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CYTOLOGICAL STUDY OF VARIOUS THYROID LESIONS AND EVALUATION OF EFFICACY OF FNAC IN DIAGNOSIS OF THYROID LESIONS.

Pathology

Dr. Vijay Kumar Jha MD, Tutor, Department of pathology, VIMS, pawapuri, Nalanda, Bihar.

Dr. Seema Sinha* MD, Tutor, Department of pathology, VIMS, pawapuri, Nalanda, Bihar. *Corresponding Author

Dr. Imtiaz Ahmad MD, Associate professor, Department of pathology, VIMS, Pawapuri, Nalanda, Bihar.

ABSTRACT

Background: Thyroid lesions are common endocrine disorders now-a-days and thyroid malignancies are most common endocrine malignancies worldwide. Fine needle aspiration cytology is one of the established firstline diagnostic techniques that is rapid, accurate and cost effective in evaluation of thyroid lesions.

Aims And Objectives: Present study was intended to know the prevalence of various thyroid lesions in our center and also to evaluate efficacy of FNAC in evaluation of thyroid lesions.

Material And Methods: This is a prospective and retrospective study comprising of 250 cases registered between July 2018 to June 2021 and whose FNAC was performed in the department of pathology and also thyroid FNAC slides obtained from outside laboratories for review and second opinion. Relevant clinical data including age, sex, clinical features, radiological and thyroid function tests were noted. Cytological reporting was done according to conventional cytopathology reporting and BETHESDA system into nondiagnostic, benign, follicular lesions of undetermined significance, follicular neoplasm/Hurthle cell neoplasm, suspicious of malignancy and malignant lesions.

Results: a total 250 FNAC were included in the study. Total 3 cases (1.2%) were inadequate, 208 (83.2%) were benign, and 39 neoplastic cases including 17 follicular neoplasm, 5 Hurthle cell neoplasm, 8 papillary carcinoma thyroid, 3 medullary carcinoma thyroid, 4 anaplastic carcinoma thyroid and 2 cases of Non Hodgkins lymphoma.

Conclusion: The results of our study are consistent with previous studies and further supports FNAC as a reliable, accurate and cost effective method in diagnosis of thyroid lesions.

KEYWORDS

FNAC, cytology, follicular neoplasm, papillary carcinoma, colloid, anaplastic carcinoma

INTRODUCTION

Thyroid disorders are one of the commonest endocrine disorders[1] and is second only to diabetes. Majority of the thyroid lesions clinically present as thyroid swellings in the form of nodular elargement or as diffuse enlargement of the gland. Prevalence of thyroid nodules is about 4-7% of general population [2,3,4,5]. Most of the thyroid nodules are benign.[2] Incidence of thyroid cancer in patients with thyroid nodules is 5-20% for the general population and about 18-30% for those exposed to ionising radiation.[6,7,8] Children and adolescents are not exempted from thyroid neoplasm and malignancies hence needs inclusion in studies.[9] Palpable thyroid nodules comprises of various nonneoplastic and neoplastic conditions including both benign and malignant lesions. The non-neoplastic lesions of thyroid gland include: goitre, dyshormonogenetic goitre, thyroiditis, hyperplastic nodule, simple cyst and thyroglossal cyst. Follicular neoplasm, Hurthle cell neoplasm, papillary carcinoma, medullary carcinoma and anaplastic carcinoma are among the neoplastic entities.

Thyroid malignancies are commonest endocrine malignancies. FNAC is one of the first line investigations which is highly accurate, widely accepted, rapid, cost effective method with minimum complications. [10,11] The thyroid gland being superficial is easily accessible for FNAC.[12.13] Prior distinction between benign and malignant lesion is essential for proper management, extent of surgery and also in decreasing unnecessary surgical interventions.[14.15] FNAC is a proven and effective method to distinguish benign from malignant lesions.[16] Ultrasound guided FNAC improves efficacy by aspirating the representative sample and decreases number of false negative cases. [17.18]

Aims And Objectives :

This study was done to know the cytological patterns of various thyroid lesions by FNAC and to evaluate the efficacy of cytological study in diagnosis and management of patients with thyroid nodules.

