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Diagnostic Accuracy of Fine-Needle Aspiration for Parotid and Submandibular Gland Lesions

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Abstract

Objective. To assess the diagnostic accuracy of fine-needle aspiration (FNA) of the parotid and submandibular glands.

Study Design. Case series with chart review.

Setting. Tertiary referral academic center.

Subjects and Methods. Retrospective analysis was performed for all parotid and submandibular gland FNAs from a single center from 2001 to 2014. There were 1283 FNAs performed for 1076 patients. Of these, 343 cases had surgical follow-up (parotid gland, n = 272; submandibular gland, n = 71). Cases were included where the patient had a preoperative FNA, followed by surgical excision. Correlation of preoperative FNA results to final surgical pathology was performed, with measures of diagnostic accuracy computed.

Results. Malignancy was identified in 29.0% of parotid tumors and 42.3% of submandibular tumors, based on final pathology. FNA was nondiagnostic due to insufficient cellularity for evaluation in 22 of 343 cases (6.4%) and indeterminate in 39 of 343 cases (11.4%). Diagnostic accuracy in the parotid and submandibular glands for distinguishing benign from malignant pathology was determined as follows, respectively: sensitivity, 75.0% and 91.3%; specificity, 95.1% and 94.1%; positive predictive value, 84.9% and 91.3%; and negative predictive value, 91.2% and 94.4%.

Conclusion. FNA has high accuracy in identifying malignancy in parotid and submandibular gland lesions when performed at a high-volume center. Preoperative FNA results provide otolaryngologists with valuable diagnostic information that may influence the surgical management of salivary gland tumors. FNA, in conjunction with cross-sectional imaging, is useful in counseling patients for a complete informed consent.

Keywords

parotid gland, submandibular gland, salivary gland, salivary tumor, fine needle aspiration, cytopathology, sensitivity and specificity

The diagnostic accuracy of fine-needle aspiration (FNA) biopsy for salivary gland lesions remains a subject of debate.[1,2] While multiple studies have demonstrated the test's diagnostic accuracy, a recent meta-analysis found that the heterogeneity of evidence did not allow a determination of the clinical usefulness of FNA.[2] This contrasts with frozen section analysis, where an evaluation by the same group demonstrated satisfactory accuracy.[3]

FNA is known to be a relatively painless, quick, and minimally invasive procedure commonly conducted in the outpatient setting.[4] Some argue that parotid masses require excision regardless of test results, and therefore obtaining the test does not sufficiently alter practice[5]; however, others state that the test result may indeed affect preoperative counseling, the timing of surgery, and the extent of surgery.[6] These latter factors may be more or less influenced by a given test result depending on the predicted accuracy of the test.

Here, we investigated the diagnostic accuracy of FNA in (1) distinguishing benign from malignant parotid and submandibular salivary gland tumors and (2) identifying specific tumor subtype by comparing FNA results with surgical histopathology results at a single high-volume center. Specific attention was given to the role of indeterminate FNA results.

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Methods

We initially reviewed all cases of parotid and submandibular salivary gland FNAs performed at a single tertiary referral center from 2001 to 2014. Subsequently, we selected all cases proceeding to surgery to allow for gold standard final histopathologic comparison. In any case where patients had preoperative FNA performed at an outside institution, these results were excluded from analysis, except in the situation where original slides were transferred to our center for review by university pathologists. It is the general practice at our institution to evaluate FNAs through smear preparations with or without liquid-based preparations. Each case had a final diagnosis rendered by a board-certified university cytopathologist. Clinical information—including age, sex, tumor location, FNA cytopathologic diagnosis, and pathologic diagnosis—was obtained from a review of the medical records. The UCLA Medical Institutional Review Board 2 (11-002014-CR-00003) approved this retrospective study.

FNA was predominantly performed by radiologists and pathologists using 23-, 25-, and/or 27-gauge needles with or without aspiration. It is the general practice of our institution to perform 2 to 8 passes on salivary gland lesions. Ultrasound guidance was utilized for lesions that were not obviously palpable.

