Original Article

Comparison of the efficacy of the palpation versus ultrasonography-guided fine-needle aspiration cytology in the diagnosis of salivary gland lesions

Nazoora Khan, Nishat Afroz, Swati Agarwal, Mohammad Amanullah Khan[1], Ibne Ahmad[2], Hena A. Ansari, Sunanda Chauhan, Divya Rabindranath, Azka Anees Khan

Departments of Pathology, [1]General Surgery and [2]Radiodiagnosis, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

ABSTRACT

Background: Fine-needle aspiration cytology (FNAC) is the initial investigation for salivary gland swellings. The aim of this study was to study the utility of ultrasonography (USG) as an adjunct to cytology in the diagnosis of salivary gland lesions and to compare the two methods, palpation-guided and ultrasound-guided FNAC in diagnosis of salivary gland lesions. **Materials and Methods:** The study comprised of 45 patients presenting with a salivary gland swelling. All the patients were subjected to USG examination and FNA of the swellings-both by palpation method and ultrasound guided, in each case. Further, the cytological features of all the cases were studied comparing the findings on palpation-guided versus USG-guided FNAC. Histopathological correlation was also done wherever possible. **Results:** Number of inadequate aspirations decreased and the number of lesions detected increased on using USG-guided FNAC. Only two cases were false negative on USG-guided FNAC, and there were no false positive cases. While on palpation-guided FNAC, three cases came out to be false negatives, and one was seen to be false positive. The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive values were higher for USG-guided FNAC than for palpation-guided FNAC. **Conclusion:** We concluded that though differentiation of salivary gland masses was difficult on USG alone due to nonspecific USG findings, combination of ultrasound with FNAC certainly improved the diagnostic efficiency. USG guidance led to more representative, meticulous sampling which helped in providing a correct diagnosis in the majority of cases.

Key words: Fine-needle aspiration cytology, salivary gland lesions, ultrasonography

INTRODUCTION

Masses of the salivary gland range from nonneoplastic lesions like inflammation and cysts to benign and malignant neoplasms. Tumors of salivary gland are relatively rare and comprise 3–6% of all head and neck neoplasms.[1] Although the main treatment modality for both benign and malignant lesions is surgery, it is necessary to differentiate between the two preoperatively, to guide the surgical approach and extent of removal of tissue.

The exact nature of salivary gland lesions cannot be determined on clinical examination alone. Ultrasonography (USG) can be a potentially useful preoperative investigation as it offers several advantages. Included among these are its widespread availability, its low cost, and the avoidance of exposure to ionizing radiation.[2,3] However, USG examination alone cannot satisfactorily differentiate between benign and malignant tumors. The sonographic appearance is nonspecific as benign and malignant tumors both are mostly hypoechoic,[4] the only clues to malignancy being irregular margins, posterior shadowing, or heterogeneous internal echogenicity.[5] Hence, pathological examination is required for a definite diagnosis in most cases.

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Address for correspondence: Dr. Hena A. Ansari, Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh - 202 002, Uttar Pradesh, India. E-mail: hena.jnmc@gmail.com

Fine-needle aspiration cytology (FNAC) of salivary gland is an accepted, sensitive, and specific technique in the diagnosis of both neoplastic and nonneoplastic lesions.[6] It is a safe and relatively nontraumatic procedure that can quickly provide important preoperative information. However, a large multicenter study showed that the sensitivity of blind aspiration of salivary gland masses for the detection of malignancy was as low as 38%.[7] US guidance increases diagnostic accuracy by enabling the avoidance of necrotic or cystic regions and targeting of higher-yield areas of the lesion for tissue extraction.[8-10] Ultrasound guided FNA has been shown to improve diagnostic accuracy when compared with FNA performed without sonographic guidance in earlier studies.[11-13]

Recently, however, USG-guided FNAC has come under criticism with some studies quoting a high rate of inadequate sampling.[14] These studies suggest core needle biopsy to be a better alternative to USG-guided FNAC. Others, however, refuted these claims quoting the higher rates of complications with core needle biopsy, and almost similar sensitivity and specificity when compared to USG-guided FNAC.[15]

We performed this study to evaluate the significance of USG as an adjunct to cytology in context of salivary gland lesions, as well as to compare USG-guided and palpation-guided FNAC in these lesions. Furthermore, there are significant variations regarding opinion about ultrasound-guided FNAC in previous studies. We also aim to clear these controversies and establish a clear understanding of the role of USG-guided FNAC in preoperative evaluation of salivary gland lesions.

