Original Article

Cytohistological Study of Head and Neck lesions and their Diagnostic Pitfalls

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ABSTRACT

Background: Head and neck swellings often present with a perplexing diagnostic dilemma and may originate from lymph nodes, thyroid and salivary glands. FNAC is presently employed for both therapeutic and prognostic reasons, thereby helping the surgeon to decide modality of treatment. Thus this study was conducted with an aim to correlate cytological diagnosis of head and neck swellings with histopathology and to compare statistical data employing sensitivity, specificity and diagnostic accuracy.

Methods: This was a retrospective study carried out for duration of 3 years and included 1231 cases referred to the Department of Pathology. FNAC was done from palpable head and neck masses and correlated with histopathology findings. Statistical analysis was done to calculate the sensitivity, specificity and diagnostic accuracy of cytological diagnosis.

Results: Of 1231 cases for which FNAC was done, 234 cases were available for histopathological correlation. There was an overall male preponderance with male:female ratio being 1.04:1. The age of patients ranged between 16 years to 90 years. The maximum number of aspirates were from lymph nodes (680 cases, 55.23%) followed by thyroid gland (324 cases 26.32%), neck and post-auricular swellings (117, 9.5%) and salivary gland (110, 8.9%). Statistical analysis was done to calculate overall diagnostic accuracy, sensitivity and specificity of FNAC and was found to be 93.4%, 72.8%, 97.3% respectively.

Conclusion: FNAC is a fairly accurate, reliable and cost effective method for rapid and reliable diagnosis of palpable lesions in the head and neck region, thus helping the surgeon modify or monitor his surgical approach.

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Introduction

The aspirates from head and neck region encompass lesions from salivary glands, thyroid, lymph node, soft tissue, blood vessels and neural tissue and have variable pathology ranging from benign inflammatory lesions to neoplasms. Fine needle aspiration cytology (FNAC) which was originally described by Martin and Ellis is considered an excellent first line method with high specificity for investigating the nature of palpable swellings in the head and neck region, thus obviating the need for surgical intervention. [1,2] It has an important role in diagnosing head and neck tumors that account for almost half of all the tumors at different body sites with high specificity. [3] Further, the lesions can be categorized into inflammatory/ benign and malignant with a high degree of specificity. [4]Thus this study was undertaken to study the spectrum of head and neck lesions and to correlate the cytological results with histopathological examination. Descriptive statistics was done to evaluate our results.

Materials and Methods

This was a retrospective study carried out for duration of 3 years and includes 1231 cases of head and neck swellings referred from department of otorhinolaryngology for pre-operative FNAC and subsequent histopathological evaluation. The study was vetted and approved by Institutional Ethics committee.

Prior to FNAC a detailed clinical history and clinico-radiological findings were noted in a preformed proforma and informed consent was taken. Subsequently fine needle aspiration was done using 22-23 G needle attached to a 10 ml plastic disposable syringe. For all the palpable swellings of head and neck region atleast four smears were made and stained by May-Grunwald Giemsa, Hematoxylin & Eosin (H&E), and Papanicolou stains. A few unstained smears were fixed and kept for Ancillary stains and/or immunochemistry as and when required.

Out of 1231 cases, surgical biopsies were available for 234 cases for histopathological correlation. The cytology results were classified into the following categories: true negative (absence of malignancy correctly diagnosed); true positive (presence of malignancy correctly diagnosed); false negative (the cytological specimen failed to diagnose as malignancy); and false positive (the cytological specimen was incorrectly considered or suspect of malignancy).

Data analysis was based on Galen and Gambino method which calculated sensitivity and specificity of cytology in differentiating benign and malignant lesions.

Results

Total number of cases for which FNAC was done was 1231. Amongst these 630 patients were males and 601 were females, with an overall male to female ratio of 1.04:1. The youngest patient in this series was 16 years old and the eldest 90 years old with the mean age of 34.24 years. Of all these cases, 234 patients were subjected to surgical intervention and subsequent histopathological examination and were thus available for cytohistological correlation. All 1231 cases were categorized cytologically, on the basis of site of origin into lesions of lymph nodes, thyroid, salivary glands and neck and postauricular swellings. They were broadly classified into inflammatory, benign and malignant lesions (Table 1).

Lymph Nodes: Of 680 cases for which FNAC was performed, 72 cases were available for cyto-histopathological correlation. The most common group of lymph nodes involved was deep jugular group (63.9%), followed by supraclavicular group (9.3%). Lymph node lesions were categorized into benign and malignant lesions. Of 72 cases the final diagnoses under benign lesions were tuberculosis (18 cases), reactive lymphadenitis (16 cases), sarcoidosis (1 case), inflammatory (1 case) and under malignant conditions were Hodgkins disease (8 cases), Non Hodgkins lymphoma (10 cases), metastatic (16 cases) and angio-immunoblastic (2 cases).There were one false positive and six false negative cases in this group (Table no 2).

