

ONCOLOGY

# Fine-needle aspiration cytology in the diagnosis of parotid lesions

## *Il ruolo dello FNAC nella diagnosi delle lesioni parotidiche*

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SUMMARY

Fine-needle aspiration cytology guided by ultrasound imaging is a widely used diagnostic tool to evaluate neoplastic or inflammatory lesions of salivary glands. From February 2002 to February 2008 all the parotid lesions removed surgically in our Unit of Otolaryngology were reviewed. Study focused on sensitivity, specificity, accuracy, predictive values, likelihood ratios, and Kappa statistics for fine-needle aspiration cytology vs histological diagnosis in 176 cases. Fine-needle aspiration cytology sensitivity and specificity were 81% and 99%, respectively. Accuracy for malignancy was 97%, accuracy for benignity was 83%; positive and negative predictive values were 93% and 98%, respectively; likelihood ratio of positive and negative test results were 100.3 and 0.19, respectively ("positive" was used to define "malignant"). The prevalence of malignancy was 0.114. Kappa statistics for the degree of agreement between fine-needle aspiration cytology and histological results were 0.85 (95% CI = 0.71-0.99). Pre-operative fine-needle aspiration cytology diagnosis improves surgical treatment of parotid masses.

KEY WORDS: Salivary glands • Parotid • FNAC • Cytology

RIASSUNTO

*L'agoaspirato eco-guidato rappresenta una metodica diagnostica ampiamente utilizzata nella valutazione delle lesioni parotidiche. È stata eseguita un'analisi retrospettiva su tutte le parotidectomie effettuate nella nostra unità operativa da febbraio 2002 a febbraio 2008. Sono state studiate la sensibilità, la specificità, l'accuratezza, i valori predittivi, la likelihood ratio e la statistica Kappa su 176 casi di agoaspirato parotideo. Sensibilità e specificità sono risultate l'81% e il 99%. Accuratezza per malignità il 97% e accuratezza per benignità 83%. Il valore predittivo positivo è risultato 93%, quello negativo 98%; la likelihood ratio del test positivo è 100,3 e del test negativo 0,19. La prevalenza di malignità è risultata 0,114. Il valore della statistica Kappa effettuato sulla corrispondenza tra esame citologico ed istologico è risultata 0,85 (95% CI=0,71-0,99). L'agoaspirato preoperatorio è utile nello stabilire l'iter terapeutico delle neoformazioni parotidiche.*

PAROLE CHIAVE: Ghiandole salivari • Parotide • Agoaspirato ecoguidato • Citologia

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## Introduction

The differential diagnosis between benign and malignant parotid lesions cannot be established by the simple physical examination but requires complementary diagnostic methods.

Fine-needle aspiration cytology (FNAC) guided by ultrasound imaging (US) is a widely used diagnostic tool to evaluate both neoplastic and inflammatory lesions of the salivary glands.

FNAC became popular 30 years ago<sup>1</sup> as it is useful in the differential diagnosis of salivary gland swellings. It is a minimally invasive procedure that does not require anaesthesia<sup>2</sup>. It is well-tolerated, simple, safe and cost-effective<sup>3,4</sup>. Moreover, it can be easily repeated in the event of non-diagnostic results, thus improving diagnostic precision<sup>5</sup>.

Nevertheless, the role of FNAC in the pre-operative evaluation is not universally established. At present, the debate

focuses on the reliability of FNAC as a diagnostic tool and its usefulness in treatment planning. Although in some Hospitals, FNAC is performed in every case of salivary gland nodule, some Authors support the role of cytology only in a selected group of patients with suspected malignancy, metastatic carcinoma or lymphoma<sup>6</sup>. However, Butsakis et al. state that pre-surgical FNAC does not impact on the surgical handling of these lesions<sup>7</sup>.

The aim of the present investigation was to assess the diagnostic accuracy of FNAC, on parotid gland swellings, in order to determine its usefulness in the planning of parotid gland surgery.

## Material and methods

A retrospective study was carried out focused on 176 consecutive patients affected by parotid disease that were referred to the Department of Otorhinolaryngology, "San

Raffaele” Scientific Institute, Milan (Italy), between February 2002 and February 2008.

