



FALSE NEGATIVE FINE NEEDLE ASPIRATION CYTOLOGY IN PAROTID MALIGNANCY

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ABSTRACT

Objective: To perform a critical histopathologic review of falsely negative fine needle aspiration cytology for the parotid gland

Study Design: Retrospective case series, academic tertiary referral center

Methods: Between the years 2005-2010, 650 patients with parotid neoplasms were reviewed. 317 patients had FNAC, frozen section, and final pathology available. Within this series, 10 false negative parotid mass FNAC results were identified. Clinical history, physical examination, operative findings, and both cyto- and histopathologic features were reviewed. Statistical analysis was performed to assess for clinical and cytopathologic predictors of FNAC false negativity.

Results: Ten patients received a false-negative diagnosis with FNAC: pleomorphic adenoma (n = 4, 40%), Warthin's tumor (n = 3, 30%), oncocytoma (n = 1, 10%) and benign lymphoepithelial cyst (n = 2, 20%). Final pathology includes low-grade mucoepidermoid (n = 5, 50%), acinic cell (n = 2, 20%), adenoid cystic (n = 1, 10%), infiltrative spindle cell (n = 1, 10%), and carcinoma ex-pleomorphic adenoma (n = 1, 10%).

Conclusion: FNAC is a well-established diagnostic technique for parotid masses. False negative FNAC will occasionally arise. Knowledge of common cyto- and histopathologic features that correlate to an increased likelihood for false negative results will benefit both surgeon and patient.



INTRODUCTION

When comparing the utility of FNAC for benign versus malignant masses, FNAC has superior sensitivity and specificity for benign lesions. Seethala *et al* report sensitivity of 88-98% for benign lesions and 58-96% for malignant. Specificity was 94% for benign and 71-88% for malignant lesions.⁶

There are a number of reasons why FNAC may be more difficult to interpret a malignant mass including the experience of cytopathologists. Specifically, since the notorious morphological heterogeneity of salivary gland carcinomas and the entire architecture of the parotid mass, including the capsule, cannot be examined by using FNAC, there is difficulty in making a definitive diagnosis as seeing capsule invasion is what defines malignancy in certain cases.

We aim to examine the FNAC results of patients with parotid gland masses, and compare these results with their final surgical pathology. We specifically are looking to report which malignant masses gave our department difficulty in diagnosing via FNAC and were instead reported as benign masses.

METHODS

Institutional Review Board approved retrospective review of the charts of patients who underwent superficial or total parotidectomy between 2005 and 2010, as identified by current procedural terminology (CPT) code. 317 patients were reviewed.

Inclusion criteria included: (1) primary parotid neoplasm without prior surgical intervention, (2) availability of FNAC, intraoperative frozen section, and final pathology, (3) a FNAC interpreted as diagnostic benign, and (4) a final histologic diagnosis interpreted as malignancy.

A total of 10 patients were identified who met the above criteria. Histologic samples from all ten patients were then reviewed by a single head and neck pathologist (CGF) for internal validity.

Clinical and demographic data were collected

RESULTS

Of the 317 reviewed cases, ten (n = 10) FNACs of parotid masses were interpreted as benign and were subsequently identified as malignant on permanent section. Mean age was 37 [range 12-68]. Additional patient demographic information and clinical exam findings are noted in Table 1. The duration of the parotid mass present prior to evaluation was quite variable (2-204 months, average 31 months).

Diagnoses based on FNAC for this series of patients include: pleomorphic adenoma (n = 4, 40%), Warthin's tumor (n = 3, 30%), oncocytoma (n = 1, 10%) and benign lymphoepithelial cyst (n = 2, 20%). The most common malignancy in this series was low-grade mucoepidermoid carcinoma (n = 5, 50%).

Interestingly, the 5 patients with final diagnosis of mucoepidermoid carcinoma originated from three different falsely benign diagnostic FNACs (Warthin's tumor, benign lymphoepithelial cyst, pleomorphic adenoma). Table 2 provides a comparison between FNAC and final pathology for this cohort.

Table 1:

Characteristic	No. (%)
Clinical History	
Gender	
Men	6 (60%)
Women	4 (40%)
Previous parotid mass	
Yes	2 (20%)
No	8 (80%)
History of tobacco use	
Yes	1 (10%)
No	9 (90%)
Reported pain	
Yes	3 (30%)
No	7 (70%)
Reported ear numbness	
Yes	0 (0%)
No	10 (100%)
Physical Exam Findings	
Facial nerve paresis	
Yes	0 (0%)
No	10 (100%)
Fixed parotid mass	
Yes	1 (10%)
No	9 (90%)
Palpable nodes	
Yes	0 (0%)
No	10 (100%)
Pathology	
FNAC impression	
Benign	10 (100%)
Malignant	0 (0%)
Frozen section impression	
Benign	5 (50%)
Malignant	5 (50%)

