymphangioma or cystic hygroma is an uncommon benign congenital tumor of lymphatics that is seen in children and, rarely, adults. The most common intraoral location of lymphangiomas is the tongue, and can be a cause of macroglossia. Aspirates showed 13 cc of yellow fluid with red blood cells, lymphocytes, and rare fragments of benign-appearing salivary gland epithelium. The main entities to be considered in the differential diagnosis of a lingual cystic lesion in an adult patient include: mucus retention cyst, lymphoepithelial cyst, lymphangioma, intraductal papilloma, polymorphous low-grade adenocarcinoma, acinic-cell carcinoma, mucoepidermoid carcinoma, squamous cell carcinoma, and pleomorphic adenoma. In this case, the fine-needle aspiration findings along with the magnetic resonance imaging (MRI) findings of a multiloculated cystic mass allowed the diagnosis of lymphangioma.

**Spindle-cell lipoma.** Intraoral lipoma is not unusual. The most common location is in the buccal mucosa, followed by the tongue and the floor of the mouth. Spindle-cell lipoma, however, is a distinct histological entity, typically located in the neck region. Our patient was a 70-year-old woman who presented with a 1-cm soft tumor of 1-year duration, located on the right lateral margin of the anterior mobile tongue. FNA material was quite sparse, showing small groups of fat cells mixed with myxoid material and scattered, spindle-shaped fibroblast-like cells with slightly pleomorphic nuclei and a collagenous material in the background. The original cytological diagnosis was “benign soft-tissue tumor”, and the tissue section disclosed a typical spindle-cell lipoma, composed of benign fat cells with broad bundles of spindle cells and relatively distinct tumor borders.

#### Group 4 (4 Cases)

Cytologic findings were benign (3 patients) and unsatisfactory (1 patient). Biopsy material was available in all cases, showing inflammatory and reactive conditions in 3 cases and hematoma in 1 case.

#### DISCUSSION

The cytomorphology of a number of tumors which might appear on the tongue has been described, and diagnostic criteria have been defined. In addition to SCC, cytologic features of NHL have been described. The cytologic diagnosis of hemangioma on the tongue, as in other sites, is based more on clinical findings and an immediate appearance of blood in the syringe, even without aspiration, than on the evaluation of scattered histiocytes and mesenchymal cells in the hemorrhagic smears (17).

The results presented in this study imply that the use of cytology in the evaluation of tongue lesions is of considerable diagnostic help. Compared to surgical biopsy, cytology is advantageous to the patient in many ways. Tongue tumors are easily accessible by cytology, and cytodiagnosis with regard to benignity or malignancy is comparable to that of histologic examination of biopsy material (1-3, 6, 8). The aspirations and brushings are most often easily performed, anesthesia is not necessary (7, 8), and a preliminary report is possible within 20 min when the cytopathologist performs the examination. The only complication is pain during the short period of performing the examination. One other advantage is the possibility of clinically staging patients with SCC; enlarged lymph nodes may be examined simultaneously. Although FNAC is most useful in the

detection of malignant lesions it can also be used to rule out malignancy (2, 3, 6-8). When clinical and radiologic findings are benign and the cytopathologist is confident that he/she has sampled the lesion, benign cytologic findings imply that expectation is an adequate follow-up. When a benign diagnosis is rendered on a tongue mass clinically suspicious for malignancy, it is very important that the material be sufficient and well-preserved, and that reliable diagnostic criteria are followed. A correct and, for the clinician, helpful final evaluation is facilitated when the cytopathologist has access to all clinical data and there is close cooperation between cytopathologist and clinician (1).

Cytology can be also used in the typing of tongue tumors (8); Acquisition of material for ancillary studies is also possible (15, 21-24).

## CONCLUSIONS

The purpose of this article was to evaluate cytology in tongue tumors, in an area in which cytology has many advantages and relatively low use. When the results were evaluated not only from the cyto-

pathologist's point of view but with the correlation of these findings with histopathologic findings and treatment modalities, questions were raised that required specific answers. One of the questions to be answered and probably the most important of all is the question of what is required to improve preoperative diagnosis. The authors believe that this question can be answered by improving the diagnostic method, with the application of more strict rules in tissue sampling, by careful evaluation of the material, by minimizing procedure limitations, and finally by improving the interpretation of the cytologic findings.

It is accepted that cytology has reached high diagnostic accuracies of 90% in the areas in which it has been used. Increasing this accuracy requires more effort than has been made so far to bring this method to today's state of the art. Further prospective and retrospective studies are required to evaluate the validity of these proposals. It is apparent that cooperation between clinicians and cytologists contributes significantly to the understanding of each other's efforts to improve disease diagnosis and treatment, with the final outcome being undoubtedly to the benefit of the patient.