Thyroid: Total number of patients who presented with thyroid swelling were 324 with commonest clinical complaint of enlargement of thyroid gland associated with voice change and difficulty in swallowing. The female to male ratio for thyroid lesions was 2.4: 1 thus exhibiting a paradox in this group with female preponderance. Of these 324 cases for which FNAC were performed, 69 cases were subjected to surgical intervention hence available for cyto-histopathological correlation. On FNAC, the thyroid lesions were classified as colloid goiter (51 cases), cystic nodule (3 case), lymphocytic thyroiditis (10 cases), granulomatous thyroiditis (1 case), follicular neoplasm (6 cases), medullary carcinoma (2 cases), papillary carcinoma (2 cases), hurthle cell neoplasm (1 case), and Non hodgkins lymphoma (1 case). Considering histopathology as gold standard, 54 cases were benign and 12 cases were malignant. There were 5 false positive in this group (Table no 3).

Salivary Glands- Of 110 salivary glands swellings 40 cases were subjected to surgical intervention hence available for cyto-histopathological correlation. Of these 40 cases, 15 cases were female and 25 were males. Parotid was the commonest salivary gland to be involved. Of all the 40 cases, 27 cases were benign and 13 cases were malignant on histopathology. The commonest salivary gland lesion

was pleomorphic adenoma (18 cases), followed by chronic sialdenitis and Warthin's tumour (4 cases each). Amongst the malignant salivary gland lesions, Mucoepidermoid carcinoma, Adenoid cystic, and Squamous cell carcinoma accounted for 2 cases each. There were 3 false positive cases in this group (Table no 4).

Neck and Post Auricular Swelling- Of 117 cases, which presented with neck and post-auricular soft tissue swellings, 53 cases were sent for histopathology and were available for cyto-histopathological correlation. Of these 53 cases, 37 were males, and 16 were female. Overall 51 cases were diagnosed as benign on histopathology. Castleman's disease, a morphologically distinct form of hyperplasia, was cytologically diagnosed as reactive hyperplasia. Two cases of Basal cell carcinoma (BCC) and metastatic deposit of squamous cell carcinoma which were diagnosed as benign cystic lesions on cytology respectively were malignant (Table no 5). There were one false positive and one false negative diagnosis in this group.

Statistical analysis was done and sensitivity, specificity and diagnostic accuracy was calculated (Table no 6). Overall diagnostic accuracy was found to be 93.4%, sensitivity 72.8%, specificity 97.3%, positive predictive value 95.5% and negative predictive value 91.9% respectively.

Table 1: Distribution of 1231 cases of head and neck swellings on cytological diagnosis.

Site	Inflammatory	Neoplastic		Inconclusive	Total
		Benign	Malignant		
Lymph node	34 (5%)	531(78.1%)	91 (13.4%)	24 (3.5%)	680
Thyroid	59 (18.2%)	230(70.98%)	20 (6.2%)	15 (4.62%)	324
Salivary glands	42 (38.2%)	47 (42.72%)	16 (14.5%)	6 (5.45%)	110
Neck and postauricular swellings	16 (13.7%)	79(67.52%)	4 (3.4%)	17 (14.5%)	117
Total	**151**	**887**	**131**	**62**	**1,231**

Table 2: Cyto-Histological Correlation of Lymph Node lesions.

Cytological diagnosis	Number of cases	Histopathological diagnosis			
		Benign (N)		Malignant (N)	
Reactive hyperplasia	21	Reactive	16	Angioimmunoblastic HL NHL	2 2 1
TB/granuloma	19	Tuberculosis Sarcoidosis	17 1	HL	1
Inflammatory	1	Inflammatory	1		
HL	5			HL	5
NHL	10	Reactive	1		
Metastatic	16			Metastatic	16

Table 3: Cyto- Histological Correlation of Thyroid lesions.

Cytological diagnosis	Number of cases	Histopathological diagnosis			
		Benign (N)		Malignant (N)	
Colloid goiter	51	Colloid goiter Graves disease Hashimoto's thyroiditis Hurthle cell Adenoma	42 3 3 1	Papillary Carcinoma	2
Cystic nodule	3	Colloid goiter with cystic degeneration	2	Papillary Carcinoma	1
Lymphocytic thyroiditis	10	Lymphocytic thyroiditis Colloid goiter	7 3		
Granulomatous thyroiditis	1	Colloid goiter with granulomatous thyroiditis	1		
Follicular neoplasm	6	Follicular Adenoma Adenomatous goiter	1 3	Folicular Carcinoma	2
Medullary carcinoma	2			Medullary carcinoma	2
Papillary carcinoma	4			Papillary Carcinoma Follicular variant of Papillary Carcinoma	3 1
NHL	1				
Hurthle cell neoplasm	1	Follicular Adenoma	1		

Table 4: Cyto- Histological Correlation of salivary Gland lesions.