MATERIALS AND METHODS

Present study was carried out in the Department of Pathology , Vardhman institute of medical sciences, Pawapuri, Nalanda, Bihar, from July 2018 to June 2021 including 250 patients with palpable thyroid lesions. Patients from various departments of our institution were included in the study. Some external cases that undergone slide review for second opinion were also included in the study.

Inclusion Criteria:

All those patients having thyroid lesions, irrespective of their age and sex, referred for cytological study from various clinical outpatient and inpatient departments were selected. In each patient detailed clinical history was obtained and through clinical examination was done prior to procuring sample for cytological study.

Exclusion Criteria:

Patients not willing for fine needle aspiration cytology of their thyroid lesions even after explaining the purpose, utility and consequence of the procedure were excluded from the study.

Procedure Methodology:

All the patients were carefully examined, well informed about the procedure and consent was taken. Aspiration was done under aseptic conditions using10 ml dispovan and 22-23 gauge needle. Aspirate was spread on properly labelled clean glass slides and both dry and wet smears were prepared. Prepared slides were stained by Papanicolaou and Giemsa stains. Reporting was done by two cytopathologists.

For histopathology specimens, tissue specimens were fixed in 10% buffered formalin. Grossing was done and sections from representative sites were taken. After tissue processing, paraffin blocks were prepared and 3 micron section were cut on microtome. Sections were stained using haematoxylene and eosin stain. Microscopy was done by two of the histopathologists.

RESULTS:

A total of 250 patients were included in this study, of which 80% were female and 20% were male with male : female ratio of 1 : 4. Age distribution ranged from 10 years to 93 years. Most of the patients (N=190) were in age range of 21–50 years accounting for 73.2% of the total cases. The youngest patient was 10 year old whereas oldest patient was 93 years old. Most of the patients(80%) were from rural area and of low socioeconomic strata, remaining 20% cases were from urban areas. Commonest clinical presentation was thyroid swelling seen in all the patients (100%). Second most common presentation was pain (24%), followed by difficulty in swallowing (16%). Pain was the commonest presentation in patients with lymphocytic thyroiditis [Fig.2], subacute thyroiditis and cystic and haemorrhagic degeneration

of thyroid nodules. Patients of anaplastic carcinoma thyroid[Fig.7] showed rapid growth of preexisting thyroid mass in two of the cases while remaining two showed recent onset of thyroid swelling in apparently normal thyroid. Two cases of Non Hodgkins lymphoma[Fig.8] thyroid showed diffuse, firm to hard, fixed multinodular mass with history of thyroid enlargement for many years. One of the patients presented with clavicular swelling and retrosternal thyroid swelling that was proved to be a case of follicular neoplasm and bony swelling revealed similar tumour with microfollicular arrangement [Fig.3]. PET scan of the same patient revealed thyroid primary with metastatic deposits in different bones including clavicle, humerus and ribs. Two cases of papillary carcinoma thyroid [Fig.4 & 5] presented with thyroid swelling and concurrent cervical lymphnodes were positive for metastatic deposits of papillary carcinoma thyroid.

According to routine cytological reporting, more than half the numbers of cases in the present study were diagnosed as goiter (54.4%, *n* = 136) which also included goiter with cystic degeneration or other secondary change as well as nodular goiter. Second most common lesion diagnosed was colloid cyst (11.2%, *n* = 28). Among other benign lesions, thyroglossal cyst 4% (n=10), lymphocytic thyroiditis accounted for 9.20% (*n* = 23), Hashimoto's thyroiditis 2%(n=5) Subacute and granulomatous thyroiditis 2.0% (*n* = 5) and one case showed microfilaria (0.4%). Among neoplastic lesions, 8.80% cases (*n* = 22) were diagnosed as follicular neoplasms (FN), 3.20% (*n* = 8) as papillary carcinoma, 1.20% (*n* = 3) as medullary carcinoma, 1.60% (*n* = 2) as anaplastic carcinoma and 0.8% (N=2) as Non- Hodgkins lymphoma.

