Pathology Section

Diagnostic Efficacy of Fine Needle Aspiration Cytology in Cystic Lesions of Head and Neck Region - A single Experience at Tertiary Health Care Centre

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ABSTRACT

Introduction: The cystic lesions of head and neck region are common presentation in the Outpatient Department and encompass a wide spectrum of differential diagnosis, ranging from inflammation to malignancy. Though, Fine Needle Aspiration Cytology (FNAC) is a well established modality for the precise diagnosis of solid lesions of head and neck region, its role in cystic lesions has not been assessed much.

Aim: To evaluate the role of fine needle aspiration cytology in the diagnosis of cystic lesions in the head and neck region and to correlate the cytology findings with histopathological diagnosis wherever possible.

Materials and Methods: This prospective study included FNAC of 162 cases of cystic lesions of head and neck region referred to the department between November 2014 and May 2016. Aspiration was done using 22-25 gauge needles. The aspirates were stained appropriately. Cytomorphology was

studied and subsequently correlated with histopathological features wherever possible.

Results: Among the 162 cases studied, 123 were negative/benign, two were suspicious of papillary carcinoma and 34 were malignant cases. The remaining three cases were inadequate for reporting and hence were excluded from statistical analysis. Among the malignant cases, metastatic squamous cell carcinoma was the commonest. Histopathological correlation was available in 88 cases with 85 cases consistent with FNAC diagnosis. Sensitivity and specificity was 85% and 100% respectively. Overall accuracy was found to be 96.59%.

Conclusion: The cytological study of cystic lesion of head and neck is important for accurate identification of the lesions preoperatively and expedite the planning of therapy. Hence, the study assumes importance. The limitation of FNAC in cystic lesions can be overcome by re-aspiration from residual solid area after draining the cyst under ultrasound guidance.

Keywords: Cystic aspirate, Cytodiagnosis, Histopathology

INTRODUCTION

Cysts and associated lesions with cystic changes are commonly encountered in the head and neck region. Pathology of these lesions is diverse and includes developmental, inflammatory, benign tumors and malignant tumors which could be primary or metastatic.

In children majority of the cysts are benign, whilst in adults, an asymptomatic neck cyst usually implicates malignancy. It is therefore essential to obtain an accurate pre-operative diagnosis for appropriate patient management. FNAC is a well established tool in the head and neck lesions. However, its usefulness in the cystic lesions has been evaluated in a limited number of studies, the major pitfall being low cellularity, reactive atypia and cellular degeneration [1-3].

Although, radiology helps to narrow down the differential diagnosis in cysts and lesions associated with cystic changes, an open surgical biopsy remains the gold standard,

thus adding burden to the patient care [4].

The aim of the study was to evaluate the usefulness of FNAC in primary investigation of the considerable spectrum of cystic lesions that occurred in the head and neck region in a developing country like ours.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Pathology at Adichunchanagiri Institute of Medical Sciences, BG Nagara, Mandya district, Karnataka, India. All the patients with cytological diagnosis of cysts or lesions with cystic change in the head and neck region over a period of 18 months were taken for the study. Institutional ethical committee clearance was obtained. Total sample size was 162. Brief clinical history including age, sex, site of the lesion, local examination findings and clinical diagnosis was recorded. Ultrasound finding was recorded wherever available. FNAC was done using 22 gauge needles. The

material aspirated was smeared on the slides, excess fluid was centrifuged and sediment smears was made wherever necessary. In all 50% of slides was fixed in 90% ethanol for Hematoxylin and Eosin (H & E) and Papanicoloau staining while 50% was air dried and stained with May-Grunwald Giemsa (MGG) stain. All the cases were categorized into four cytodiagnostic categories as negative/benign, suspicious, positive/malignant and inadequate. Cases in whom frank blood was aspirated (hemangioma)/haematoma and those with uncontrollable bleeding diathesis were excluded from the study. Cystic Lesions were those which on microscopy showed cyst fluid or cyst macrophages.

In cases where surgical excision was performed, the specimen was fixed in 10% formalin and processed routinely for H&E staining. Cytohistopathologic correlation was performed.

