

Original Article

Differentiating Malignant from Benign Lesions- The Value of Preoperative Cytology in the Management of Parotid Neoplasms

Khurshid Anwar *
Johar Iqbal**
Raza Mohammad**
Muneeb Khan**
Bakht Zada***

**Senior Registrar, Deptt; of ENT and Head & Neck Surgery KGN Teaching Hospital/Bannu Medical College, Bannu*

***Postgraduate Trainees, Deptt; of ENT and Head & Neck Surgery PGMI/ Hayatabad Medical Complex, Peshawar*

****Assistant Professor, Deptt; of ENT and Head & Neck Surgery PGMI/ Hayatabad Medical Complex, Peshawar*

Objective: To determine the sensitivity and specificity of fine needle aspiration cytology (FNAC) with respect to determination of malignancy in tumours of the parotid glands.

Place and Duration of the Study: This prospective study was conducted at the department of ENT, PGMI/HMC, Hayatabad Medical Complex, Peshawar and a Department related consultant's private clinic located at Peshawar from January 1, 2010 to May 31, 2011.

Study Design: Analytical Study

Materials and Methods: The study included all patients with a palpable mass in relation to the parotid glands. All the patients underwent needle aspiration of the parotid gland followed by excision biopsy. A comparison of FNAC and biopsy results was made.

Results: Biopsy examination for comparison was available in all the 57 cases. The FNAC findings in this series were: Benign 43, Malignant 11 and Suspicious 'Malignant Neoplasms' 3. The biopsy findings were: Benign 42 and Malignant 15. The diagnostic value of FNAC was; Sensitivity 86.67%, Specificity 97.62%, Positive Predictive Value 92.86%, Negative Predictive Value 95.35% and Diagnostic Accuracy 94.74%.

Conclusion: FNAC is a reliable technique and is a useful tool for identifying the nature of parotid tumours. However, in view of the occurrence of false negative cases, a cautious approach is recommended while planning management on its basis. The findings of FNAC should be read in conjunction with clinical and imaging studies and in doubtful cases the true nature of the lesion should be confirmed by biopsy examination.

Key words: Fine Needle Aspiration Cytology, Neoplasm, Parotid Gland, Histopathology.

Address for Correspondence

*Dr. Khurshid Anwar
 Senior Registrar, Department of ENT and Head & Neck Surgery, Khalifa Gul Nawaz Teaching Hospital / Bannu Medical College, Bannu.
 E-mail: dr.khurshidanwar@yahoo.com*

Introduction

FNAC is a well accepted procedure for diagnosing soft tissue tumours.¹ Aspirations are made employing the commonly used syringes with fine needles (22- to 23-gauge). Superficial lobe tumours can be aspirated easily whereas tumours in relation to the deep lobe can be accessed using image guidance for localization. Tumor marker studies, special stains and bacteriological & immunological studies have further improved upon the diagnostic accuracy of FNAC.²

Majority of salivary gland malignancies are slow growing and mimic benign lesions and preoperative open biopsy of parotid gland tumours is inadvisable; cytology becomes the only means for identifying the nature of the lesion. Though infectious and inflammatory conditions can also be diagnosed on cytology, it is usually not performed for these clinical conditions. Due to its

inherent limitations such as missing the target lesion, haemorrhagic smears, inadequate aspirates and a very small amount of cellular material available for histopathological examination, both the clinicians and histopathologists have been reluctant to accept cytological diagnosis as final. The definitive diagnosis is, therefore, based on examination of biopsy specimens. However, as compared to the past, more patients are referred by clinicians for cytological diagnosis as their confidence in the use of FNA cytology increases.

In the parotid gland, FNAC is fairly reliable for the diagnosis of pleomorphic adenomas; it has difficulty identifying carcinoma ex-pleomorphic adenoma. Differentiation between pleomorphic adenomas, adenoid cystic carcinoma, monomorphic adenoma and mucoepidermoid carcinoma may be difficult. The

distinction between poorly differentiated squamous cell carcinoma and high grade mucoepidermoid carcinoma is also difficult on cytology.^{3,4}

The technique is less invasive, safe and no sophisticated equipment is required to perform it. Diagnosis is made quickly and it is virtually free of serious complications. It has therefore become the initial investigation for evaluating parotid gland masses. However, reliance solely upon FNAC findings at the expense of clinical, radiographic, or other findings is unsafe.⁵ Therefore, using this technique in combination with clinical examination and imaging studies in the parotid glands, management can be planned and therapy individualized.