Table 1: Distribution Of Various Thyroid Lesions

Diagnosis	No of Cases (n=250)	Percentage (%)
Non-neoplastic thyroid lesions	208	83.20
Neoplastic thyroid lesions	39	15.60
Inconclusive	03	1.20

Among 250 cases, benign follicular lesions were commonest including follicular lesion (Colloid/ Nodular/ Adenomatoid/ thyroglossal cyst) 174 (69.60%) followed by lymphocytic thyroiditis + Hashimoto's thyroid 28(11.2%), granulomatous /subacute thyroiditis 5(2.0%) Filarial thyroiditis 1 (0.4%)[Table 2].

Table 2: Cyto-morphological Spectrum Of Various Thyroid Lesions

Diagnosis	No of Cases (n= 250)	Percentage (%)
Colloid cyst	28	11.20
Benign follicular lesion	136	54.40
Thyroglossal cyst	10	4.00
Lymphocytic thyroiditis	23	9.20
Hashimoto thyroiditis	05	2.00
Granulomatous/subacute thyroiditis	05	2.00
Filarial thyroiditis	01	0.40
Follicular neoplasm	22	8.80
Papillary carcinoma	08	3.20
Medullary carcinoma	03	1.20
Non Hodgkins lymphoma	02	0.80
Anaplastic carcinoma	04	1.60
Inconclusive	03	1.20

Table 3: Age Wise Distribution Of Various Thyroid Lesions

Diagnosis	Age groups (yrs)							
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	>70
Colloid cyst	01	02	10	07	02	04	01	01
Benign follicular lesions	01	05	27	31	49	17	04	02
Thyroglossal cyst	00	07	03	00	00	00	00	00
LymphocyticThyroiditis	00	05	08	06	02	01	01	00
Hashimoto's thyroiditis	00	00	03	02	00	00	00	00
Granulomatous/sub- acute thyroiditis	00	00	04	01	00	00	00	00
Filarial thyroiditis	00	00	00	01	00	00	00	00
Follicular neoplasm	00	03	04	07	06	02	00	00
Papillary carcinoma	00	02	04	02	00	00	00	00
Medullary carcinoma	00	00	01	01	01	00	00	00
Non Hodgkins lymphoma	00	00	00	00	00	01	01	00
Anaplastic carcinoma	00	00	00	00	01	03	00	00
Inconclusive	00	01	02	00	00	00	00	00
Total	02	25	66	58	61	28	07	03

According to the Bethesda system of reporting thyroid lesions, distribution of lesions was as given in the **table 4 :**

BETHESDA Category	No. of cases	Percentage (%)
CategoryI - Non diagnostic	3	1.20
Category II- Benign	208	83.2
Category III - AUS/FLUS	0	0
Category IV - SFN/FN	3	1.2
Follicular neoplasm (FN)	14	5.6
FN - Hurthle cell type	5	2.00
Category V- suspicious of malignancy	3	1.2
Suspicious for papillary Carcinoma	2	0.8
Suspicious for medullary Carcinoma	1	0.4
Category VI - Malignant	14	5.60
Papillary thyroid carcinoma	6	2.40
Medullary thyroid carcinoma	2	0.80
Non Hodgkins Lymphoma	02	0.80
Anaplastic carcinoma	04	1.60