STATISTICAL ANALYSIS

Data was expressed as mean values, percentages and proportions. Sensitivity, specificity, positive predictive value and negative predictive value was analyzed.

RESULTS

During this study period, out of total 1800 cases came to our institute, FNAC was done for 162 cases with all the cystic lesions of head and neck region, which accounted 8% of the cystic lesions cases in head and neck region. Three samples yielded only hemorrhagic material even after repeated aspirations and were thus concluded in inadequate smear. Histopathological correlation was available in 88 cases.

Demography

Mean age of patients was 42.75±17.02 years. Male to female ratio was found to be 1:1.9.

Cytodiagnotic Categories

[Table/Fig-1] shows all the 162 cases which were classified into four categories

Categories	Number of cases	Percentage	
Negative/Benign	123	75.92%	
Suspicious	2	1.23%	
Positive/Malignant	34	20.98%	
Inadequate	3	1.87%	
Total	162	100%	

[Table/Fig-1]: Distribution of all the cases according to cytodiagnostic categories.

Cytological Diagnosis in all Cystic Thyroid Lesions

[Table/Fig-2] shows, cytological diagnosis of all the cystic thyroid lesions in 79 cases.

Cytological Diagnosis in all Cystic Salivary Gland Lesions

[Table/Fig-2] shows, cytological diagnosis of all the cystic salivary gland lesions in 15 cases.

Among these 15 cases, benign lesions superseded the malignant lesions (66.6% versus 33.3%), with pleomorphic adenoma and mucoepidermoid carcinoma being the most common tumors encountered in each category.

Categories	Number	Percentage			
Thyroid					
Developmental Thyroglossal Duct Cyst	3	3.79%			
Goitre/ Hyperplastic Colloid Goiter With Cystic Change	47	59.49%			
Adenomatous Goiter with Cystic Change	6	7.5%			
True Cyst Colloid Cyst	7	8.86%			
Inflammatory Hashimoto's Thyroiditis with Cystic Change	2	2.53%			
Suspicious Papillary Carcinoma	2	2.53%			
Malignant Papillary Carcinoma	9	11.39%			
Inadequate	3	3.79%			
Total	79	100%			
Salivary Gland					
Benign Non-Neoplastic Benign Mucinous Cyst	4	26.66%			
Neoplastic • Pleomorphic Adenoma	2	13.33%			
Warthin's Tumor	4	26.66%			
Malignant • Mucoepidermoid Carcinoma • Acinic Cell Carcinoma	3 2	20% 13.33%			
Total	15	100%			

[Table/Fig-2]: Distribution according to cytological diagnosis in all the cystic lesions of thyroid and salivary gland.

Cytological Diagnosis in all Cystic Lymph Nodes Lesions

Out of total 18 cases of cystic lesions in lymph node region, all the 18 cases (100%) were of malignant squamous cell carcinoma.

Cytological Diagnosis in all Cystic Skin Lesions

In the present study out of 45 cases of all the cystic lesions in skin region, 43 cases were keratinous cyst which included 12 cases (26.67%) in scalp, three (6.67%) in eyebrow, six (13.34%) behind and front of ear, eight (17.78%) in lateral side of neck, seven cases (15.56%) in cheek, one case

(2.23%) in nose, five cases (11.12%) in nape of neck and one case (2.23%) on the forearm. Two of the cases (4.45%) were diagnosed as epithelial malignancy on FNAC.

Cytological Diagnosis in all Miscellaneous Cystic Lesions

Out of five cases, all were benign lesions. Four (80%) were cold abscess and one (20%) was lymphatic cyst.

Correlation of Cytologic Diagnosis and Histopathologic Diagnosis

[Table/Fig-3] shows cytological and histopathological diagnosis correlation in total 88 cases of all the cystic lesions of head and neck region.