MATERIALS AND METHODS

The present study comprised of 45 patients presenting with a swelling in salivary gland region. After clinical examination, all the patients underwent USG examination followed by USG-guided as well as palpation-guided FNAC. It/FNAC was performed under sterile conditions with 18–22 gauge fine-needle of variable length attached to 10 ml plastic disposable syringe. The aspirated material was then spread on clean glass slides which were immediately immersed in 95% alcohol for fixation or air-dried depending on the stain to be used.

Ultrasound-guided fine-needle aspiration cytology

First, the site was scanned using GE LOGIQ500 machine noting the presence, location, size, and the number of lesions. USG-guided FNA was performed with an 18–22 gauge needle attached to 10 ml syringe. The aspiration was performed under direct USG monitoring. The aspirated material was then spread onto clean numbered slides, which were immediately immersed in 95% alcohol for fixation or air-dried depending on the stain to be used.

In cases where surgery was performed, the tissue obtained was processed routinely and stained by hematoxylin and eosin stain.

After microscopic examination of all the smears and their correlation with each other, statistical evaluation was made to calculate the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of both the methods of aspiration. The test of significance used was the *z*-test for proportions.

RESULTS

Male to female ratio for benign salivary gland lesions was 3:1 (male = 23, female = 7). Most of these cases presented in the fourth decade followed by third decade of life. For malignant lesions, male to female ratio was 2:1 (male = 8 and female = 4) and the age of presentation for most ranged from fourth to sixth decade.

Most of the lesions were located in the parotid gland ($n = 31$, 69.9%) followed by submandibular gland ($n = 14$, 31.1%).

On USG, sialadenitis (5 cases) showed hypoechoic gland with multiple small hyperechoic foci, pleomorphic adenoma (11 cases) showed lobulated hypoechoic lesion which seemed to arise from parotid gland in 10 cases and submandibular gland in 2 cases, Warthin's tumor (4 cases) showed a sharply delineated ovoid lesion, with partially cystic area in one case, basal cell adenoma (3 cases) revealed only anechoic mass and myoepithelioma (1 case) showed inconclusive findings on USG.

All malignant salivary gland lesions revealed sharply marginated, inhomogenous lesions. No definite distinguishing feature was found.

As tabulated in Table 1, a total of 42 cases yielded adequate aspirates on image-guided aspiration. Benign neoplasms were subdivided into 11 cases of pleomorphic adenoma (36.7%) [Figure 1a], 3 cases of basal cell adenoma (10%) [Figure 2a], one case of myoepithelioma (3.3%) [Figure 2b]; and 4 cases of Warthin tumor (13%) [Figure 3a], nonneoplastic benign lesions included 6 cases (20%) of retention cysts and 5 cases (17%) of chronic sialadenitis. Three aspirates were inadequate. Of these, 2 cases were clinically and ultrasonographically diagnosed as a case of hemangioma but repeated aspirations yielded only hemorrhage. The other case was diagnosed as lipoma on clinical ground. On cytopathology, this showed only fibrofatty material with scant epithelial cells, and therefore was inconclusive for diagnosis.

Table 1: Correlation between cytological (USG-guided) and histopathological diagnosis of different salivary gland lesions

Lesion	Cytology (number of cases) (%)	Histopathology	Concordant	Discordant
Benign (*n*=30)				
Pleomorphic adenoma	11 (36.7)	8	7	1
Warthin tumor	4 (13.3)	4	3	1
Basal cell adenoma	3 (10)	3	2	1
Myoepithelioma	1 (3)	1	1	-
Retention cysts	6 (20)	-	-	-
Sialadenitis	5 (17)	-	-	-
Malignant (*n*=12)				
Mucoepidermoid carcinoma	5 (41.7)	4	3	1 (SCC)
Adenoid cystic carcinoma	2 (16.7)	2	2	-
Acinic cell carcinoma	1 (8.3)	1	1	-
Carcinoma ex pleomorphic adenoma	1 (8.3)	1	1	-
Polymorphous low grade adenocarcinoma	1 (8.3)	1	1	-
Adenocarcinoma	1 (8.3)	-	-	-
Lymphoma	1 (8.3)	-	-	-
Total	42	25	21	4