Cytological diagnosis	Number of cases (n)	Histopathological Diagnosis			
		Benign (N)		Malignant (N)	
Lipoma	2	Lipoma	2		
Chronic Sialadenitis	5	Sialadenosis Chronic sialadenitis	1 4		
Haemorrhagic cyst	1	Hemangioma	1		
Pleomorphic Adenoma	21	Pleomorphic adenoma Basal cell adenoma	18 1	Mucoepidermoid Carcinoma Adenoid cystic carcinoma	1 1
Mucoepidermoid Carcinoma	1			Mucoepidermoid Carcinoma	1
Squamous cell Carcinoma	3			Squamous cell Carcinoma Adenoid cystic carcinoma	2 1
Oncocytoma	1			Acinic Cell Carcinoma	1
Warthin's tumour	5	Warthin's tumour	1		
Oncocytic carcinoma	1			Salivary duct carcinoma	1

Table 5: Cyto-Histological Correlation of Neck and Post auricular Swellings.

Cytological diagnosis	Number of cases (n)	Histopathological diagnosis			
		Benign (N)		Malignant (N)	
Granulomatous Inflammation/ TB	5	Tuberculosis Sarcoidosis Castleman disease	3 1 1		
Lipoma	12	Lipoma	12		
Epidermoid cyst	21	Epidermoid cyst ProliferatingTrichilemmal Cyst Mature teratoma	19 1 1		
Sebaceous cyst	1	Sebaceous cyst	1		
Spindle cell lesion	1	Neurofibroma	1		
Neurofibroma	1	Neurofibroma	1		
Basal cell carcinoma	1			Basal cell carcinoma	1
NHL/PNET	1	Calcifying Epithelioma of Malhurbe (Pilomatricoma)	1		
Benign Vascular lesion	5	Hemangioma	5		
Benign cystic lesion	5	Thyroglossal cyst Brachial cyst	3 1	Metastatic deposit of Squamous cell carcinoma	1

Table 6: Sensitivity, Specificity and Diagnostic Accuracy of FNAC in diagnosis of Head and Neck lesions in this study.

Organ of origin	HPE/FNAC	Sensitivity	Specificity	Accuracy
Lymph node	72/680	83.3%	97.2%	90.3%
Thyroid	69/324	58.33%	100%	93.7%
Salivary Glands	40/110	56%	100%	90%
Neck and Post Auricular swelling	53/117	50%	95.23%	95.5%
Total	**234/1231**	**72.8%**	**97.3%**	**93.4%**

