Evaluation of Fine Needle Aspiration Cytology in the Diagnosis of Cancer of the Parotid Gland

Álvaro Antonio Herrera Hernández, Julio Alexander Díaz Pérez, Carlos Andrés García, Loren Paola Herrera, Paola Aranda Valderrama, and Luis Carlos Orozco Vargas
Grupo de Investigación en Cirugía y Especialidades (GRICES), Universidad Industrial de Santander, Bucaramanga, Colombia

Background: Fine needle aspiration (FNA) is commonly used in the study of neoplastic lesions of the parotid gland, however controversy exists regarding its diagnostic accuracy.
Objective: To evaluate the performance of FNA biopsy as compared to open surgical biopsy in the diagnosis of carcinoma of the parotid gland.
Material and method: Forty-six patients with parotid masses from 7 health centres in Bucaramanga, Colombia, were identified and included in the study. All patients underwent FNA and open surgical biopsy, with the latter considered the diagnostic gold standard. The FNA and final surgical histopathology were interpreted as either positive or negative for malignancy by pathologists blinded to the FNA outcome. Only standard histological stains were used. The data were compared in a contingency table and analyzed statistically to determine the accuracy of FNA to predict the surgical pathology according to standard measures.
Results: The mean age of patients was 52 (16) years old and 59% were female. Using FNA, 18% of the initial diagnoses were found to be erroneous at final pathology. FNA had a sensitivity of 0.54, a specificity of 0.90, a PPV of 0.70, an NPV of 0.83, an LR+ of 5.92, an LR– of 0.5, and kappa of 0.48 in the identification of parotid gland carcinoma from referral population with a disease prevalence of 28.3%.
Conclusions: In line with other previous studies, FNA biopsy alone was unreliable to diagnose parotid gland carcinoma. Its low sensitivity and LR– indicates its limitations as a screening test; in addition its low kappa shows a modest correlation to the eventual diagnosis. Therefore, further critical examination of techniques and interpretation of parotid FNA are recommended. The development of new methods allowing a valid and precise diagnosis of this pathology and that, like the FNA, have low cost and ease of application is recommended.

Key words: Parotid gland. Parotid neoplasms. Carcinoma. Fine-needle aspiration. Validation studies (source: MeSH).

Evaluación de la citología por punción-aspiración con aguja fina en el diagnóstico de cáncer de la glándula parótida
Contexto: La punción-aspiración con aguja fina (PAAF) se utiliza con frecuencia en el estudio de las lesiones neoplásicas de la glándula parótida, a pesar de que se mantiene la controversia respecto a su precisión diagnóstica.
Objetivo: Evaluación del rendimiento de la PAAF en comparación con la biopsia quirúrgica abierta para el diagnóstico del carcinoma de la glándula parótida.
Material y método: En el estudio participaron 47 pacientes con lesiones ocupantes de espacio en la glándula parótida y que fueron atendidos en 7 centros sanitarios de Bucaramanga, Colombia. Todos los pacientes fueron evaluados mediante PAAF y biopsia quirúrgica abierta, considerada esta última como la prueba diagnóstica de referencia. La PAAF y el estudio anatomopatológico final efectuado sobre la biopsia quirúrgica abierta fueron interpretados como positivos o negativos para lesión maligna por anatomopatólogos que desconocían el resultado obtenido en la PAAF. Sólo se utilizaron técnicas de tinción histológicas convencionales. Los datos fueron comparados mediante una tabla de contingencia y analizados estadísticamente para determinar la precisión de la PAAF en la predicción del resultado diagnóstico anatomopatológico obtenido en la biopsia quirúrgica abierta mediante muestreo y análisis transversal.
Resultados: La media ± desviación estándar de edad de los pacientes fue 52 ± 16 años; el 59 % eran mujeres. El 18 % de los diagnósticos establecidos mediante la PAAF fue erróneo en comparación con el diagnóstico anatomopatológico final. La PAAF presentó una sensibilidad y una especificidad de 0,54 y 0,90, respectivamente; unos valores predictivo positivo y predictivo negativo de 0,90 y 0,70, respectivamente; unos cocientes de probabilidad positivo y negativo de 5,92 y 0,5, respectivamente, y un

Correspondence: Dr. J. Díaz.
Departamento de Patología. Escuela de Medicina.
Universidad Industrial de Santander.
Cra. 32, N.º 29-31. Bucaramanga. Colombia.
E-mail: gricesuis@yahoo.com

Received November 19, 2007.
Accepted for publication January 28, 2008.

estadístico kappa de 0,48, respecto a la identificación del carcinoma de la glándula parótida en la población evaluada, en la que la prevalencia de la enfermedad fue del 28,3 %.