USG: Ultrasonography, SCC: Squamous cell carcinoma

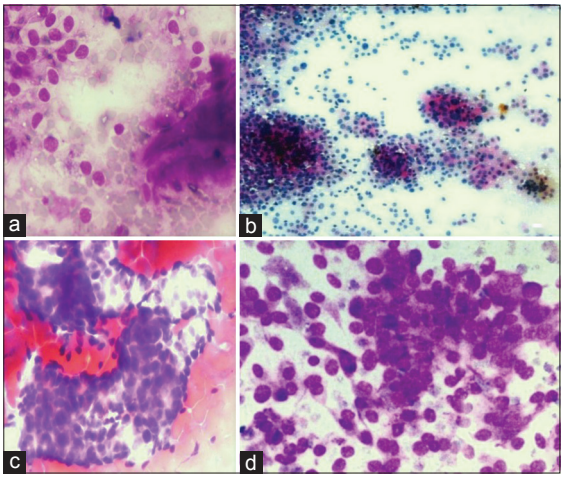

Figure 1: (a) Pleomorphic adenoma: Groups of plasmacytoid epithelial and myoepithelial cell and chunks of chondromyxoid material (May Grünwald Giemsa [MGG], ×40). (b) carcinoma ex pleomorphic adenoma-malignant cells in a preexisting pleomorphic adenoma (Pap, ×10). (c) Adenoid cystic carcinoma-papillary clusters of malignant cells with hyperchromatic nuclei and scanty cytoplasm with some hyaline globules (H and E, ×40). (d) Acinic cell carcinoma: Malignant acinic cells exhibiting little nuclear pleomorphism and granular cytoplasm (MGG, ×40)

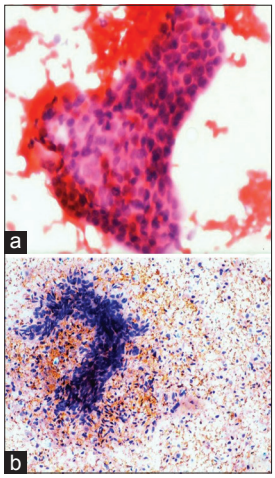

Figure 2: (a) Basal cell adenoma: tight cluster of benign monomorphic basaloid cells with hyaline globules (Pap, ×10). (b) Myoepithelioma-tight as well loose clusters of benign appearing spindly cells (Pap, ×10)

Of all the malignant cases, mucoepidermoid carcinoma [Figure 3b] formed the largest group of 5 cases. Two cases were of adenoid cystic carcinoma while acinic cell carcinoma, carcinoma ex pleomorphic adenoma, lymphoma, adenocarcinoma, and polymorphous low-grade adenocarcinoma constituted one case each [Figure 1b-d].

Histopathological correlation was available in 25 cases (16 benign tumors and 9 malignancies). A concordant diagnosis was obtained in 21 cases. One case diagnosed as pleomorphic adenoma on cytology but turned out to be adenoid cystic carcinoma on histopathology. The second discordant case was of a cytologically diagnosed basal cell adenoma which turned out to be adenoid cystic carcinoma on histopathology. The third case was of a Warthin's tumor diagnosed on cytology which turned out to be a lymphoepithelial cyst on histopathological examination. The fourth case was earlier diagnosed as mucoepidermoid carcinoma on cytology but finally turned out to be squamous cell carcinoma (SCC) on histopathology.

There was no false positive diagnosis among the malignancies.

On palpation-guided FNAC, 26 of the total 45 cases (57.8%) were diagnosed as benign. Ten (22.2%) were malignant, while 9 (20%) were inadequate to form any diagnosis. Comparison with USG-guided FNAC and histopathology.

Of the 26 cases diagnosed as benign on palpation-guided FNAC, 3 cases showed discordant results (false negative) with respect to histopathology. Of these, 2 cases were diagnosed as pleomorphic adenoma on palpation-guided FNAC but turned out to be CA ex pleomorphic adenoma both on USG-guided FNAC as well as on histopathology.

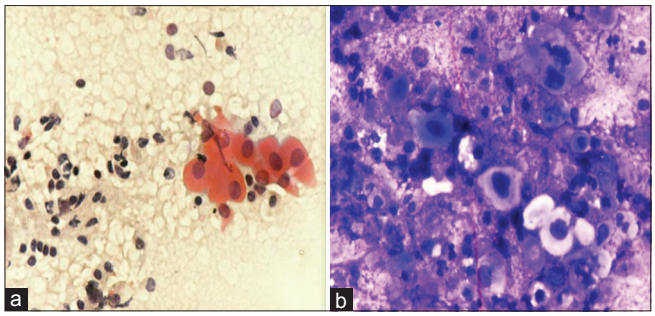

Figure 3: (a) Warthin's tumor-sheets of benign oncocytic cells with few lymphocytes (Pap, ×40). (b) Mucoepidermoid carcinoma-admixture of malignant squamous, clear and mucous cells (H and E, ×40)

Further, one case was diagnosed as basal cell adenoma both on palpation-guided and USG-guided FNAC, but was finally proven to be adenoid cystic carcinoma on histopathological examination.