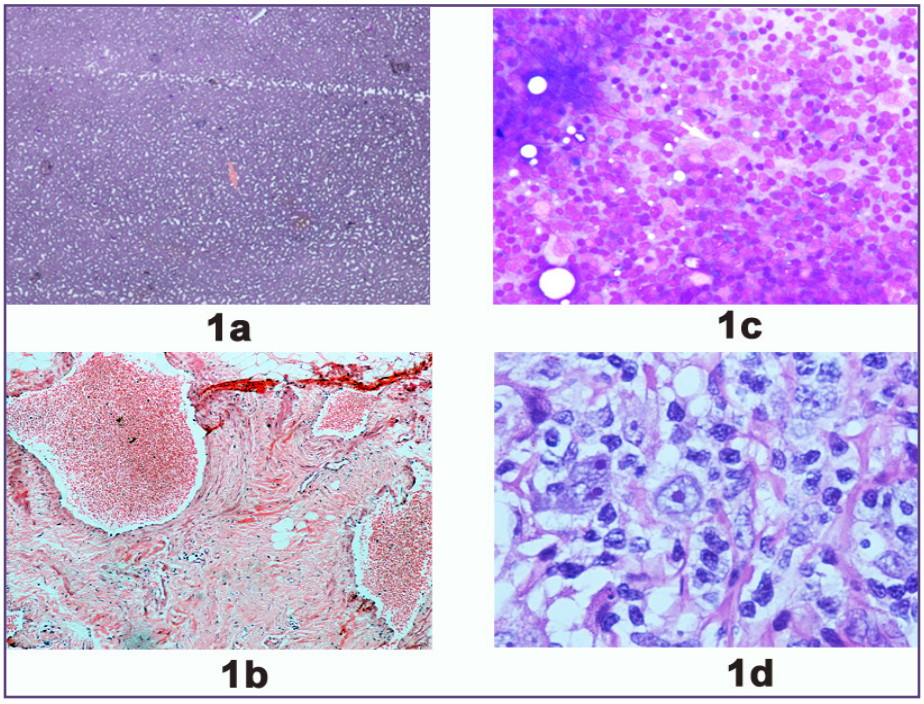

Fig. 1a: Cytology smears showing only RBC (MGG,100X) suggestive of Heamorrhagic cyst with corresponding tissue section showing dilated cavernous spaces filled with RBC seperated by connective tissue stroma in 1b (H&E,100X) 1c. Cytology smears showing RS cell diagnosed as Hodgkins lymphoma (MGG, 400X) with tissue section exhibiting mononuclear variant of RS cell in 1d (H&E, 400X).

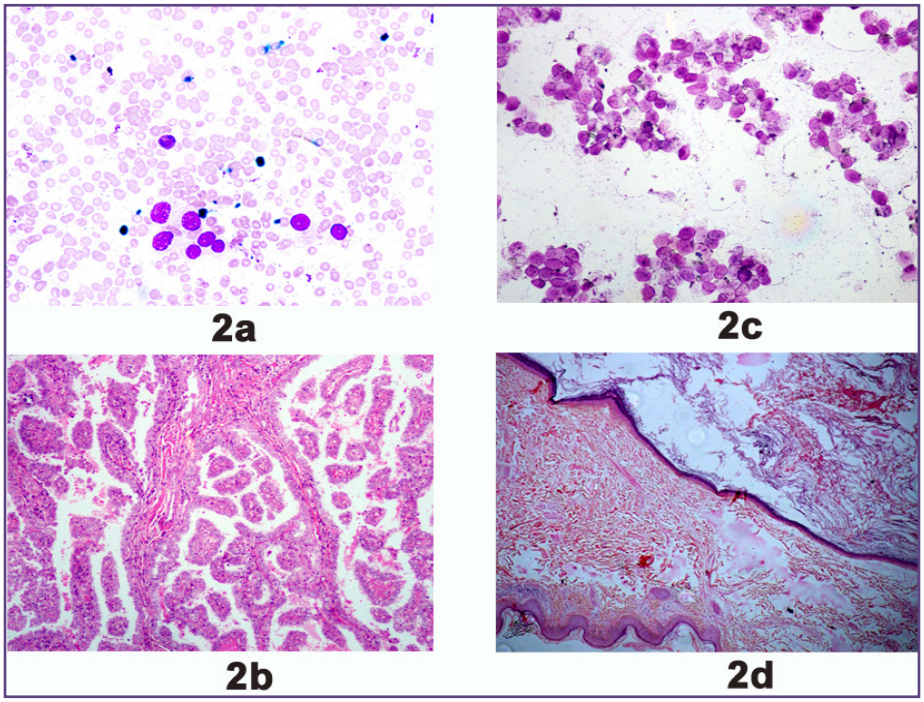

Fig. 2a: Cytology smear from nodule thyroid showing prominent intranuclear inclusion against haemorrhagic background (MGG,100X) with corresponding tissue section showing papillae and cells exhibiting Orphan Annie Eye nuclei in 2b (H&E, 100X). 2c. Cytology smears shwing numerous anucleate squames diagnosed as sebaceous cyst (MGG, 100X) with corresponding tissuesection showing well formed cyst filled with abundant keratin in 2d (H&E, 100X).