The present study was carried out to determine the diagnostic accuracy of FNAC in parotid gland masses, taking excision biopsy as the gold standard.

Materials and Methods

Sample size: The study included 57 cases of masses of the parotid glands. Sample size was calculated assuming 80% proportion of tumours of salivary glands occurring in the parotid, 95% confidence level and 10.5% margin of error under WHO software for sample size determination.

Inclusion criteria: Patients of all ages and either gender who had initial FNAC followed by open biopsies.

Exclusion criteria: Acute and chronic inflammatory lesions of the parotid glands.

Haemorrhagic aspirates and inadequate smears obtained on repeat FNAC. Frank abscesses whose aspirates were lacking in diagnostic cellular details.

All the patients having a palpable lump in relation to parotid gland were included in the study. After obtaining informed consent, patients were thoroughly examined and the management plan shared with them and their relatives after adequate explanation. Ultrasonography was carried out before advising needle aspiration. FNAC was advised in those cases fulfilling the laid down criteria. Other laboratory investigations were strictly individualized. The following laboratory investigations were carried out, as and when necessary to determine the patients' fitness for the procedure and subsequent surgery:

Blood Complete picture, screening for hepatitis B and C, Blood Sugar and Urea Levels, Serum Creatinine and Electrolytes Estimation and LFTs, Urine R/E, ECG, Echoardiography, X-Ray Chest and other Imaging Studies such as CT and MR Imaging.

All the aspirations were performed by qualified histopathologists. The results obtained on FNAC were categorized into three categories; Benign, Malignant and Suspicious. Frankly hemorrhagic and purulent aspirates were excluded from the study. Inconclusive aspirates

were also excluded from the study when a repeat aspiration was also 'inconclusive'. Ultrasonography was used for localization of target tissues in selected cases. A case was considered as "suspicious" when the cytology showed atypical cells without having overt features of malignancy. For the purpose of analysis the "suspicious" cases on cytology were regarded as malignant and were grouped under the heading of "Malignant Neoplasms". Final diagnosis was made on the basis of histopathological examination of biopsy specimens. A comparison of these results was made to determine the diagnostic value of FNAC. The data were analyzed using SPSS 16.0 for windows and the diagnostic accuracy of FNAC was determined using the Diagnostic or Screening Test Evaluation Program (STEP).

Results

A total of 57 cases were included in the study. The ages of the patients ranged from 20 to 78 years with the mean age of 41.28 years and a standard deviation of ± 13.06 . The male: female ratio was 1.28:1. No anaesthetic agent was employed for needle aspiration in any case. In 8.77% (n=5) cases a repeat aspiration was made due to the initial inconclusive results and in 3.5% (n=2) cases ultrasonography was employed to localize target tissues. Pleomorphic adenoma was the commonest benign tumor (n=38). The frequency of various types of tumours as determined by cytology is given in Table I. The number of benign and malignant cases as determined on biopsy examination was 42 and 15 respectively. Pleomorphic adenoma was the commonest benign tumour (n=36) and adenoid cystic carcinoma was the commonest malignancy (n=06) found on biopsy. The spectrum of lesions identified on biopsy is listed in Table II. Parotid gland tumours were the commonest in age group ≤ 40 comprising 59.6% of all the tumours in the study. Males and females were equally affected by parotid malignancies found in the study. The number of benign, malignant and suspicious cases as determined on FNA cytology was 43, 11 and 3 respectively. The histopathological findings as determined on examination of biopsy specimens were; benign 42 and malignant 15. FNAC was unable to correctly identify one malignant and two benign lesions; a case each of adenocarcinoma and carcinoma-ex-pleomorphic adenoma was wrongly diagnosed as pleomorphic adenoma and a case of basal cell adenoma was suspected to be malignant. For the purpose of analysis the suspicious cases were considered as "Malignant Neoplasms". The diagnostic value of FNAC in the parotid gland calculated after comparison with biopsy was; Sensitivity 86.67% and Specificity 97.62% as shown in Table III.