Correlation of FNA results to final surgical pathology was performed. FNA reports were classified as benign, malignant, or indeterminate; indeterminate classification was applied when both benign and malignant processes were included in a differential diagnosis or when cellularity was sufficient but no diagnosis could be rendered. In cases in which the diagnosis was considered indeterminate, the pathologist's interpretation that the lesion was more likely to be benign or more likely to be malignant was separately recorded. Cases without sufficient cellularity were distinctly categorized.

Measures of diagnostic accuracy were thereafter computed. All relevant aspects of the STARD checklist (Standards for Reporting of Diagnostic Accuracy) were included.[7] The primary outcomes were the sensitivity, specificity, positive predictive value, and negative predictive value of FNA for the parotid and submandibular lesions; 95% confidence intervals were calculated for each measure. Statistical analyses were performed with SPSS 22.

Results

There were 1283 FNA biopsies performed for 1076 patients between 2001 and 2014. Parotid gland lesions were biopsied in 655 cases relative to submandibular lesions in 421 cases. Of these, 343 cases had surgical follow-up (parotid gland, n = 272; submandibular gland, n = 71). Malignancy was identified in 29.0% of parotid tumors and 42.3% of submandibular tumors based on final pathology. Among the 272 patients with parotid FNAs, there were 131 men (48.2%) and 141 women (51.8%), with a mean age of 56.6 years. Among the 71 patients with submandibular FNAs, there were 31 men (43.7%) and 40 women (56.3%), with a mean age of 58.1 years. The most common benign diagnoses among parotid lesions were pleomorphic adenoma (n = 98, 36.0%) and Warthin's tumor (n = 22, 8.1%), while the most common malignant lesions were squamous cell carcinoma (n = 23, 8.5%), mucoepidermoid carcinoma (n = 12, 4.4%), and acinic cell carcinoma (n = 9, 3.3%; **Table 1**). All cases of squamous cell carcinoma included in this analysis presented as a parotid mass; cases of cutaneous tumors with direct spread to the parotid gland were not part of this study as these patients had cutaneous biopsies performed rather than parotid FNA. With consideration for patient history of prior cutaneous squamous cell carcinoma, these parotid tumors were determined to be either primary parotid tumors (6 of 23, 26.1%) or metastatic disease (17 of 23, 73.9%). The most common benign diagnoses among submandibular lesions were sialadenitis/inflammation (n = 16, 22.5%) and pleomorphic adenoma (n = 12, 16.9%), while the most common malignant lesion was squamous cell carcinoma (n = 10, 14.1%; **Table 2**).

A cytopathologic diagnosis of benign or malignant was obtained with FNA in 282 of 343 patients (82.2%). FNA

Table 1. Final Histopathologic Diagnosis of Parotid Gland Tumors.

	n	%
Benign (n = 193)		
Pleomorphic adenoma	98	36.0
Warthin's tumor	22	8.1
Inflammation/sialadenitis	15	5.5
Benign salivary tissue	13	4.8
Basal cell adenoma	9	3.3
Cyst	9	3.3
Oncocytoma	6	2.2
Benign lymph tissue	5	1.8
Monomorphic adenoma	4	1.5
Lipoma	4	1.5
Schwannoma	3	1.1
Sebaceous adenoma	1	0.4
Paraganglioma	1	0.4
Hemangioma	1	0.4
Kuttner's tumor (IgG4)	1	0.4
Indeterminate	1	0.4
Malignant (n = 79)		
Squamous cell carcinoma	23	8.5
Mucoepidermoid carcinoma	12	4.4
Acinic cell carcinoma	9	3.3
Salivary duct carcinoma	8	2.9
Lymphoma	8	2.9
Carcinoma not otherwise specified	7	2.6
Carcinoma ex-pleomorphic adenoma	4	1.5
Adenocarcinoma	3	1.1
Myoepithelial carcinoma	2	0.7
Melanoma	2	0.7
Merkel cell carcinoma	1	0.4