Conclusiones: La PAAF, utilizada como método diagnóstico aislado, careció de fiabilidad para el diagnóstico del carcinoma de la glándula parótida, en concordancia con los resultados obtenidos en otros estudios previos. Sus bajos valores de sensibilidad y de cociente de probabilidad negativo indican sus limitaciones como prueba de detección o cribado; además, el escaso valor del estadístico kappa demuestra que esta técnica posee una correlación modesta con el diagnóstico final. Por tanto, se recomienda el análisis crítico adicional con otras técnicas de análisis adicionales que mejoren la interpretación de la PAAF sobre la glándula parótida. También se considera importante el desarrollo de nuevos métodos que permitan establecer un diagnóstico válido y preciso de este problema y que, de la misma manera que la PAAF, tengan un coste económico bajo y sean fáciles de utilizar.

Palabras clave: Glándula parótida. Tumores de glándula parótida. Carcinoma. Punción-aspiración con aguja fina. Estudios de validación (fuente: MeSH).

INTRODUCTION

Upon evaluating neoplastic diseases of the parotid gland, clinical findings, and imaging techniques lack the necessary precision for differentiating benign lesions from malignant tumours. Because of this, fine-needle aspiration (FNA) has played a relevant role that is constantly increasing in preoperative diagnosis of parotid gland tumours.[1-3] This cytological diagnostic tool has been used for over 150 years and was initially applied by Martin et al[4,5] for studying parotid gland lesions. The procedure does not require the use of general anaesthesia and interpretation of the samples can be done without using sophisticated equipment. It does not have contraindications and its few adverse effects include haematoma, pain, and local haemorrhage (which can generally be avoided by using a very fine needle), as well as infection. In some situations it is thought that a detailed interpretation of the FNA allows for a precise diagnosis to be made in most cases. This precise diagnosis may then lead to a conservative treatment in the case of benign lesions, which would decrease treatment costs and allow for FNA to be a safe, fast, and a better financial choice as opposed to open surgical biopsy. FNA may also be very useful in detecting metastasis and lymphoma, and therefore makes surgical planning easier. Because of all this, FNA performed on the parotid gland has been considered a first-line tool of defence for diagnostic evaluation of palpable masses of the parotid gland.[6] However, there is still controversy regarding its usefulness for studying neoplastic lesions, with significant differences between the results obtained in several validation tests,[1,7,8] including observance of a high rate of false negatives in the group of malignant lesions.[9-16] In our study we have evaluated the cytological precision of FNA in diagnosing malignant lesions of the parotid gland using the final pathological test of the gland as the diagnostic gold standard.

MATERIAL AND METHOD

Patients and Health Centres

The study participants were those patients seen at the head and neck department of 7 health centres in Bucaramanga, Colombia, during the period 2004-2005, due to having a palpable mass in the parotid area. The health centres were: Hospital Universitario de Santander, Clínica Chicamocha, Clínica Comuneros, Clínica Carlos Ardila Lulle, Clínica Bucaramanga, Clínica de Salud Coop, and Clínica Metropolitana. The surgeons in the corresponding departments took a complete medical history and performed a complete physical examination, and were also responsible for performing the FNAs. Histological samples were stained using the Papanicolaou technique and were interpreted by an pathologist specializing in cytolopathology who was unaware of the clinical presentations of the patients. The diagnostic results were evaluated according to the World Health Organization (WHO) classification, which recognizes 13 benign adenomas and 24 primary carcinomas of the parotid gland.[17] During the following 30-60 days, a partial or total parotidectomy was performed and the masses removed during surgery were sent for pathology testing. The histological samples stained with haematoxylin-eosin were evaluated by pathologists who were unaware of the clinical data and the results obtained with the FNA. The resulting diagnoses were evaluated once again under the WHO classification referred to above. The study included all those patients who, during the period from 2004 to 2005, had a parotid mass and who underwent FNA and parotidectomy, independent of the outcome.

Ethical Issues

This research study was done according to the 1991 National Constitution, under the 1993 resolution 008430 by the Colombian Ministry of Social Welfare, and the Helsinki Declaration. The health authorities of those health centres taking part also approved it.