S. No.	Site	FNAC con- sistent	FNAC non- consistent	HP				
1.	Thyroid							
	Thyroglossal cyst	3		3				
	Colloid goiter with cystic change	17	2	19				
	Adenomatoid goiter with cystic change	2		2				
	Suspicious papillary carcinoma	2		2				
	Papillary carcinoma	9		9				
2.	2. Salivary Gland							
	Benign mucinous cyst	2	1	3				
	Pleomorphic adenoma	2		2				
	Warthin's tumor	4		4				
	Mucoepidermoid cyst	3		3				
	Acinic cystic carcinoma	2		2				
3.	Lymph Node							
	Metastatic SCC	1		1				
4.	Skin							
	Keratinous cyst	35		35				
5.	Miscellaneous							
	Cold abscess	2		2				
	Lymphatic cyst	1		1				
	Total	85	3	88				
[Table/Fig-3]: Cytological and histopathological diagnos								

Histopathology was obtained in 88 cases out of which 85 cases were diagnosed by FNAC.

correlation in all cystic lesions of head and neck region.

Out of the 85 cases of FNAC for which histopathology was available, consistent diagnosis was obtained in 33 cases of thyroid lesions in which three cases were thyroglossal cyst, 17 cases of colloid goiter with cystic change, two cases of adenomatoid goiter with cystic change, two cases of suspicious papillary carcinoma and nine cases of papillary carcinoma.

Among salivary gland lesions 13 cases were consistent with histopathology, two were benign mucinous cyst, two cases of pleomorphic adenoma, four cases of Warthin's tumor, three cases of mucoepidermoid cyst, two cases were of acinic cell carcinoma.

Among lymph node, one case of metastatic squamous cell carcinoma was consistent and 35 cases of keratinous cyst from skin were consistent.

Miscellaneous category included total three consistent cases, which included 2 cases of cold abscess and one case of lymphatic cyst.

Among these 88 cases of FNAC, non-consistent diagnosis was obtained in total 3 cases. The two among these were diagnosed as colloid goiter with cyst change on FNAC, which turned out to be papillary carcinoma on histopathology.

The third case was of benign mucinous cyst on FNAC which was diagnosed as low grade mucoepidermoid carcinoma histologically.

Lesions with cytological diagnosis of inadequate sample were excluded from following calculations

[Table/Fig-4] shows, sensitivity, specificity, positive predictive value, negative predictive value and accuracy in overall cystic head and neck lesions, in thyroid and salivary glands.

	Overall	Thyroid	Salivary Gland
Sensitivity	83.33%	84.62%	83.33%
Specificity	100%	100%	100%
Positive Predictive Value	100%	100%	100%
Negative Predictive Value	88.89%	91.67%	88.89%
Accuracy	92.85%	94.28%	92.85%

[Table/Fig-4]: Shows sensitivity, specificity, positive predictive value, negative predictive value and accuracy in overall cystic head and neck lesions, in thyroid and salivary glands.

DISCUSSION

The major drawback of FNAC in head and neck region is the presence of cysts and cystic change. This cystic transformation has been noted in plethora of lesions ranging from most innocuous benign cyst to the malignant ones with aggressive biologic behavior.

The present study was conducted to evaluate the efficacy of FNAC in the diagnosis of cystic lesions of head and neck region.

Age Distribution

Mean age was found to be 42.75±20 years. This was in accordance with the study of Dejmek A et al., where they reported mean age of 51±25 years [2]. Mean age of cystic lymph node metastasis in the present study was 60 years. This was similar to the study of Ustun M et al., who reported a significantly higher mean age for patients with malignant cysts as compared to benign cyst in lymph node [5]. Several

studies have stated that any cystic lymph node mass in head and neck region over 40 years of age should be considered as malignant unless proven otherwise.

In the present study, mean age of cystic thyroid nodule was 33.9 ± 19 years. This was similar to the findings of de los Santos ET et al., who reported mean age of 47.7 ± 21 years [6].

Male to female ratio was 1:1.9. This was in accordance with the study of Dejmek A et al., wherein authors reported male to female ratio of 1:1 [2]. A slight female preponderance in the present study is explained by the inclusion of thyroid lesions in the present study.

The most common site aspirated in the present study was thyroid. In various other studies lymph node was the most common site followed by thyroid and other organs. The probable reason for this difference may be the higher incidence of thyroid illness encountered in South India as compared to North Indian population [7].