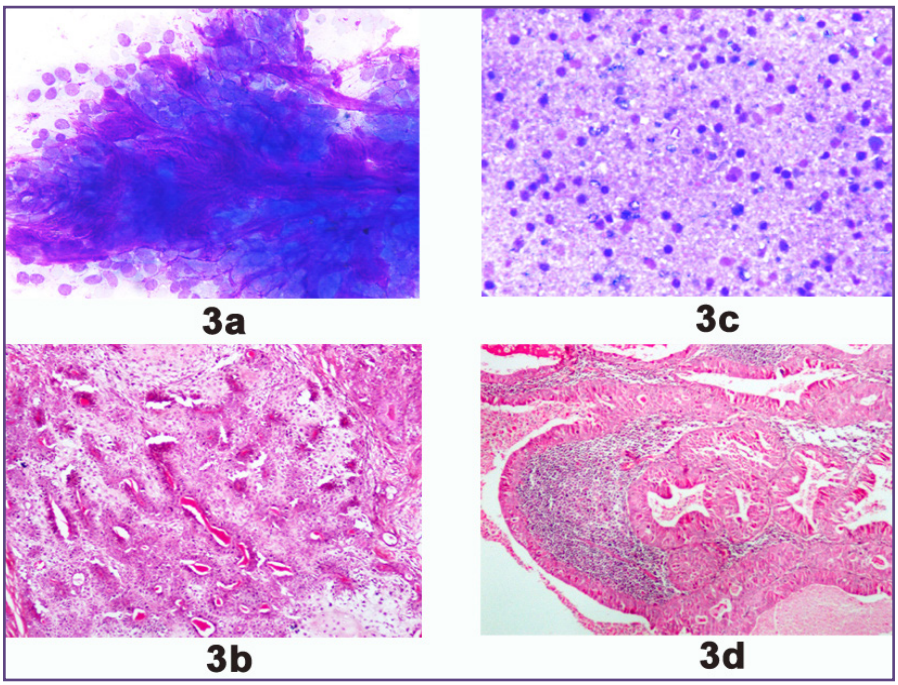

Fig. 3a: Cytology smears showing epithelial cells associated with fibrillar myxoid background in Pleomrphic Adenoma (MGG,100X) with corresponding tissue section exhibiting bimodal population of epithelial and myoepithelial cells in 3b (H&E, 100X) 3c Cytology smear showing monolayered sheets of uniform oncocytic cells, lymphocytes against amorphus background in Warthin's tumour (MGG, 100X) with corresponding tissue section showing oncocytic epithelium resting on lymphocytes in 3d (H&E,100X).

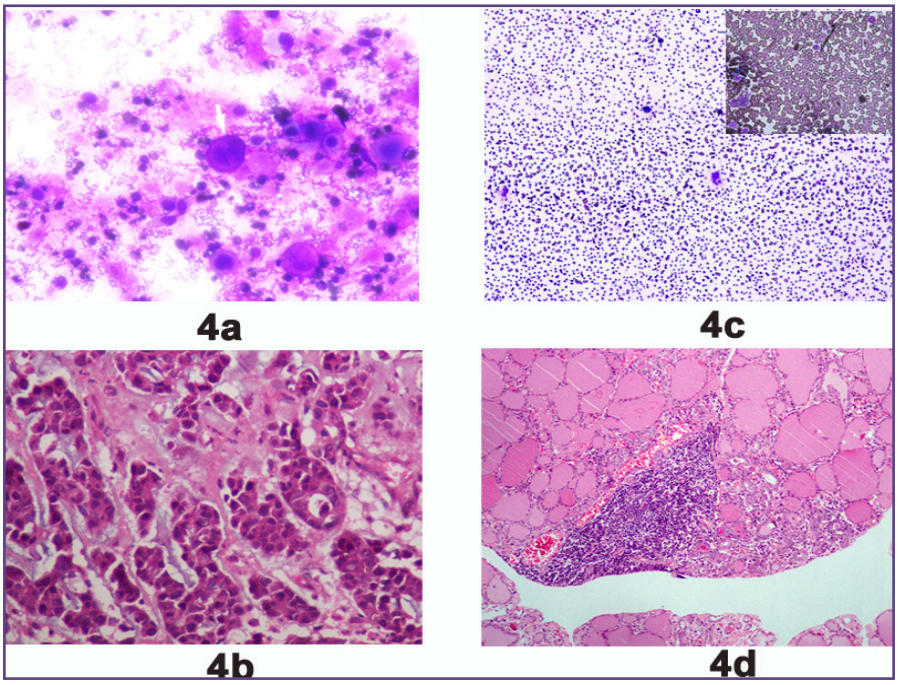

Fig. 4a: Smear showing poorly cohesive malignant epithelial cells with hyperchromatic nuclei against necrotic background diagnosed as Squamous Cell Carcinoma (MGG, 400X) with corresponding tissue section in 4b showing Adenoid Cystic Carcinoma (H&E, 400X) 4c. Smear showing thin colloid and follicular epithelial cells diagnosed as colloid goiter (MGG 100X) with corresponding tissue section in 4d showing destruction of thyroid follicles by lymphocytes in Hashimoto's thyroiditis (H&E, 100X)