Moreover, of the 10 malignant cases on palpation-guided FNAC, 1 case of carcinoma ex pleomorphic adenoma did not show correlation (false positive) with respect to USG-guided FNAC and histopathology as it was confirmed to be a case of benign salivary gland tumor, that is, pleomorphic adenoma.

Hence, the number of false positives and false negatives on palpation-guided FNAC were 1 and 3, respectively.

Chart 1 shows comparison between palpation-guided and USG-guided FNAC. USG-guided aspirations reduced the number of inadequate aspirates to almost one-third of the palpation-guided aspirates (9 inadequate aspirates by palpation-guided versus 3 inadequate by USG-guided FNAC). There were no significant differences in the number of benign and malignant lesions found by both the methods.

The diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of USG-guided FNAC for salivary gland lesions were calculated to be 92.0%, 81.9%, 100%, 100%, and 87.5%, respectively, while that of palpation-guided FNAC were 88.9%, 75.0%, 95.8%, 90.0%, and 88.4%, respectively.

DISCUSSION

Through this study, we observed that the differentiation of salivary gland masses was difficult by USG alone as neoplastic lesions did not show any specific features except for inhomogenous sharply marginated lesions. The role of USG in the diagnosis of salivary gland lesions has been studied in detail earlier also.[16,17] It has been proven that though USG should be the first imaging modality for patients with salivary gland masses, further investigation should be done when neoplasms are suspected, particularly if deep areas of the gland are involved, which cannot

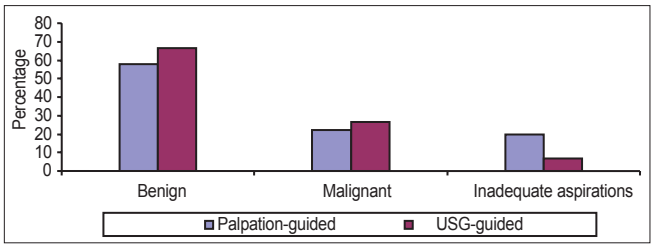

Chart 1: Comparison of palpation-guided and ultrasonography-guided fine-needle aspiration cytology of salivary gland lesions

be visualized by USG.[18] It was further proven that it is challenging to use sonography for differentiating between benign and malignant salivary gland masses. Hence, to make a definite diagnosis, ultrasound-guided FNA should be performed.[4]

Combination of ultrasound with FNAC certainly improved the diagnostic efficiency in our study. We found that of the total 45 salivary gland lesions, palpation-guided FNAC yielded 26 cases (57.8%) of benign and 10 cases (22.2%) of malignant lesions while USG-guided FNAC resulted in 30 (66.7%) benign and 12 (26.7%) malignant lesions. Though the difference in the number of benign and malignant cases detected by the two methods was not significant, but certainly more number of benign and malignant lesions were diagnosed on USG-guided FNAC than on palpation-guided FNAC.

There were only three inadequate aspirates on USG-guided FNAC, in contrast to nine nondiagnostic aspirates on blind FNAC. This is comparable with the results of previous studies who reported a decrease in the number of inadequate specimens with the use of USG-guided FNAC.[11,19]

Regarding the distribution of cases, we observed a higher incidence of neoplastic salivary gland masses (31 cases-73.8%) as compared to nonneoplastic lesions (11 cases-26.2%). This is in contrast to the study where 73% of their cases comprised of benign nonneoplastic lesions.[20] Our findings, however can be validated by the fact that earlier investigators have also reported the proportion of noneoplastic lesions in the medical literature to range from 20% to 74.5% with an average of 37%.[6,21,22] Of the neoplastic lesions in our study, 19 cases (61.2%) were clearly benign while 12 cases (38.7%) were malignant.

The two most common benign neoplasms in our study were pleomorphic adenoma (11 cases) and Warthin's tumor (4 cases). This is similar to the findings of different researchers earlier.[12,20,22] The most common malignant neoplasm in our study was mucoepidermoid carcinoma (5 cases).