Discussion

Table I. FNAC Findings among the patients. (n=57)

S. No	Type of Tumour	Frequency	Percentage
1.	Pleomorphic adenoma	38	66.7
2.	Warthin tumour	3	5.3
3.	Oncocytoma	1	1.8
4.	Lipoma	1	1.8
5.	Mucoepidermoid carcinoma	3	5.3
6.	Adenoid cystic carcinoma	6	10.5
7.	Malignant Neoplasms (Suspicious)	3	5.3
8.	Acinic Cell carcinoma	2	3.5
Total		57	100.0

Table II. Biopsy Findings: Type of parotid tumours

S.No	Type of Tumour	Frequency	Percent
1.	Pleomorphic adenoma	36	63.2
2.	Warthin tumour	3	5.3
3.	Oncocytoma	1	1.8
4.	Lipoma	1	1.8
5.	Mucoepidermoid carcinoma	3	5.3
6.	Adenoid Cystic carcinoma	8	14.0
7.	Ca ex Pleomorphic Adenoma	1	1.8
8.	Acinic Cell Carcinoma	2	3.5
9.	Adenocarcinoma	1	1.8
10.	Basal Cell Adenoma	1	1.8
Total		57	100.0

Table III. The Diagnostic Accuracy of FNAC in Parotid Glands

		FNAC		
		Positive	Negative	Total
Histopathology	Positive	13	1	14
	Negative	2	41	43
	Total	15	42	57

Salivary glands tumours represent about 3% of all the neoplasms. 80% of these tumours occur in the parotid gland and 80% of the parotid tumours are benign.⁶ The gland has a complex structure, consisting of secretory cells, acini and a duct system. The acini are surrounded by myoepithelial cells which have features common to both epithelial and smooth muscle cells.⁷ Because of complex anatomy, parotid gland neoplasms pose many problems to the pathologist. These tumours are rarely homogenous in structure and many present in a variety of combinations and patterns. Fine-needle aspiration (FNA) biopsy as a diagnostic technique is well established and lesions of the salivary glands frequently are evaluated by this technique; in fact in many centers, this is the first tissue-based procedure applied to establish a diagnosis before any surgical intervention.^{3,4}

FNAC can readily identify pleomorphic adenomas because of their biphasic pattern, epithelial/myoepithelial cells and fibromyxochondroid stroma. The components may be arranged in a wide spectrum of microscopic appearances with a potential for errors in cytological interpretation.⁷ It can be a source of confusion with tumours such as basal cell adenoma, adenoid cystic carcinoma and mucoepidermoid carcinoma on cytology.⁸ In our series 36 cases of pleomorphic adenoma were correctly identified on cytology. Carcinoma-ex-pleomorphic adenoma is difficult to identify on cytology probably because of lack of a representative sample. It is a highly aggressive tumour of no specific type.⁴ In this study a false negative case proved to be carcinoma-ex-pleomorphic adenoma on subsequent histopathology. According to by Kljanienco et al, carcinoma ex pleomorphic adenoma has the highest false negative rate (35.3%) of all malignant salivary gland tumours.⁹ Warthin tumours are the second most common benign neoplasm occurring in the parotid gland. The three main components that characterize the FNA cytology of Warthin tumor are oncocytes, lymphocytes, and the fluid background. Cytology was able to correctly identify all the cases of Warthin tumour in this study. A Rotterdam study by Veder et al found 95.5% diagnostic accuracy of FNA cytology for identification of Warthin tumour.¹⁰

Monomorphic adenoma constitutes 1.8% of benign epithelial salivary gland tumors. Basal cell adenomas are the commonest and the majority occurs in the parotid gland.⁶ Basaloid neoplasms are the most difficult problem in salivary gland FNAC. In this study a suspicion of being malignant was laid on a single case of basal cell adenoma. The diagnosis of basaloid neoplasms includes; cellular pleomorphic adenoma, adenoid cystic carcinoma and other rare benign and malignant neoplasms which cannot frequently be differentiated by cytology alone.¹¹

Oncocytomas are rare, benign salivary gland tumors most commonly encountered in the parotid of older people. Although most have benign nature, malignant cases have also been reported. The differentiation between benign and malignant oncocytoma is largely based on the clinical findings since the malignant counterpart has no sufficient histological and ultrastructural differences from the benign variant. Malignant oncocytoma has typical recurrences and sometimes nodal metastases. Histologically atypical oncocytic cells increased mitotic activity, local infiltration with perineural, vascular or soft tissue infiltration and absence of capsule may be seen. The majority of oncocytic neoplasms are benign, even if nuclear atypia is present. Nevertheless, the cytologic distinction of oncocytoma from the extremely rare oncocytic carcinoma is difficult and may be impossible on FNAC.^{12,13} The single case of oncocytoma in our study was correctly identified on cytology as the smear consisted largely of oncocytes with no nuclear atypia or increased mitotic activity.