Among salivary gland, parotid was the most common organ involved (60.01%), followed by submandibular gland (20.01%), sublingual gland (6.66%) and lip (6.66%). Similar predilection of parotid gland was documented by Edwards PC et al., in 95.2% of the cases [8].

Maximum number of cases were in the benign category (75.92%) followed by malignant (20.98%) and suspicious (1.23%) category. Dejmek A et al., documented similar findings i.e. maximum cases in the study belonged to benign category (66%) followed by malignant cases (18%) [2].

Thyroid

Most common lesion in present study was diagnosed as colloid goiter with cystic change. Similar findings were reported by Choi KU and Gupta C et al., [9,10].

Carcinoma in thyroglossal duct cyst is rare, the incidence being <1%. FNAC is important in pre-operative diagnosis, and literature on FNAC findings of a carcinoma in TDC is limited. Diligent search for tumor cells and repeat aspirate is mandatory for accurate diagnosis [11].

In the present study there were seven cases of colloid cyst (8.86%). These findings were similar to the findings of Amita K et al., (6%) [12].

In the present study Hashimoto's thyroiditis with cystic change was found in 2.53% of the cases. Cystic change in Hashimoto's thyroiditis is a well-documented phenomenon and a source of pitfall [13]. Hashimoto's thyroiditis can present as solitary thyroid nodule, which may undergo cystic change. Singh A et al., reported a case of solitary nodule with cystic change which was misinterpreted at FNAC as follicular neoplasm with cystic change and which turned out to be Hashimoto's thyroiditis on histopathology [14].

Follicular and Hurthle cell neoplasm is a grey zone area at cytology, since the capsular and vascular invasion, mandatory for the diagnosis of carcinoma cannot be established at

FNAC. Suspicious for papillary carcinoma is a category wherein nuclear changes are patchy and the smears are sparsely cellular. Cystic degeneration pattern is noted. Olson T et al., reported the increase in risk of malignancy in suspicious category after the introduction of the Bethedsa system [15]. In the present study two cases (1.23%) were diagnosed as the suspicious for papillary carcinoma which were confirmed on histopathology.

In the present study, all the nine cases of malignancy (11.39%) were papillary carcinoma. Cystic change is seen in 25% of papillary carcinoma [16]. In these cases, sampling error rather than misinterpretation by pathologist is the cause of high false negative rate ranging from 45% to 67% as reported in various studies [17]. Re-aspiration from the residual solid area after draining the colloid and repeat aspiration are useful in these cases [Table/Fig-5]. Ultrasound guided FNAC allows precise localization of needle in suspicious area and hence improves diagnostic accuracy [12].

Out of 79 cases of thyroid lesions aspirated, surgery was performed in 35 cases (44.30%). Concordant diagnosis was obtained in 33 cases. Discordant diagnosis was obtained in two cases. Both the cases were diagnosed as colloid goiter with cystic change on FNAC, which proved to be papillary carcinoma on histopathology. This inherent limitation of FNAC can be avoided by re-aspiration from solid area, under ultrasound guidance. de Los Santos ET et al., reviewed 221 cases of surgically resected thyroid. The authors observed that the major cause of false negative diagnosis in their study was a cystic papillary carcinoma [6]. The authors observed that the risk of malignancy is same for both solid and cystic lesions [12].

Salivary Gland

In the present study benign lesions out numbered malignant ones. Among the benign lesions, benign mucinous cyst (26.66%) and Warthin's tumor (26.69%) were the most common lesions encountered. This was similar to the findings of Layfield LJ et al., [18].

A systematic approach is recommended for cystic lesions of salivary glands akin to that described for the solid salivary gland lesions. The fluid aspirated is either proteinaceous with lymphohisticocyte rich smear pattern or mucoid in nature. Based on this and nature of the secondary epithelial component seen, a specific diagnosis could be rendered in majority of the cases.

One of the most error prone and clinically significant diagnostic pitfalls of FNAC of salivary gland lesion is a false negative diagnosis in case of low grade MEC. Similar problem was encountered in the present study in one case (7.14%). Most of the time only mucoid material is aspirated and smears show only mucin [19,20].