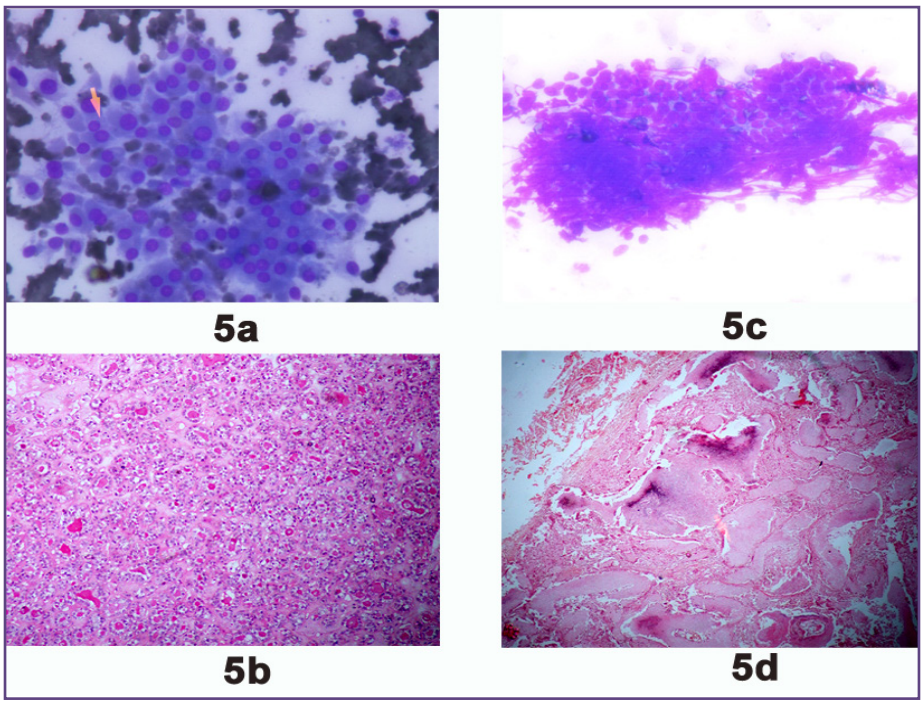

Fig. 5a: Smear showing sheets of oxyphill cells diagnosed as Hurthle cell Adenoma (MGG, 400X) with corresponding tissue section in 5b showing well circumscribed Follicular Adenoma(H&E, 100x). 5c Smear showing monotonus population of cells diagnosed as NHL/PNET (MGG,400X) with tissue section corresponding tissue section showing ghost cells diagnosed histologically as Pilomatricoma in 5d (H&E, 100x).

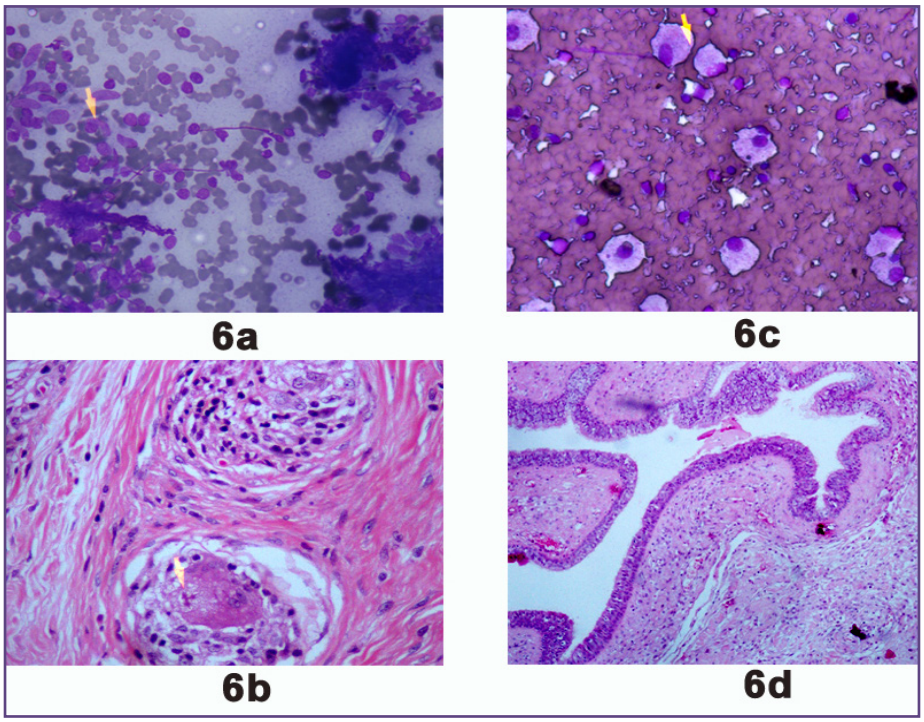

Fig. 6a: Smear showing epithelioid cells cytologically diagnosed as granulomatous lesion (MGG, 400x) with tissue section showing solid granulomas, Arrow showing: giant cell with Asteroid body in Sarcoidosis (H&E, 400X). 6c Smear showing many cyst macrophages against diagnosed as benign cystic lesion (MGG 400X) with Corresponding tissue section in 6d showing Thyroglossal cyst (H&E, 100X).