Statistical and Epidemiological Analysis

The sample size (25 patients) was calculated using Kraemer's method.[18,19] The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive and negative probability ratios, and the kappa statistic were calculated by cross-sectional sampling.[20] The numbers shown in Figure were used in Table 1 (the contingency table). The 95% confidence intervals (CI) were calculated using the binomial analysis of the sensitivity, specificity, PPV, NPV, positive and negative PR, and kappa. Prevalence was estimated by using normal approximation. For the statistical analysis, EpiInfo 2004 (CDC, United Sates)[21] and Stata 8.022 were used.

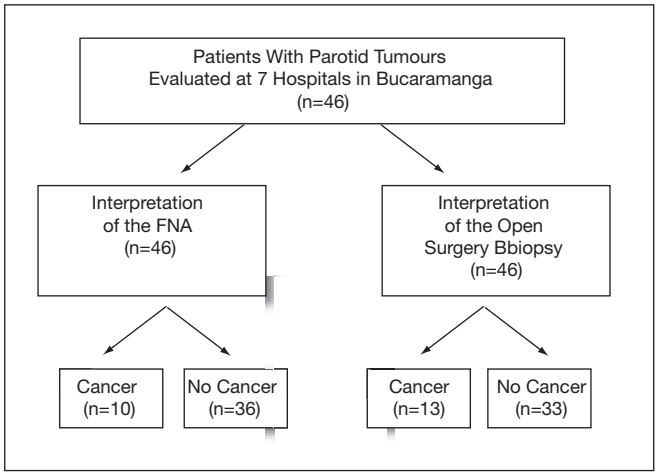

Figure. Sample.

Table 1. Contingency Table[a]

Parotid FNA	*Final Pathology Diagnosis*		
	Positive	*Negative*	*Total*
Positive	7 (TP)	3 (FP)	10 (Q)
Negative	6 (FN)	30 (TN)	36 (Q')
Total	13 (P)	33 (P')	46 (No)

[a]FN indicates false negative; FP, false positive; TP, true positive; TN, true negative.

Table 2. Evaluation of the Usefulness of Fine-Needle Aspiration for Diagnosing Parotid Cancer in this Population

	Value, %	*95% Confidence Interval*
Sensitivity	53.8	25.1-80.8
Specificity	90.9	75.7-98.1
Positive predictive value	70	34.8-93.3
Negative predictive value	83.3	67.2-93.6
+ Probability ratio	5.92	1.8-19.5
– Probability ratio	0.508	0.279-0.922
Kappa	48.12	33.6-62.64
Prevalence	28.26	14.16-42.36

RESULTS

A total of 46 patients were studied, with 58.7% (27 patients) being women and the age distribution ranged between 22 and 80 years old, with a mean of 52 (16). The false positive (FP) and false negative (FN) results are shown in Table 1 (the contingency table). The usefulness of fine-needle aspiration for diagnosing parotid cancer in this population is shown in Table 2. Table 3 shows the relative ratio of the

Table 3. False Positive and False Negative Results of FNA Compared to the Final Pathology Result

Type of Tumour	*No. (%)*
False positive results	
Pleomorphic adenoma	3 (6.5%)
False negative results	
Cystic adenoid carcinoma	2 (4.3%)
Lymphoma	2 (4.3%)
Mucoepidermoid carcinoma	1 (1.6%)
Acinar cell carcinoma	1 (1.6%)
Total	9 (18.1%)

Table 4. Frequent Diagnostic Errors During Fine-Needle Aspiration (FNA) of the Parotid Gland

FNA Diagnosis	*Final Pathology Diagnosis*
False negative results	
Benign lymphatic node	Lymphoma
Normal parotid tissue	Acinar cell carcinoma
Benign cyst	Mucoepidermoid carcinoma
Benign mixed tumour	Cystic adenoid carcinoma
Sialadenitis	Metastasis of epidermoid carcinoma
Benign mixed tumour	Carcinoma on mixed tumour
False positive results	
Cystic adenoid carcinoma	Monomorphous adenoma
Lymphoma	Intraparotid lymphatic node
Lymphoma	Warthin's tumour

patients (18.1%) in whom the erroneous FNA diagnosis was due to FP results (6.5%) and FN results (11.8%), while Table 4 compares the specific FNA diagnoses and the final pathological study regarding the total number of FP and FN cases.