In USG-guided FNAC, as described earlier, 3 of our cases diagnosed as benign on USG-guided FNAC

showed discordant results on histopathology. Two histopathologically confirmed cases of adenoid cystic carcinoma were misdiagnosed as pleomorphic adenoma and basal cell adenoma on cytology. It is a common error because both pleomorphic adenoma and adenoid cystic carcinoma have relatively uniform epithelial-like cells, and both may have a fibrillar myxoid stromal component.[23] Distinction between adenoid cystic carcinoma and basal cell adenoma on cytology can also be a problem as both these lesions can demonstrate hyaline globules which are otherwise characteristic of adenoid cystic carcinoma.[23] The third case was misdiagnosed as Warthin's tumor on cytology, but histopathology revealed it to be a lymphoepithelial cyst. Clinically, both lesions can present as cystic lesions and majority of cysts occurring in the major salivary glands are associated with neoplasm, which may lead to false diagnosis.[24]

In palpation-guided FNAC, 3 cases were found to be false negative on further follow-up by USG-guided FNAC and histopathology. Out of three, 2 cases were reported as pleomorphic adenoma on cytology but on histopathology they turned out to be pleomorphic adenoma with carcinomatous change. This was due to sampling error because the proportion of benign and malignant areas is variable in these lesions, and the diagnosis requires demonstration of pleomorphism and atypical cell.[25] In this case, most of the tumor was benign, and only a small area showed malignant transformation which was missed on conventional FNAC. The cytologically diagnosed basal cell adenoma (third case) was reported as adenoid cystic carcinoma on histopathological examination. This was due to the overlapping morphological features as has already been mentioned.

In USG-guided FNAC, a single case showed discordant results on histopathology. The case was cytologically diagnosed as mucoepidermoid carcinoma but on histopathological examination proved to be a case of high grade SCC. This was because distinction between high-grade mucoepidermoid carcinoma and SCC is difficult on cytology unless a mucinous component is demonstrated.

On palpation-guided FNAC, one false positive diagnosis was found. A case of pleomorphic adenoma was overdiagnosed as carcinoma ex pleomorphic adenoma due to cytological misinterpretation. As a general rule, a few atypical cells in classic pleomorphic adenoma should not be regarded as evidence of malignancy.[6] This discrepancy was overcome by USG-guided FNAC because combined ultrasound findings and FNAC avoided the false positive diagnosis.

Mucoepidermoid carcinoma, pleomorphic adenoma, chronic sialadenitis, and malignant lymphoma are responsible for most of the diagnostic errors.[26] Similarly, the present study showed that the diagnostic pitfalls of FNAC were in relation to mucoepidermoid carcinoma, adenoid cystic carcinoma, and carcinoma ex pleomorphic adenoma.

In the present study, palpation-guided FNAC showed the diagnostic accuracy of 88.9%, sensitivity 75.0%, specificity 95.8%, positive predictive value 90% and negative predictive value of 88.4%. In comparison, the sensitivity of USG-guided FNAC of the salivary gland lesions was 81.9%, specificity 100%, positive predictive value 100%, negative predictive value 87.5%, and diagnostic accuracy of 92.0%. This was comparable with previous studies who also showed that the overall sensitivity and specificity of USG-guided FNAC were higher than the palpation-guided FNAC.[27,28] The reported incidence of sensitivity and specificity for USG-guided FNAC is varied with sensitivity ranging from 62% to 98% and the specificity ranging from 94% to 100%.[12,29,30]

In our study, the findings on USG-guided FNAC were diagnostic in 42 out of 45 cases, that is, in 93% of the cases. Inadequate aspirations were obtained in 3 cases (6.7%). We are against the opinion that USG-guided FNAC leads to a high rate of inadequate aspirations,[14] and agree with studies who suggested that US-guided FNA represents a diagnostically adequate method for sampling lesions of the salivary glands, with accuracy similar to that of US-guided core needle biopsy.[15]

All the parameters obtained by palpation-guided FNAC were lower than that obtained by USG-guided FNAC. We found that ultrasound guidance can help in aspirating smaller salivary gland lesions, leading to a larger number of lesions being detected and therefore better sensitivity. It can also lead to more accurate sampling, hence improving the specificity also. It has been suggested earlier that USG-guided FNAs performed by a cytopathologist could significantly improve the specificity and negative predictive value while preserving virtually the same excellent sensitivity and positive predictive value as those of palpation-guided FNAs.[19]

CONCLUSION

It is well-known that there are insufficient characteristic USG features to distinguish between neoplastic and nonneoplastic lesions of salivary glands. Hence, further imaging is necessary using computed tomography or magnetic resonance imaging. We suggest that USG-guided FNAC of salivary gland lesions can be a useful alternative to expensive imaging techniques especially in poor resource countries like India. USG-guided FNAC has an added advantage of better visualization of lesions, needle

placement, and hence less number of inadequate samples as compared to routine palpation-guided method.

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