The retrospective review of case notes was performed maintaining an anonymous evaluation of the data. The study protocol is in accordance with the Helsinki Declaration of 1975, as revised in 1983.

All patients underwent FNAC under US guidance following clinical examination. In order to obtain homogeneous and comparable data, only FNAC performed in our Institute were considered. All details regarding demographic and clinical data, including age, sex, previous surgery, timing of symptoms, cytological and histological results, site and volume of the lesions, involvement of histological sample margins and relapses were saved in an electronic database.

In our Institute, FNAC is always performed by radiologists under US-guidance (with the use of a 23-gauge needle). Cytology is performed in all cases by the same pathologist.

The cytological results were classified as: “inflammatory/benign lesion”, “malignant neoplasm”, or “non-diagnostic” when the cytological analysis was inconclusive.

A statistical analysis was performed with the specific software JMP IN 5.1 (a Business Unit of SAS Copyright ©1989-2003 SAS Institute Inc., Cary, NC, USA). Sensitivity, Specificity, Accuracy, Positive Predictive Value (PPV), Negative Predictive Value (NPV), Likelihood Ratio of Positive test results (LR<sup>+</sup>), Likelihood Ratio for Negative test results (LR<sup>-</sup>) and Prevalence of Malignancies were calculated for FNAC by using the post-operative histological diagnosis as the reference standard. Kappa statistics for agreement were also calculated together with the 95% confidence interval (95% CI).

## Results

FNAC samples were obtained in 176 cases. FNAC results were “non-diagnostic” in 36 cases (20.45%), “inflammatory/benign lesion” in 126 (71.59%), “malignant neoplasm” in 14 (7.95%) (Table I). The cytological diagnosis in this series is reported in Table II.

The correlation between the cytological and histopathological diagnosis was assessed in the 140 patients with a diagnostic FNAC (Table III).

The most common histopathological diagnosis was “benign lesion”, that occurred in 124 patients (88.57%) and included pleomorphic adenoma in 81 patients (57.85%) and Warthin’s tumour in 42 (30%). Mucoepidermoid carcinoma (2.85%) was the most common malignancy, followed by adenocarcinoma (2.14%) and squamous cell carcinoma (2.14%).

FNAC showed a sensitivity of 81% and a specificity of 99%. Accuracy for malignancy was 97%, accuracy for a benign lesion was 83%, overall diagnostic accuracy was 97%. The FNAC PPV for malignancy was 93% and the

**Table I.** The FNAC results classification.

| Diagnosis                   | FNAC no. (%) | Histology no. (%)   |
|-----------------------------|--------------|---|
| Benign/Inflammatory lesions | 126 (71.59%) | 124 (70.45%)  |
| Malignant tumours           | 14 (7.95%)   | 16 (9.09%)  |
| Non Diagnostic              | 36 (20.45%)  | 19 (10.79%) benign lesions<br>6 (3.40%) malignant tumours |

**Table II.** Cytodiagnosis of salivary gland tumours by aspiration biopsy.

| Lesion                     | No. cases | Percentage |
|----------------------------|-----------|------------|
| Pleomorphic adenoma        | 81        | 57.8%      |
| Warthin’s tumour           | 42        | 30.1%      |
| Mucoepidermoid carcinoma   | 4         | 2.9%       |
| Adenocarcinoma             | 3         | 2.1%       |
| Indifferentiated carcinoma | 3         | 2.1%       |
| Lymphoma                   | 2         | 1.5%       |
| Adenoid cystic carcinoma   | 1         | 0.7%       |
| Ductal adenoma             | 1         | 0.7%       |
| Oncocytoma                 | 1         | 0.7%       |
| Monomorphic adenoma        | 1         | 0.7%       |
| Lipoma                     | 1         | 0.7%       |
|                            | 140       | 100%       |

**Table III.** Contingency table between cytologic and histologic diagnosis.

| Parotid FNAC   | Benign histology | Malignant histology | Total |
|----------------|------------------|---------------------|-------|
| Benign FNAC    | 123<br>97.62     | 3<br>2.38           | 126   |
| Malignant FNAC | 1<br>7.14        | 13<br>92.86         | 14    |
| Total          | 124              | 16                  | 140   |

NPV was 98%. The Likelihood Ratio of Positive test results was 100.3 and the likelihood ratio of negative test results was 0.19, where “positive” was meant as “malignant”. The prevalence of malignancy was 0.114.