DISCUSSION

FNA on the parotid gland is performed because of its technical simplicity and the minimal risk associated with the procedure, in spite of it having a more imprecise diagnostic outcome.[8,10,12-14] This lack of precision has been blamed on several factors,[6] such as the fact that parotid tumours are morphologically very complex with multiple cell types and growth patterns, and the characteristics of the overlapping between different pathological bodies. Because of this, the cytopathologist's experience regarding

parotid gland pathology affects diagnostic precision. On the other hand, only 25% of the parotid lesions that show up as clinically palpable masses truly correspond to a malignant tumour and in most cases these lesions are benign mixed tumours (pleomorphic adenomas). This means that the limited sampling that FNA offers is of considerable importance. Since the parotid lesions are usually heterogeneous, cytological atypia may only appear locally and, therefore, it may not be seen on an FNA sample. Finally, a certain number of malignant tumours have cytological characteristics that are untypical and the probability they become malignant can only be determined based on capsular infiltration, a characteristic that is impossible to assess by means of FNA.

In our study FNA had sensitivity and specificity of 0.54 and 0.90, which indicates its usefulness for confirming diagnosis more than determining it in a reference population. The PPV was low, which indicates a high rate of false positive results. Positive and negative PRs reflect the probability that there is or is not a malignant neoplastic lesion, based on the FNA's positive or negative result. If we use Fagan's nomogram[23] on this group of patients with a parotid mass, a positive PR indicates that when the result of the FNA is positive the probability that the tumour is truly a malignant lesion is approximately 80%. On the other hand, a negative PR indicates that if the FNA result is negative, the probability that the patient really does have a malignant tumour only changes slightly. In last place, the kappa value of 0.48 shows that the correlation existing between FNA and the final pathology result is only slightly higher than what could randomly appear. All this information indicates that FNA has limited validity and precision, and should not be used as the sole diagnostic tool for parotid gland lesions.

Our results concur with those obtained in previously published studies,[1-4,8,12-16] which show that the sensitivity for malignant lesions varies between 38%[24] and 97%,[28] while the specificity varies between 82%[1] and 100%.[30] These variations may be due to differences in the populations clinically evaluated, to variations in the sampling technique and interpretation of the FNA and to the use of additional techniques, such as immunohistochemistry or flow cytometry, in order to obtain more information from the sample retrieved by FNA in those cases where lymphoma is suspected. In our study, interpretation of the FNA was done using traditional techniques and without using immunohistochemistry or molecular analysis techniques, which may have increased diagnostic precision.[29]

Generally speaking, it has been determined that FNA only offers a precise diagnosis for a third of parotid gland lesions prior to performing an open surgery procedure.[1,6,13,25] The predictive values obtained in the different studies cannot be compared since the prevalence has presented large differences.[1-4,8,12-16,26]

In our study 3 FP results (6.5%) were identified, 2 of which correspond to lymphoma. The 6 FN results (13%) correspond to cystic adenoid carcinoma (2 cases), lymphoma (2 cases), mucoepidermoid carcinoma (1 case), and acinar cell carcinoma (1 case). These results concur with the false negatives seen regularly in other studies[6,27] (Table 4).

In conclusion: FNA evaluated in our study has a low level of diagnostic precision for malignant tumours of the parotid gland. The low levels of sensitivity and the negative probability level limit the usefulness of FNA as a technique for detection or screening techniques, while the low kappa value shows a low correlation with the final pathology evaluation. This is why we recommend that FNA evaluated by conventional staining methods should not be done systematically. Even though FNA is a relatively low-cost and simple technique, it seems that it needs to be used along with other techniques, such as immunocytochemistry and flow cytometry, in order to increase its precision diagnosis value for parotid lesions.