Out of 250 cases, histopathology was available in 50 of the cases including 22 cases diagnosed as neoplastic in FNAC. Among surgically resected histopathology specimens distribution of lesions were as given in Table 5. Out of 28 benign cases, 26 cases were benign including colloid goiter, thyroglossal cyst, adenomatous goiter and adenomatous goiter with associated Hashimoto's thyroiditis. Two of the cases diagnosed as colloid goiter with cystic degeneration in FNAC , proved to be the case of papillary carcinoma thyroid with cystic degeneration. Remaining 22 neoplastic cases showed follicular adenoma (12), Hurthle cell adenoma (3) and papillary carcinoma thyroid in 7 cases. One case of follicular neoplasm diagnosed in FNAC showed features of follicular variant of papillary carcinoma thyroid in histopathological study. Histopathological findings of all seven cases of papillary carcinoma were consistent with cytological diagnosis. Other malignant cases were lost in follow up.

Table5: Comparison Of Cytological Diagnosis And Histopathological Findings

Cytological Diagnosis	Number of cases	Benign / Neoplastic	Histopathological Diagnosis	No. of cases
Colloid goiter	10	Benign	colloid goiter Papillary carcinoma thyroid	08 02
Thyroglossal cyst	03	Benign	Thyroglossal cyst	03
Adenomatous goiter	12	Benign	Adenomatous goiter Follicular adenoma	10 02
Adenomatous goiter with Hashimoto's thyroiditis	03	Benign	Hyperplastic nodule with associated Hashimoto's thyroiditis	03
Follicular+Hurthle cell neoplasm	15	neoplastic	Follicular adenoma/Hurthle cell adenoma Follicular variant of papillary carcinoma thyroid	14 01
Papillary carcinoma thyroid	07	malignant	Papillary carcinoma thyroid	07

DISCUSSION:

Fine needle aspiration cytology is a simple, minimally invasive, rapid,

cost effective, gold standard first line investigation in the evaluation and management of patients with thyroid nodules. [2,16,20] Nowadays, FNAC is practiced world wide to evaluate thyroid lesions for proper management. Various previous studies have established FNAC as a valuable first line investigation for the evaluation of thyroid lesions. Out of 250 cases in this study, FNA smears in total 3 cases were inadequate due to scanty cellularity and markedly haemorrhagic smears. Rich vascular supply of thyroid gland results in such haemorrhagic smears.[6,28] Limiting the number of passes and aspiration without negative pressure helps decrease chances of such inadequate samples. The mean age of patients of thyroid lesions in various studies ranged from 36.5 to 46.0 years and age distribution in present study was almost comparable with the studies by Sathiyamurthy K. et al 2014, [12] Arvinthan T et al 2007[30] and Gupta M et al 2010.[31]

Male female ratio was 4:1 which is consistent with most of the previous studies [30,13,35,36] The ratio between non-neoplastic and neoplastic lesions of thyroid gland was in between 2.41:1 to 12.29:1. Present study included total 208 benign cases and 39 neoplastic lesions with a ratio of 5.33:1, which is very close to the studies by Sathiyamurthy K et al 2014, [12] Godinho-Matos L et al 1992, [32] Handa U et al 2008, [13] Sengupta A et al 2011[33] and Sekhar A et al 2015.[35] The commonest non-neoplastic thyroid lesions found in this study were goitres which was comparable to the studies by Sathiyamurthy K et al 2014, [12] and Gupta M et al 2010.[31]The diagnostic accuracy of thyroid lesions by cytology in previous studies was about (65-98%). Present study showed diagnostic accuracy as 98.00%, which was well within this range and was similar to the studies by Gharib H 1994, [6] Bagga PK et al 2010[7] and Likhar KS et al 2013.[15]

Two cases which were reported as colloid goiter in FNAC proved to be the cases of papillary carcinoma thyroid in histopathological examination. In such cases aspiration from multiple sites and in ultrasound guidance will improve result[13,14]. Differentiating follicular adenoma from follicular carcinoma is not possible. But in one of our cases thyroid swelling was present with pathological fracture of clavicle and interestingly FNAC from both the swellings revealed increased cellularity with predominantly microfollicular arrangement. PET scan of the same patient in higher center confirmed thyroid primary with multiple bony metastasis involving clavicle, humerus and ribs.