Table 2. Final Histopathologic Diagnosis of Submandibular Gland Tumors.

	n	%
Benign (n = 41)		
Inflammation/sialadenitis	16	22.5
Pleomorphic adenoma	12	16.9
Kuttner's tumor (IgG4)	5	7.0
Oncocytoma	2	2.8
Lipoma	2	2.8
Warthin's tumor	1	1.4
Schwannoma	1	1.4
Benign lymph tissue	1	1.4
Cyst	1	1.4
Malignant (n = 30)		
Squamous cell carcinoma	10	14.1
Lymphoma	7	9.9
Adenoid cystic carcinoma	3	4.2
Carcinoma ex-pleomorphic adenoma	3	4.2
Carcinoma not otherwise specified	3	4.2
Salivary duct carcinoma	2	2.8
Adenocarcinoma	1	1.4
Melanoma	1	1.4

Table 3. Distribution of FNA Results among Parotid and Submandibular Gland Tumors.

	Surgical Follow-up, n (%)		
FNA Diagnosis	Benign	Malignant	Indeterminate
Parotid gland			
Benign (n = 172)	156 (90.7)	15 (8.7)	1 (0.6)
Malignant (n = 53)	8 (15.1)	45 (84.9)	0 (0)
Indeterminate (n = 47)	28 (59.6)	19 (40.4)	0 (0)
Submandibular gland			
Benign (n = 34)	32 (94.1)	2 (5.9)	0 (0)
Malignant (n = 23)	2 (8.7)	21 (91.3)	0 (0)
Indeterminate (n = 14)	7 (50)	7 (50)	0 (0)

Abbreviation: FNA, fine-needle aspiration.

was nondiagnostic due to insufficient cellularity in 22 patients (6.4%) and indeterminate in 39 patients (11.4%). In the parotid gland, FNA results were benign in 63.2%, malignant in 19.5%, and indeterminate in 17.3% (**Table 3**). In the submandibular gland, FNA results were benign in 47.9%, malignant in 32.4%, and indeterminate in 19.7%. Among parotid gland FNA results, a benign FNA resulted in benign final pathology in 90.7% of cases, whereas a malignant FNA resulted in malignant pathology in 84.9% of cases (**Table 3**). When FNA of the parotid gland was indeterminate, the final pathology was more likely to be benign (59.6%) than malignant (40.4%; **Table 4**). Among submandibular gland FNA results, a benign FNA resulted in benign final pathology in 94.1% of cases, whereas a malignant FNA resulted in malignant pathology in 91.3% of cases. When FNA of the submandibular gland was indeterminate, the final pathology was equally likely to be benign versus malignant.

Measures of diagnostic accuracy were therefore computed according to the preceding results. Diagnostic accuracy in the parotid gland for distinguishing benign from malignant pathology was as follows: sensitivity, 75.0%; specificity, 95.1%; positive predictive value, 84.9%; and negative predictive value, 91.2% (**Table 5**). Diagnostic accuracy in the submandibular gland for distinguishing benign from malignant pathology was as follows: sensitivity, 91.3%; specificity, 94.1%; positive predictive value, 91.3%; and negative predictive value, 94.4%.

FNA results classified as indeterminate were further analyzed with pooled results for parotid and submandibular lesions (**Table 4**). Among lesions classified strictly as indeterminate—that is, sufficient cellularity for evaluation but uncertainty of diagnosis—the final histopathology was more likely to show benign (n = 13, 72.2%) than malignant results (n = 5, 27.8%). When lesions were classified as indeterminate but the pathologist favored a benign result, the final histopathology was more likely to show benign (n = 9, 75%) than malignant results (n = 3, 25%). Among those lesions classified as indeterminate but where the pathologist favored a malignant result, the final histopathology always showed a malignant tumor (n = 9, 100%).