Discussion

Head and neck masses are common clinical conditions and FNAC serves an important first line investigation thus providing useful information to surgeon to determine further management. Being minimally invasive it is a preferred investigation particularly in young patients who have low incidence of malignancy and in patients who are in palliative settings. [2] Furthermore, most head and neck masses of distinct cause present in fairly predictable locations within specific age group. This permits a methodical approach to clinch a working diagnosis and a differential diagnosis and appropriate treatment protocol for the patients.

Of all the 1231 cases for which FNAC was done, histopathological correlation was available for 234 cases. Evaluation of palpable head and neck swellings demands a systematic and rational approach. Organ wise cytological findings were thus correlated with histopathological diagnosis (Table no 7). Establishing the exact nature of swellings and preliminary identification of lesion as cystic, inflammatory or neoplastic substantially obviates unnecessary surgeries in a significant number of cases.

All 1231 cases were divided into inflammatory, benign and malignant lesions. In the present study 62 cases (5.04%) were rendered inconclusive. The inconclusive lesions in head and neck masses ranged between 0-22% and 3-30% which correlates well with our study. [6,7] The inconclusive cases were mainly due to small size of swelling (<1cm), hemorrhagic aspirate and lesions with extensive fibrosis and necrosis.

In the present study maximum number of aspirates were from lymph nodes (680 cases, 55.23%) followed by thyroid gland (324 cases 26.32%), neck and post-auricular swellings (117, 9.5%) and salivary gland (110, 8.9%) which Correlates well with other studies. [5,8]

Lymph Node: Highest degree of sensitivity (83.3%) was seen in diagnosing lymph node pathologies. Of 72 cases for which histological correlation was available there were one false positive and six false negative cases. Tubercular lymphadenitis was the commonest diagnostic pathology which correlated well with studies by other authors. [9] Tuberculosis is widely prevalent in developing countries with prevalence as high as 1.5% and tubercular cervical lymphadenopathy being the most common form of extrapulmonary tuberculosis. FNAC has been reported to have 90-100 % diagnostic accuracy in detection of tuberculous affliction of nodes. [7,10]

The percentage of reactive lymphadenitis (22.2%) was next only to Tubercular lymphadenitis (23.6%) and is comparable to studies by other authors. [11]

In our study two cases diagnosed as reactive lymphadenitis were histologically diagnosed as Hodgkin's disease and Non Hodgkin Lymphoma respectively on histopathology. The diagnostic dilemma arising in distinguishing cytologically between reactive lymphadenitis and TB from lymphomas may be due to cluster of epithelioid cells, tingible body macrophages and polymorphous population of lymphocytes found in lymphomas.[13] Thus the presence of these features does not necessarily rule out lymphoma and its classification must be made on adequate tissue biopsy. [9]

Likewise one case was diagnosed as NHL on cytology turned out to be reactive lymphadenitis on histopathology. Aspirates from germinal centers from reactive hyperplasia may lead to erroneous results owing to increased number of large cells and increased mitosis and is well known to produce False Positive diagnosis.[13]

Two cases of Angioimmunoblastic lymphadenopathy (AILD) were cytologically diagnosed as reactive hyperplasia. AILD is referred by most authors as a form of peripheral T- cell Lymphoma. [14] An exuberant benign reactive host inflammatory reaction is characteristic in producing difficulty in its separation from reactive lymphadenopathy. Initial diagnosis is usually confirmed by tissue biopsy. Ancillary test to confirm diagnosis is by flow cytometry which detects abnormal T- cell antigen expression. [15,16] According to Frable et al cytological diagnosis was used preliminary for the documentation of residual or recurrent lymphomas and to assess the stage of disease. The use of FNAC to render preliminary diagnosis of lymphomas remains controversial. [17]

Table 7: Organ wise FNAC diagnosis correlation with HPE.

FNAC diagnosis	Correlation with Histopatholgy			
	Total Number (n)	Present	FP	FN
Lymph Node	72	65	1	6
Thyroid	79	74	0	5
Salivary gland	40	36	0	4
Neck & Post auricular swelling	53	5	1	1

FP- False Positive FN-False Negative

The diagnostic accuracy in diagnosing metastatic deposits involving cervical lymph nodes was 100% in our study. However, partial lymph node involvement, micro metastases in sub capsular sinus or scattered single cells are unlikely to be sampled by repeated aspiration hence are the main causes of false negative cytological reports. [13]

Thyroid: Out of 324 aspirates of thyroid lesions, 79 surgical biopsies were available for histopathological correlation. Of 79 cases, 67(84.8%) were benign lesions and 12 (15.2%) were neoplastic lesions. Out of these 67 benign lesions 53 cases were diagnosed as colloid goiter (67.1%), which was the commonest pathology observed in this group. Amongst the malignant lesions, Papillary carcinoma thyroid was the commonest neoplasm (7.6%).