Proper sampling from a representative site is important for adequacy of sample and correct diagnosis. According to most of the authors, preparation of atleast 4-6 smears from different areas of nodule gives better result. Strict criteria for specimen adequacy could help to reduce erroneous diagnosis [25]. Ultrasound guided FNAC improves sampling, accuracy and decreases rate of non-diagnostic smears[26].

In present study, all the cases of papillary carcinoma thyroid were female, two of them were less than twenty years of age and 6 were in their 3rd decade. These patients gave history of slow growing thyroid swelling, associated with pain, discomfort and hoarseness of voice. Cytological examination revealed high cellularity, syncytial sheets, papillaroid fragments with distinct anatomical borders and clusters of follicular epithelial cells showing nuclear enlargement, overlapping, grooves, intranuclear cytoplasmic inclusions and thick colloid[Fig 5]. Three cases of cases of medullary carcinoma thyroid was reported in patients in their 5th decade. 4 cases of anaplastic carcinoma was reported in 5th and 6th decade. 3 cases of anaplastic carcinoma thyroid presented with rapid enlargement of preexisting thyroid swelling with compressive symptoms like difficulty in deglutition and breathlessness.

One of the cases presented with rapidly growing mass without visible preexisting thyroid enlargement. Out of four cases of anaplastic carcinoma thyroid one was associated with papillary carcinoma thyroid and another was associated with medullary carcinoma thyroid. Two cases of Non Hodgkins lymphoma were seen in older patients in their seventies. These patients presented with diffuse, multinodular, fixed, firm to hard mass encircling anterior aspect of neck. Microscopic features revealed predominantly scattered atypical large lymphoid cells with indented nuclei and prominent nucleoli in many and scanty cytoplasm. Cytological examination of anaplastic carcinoma revelead bizarre pleomorphic tumor cells with increased mitotic activity and necro-inflamatory background.[Fig 6].

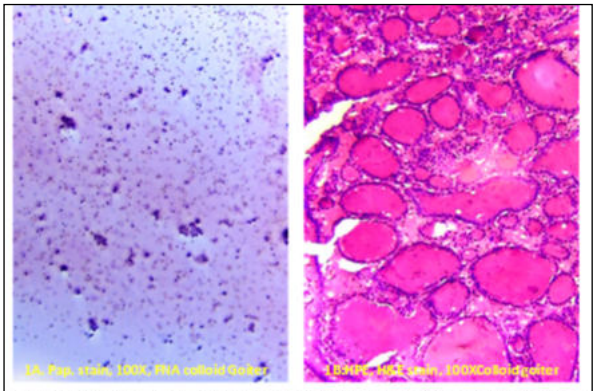

Fig.1A: FNAC colloid goiter –abundant colloid and sparsely scattered follicular cells ,1B: HPE shows colloid distended follicles.

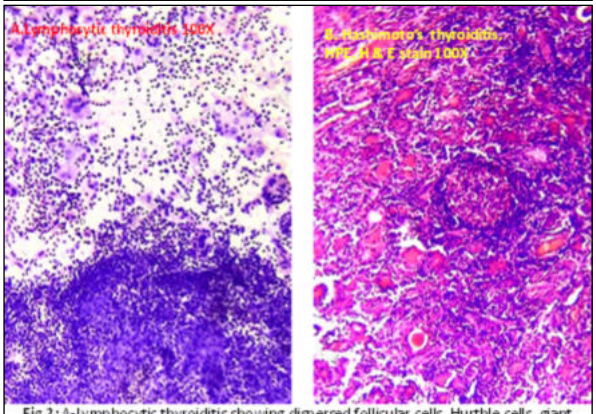

Fig.2: A-Lymphocytic thyroiditis showing dispersed follicular cells, Hurthle cells, giant cells and abundant lymphocytes infiltrating follicular cells
Fig.2: B: HPE, H & E stain Hashimoto's thyroiditis with degenerated follicles and dense lymphocytic infiltrate with lymphoid follicle formation