Clue to the diagnosis of low grade MEC include stringy mucin [Table/Fig-6]. Similarly, diligent search for the presence of clear, mucin secreting cells and intermediate cells should be

made as these have high Positive Predictive Value (PPV) for cytologic diagnosis of MEC. However, at times extremely low grade MEC may have large cystic spaces lined by single row of columnar mucin secreting epithelium which may not find way in smears [18]. Hence, it is advocated that in salivary gland cytology, while reporting a benign mucinous lesion, a note with a caution that a possibility of low grade MEC has to be ruled out should be delivered.

Pleomorphic Adenoma (PA) can at times show cystic change harbouring mucin [Table/Fig-7]. This is a potential trap and can lead to an erroneous diagnosis of MEC [21].

In the present study, Warthin's tumor was reported in 26.69% of salivary gland aspirated and histopathologic correlation was obtained in all the cases. This was in accordance with a study of Layfield LJ et al.,[18]. The presence of characteristic triphasic appearance of oncocytes, lymphoid cells and a dirty debritic background makes diagnosis easy at cytology [Table/Fig-8]. Nevertheless, many a times, this pattern may not be discernable. Predominance of lymphoid cells may lead to a misdiagnosis of lymphoepithelial cyst. Also, Warthin's tumor can be easily missed at cytology if one fails to recognize oncocytes in smears [18].

Moreover, at times presence of atypical squamous metaplastic cells may lead to be false diagnosis of squamous cell

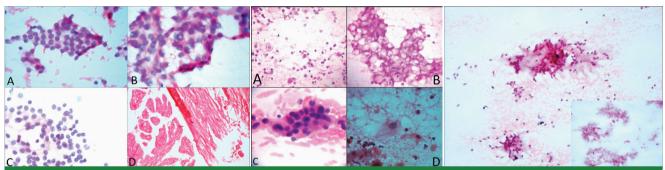
carcinoma. In all such cases careful search for oncocytes will avoid false negative and false positive diagnosis increasing the diagnostic accuracy. In the present study none of this error was observed which is in accordance with the study of Edwards PC et al., [8].

Acinic cell carcinoma- papillary cystic variant (ACC PV) accounted for 13.3% of salivary gland lesions, in the present study [Table/Fig-9]. Ali SZ, in their study involving seven cases of ACC PV, reported that the rarity of this variant and cystic nature often leads to it being misinterpreted as other benign or malignant salivary gland lesions [22].

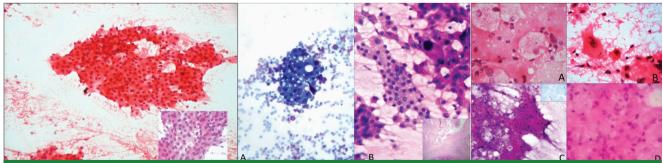
The presence of mono-layered and tight cohesive sheets, high N:C ratio, squamoid, vacuolated, duct like, oncocyte like cells and bare nuclei in a cystic background aids in correct diagnosis.

Lymph Node Lesions

In the present study, 18 out of total 162 cases (11.11%) aspirated were reported as metastatic lymph nodes with cystic change. All of them (18/18) were Squamous Cell Carcinoma (SCC). Tonsil was the most common primary site (44.44 %), followed by tongue (33.33%) and oropharynx (11.11%). In remaining two cases, no primary site could be attributed in spite of thorough work-up. Cystic mass



[Table/Fig-5]: Smears showing anatomical bordering (a) intranuclear inclusion; (b) and intranuclear grooving; (c) - papillary carcinoma with cystic change (H& E, ×100); (d) -histopathology (H& E, ×400). **[Table/Fig-6]:** Smear showing mucinoophages, chronic inflammation and mucin in benign mucinous cyst (a) mucin secreting cells; (b) intermediate cells; (c) and dykeratotic cells in low grade MEC with cystic change. **[Table/Fig-7]:** Smear showing oncocytes in WT with cystic change (H & E, ×40). Inset - high power (H & E, ×400).