Discussion

In the present large series of parotid and submandibular FNA biopsies performed at a single institution with subspecialist head and neck pathologists, we demonstrate high accuracy in the preoperative diagnosis of salivary gland lesions. The positive and negative predictive values within parotid lesions were 84.9% and 91.2%, respectively, while the positive and negative predictive values within submandibular lesions were 91.3% and 94.4%, respectively. Single-institution studies of parotid gland lesions, as included in a recent meta-analysis,[2] demonstrated a positive predictive value of 98.3% among 552 cases,[6] an accuracy of 98% among 341 cases,[8] an accuracy of 86% among 228 cases,[9] and a positive predictive value of 83% among 150 cases.[1] Some institutions utilize both FNA and frozen section, with 1 group comparing the 2 techniques and demonstrating that FNA had an accuracy of 90% relative to frozen section with 88%.[10] Others feel that FNA is unacceptably inaccurate and therefore rely strictly on frozen section results for surgical decision making.[11] A recent study from the University of Iowa, published after the meta-analysis, reviewed 543 cases and noted a positive predictive value of 98.6% and a negative predictive value of 94.3%.[12] These findings suggest

Table 4. Indeterminate FNA Results among Parotid and Submandibular Lesions.

FNA Diagnosis	Surgical Follow-up, n (%)	
	Benign	Malignant
Indeterminate due to uncertainty in diagnosis (n = 18)	13 (72.2)	5 (27.8)
Indeterminate		
Favor benign (n = 12)	9 (75)	3 (25)
Favor malignant (n = 9)	0 (0)	9 (100)

Abbreviation: FNA, fine-needle aspiration.

Table 5. Measures of Diagnostic Accuracy among Parotid and Submandibular Gland Tumors.[a]

	Parotid Gland	Submandibular Gland
Sensitivity	75 (61.9-84.9)	91.3 (70.5-98.5)
Specificity	95.1 (90.3-97.7)	94.1 (78.9-99)
Positive predictive value	84.9 (71.9-92.8)	91.3 (70.5-98.5)
Negative predictive value	91.2 (85.7-94.8)	94.4 (78.9-99)

[a]Values presented in % (95% confidence interval).

that FNA is an accurate diagnostic tool in salivary gland lesions when used in conjunction with the history and physical examination and cross-sectional imaging.

Some institutions predominantly utilize frozen section analysis for surgical decision making.[11] Sensitivity and specificity for malignant lesions were reported as 98.5% and 99%. Although some expert head and neck pathologists are comfortable with this approach, others feel that frozen section for salivary tumors is not optimal given the increasing availability of advanced diagnostic techniques, such as immunohistochemistry and genetic analysis. Reliance on frozen section could allow for overtreatment or undertreatment. Patients diagnosed with carcinoma instead of lymphoma or benign disease could be subject to unnecessary facial nerve resection,[13] and adjunctive procedures such as neck dissection and mandibulectomy might be undertaken. Patients incorrectly diagnosed with benign disease may require reoperation, and revision surgery entails a higher risk of complications. Furthermore, frozen section requires additional time under anesthesia, which is known to be associated with perioperative morbidity.[14,15]

As all cases were rendered by board-certified university cytopathologists, a comparison cannot be made between diagnoses made by board-certified cytopathologists and general surgical pathologists. The experience among the cytopathologists varied from being directly out of fellowship to having 22 years of experience. Cytopathologists rely on certain features of the specimen to distinguish between benign and malignant pathology. For example, a specimen with basaloid cells may indicate chronic sialadenitis, cellular pleomorphic adenomas, basal cell adenomas/adenocarcinomas, or an adenoid cystic carcinoma. The additional presence of chondromyxoid stroma may favor a pleomorphic adenoma; however, if this feature is only focally present or clinical and imaging features are discordant, the pathologist is precluded from being more definitive. Similarly, a specimen with oncocytic cells could represent oncocytomas/oncocytic carcinomas, Warthin's tumors, pleomorphic adenomas, mucoepidermoid carcinomas, or acinic cell carcinomas. The presence of metaplasia may also lead a pathologist into an indeterminate diagnosis—for example, in the event of finding squamous or mucinous metaplasia within Warthin's tumors. Squamous or mucinous cells suggest a diagnosis of squamous cell carcinoma or mucoepidermoid carcinoma, and these entities therefore remain on the differential, although the presence of lymphocytes and oncocytes would lead a pathologist to favor the benign entity of a Warthin's tumor.