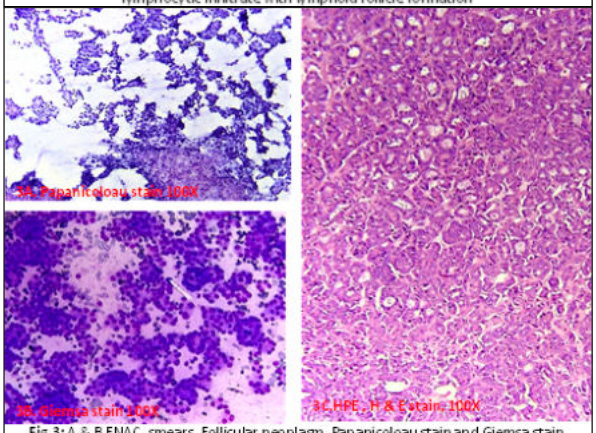

Fig.3: A & B FNAC smears, Follicular neoplasm, Papanicoloau stain and Giemsa stain showing cellular smears with predominantly microfollicular pattern. C, H& E satin , follicular adenoma, crowded microfollicles.

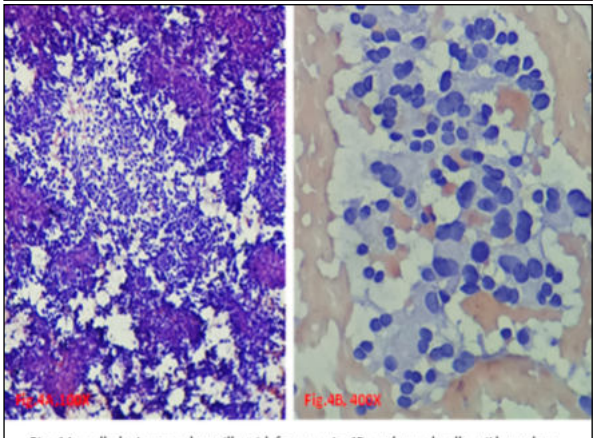

Fig. 4A- cell clusters and papillaroid fragments 4B- enlarged cells with nuclear overlapping, cytoplasmic pseudoindusions and grooves

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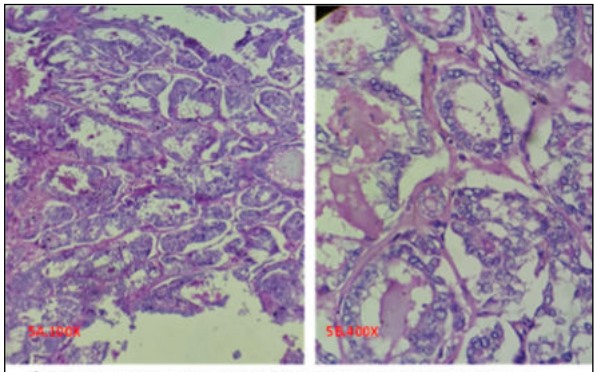

Fig.5: Papillary carcinoma thyroid , H & E stain, Micrograph (A) shows well formed papillae (B) shows tue papillae containing central fibrovascular core lined by follicular cells displaying nuclear grooves, pseudoinclusion and ground glass appearance.

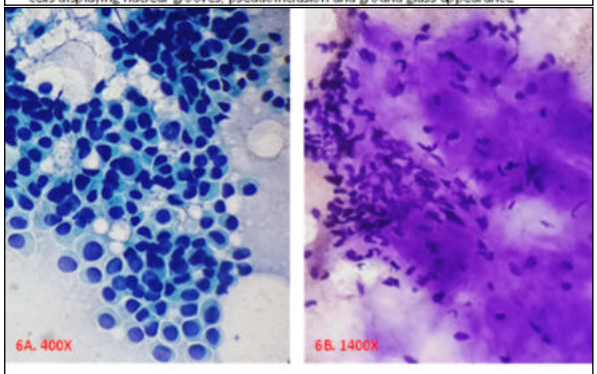

Fig.6: FNAC Medullary carcinoma thyroid, micrograph6A shws sheets and clusters of atypical plamacytoid cells, micrograph B show purple amorphous deposits of amyloid and many spindled tumour cells.