## REFERENCES

1. Frable W, Frable MAS. Thin-needle aspiration biopsy. The diagnosis of head and neck tumors revisited. *Cancer* 1979;43:1541-8.
2. Platt JC, Rodgers SF, Davidson D, Nelson C. Fine-needle aspiration biopsy in oral and maxillofacial surgery. *Oral Surg Oral Med Oral Pathol* 1993;75:152-5.
3. Schelkun PM, Grundy WG. Fine-needle aspiration biopsy of head and neck lesions. *J Oral Maxillofac Surg* 1991;49:262-7.
4. Cramer H, Lampe H, Downing P. Intraoral and transoral fine needle aspiration. A review of 25 cases. *Acta Cytol* 1995;39:683-8.
5. Bhamhani S, Das DK, Luthra UK. Fine needle aspiration cytology in the diagnosis of sinuses and ulcers of the body surface (skin and tongue). *Acta Cytol* 1991;35:320-4.
6. Das KD, Gulati A, Bhatt NC, Mandal AK, Khan VA, Bhamhani S. Fine needle aspiration cytology of oral and pharyngeal lesions. *Acta Cytol* 1993;37:333-42.
7. Malberger E. Aspiration cytology in the diagnosis of orofacial masses. *Int J Oral Surg* 1974;3:137-43.
8. Scher RL, Oostingh PE, Levine PA, Cantrell RW, Feldman PS. Role of fine needle aspiration in the diagnosis of lesions of the oral cavity, oropharynx, and nasopharynx. *Cancer* 1988;62:2602-06.
9. Verbin RS, Bouquot JE, Guggenheimer J, Barnes L, Peel RL. Cancer of the oral cavity and oropharynx. In: Barnes L, ed. *Surgical pathology of the head and neck*. New York: Marcel Dekker, 1985:343-8.
10. Pellagrino SV. Glossopyrosis due to adenoid cystic carcinoma. *Oral Surg* 1977;43:521-3.
11. Mockli GC, Ljung B-M, Goldman RL. Fine needle aspiration of intramuscular myxoma of the tongue. A case report. *Acta Cytol* 1993;37:226-8.
12. Deery A. Oral cavity. In: Grey W, ed. *Diagnostic cytopathology*. Edinburgh: Churchill Livingstone; 1995. P. 315-20.
13. Naish SJ. Handbook: immunochemical staining methods. Carpinteria, CA: DAKO Corporation; 1989. p. 2-3.
14. Tani EM, Christensson B, Porwit A, Skoog L. Immunocytochemical analysis and cytomorphologic diagnosis on fine needle aspirates of lymphoproliferative disease. *Acta Cytol* 1988;32:209-15.
15. Liljemark J, Tani E, Mallsted H, Skoog L. Fine-needle aspiration cytology and immunocytochemistry of malignant non-Hodgkin's lymphoma in the oral cavity. *Oral Surg Oral Med Oral Pathol* 1989;68:599-603.
16. Barnes L. Tumors and tumorlike lesions of the soft tissues. In: Barnes L, ed. *Surgical pathology of the head and neck*. New York: Marcel Dekker; 1985.
17. Gunhan O, Dogan N, Celasun B, Sengun O, Onder T, Finci R. Fine needle aspiration cytology of oral cavity and jaw bone lesions. A report of 102 cases. *Acta Cytol* 1993;37:135-41.
18. Guggenheimer J, Appel BN, Verbin RS, Barnes L. Benign neoplastic and non-neoplastic lesions. In: Barnes L, ed. *Surgical pathology of the head and neck*. New York: Marcel Dekker; 1985. p. 252-260.
19. Daskalopoulou D, Ravidis AD, Maounis N, Markidou S. Fine-needle aspiration cytology in tumors and tumor-like conditions of the oral and maxillofacial region: diagnostic reliability and limitations. *Cancer* 1997;81:238-52.
20. Tamiolakis D, Antoniou C, Venizelos J, Lambropoulou M, Alexiadis G, Economou C, et al. Papillary thyroid carcinoma metastasis most probably due to fine needle aspiration biopsy: a case report. *Acta Dermatoven APA* 2006;15:169-72.
21. Domanski H, Akerman M. Fine needle aspiration cytology of tongue swellings: A study of 75 cases. *Diagn Cytopathol* 1998;18:387-92.
22. De Las Casas LE, Hoerl HD, Oberley TD, Hafez GR, Sempf JM, Shalkham JE, Kurtycz DF. Myoepithelioma presenting as a midline cystic tongue lesion: cytology, histology, ancillary studies, and differential diagnosis. *Diagn Cytopathol* 2001;24:403-7.

23. De Las Casas, LE; Bardales, RH Fine-needle aspiration cytology of mucous retention cyst of the tongue: Distinction from other cystic lesions of the tongue. *Diagn Cytopathol* 2000;22:257-62.
24. Ashraf MJ, Azarpira N, Hashemi SB. Fine needle aspiration cytology of malignant peripheral nerve sheath tumor of the tongue. *Acta Cytol* 2010;54:117-9.

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