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Fine Needle Aspiration Cytology Correlates with Histopathology – A Diagnostic Tool in Children.

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Abstract: *Fine Needle Aspiration Cytology (FNAC) in simple words is "aspiration by fine needle". It is the study of cells obtained by puncturing organs of human body with the use of a small-gauge needle. It has become an increasingly popular and widely accepted procedure for evaluating palpable, nonpalpable, superficial, deep masses and can be readily applied for providing diagnosis in pediatric patients. This research aims to study the spectrum of lesions aspirated in pediatric patients and to correlate the cytological diagnosis with the histopathological diagnosis.*
Materials & methods: *This is the prospective study which included children aged 0-18 years of either sex with swelling in any part of the body during the years 2008-2010 investigated by FNAC with/without a biopsy. FNAC smears were stained with haematoxylin and eosin (H&E) and special stains. Histopathological slides were prepared using the paraffin-embedding method and stained with H&E.*
Results: *A wide spectrum of lesions were aspirated. The total number of aspirates was 495; only 15.75% were unsatisfactory. Of the 84.24% satisfactory aspirates, the majority were benign 82.82%.The benign cytological diagnosis revealed lymphadenitis in the majority 60.73%. Of the malignant cases, the maximum were small round cell tumours 42.85%. Histopathological examination was possible in 64 cases and 56 were confirmed on histology. The diagnostic accuracy of FNAC was 87.50%. Its sensitivity, specificity, positive and negative predictive value was 90.32%, 100%, 100% and 25.00% respectively. p value <0.05 indicated statistical significance.*
Conclusion: *FNAC is a simple, safe, rapid, sensitive, specific and an inexpensive bedside method. It provides diagnostic and therapeutic advantages. It helps the surgeon to select, guide and modify surgical treatment. FNAC is recommended as a first line of investigation and a diagnostic modality in children.*
Keywords: *FNAC, Histopathology, Pediatric.*

I. Introduction

Fine Needle Aspiration Biopsy (FNAB)/ Fine Needle Aspiration Cytology (FNAC) in simple words is "aspiration by fine needle" [1,2]. FNAC is a simple, safe, rapid, accurate and an inexpensive bedside method to obtain a tissue specimen for diagnosis of suspicious lesions. In this era of cost conscious medicine, FNAC is a technique which speeds up the process of diagnosis, limits the physical and psychological discomfort to the patient and saves the expenditure of hospitalization. It helps the surgeon to select, guide and modify surgical planning in patients requiring surgery. It is a valuable tool to follow up patients with a history of malignancy and also reduces the necessity to perform excision biopsy in many cases, where the diagnosis is definite, saving the children from surgical complications and thus it can be recommended as a first line of investigation in the diagnosis of swellings in the pediatric age group [3-5].

II. Materials and Methods

All the cases of FNAC reported during the period May 2008 to May 2010 in the pediatric age group i.e. 0-18 years were reviewed. The corresponding histopathological diagnosis in those cases that were subsequently biopsied was also reviewed and a correlation between the two diagnoses was made. Children aged 0-18 years of either sex were included with swelling/s in any part of the body/organ during the years 2008-2010 which was investigated by FNAC with/without a biopsy. FNAC smears were stained with haematoxylin and eosin (H&E), Papanicolaou, May Grunwald Giemsa and special stains. Histopathological slides were prepared using the paraffin-embedding method and stained with H&E.

III. Results

A wide spectrum of lesions were aspirated. The total number of aspirates was 495. In this study of pediatric FNACs the age range included was 0-18 years, which was subdivided into four groups: 0-1 year, 1-6 years, 7-12 years and 13-18 years. The aspirates were more in the older age group (13-18 years) – 66.26%. The majority of aspirates were of benign nature 82.82% and very few were malignant 1.41%. The rest of the aspirates were unsatisfactory 15.75% (Table 1). The youngest patient was 11 months old and the oldest was 18