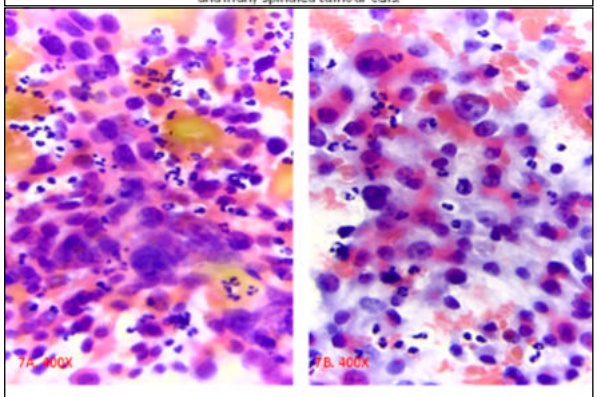

Fig.7 A &B : Anaplastic Carcinoma thyroid, Papanicolaou stain showing pleomorphic tumour cells on a necroinflamatory bckground, B . Atypical and bizarre tumour cells

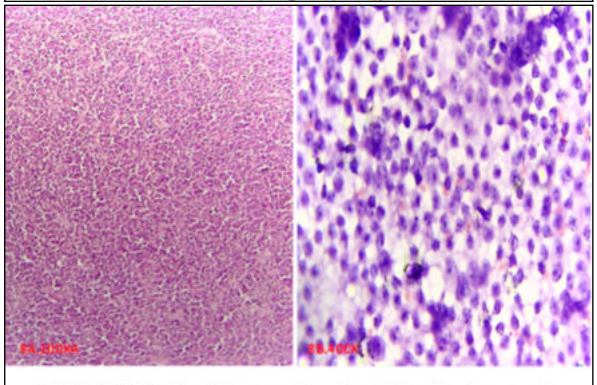

Fig8. A & B: NHL thyroid – cellular smears with predominantly scattered monomorphic atypical large lymphoid cells with prominent nucleoli

CONCLUSION:

FNAC is one of the first line investigations for management of thyroid lesions. With proper sample collection and evaluation by experienced and trained pathologist FNAC effectively delineates benign thyroid lesions from neoplastic lesions that determines the course of treatment and also decreases surgical interventions in various benign conditions. Various limitations of FNAC needs consideration while reporting. Common false negative reporting is encountered in cases with follicular variant of papillary carcinoma thyroid that needs meticulous examination to identify characteristic nuclear features. Follicular adenoma and follicular carcinoma cannot be distinguished on FNAC. Cases of micropapillary carcinoma thyroid and papillary carcinoma thyroid with cystic changes are prone to be missed by conventional FNAC. Ultrasound guided FNAC and excision biopsy helps in such cases. Thyroid malignancies are common in younger patients and need proper early evaluation. False positive diagnosis of papillary carcinoma thyroid is seen in cases of Hashimot's thyroiditis, follicular neoplasm due to presence of nuclear grooves and inclusion in some of these cases.

Presence of cases of undifferentiated or anaplastic carcinoma thyroid with foci of papillary and medullary carcinoma thyroid supports that anaplastic carcinoma of thyroid develops from transformation of pre-existing differentiated carcinomas. Hence early diagnosis and proper surgical intervention of thyroid malignancies is essential to decrease the morbidity and mortality associated with undifferentiated malignancies.

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Conflict Of Interest: There is no conflict of interest regarding the publication of this article

Ethical Approval: The study was approved by the Institutional Ethics Committee

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