Table 2:

Patient #	Age	Gender	Previous parotid mass	FNAC diagnosis	Permanent section diagnosis
1	44	F	No	Pleomorphic adenoma	Adenoid cystic
2	12	F	No	Benign lymphoepithelial cyst	Acinic cell carcinoma
3	68	M	No	Oncocytoma	Acinic cell carcinoma
4	12	M	No	Warthin's	Low-grade mucoepidermoid
5	22	M	No	Warthin's	Low-grade mucoepidermoid
6	53	M	Yes	Warthin's	Low-grade mucoepidermoid
7	58	M	No	Benign lymphoepithelial cyst	Low-grade mucoepidermoid
8	27	F	Yes	Pleomorphic adenoma	Low grade mucoepidermoid
9	27	M	No	Pleomorphic adenoma	Infiltrative spindle cell carcinoma
10	48	F	No	Pleomorphic Adenoma	Carcinoma ex pleomorphic adenoma

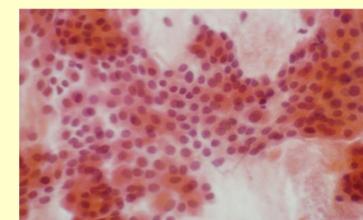


FIGURE 1: FNA sample from patient #6. The epithelial cells are arranged in a monolayer within a cystic background and appear "oncocytic" with eosinophilic cytoplasm, suggesting a Warthin's tumor. The final histologic diagnosis was low grade mucoepidermoid carcinoma.

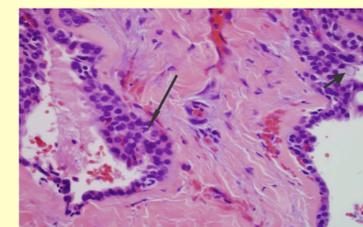


FIGURE 2: Histologic section from patient #6. The intermediate cells (long arrow) may mimic oncocytes. Mucocytes (short arrow) admixed with intermediate cells confirm the histologic diagnosis of low grade mucoepidermoid carcinoma.

DISCUSSION

Mucoepidermoid carcinoma is commonly noted as a difficult parotid neoplasm to diagnose with FNAC.⁷ The low-grade variant is primarily cystic with mucous-containing cells. Due to these features, low-grade mucoepidermoid carcinoma may be misinterpreted as pleomorphic adenoma, Warthin's tumor, or a benign lymphoepithelial cyst.

Furthermore, low-grade mucoepidermoid carcinomas will frequently cause a lymphocytic response, and lymphocytes are also commonly seen within a Warthin's tumor aspirate. Finally, the intermediate-type epithelial cells observed in low-grade mucoepidermoid carcinoma are similar in appearance to the oncocytes noted in Warthin's tumor.

Pleomorphic adenomas are noted to contain three distinct morphological features: extracellular matrix, myoepithelial cells and bland ductal cells. Varying proportions of these three components may or may not be present when an FNAC sample is obtained.⁹ Interestingly, the myoepithelial cells within a pleomorphic adenoma may be spindle, a cellular characteristic commonly noted in malignancies or non-epithelial salivary gland tumors.¹⁴ As pleomorphic adenoma is the most common tumor of the parotid gland, cytologists commonly interpret spindle cells as a benign pleomorphic variant rather than malignancy when the clinical suspicion is low. The chondromyxoid stroma of the pleomorphic adenoma is helpful for cytopathologic diagnosis, though depending on the variant and sampling, may be masked by high cellularity.

In this series, acinic cell carcinoma was discovered from two false negative FNACs (oncocytoma, benign lymphoepithelial cyst). As these tumors are inherently comprised of cells which resemble the acinar cells of the salivary gland, it is quite difficult to diagnose this tumor-type via FNAC.

Lastly, adenoid cystic carcinoma may appear very similar to pleomorphic adenoma or Warthin's tumor, as it consists of with small basophilic cells with very little cytoplasm or cytologic atypia. Thus, it is difficult for the cytopathologist to diagnose adenoid cystic carcinoma unless the surgeon states an index of suspicion for facial nerve invasion.

When utilizing FNAC as an adjunct for the diagnosis of parotid masses, one must consider the diagnostic limitations to not be necessarily related to the technique itself, but to the nature of both the lesion and unique characteristics of the salivary gland cells themselves.

As FNAC cannot assess for cellular architecture nor presence of invasion, the clinical impression of the practitioner may commonly serve as a useful adjunct for diagnosis.

CONCLUSION

- Unique characteristics of salivary gland architecture and similarity of cytology between tumors produce a difficult diagnostic situation for the cytopathologist.
- Newly developed molecular and immunocytochemical assays may significantly improve the accuracy salivary gland FNAC and reduce the number of false negative cases.

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