years old. The sex distribution of the FNA diagnosis revealed a female preponderance 61.01% as compared to males 38.98% were from males (Table 2). A subdivision of the FNA diagnosis according to anatomic site revealed a distinct preponderance of head, neck and face region over all other sites 67.47%. The least number of aspirates were from lower extremity 2.02%. At all anatomic sites, benign diagnoses exceeded malignant cases (Table 3). A subdivision of the FNA diagnosis according to specific organs revealed a distinct preponderance of cases involving the lymph nodes 60.20%. This was followed by breast 13.93%, bone and soft tissue 10.90%. The least number of aspirates were from retroperitoneal structures and male gonad 0.20% each (Table 4). In all organs, benign diagnosis was found in the majority except for the retroperitoneal structures and male gonad where malignancy was the sole finding. In breast, thyroid, salivary gland, skin and sub cutis (epidermal/sebaceous/dermoid cysts) all the aspirates were benign. When the benign cytological diagnosis were subtyped, the maximum number of aspirates were from lymph nodes 60.73%; of which majority were inflammatory 57.42%. In the inflammatory category, the majority were specific infections i.e. tuberculous 89.51% (Fig 1a,b,c,d, Fig 2a & 2b). The lymphadenitis category was followed by fibroadenoma of the breast (Fig 3a,3b,4a,4b) (Table 5). In this study, AFB smears were studied in all 128 TB cases. The smears were positive in 45.31% cases and negative in 54.68% cases (Fig 5). The other systemic diseases associated with lymphadenopathy were pulmonary Koch's 10% followed by HIV 2% cases (Table 6). There were only 07 aspirates which were positive for malignancy. Out of these the maximum number were malignant small round cell tumour 42.85% (Fig 6) followed by lymphomas 28.57% (Fig 7) which could not be sub-typed on FNAC (Table 7). In this study, 64 cases were examined histopathologically and correlation between the FNA smear diagnosis and histopathological diagnosis was done with the help of statistical analysis and the sensitivity, specificity, predictive value and test of significance applied for the test. Amongst the 64 cases diagnosed on cytology, 56 cases were confirmed on histology. Diagnosis changed on histopathology in 06 cases and 02 cases showed normal histology (Table 8). In this study, sensitivity of FNA was found to be 90.32% and the specificity was 100%. On referring to χ^2 table, with degree of freedom, $p < 0.0066$ was statistically significant. According to Fisher's test, p value equalled 0.0139 ($p < 0.05$), indicating the test to be statistically significant. The test is more significant and is to be used for diagnostic purposes with significant diagnostic accuracy value. The predicative power of the FNA test in the pediatric population is very high (i.e. PPV = 100%) and the test is statistically significant ($p < 0.05$). Hence this study proves that FNA is a very important diagnostic modality in the pediatric age group.

IV. Discussion

Fine needle aspiration biopsy is a very sensitive, specific and an accurate method for evaluating both palpable and non-palpable, superficial and deep masses in pediatric patients[1,3,4]. It provides diagnostic and therapeutic advantages in cases of superficially accessible organs and tissues e.g. lymph nodes, breast, thyroid, skin and also in cases of deep solid enlarged intra-abdominal lymph nodes, space occupying lesions of kidney, liver, pancreas and a few cystic masses [1]. FNA is an operator dependent procedure, which for optimal results requires a good co-operation between the clinician and the pathologist. In case of lymph node malignancy such as Non-Hodgkin's lymphoma, FNAC provides a quick diagnosis; thus surgical biopsy and inappropriate procedures can be avoided. FNA of the testis enables us to distinguish between inflammatory and neoplastic lesions pre-operatively [6]. While the type of malignancy can be diagnosed, FNA does not give information about the architecture of the tumour. In order to improve resectability, patients receive pre-operative chemotherapy such as in Wilm's tumour and rhabdomyosarcoma. Pre-treatment has been shown to downgrade the atypia seen in some Wilm's tumours which could result in under treatment if complete histology is not obtained prior to treatment. This difference in information obtained from FNA biopsy and open biopsy and how this subsequently affects treatment must be weighed against the risk of gross tumour spillage, infection and delay in therapy with open biopsy. FNA should be utilized for the diagnosis of recurrent lesions; tumours that do not appear readily resectable; in an obvious disseminated disease to allow for early initiation of therapy [7].

In our study, as in Table 1, we have included the age range of 0-18 years and further subdivided this age range into four categories Our findings were similar to the series of Taylor et al [8], Silverman et al [9] and Smith et al [7], they took 18 years as age range. In our study, the majority of aspirates were benign 83% and revealed a female preponderance. This finding correlates well with the findings of Wakely et al [10] who also found the maximum number of cases (62.5%) in the benign category with a female preponderance. The number of aspirates according to anatomic site, revealed a distinct preponderance of head, neck and face 67% over all other sites. Our findings correlate with Howell et al [4] who also found the maximum number of aspirates in head, neck and face region (64.81%). A subdivision of the FNA diagnosis according to the organ involved, revealed a distinct preponderance of lymph node aspirates 60% over all other organs. Our findings correlate well with the studies of Wakely et al [10], Cohen et al [3], Howell et al [4], Mobley et al [11]. They also found the maximum number of benign aspirates from lymph nodes and also benign aspirates in all other organs. We subtyped the benign cytological diagnosis and lymphadenitis (60.73%) was the diagnosis in the majority of the aspirates. Our

findings correlate well with studies of Wakely et al [10] (44.28%), Howell et al [4] (62.96%), Mobley et al [11] (78.57%) where the majority of cases were of lymphadenitis. In our study, in the lymphadenitis category, the majority of the aspirates were inflammatory (57.42%) followed by reactive lymphadenitis (42.57%). These findings correlate with those of Howell et al [4]. Amongst the malignancies, we found maximum number of cases of malignant small round cell tumour (42.85%) which could not be sub-typed on FNAC. Our findings correlate with Taylor et al [8] (73.68%), Cohen et al [3] (66.66%), Smith et al [7] (38.40%) they also found maximum number of cases of malignant small round cell tumour.