Kappa statistics for the degree of agreement between FNAC and histological examinations was 0.85 (95% CI = 0.71-0.99) (Table IV).

## Discussion

Most publications focus attention on the efficacy of FNAC but at present, there is no consensus regarding its effective role in the diagnostic work-up of parotid masses<sup>6,8</sup>.

In our Department, FNAC is performed in every case of parotid lesion, benign or malignant, palpable or not, in order to correctly plan surgery. The most important goal of this examination is to distinguish a benign, from a malig-

**Table IV.** Evaluation of the usefulness of FNAC.

|  | Value, % | 95% Confidence Interval |
|--|----------|-------------------------|
| Sensitivity                                | 81       |                         |
| Specificity                                | 99       |                         |
| Positive Predictive Value (PPV)            | 93       |                         |
| Negative Predictive Value (NPV)            | 98       |                         |
| Likelihood Ratio for Positive test results | 100.3    |                         |
| Likelihood Ratio for Negative test results | 0.19     |                         |
| Kappa                                      | 0.85     | 0.707 – 0.993           |
| Prevalence of malignancies                 | 0.1143   |                         |
| Prevalence of benign findings              | 0.8857   |                         |
| Accuracy for malignancy                    | 97       |                         |
| Accuracy for benign findings               | 83       |                         |

nant mass. 20.6% of FNAC are non-diagnostic; this could be due to the complexity of the tissue architecture.

In the recent scientific literature, sensitivity ranges from 57% to 98%, specificity from 56% to 100%, and accuracy from 78% to 98%<sup>1 5 6 9-17</sup>. Different causes could account for this variability. It is difficult to compare data from different studies because of the different methods adopted to classify patients, exams and results.

In many papers, cytological and histological results obtained from both parotid and submandibular glands are analysed together. Moreover, sensitivity, specificity and accuracy are sometimes calculated for each single histological subtype, such as pleomorphic adenoma or mucoepidermoid carcinoma. In some studies, patients underwent FNAC only in cases of suspected malignancy and this clearly affects sensitivity, specificity and accuracy. On the contrary, in other studies, FNAC is performed routinely and the rate of malignancies is very low<sup>6</sup>.

Some Authors highlighted the potential for false-negative FNAC<sup>9 11 14</sup>. In the retrospective study reported Atula

et al.<sup>11</sup>, diagnosis of mucoepidermoid carcinoma, adenoid cystic carcinoma, lymphoma and squamous cell carcinoma was frequently missed by FNAC alone. In our series, FNAC false-negative findings occurred in one case of acinic cell carcinoma, in one of mucoepidermoid carcinoma and in one of lymphoma. In all of these cases, the cytological diagnosis was Warthin's tumour. Que Hee et al.<sup>15</sup> reported a low accuracy of FNAC (56%), but the specimens were collected by several different clinicians with varying degrees of experience and not by pathologists. In fact, the FNAC result depends both on the operator's experience and the diagnostic skill of the cytopathologist. Good collaboration between the clinician and the pathologist guarantees the best results.

In some studies on the parotid gland, FNAC PPV and NPV have been calculated: these values varied considerably between the different studies. The low value of NPV reported by Cohen et al.<sup>6</sup> means that more than half of the FNAC specimens, without neoplastic cells, were actually obtained from neoplastic lesions, as assessed by histology. In agreement with our results, Zurrida et al. reported both a high PPV and a high NPV (of 100% and 90%, respectively)<sup>9</sup>.

The results of the likelihood ratio of positive and negative were 100.3 and 0.19, respectively. This means that FNAC can be considered useful in predicting the histopathological diagnosis of the parotid masses.

Kappa statistics for the degree of agreement between FNAC and histological examinations was 0.85 (95% CI = 0.707-0.993), which means that the agreement lies between substantial and almost perfect (Table IV).

## Conclusions

FNAC is a well-established tool to investigate parotid swellings but its role still remains controversial. Our data support the hypothesis that FNAC is effective in this setting. Moreover, FNAC may be considered safe. Good collaboration between the clinician and the pathologist is, in our opinion, important to obtain the best results.

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