Surgery of the parotid gland entails a well-known risk profile. Previous studies have demonstrated temporary facial palsy in 25.0% to 46.1% of patients and permanent facial palsy in 2.3% to 6.0% of patients.[16-18] Facial nerve sacrifice has also occurred in 6.4% of patients with parotid gland lymphoma, where surgery is not the preferred treatment modality.[13] Other concerns include pain, salivary fistula, sensory deficit in the region of the great auricular nerve, and Frey's syndrome. Surgery of the submandibular gland carries similar risks, with marginal mandibular nerve palsy occurring temporarily in up to 29.8% of patients and permanently in 5.7% to 7.7%, along with hypoglossal and lingual nerve palsies in 1.1%-2.9% and 1.4%-5.7% of patients, respectively.[19-21]

Given these considerable risks, preoperative knowledge of the likelihood that a given lesion is benign or malignant allows for enhanced preoperative patient counseling and improved surgical planning. Various scenarios depict the utility of FNA:

- A patient with a palpable parotid lesion is recommended for surgery. After obtaining an FNA demonstrating malignancy, the surgeon orders cross-sectional imaging and determines that adjunctive procedures or additional imaging are required. Whole-body positron emission tomography–computed tomography may be ordered to evaluate for distant metastatic disease that could preclude surgery.
- An elderly patient with multiple comorbidities challenging his candidacy for anesthesia presents with a growing submandibular lesion. Cross-sectional imaging is reassuring, and the FNA provides a benign result, allowing the patient to elect observation in lieu of an immediate operation that might risk medical complications.
- A patient with an enlarging parotid lesion undergoes multiple FNAs, which are indeterminate. Surgery is recommended: the surgeon counsels the patient on the full range of procedures and

outcomes that might be necessary, and head and neck pathologic expertise is arranged for frozen section analysis.

One major limitation of this analysis is that only patients proceeding to surgery were included. Histopathology remains the gold standard in salivary disease diagnosis; thus, FNA results for patients who did not elect surgery or who pursued surgery elsewhere could not be assessed for accuracy. Because some patients did not have long-term follow-up available, we did not assess complication rates from FNA or surgery in this study out of concern for bias.

Another limitation of this study is that the uniformity of FNA technique cannot be assessed. This study was performed at a large academic center where different skill levels (residents/fellows/attendings) and departments (radiology, pathology, head and neck surgery) were involved in performing the FNAs, and these factors were not specifically addressed in this study.

Conclusion

In this series of FNA biopsies of the parotid and submandibular glands from a large referral center with fellowship-trained cytopathologists, we demonstrate that there is high accuracy, particularly for ruling out the presence of malignancy. We again confirm that the proportion of malignant tumors is higher in the submandibular gland than in the parotid gland, and we present a current assessment of the distribution of pathologic diagnoses of the salivary glands. FNA results provide valuable diagnostic information that may influence surgical management and should be routinely obtained in conjunction with cross-sectional imaging when evaluating patients with salivary gland lesions.

Author Contributions

Aaron J. Feinstein, conception, data acquisition, analysis and interpretation, drafting, final approval, accountability for all aspects of the work; **Jose Alonso**, data acquisition, analysis and interpretation, revising, final approval, accountability for all aspects of the work; **Sung-Eun Yang**, data acquisition, analysis and interpretation, revising, final approval, accountability for all aspects of the work; **Maie St. John**, conception, data interpretation, revising, final approval, accountability for all aspects of the work

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