[Table/Fig-8]: Smears showing epithelial cells along with inset showing chondromyxoid stroma in mucinous background in PA with cystic change (H & E, ×100). [Table/Fig-9]: Smears showing tumor cells with vacuolated cytoplasm (a), duct like cells, vacuolated cells, oncocytic like cells anisokaryosis (b) in acinic cell and carcinoma and cystic change (H & E, ×100). Histopathology of same (Inset in B) (H & E, ×100). [Table/Fig-10]: FNAC smears showing foamy histiocytes and proteinaceous material representing cystic change from a case of metastatic squamous cell carcinoma in lymph node (a) dyskeratotic cells in metastatic deposit of squamous cell carcinoma (b) (H & E, ×400). (c) shows caseous necrosis and (d) shows granulomas - cold abscess (H & E, ×400). Inset shows acid fast bacilli (Zeihl Neelsen stain x 1000).

in the head and neck region is the most common mode of presentation of metastatic deposits of head and neck malignancy, more so in adults above 40 years of age. Most common malignancy metastasizing being SCC and papillary carcinoma thyroid. Studies have affirmed to the finding that metastasis of squamous cell carcinoma from tonsils have a propensity to produce cystic masses [Table/Fig-10] [23].

The mechanism of cystic change in lymph node metastasis has been a matter of speculation. One hypothesis is the phenomenon of true cyst formation lined by malignant cells and lymphoid tissue. These true cysts have an origin from salivary duct epithelium or transitional keratinocytes which have ability for cyst formation.

The necrosis over time undergoes liquefaction and on aspiration appears as yellow dirty material. After aspiration, swelling reduces in size. Furthermore, superadded acute inflammation may render the picture murkier.

Significance of FNAC in diagnosis of metastatic deposits in solid lymph node is 100%, while in cyst it is 50-60%. Similarly, false negative rate in solid lesion is 3% while in cystic lesion, it is 63%. Taking into consideration all these aspects, it is wise to follow certain principles-

- Any cystic mass over 40 years of age, which yields necrotic material-consider metastatic deposits, unless proven otherwise.
- 2) Centrifuge the fluid and examine sediment smears diligently for dyskeratotic cells.
- 3) In presence of acute inflammation masking the true nature, advise repeat FNAC after a short course of antibiotic.
- 4) Ultrasound guided FNAC can be helpful.

One of the major pitfalls is the difficulty encountered in differentiating metastatic squamous cell carcinoma with cystic change from an infected keratinous cyst in presence of reactive atypia, branchial cyst and Warthin's tumor with squamous metaplasia.

At such time, importance to the nuclear features like hyperchromasia, irregularities in nuclear membrane, anisokaryosis and dyskeratotic cells avoid false diagnosis.

Occasionally granulomatous reaction to keratin may supervene the smears and a false diagnosis of Tuberculosis (TB) is rendered [Table/Fig-10]. Presence of keratin and foreign body giant cells are clues to the cytologic diagnosis of keratinizing squamous cell carcinoma.

Inflammatory Lesions-Miscellaneous

Various infections and inflammatory lesions presenting as cystic head and neck masses include abscess of bacterial, fungal or tubercular origin and cellulitis. Viswakarma SK et al., reported a case of 13-year-old female with cystic swelling on the tongue. Cytology of tongue swelling and lymph node established the diagnosis of cold abscess and patient responded well to anti-tubercular therapy [24].

Dermoid and Epidermoid Cyst

Keratinous cyst has predilection for head and neck region. At cytology both dermoid and epidermoid cyst show nucleate and anucleate squamous in a keratinous debritic background. Rarely a hair shaft or a sebaceous lobule may appear in the cytology smear of dermoid cyst allowing type specific diagnosis.

Subtyping keratinous cyst has no clinical connotation, except for the fact that 5% of these cysts may undergo malignant transformation. Thus, FNAC is useful in pre-operative diagnosis of all keratinous cysts in such suspected cases [25].

Hence, the sensitivity and specificity of FNAC in cystic lesions of head and neck region is similar to that reported in the literature.

LIMITATIONS

Major limitation is the small number of cases with surgical follow-up. Further studies involving a large number of cases with surgical follow-up are necessary.

CONCLUSION

Many head and neck lesions ranging from non-neoplastic to malignant tumors can undergo cystic change. FNAC is a simple, safe and effective tool and can be used in preoperative diagnosis of cystic lesions of head and neck.

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