REFERENCES

1. Al-Khafaji BM, Nestok BR, Katz RL. Fine-needle aspiration of 154 parotid masses with histologic correlation: ten-year experience at the University of Texas MD Anderson Cancer Center. Cancer. 1998;84:153-9.
2. Ljung BME, Hanafee W. CT scanning and aspiration cytology in the management of parotid lesions. Rev Laryngol Otol Rhinol (Bord). 1984;105: 21-4.
3. Owen EERTC, Banerjee AK, Prichard AJN, Hudson EA, Kark AE. Role of fine-needle aspiration cytology and computed tomography in the diagnosis of parotid swellings. Br J Surg. 1989;76:1273-4.
4. Martin AM, Ellis EB. Biopsy by needle puncture and aspiration. Ann Surg. 1930;92:169-81.
5. Amedee RG, Dhurandhar NR. Fine-needle aspiration biopsy. Laryngoscope. 2001;111:1551-7.
6. Alphs HH, Eisele DW, Westra WH. The role of fine needle aspiration in the evaluation of parotid masses. Curr Opin Otolaryngol Head Neck Surg. 2006;14:62-6.
7. Qizilbash AH, Sianos J, Young JEM, Archibald SD. Fine needle aspiration biopsy cytology of major salivary glands. Acta Cytol. 1985;29:503-12.
8. Carroll CMA, Nazeer U, Timon CJ. The accuracy of fine needle aspiration biopsy in the diagnosis of head and neck masses. Ir J Med Sc. 1998;167: 149-51.
9. McGuirt WF. The neck mass. Med Clin North Am. 1999;83:219-34.
10. Frable MAS, Frable WJ. Fine-needle aspiration biopsy of salivary glands. Laryngoscope. 1991;101:245-9.
11. Batsakis JG, Sneige N, El-Naggar AK. Fine-needle aspiration of salivary glands: its utility and tissue effects. Ann Otol Rhinol Laryngol. 1992;101: 185-8.
12. Sergi B, Contucci AM, Corina L, Paludetti G. Value of fine-needle aspiration cytology of parotid gland masses. Laryngoscope. 2004;114:789.
13. Zbaren P, Schar C, Hotz MA, Loosli H. Value of fine-needle aspiration cytology of parotid gland masses. Laryngoscope. 2001;111:1989-92.
14. Atula T, Grenman R, Laippala P, et al. Fine needle aspiration biopsy in the diagnosis of parotid gland lesions. Diagn Cytopathol. 1995;15:185-90.
15. Pitts DB, Hilsinger RL, Karandy E, et al. Fine-needle aspiration in the diagnosis of salivary gland disorders in the community hospital setting. Arch Otolaryngol Head Neck Surg. 1992;118:479-82.
16. Zurrida S, Alasio L, Tradati N, et al. Fine-needle aspiration of parotid masses. Cancer. 1993;72:2306-11.
17. Eveson JW, Auclair P, Gnepp DR, El-Naggar AK. Tumours of the salivary glands. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. World Health Organization Classification of Tumours. Pathology and genetics of head and neck tumours. Lyon: IARCPress; 2005. p. 209-82.
18. Kraemer HC. Evaluating medical tests. Objective and quantitative guidelines. Newbury Park: Sage; 1992.
19. Obuchowsky N. Sample size calculations in studies of test accuracy. Stat Methods Med Res. 1998;7:371-92.
20. Orozco LC, Camargo DM. Evaluación de tecnologías diagnósticas y tipos de muestreos. Biomédica. 1997;17:321-4.
21. CDC. Division of Public Health Surveillance and Informatics, EpiInfo™ Version 3.2.2 [Release Date: April 14, 2004]. Available at: http://www.cdc.gov/epiinfo/
22. STATACorp LP. Statistical Software for Professionals, Version 8.0. 2004. Available at: http://www.stata.com
23. Fagan TJ. Nomogram for Bayes's theorem. N Engl J Med. 1975;293:257.
24. Balakrishnan K, Castling B, McMahon J, et al. Fine needle aspiration cytology

in the management of a parotid mass: a two centre retrospective study. Surgeon. 2005;3:67-72.
25. Weinberger MS, Rosenberg WW, Meurer WT, Robbins KT. Fine-needle aspiration of parotid gland lesions. Head Neck. 1992;14:483-7.
26. Boccato P, Altavilla G, Blandamura S. Fine needle aspiration biopsy of salivary gland lesions. A reappraisal of pitfalls and problems. Acta Cytol. 1998;42:888-98.
27. Cajulis RS, Gokaslan ST, Yu GH, Frias-Hidvegi D. Fine needle aspiration biopsy of the salivary glands. A five-year experience with emphasis on diagnostic pitfalls. Acta Cytol. 1997;41:1412-20.
28. Stow N, Veivers D, Poole A. Fine-needle aspiration cytology in the management of salivary gland tumors: an Australian experience. Ear Nose Throat J. 2004;83:128-31.
29. Moore JG, Bocklage T. Fine-needle aspiration biopsy of large-cell undifferentiated carcinoma of the salivary glands: presentation of two cases, literature review, and differential cytodiagnosis of high-grade salivary gland malignancies. Diagn Cytopathol. 1998;19:44-50.
30. Longuet M, Nallet E, Guedon C, Depondt J, Gehanno P, Barry B. Diagnostic value of needle biopsy and frozen section histological examination in the surgery of primary parotid tumors. Rev Laryngol Otol Rhinol (Bord). 2001; 122:51-5.