Mucoepidermoid carcinoma is the most common childhood parotid gland malignancy and accounts for 45-70% of the parotid gland malignancies. A low grade tumour is likely to be confused with pleomorphic adenoma whereas the high grade tumors are often mistaken for squamous cell carcinoma. Positive immunohistochemical staining for mucin would indicate a mucoepidermoid carcinoma.¹⁴ Adenoid cystic carcinoma is the second most common parotid gland malignancy. The cribriform pattern is the most common and easily recognizable on cytology.¹⁵ Acinic cell carcinoma is the third major common malignant tumor of the parotid gland. Cytologic diagnosis depends on the identification of acinar cells and/or recognition of the acinar-glandular arrangement.¹⁵ All these malignancies were correctly identified on cytology in the study.

The overall accuracy of FNA cytology in diagnosis of parotid neoplasms has been reported in the literature to be 87% to 100% with sensitivity of 87% to 100% and a specificity of 90% to 100% in distinguishing benign from malignant lesions.^{16,17} The diagnostic accuracy of FNAC in our study was 94.74% with sensitivity of 86.67% and specificity 97.62%. In a retrospective review of cases conducted at the Pakistan Institute of medical Sciences, Islamabad the diagnostic accuracy of FNAC in salivary glands was found to be; positive predictive value 100%, negative predictive value 91.4% and diagnostic efficacy 91.8%. The study reported positive correlation for neoplastic lesions to be 93.9%.¹⁸ Another similar study conducted at the Aga Khan University Hospital Karachi, reported three false negative and one false positive case. The diagnostic accuracy of FNAC in the study was 92% with sensitivity, specificity, positive predictive and negative predictive values of 70%, 97%, 87% and 92% respectively.¹⁹ Obaid MA and colleagues found FNAC

as a useful adjunct in the management of epithelial parotid tumours and recommend the pre operative use of FNAC on such cases.²⁰ In 2010, a study conducted at Department of Pathology, Fatima Jinnah Medical College, Lahore, Pakistan, Ashraf and colleagues found sensitivity, specificity, positive predictive value, and negative predictive value of FNAC for benign neoplastic lesions at 98.52, 87.05, 94.36, and 96.55%, respectively, whereas for malignant neoplastic lesions these values were 77.77, 98.78, 93.33, and 95.29%, respectively.²¹

No different figures for the diagnostic accuracy on the subject can be found in the international literature. In 1991, Frable and Frable studied 227 aspirations from salivary glands. FNA had 92% sensitivity for tumor and specificity of 99% for the absence of tumor. The diagnostic efficiency in their series was 96.4%, with an overall predictive value of 98.3% for malignancy.²² Basavanandswami and colleagues in India in a similar study found that sensitivity of needle aspiration for malignancy was 90.9% while the specificity was 96.6%. There was 1 false negative case and 1 false positive case. The positive predictive value for cytology was 90% and negative predictive value was 96 %. The diagnostic accuracy of test was 95.1%.¹⁷ Hee and Perry in a study of 169 patients on parotid found that fine-needle aspiration cytology had an overall accuracy of 56%. The sensitivity and specificity for the following diagnoses were, respectively: benign 86% and 61%; malignant 57% and 100%; pleomorphic adenoma 78% and 95%; mucoepidermoid carcinoma 14% and 99% and adenocarcinoma 20% and 100%. They concluded that FNA cytology was highly specific for malignancy but its sensitivity for malignancy was poor. So while FNA is the mainstay of diagnosis of salivary gland tumours, it cannot always be relied upon in isolation, and should be used in conjunction with other investigations.²³

Conclusion

FNAC is a useful tool for identifying the nature of parotid tumours. It is a reliable technique and helps in planning management in the vast majority of patients. However, in view of its limitations and in particular, the occurrence of false negative cases, a cautious approach towards parotid tumours is recommended. The findings of FNA should be read in conjunction with clinical and imaging studies and in doubtful cases the true nature of the lesion should be confirmed by biopsy examination.

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