Two cytologically diagnosed cases of colloid goiter turned out to be papillary carcinoma on histopathology. Such erroneous interpretations have also been reported by other authors. [9] The cause of false negative results may be due to poor cellularity, sampling error in case of small focus of neoplasm, absence of papillary fragments that fail to demonstrate intranuclear inclusions and nuclear grooves.[18]

One case diagnosed as thyroid cyst on FNAC on the basis of scant cellularity, foamy macrophages, few follicular cells and colloid was histologically confirmed as Papillary carcinoma. Cystic lesions of thyroid pose diagnostic difficulties which have been well observed by other authors. [19] Recurrent cysts, incompletely decompressed lesions, lesions greater than 3- 4 cm in diameter in which aspiration of several areas does not give evidence of colloid nodule and lesions in young male are indications for surgical excision. [20]

Another diagnostic dilemma in FNAC of thyroid lesion is to differentiate follicular adenoma from follicular carcinoma. Similarly, colloid goiter may be difficult to differentiate from adenoma. Similar observations have beencited by other authors who have stressed that the cytological appearance in colloid goiter and follicular adenoma is overlapping and the cytological criteria cannot distinguish between the two. [19] Three cases of Hashimoto's thyroiditis were cytologically diagnosed as nodular colloid goiter. On reviewing slides, they revealed hypocellular smears comprising few follicular cells and scant colloid. Studies by other authors suggest similar diagnostic dilemma. [21]

One case in this group demonstrated dual pathologies as colloid goiter with granulomatous thyroiditis on histopathology. Studies by other authors have emphasized the same observation of finding two or more surgical pathology on histology amongst thyroid lesions. Multiple aspirations in a thyroid swelling in order to obtain representative material from different areas is indicated since the thyroid may be affected by more than one disease process.[22]

Salivary Gland: In our study, of all the salivary glands, Parotid were most frequently involved salivary gland and Pleomorphic Adenoma was the commonest lesion reported. There were 4 false negative cases, however no false positive case was seen in this group. A case of Mucoepidermoid carcinoma was diagnosed as pleomorphic adenoma on FNAC. Studies by other authors suggest that low grade mucoepidermoid carcinoma is one of the most difficult entities to diagnose cytologically and is the source of false negative results.

One case of Pleomorphic Adenoma was found to be Adenoid Cystic carcinoma on histopathology. On reviewing the smears, cluster of uniform cells in myxoid stromal background were noted with notable absence of hyaline globules. Similar findings were noted by other authors.[23]

One case of acinic cell Carcinoma was misdiagnosed as Warthin's tumour on cytology hence reported as false negative. Studies by authors have documented that Acinic Cell carcinoma is most frequently misdiagnosed as Warthins tumour. Such difficulties arise because of close resemblance of acinar cells of acinic carcinoma with sheets of oncocytes. [24]

Neck and Post Auricular Swellings: Amongst the miscellaneous lesions from Neck and Posterior auricular swellings 1 case was false positive and 1 false negative. A case of Pilomatricoma was given as NHL on cytology and hence rendered False Positive. On reviewing smears hyperchromatic cells with prominent nucleoli were seen that were misdiagnosed as Lymphoma. Wrong et al in his study of 16 cases on Pilomatricoma observed that a correct diagnosis could be given only in 25% of the cases. The most common diagnostic pitfall was a false positive or suspicious diagnosis of carcinoma. [25]

A case of metastatic deposit of well differentiated squamous cell carcinoma was cytologically diagnosed as benign cystic lesion (brachial cyst) since smears revealed only necrotic material due to liquefactive necrosis.[26]

Another case of Post auricular swelling cytologically diagnosed as Reactive hyperplasia proved out to be Castleman's disease on histopathology. On reviewing the smears they showed abundant plasma cells. The plasma cell

lesion represents an earlier and active stage of disease that may lead to diagnostic errors on cytology. The cytologic characterization of Castleman's disease may be difficult. [27]

The sensitivity, specificity and Accuracy of present study were 72.8%, 97.3%, 93.4% respectively and are comparable with studies by other authors and are fairly accurate.[6,9,28]

Conclusion

FNAC is simple and fairly accurate method of diagnosing palpable head and neck swellings with a high diagnostic accuracy. It can be employed for both the neoplastic and non neoplastic lesions and is a highly effective diagnostic procedure in the diagnosis and management of head and neck masses. In the present study there were only 2 false positive cases and 16 false negative cases.

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