We examined 64 cases on histopathology, and correlation between the FNA smear diagnosis and histopathological diagnosis was done with help of statistical analysis. Of the 64 FNACs, 56 were confirmed on histopathology and the diagnosis changed with histopathology in 06 cases. So the diagnostic accuracy was 87.50% which indicates a good correlation. Other authors Jereb et al [12] (93%), Taylor et al [13] (89%) have also found a good correlation. We found the sensitivity of the FNAC procedure to be 90.32% while its specificity was 100%. The positive predictive value (PPV) was 100% and the negative predictive value was 25.00%; false positive rate being 9.67% and false negative rate was 0%. The p value < 0.05 indicated that the test was very significant. The sensitivity and specificity reported by other authors ranged from 76% - 97% and 95% - 100% respectively. The positive predictive value (PPV) reported by other authors ranged between 89.4% - 100% while the negative predictive value was 94.7% reported by Silverman et al [9]. Other studies have shown a false positive rate in the range of 2 - 0% and a false negative rate in the range of 7 - 0%. Our findings match with those found in other studies, except for a negative predictive value which is much lower at 25% and a false positive rate of 9.67%

V. Conclusion

"Diagnosis by aspiration is as reliable as the combined intelligence of the clinician and the pathologist make it". This was emphasized about seventy years ago by Stewart [14] FNAC may be performed by a clinician, pathologist or radiologist as an outpatient procedure. So along with other advantages it brings a new dimension of cooperation between the medical specialist, cytopathologist and radiologist in this era of emphasis on ambulatory care [1].

Table 1: Age range and FNA diagnosis

Age (years)	Benign	Malignant	Inadequate	Total
0-1	**02**	**00**	**01**	**03 (0.60%)**
1-6	**45**	**03**	**20**	**68 (13.73%)**
7-12	**86**	**00**	**10**	**96 (19.39%)**
13-18	**277**	**04**	**47**	**328 (66.26%)**
Total	**410 (82.82%)**	**07 (1.41%)**	**78 (15.75%)**	**495 (100%)**

Mean age – 9.5 years

2: Sex distribution and FNA diagnosis

Sex	Benign	Malignant	Unsatisfactory	Total
Male	**156**	**04**	**33**	**193 (38.98%)**
Female	**254**	**03**	**45**	**302 (61.01%)**
Total	**410 (82.82%)**	**07 (1.41%)**	**78 (15.75%)**	**495 (100%)**

Table 3: Anatomic sites and FNA diagnosis

Site	Benign	Malignant	Inadequate	Total
Head, Neck and Face	280	03	51	334 (67.47%)
Chest and Back	89	00	18	107 (21.61%)
Abdomen	12	03	05	20 (4.04%)
Upper Extremity	20	01	03	24 (4.84%)
Lower Extremity	09	00	01	10 (2.02%)
TOTAL	410	07	78	495 (100%)

Table 4: Specific organs and their FNA diagnosis

Organ	Benign	Malignant	Inadequate	Total
Eye and Adnexae	00	01	01	02 (0.40%)
Skin and Subcutis	24	00	02	26 (5.25%)
Salivary Gland	04	00	01	05 (1.01%)
Thyroid	29	00	10	39 (7.87%)
Breast	63	00	06	69 (13.93%)
Lymph Nodes	249	02	47	298 (60.20%)
Bone and Soft Tissue	41	02	11	54 (10.90%)
Retroperitoneal Structures	00	01	00	01 (0.20%)
Male Gonad	00	01	00	01 (0.20%)
TOTAL	410	07	78	495 (100%)

Table 5: Benign Cytologic Diagnosis

FNA DIAGNOSIS	*NO.OF ASPIRATES*
Inflammatory lesions Tuberculous LN*= 128 (31.21%) Suppurative LN*= 15 (3.65%)	143 (34.87%)
Reactive Lymphadenitis	106 (25.85%)
Fibroadenoma of breast	57 (13.90%)
Cysts**	39 (9.51%)
Colloid Goitre	25 (6.09%)
Abscess***	14 (3.41%)
Lipoma	07 (1.70%)
Lymphocytic Thyroiditis	04 (0.97%)
Fibrocystic disease of breast	03 (0.73%)
Gynecomastia	03 (0.73%)
Pleomorphic Adenoma	03 (0.73%)
Benign Spindle Cell tumour	03 (0.73%)
Fibroma	02 (0.48%)
Sialadenitis	01 (0.24%)
TOTAL	410 (100%)

**Lymph node **Epidermal, Thyroglossal, Ganglion Cyst ***Breast, shoulder, thigh.*

Table 6: Cytological diagnosis of Lymphadenopathy

DIAGNOSIS	***NO.OF ASPIRATES***
Reactive Lymphadenitis	***106 (35.57%)***
Inflammatory lymphadenitis ***Tuberculous lymphadenitis 128 (42.95%)*** ***Suppurative lymphadenitis 15 (5.03%)***	***143 (47.98%)***
Malignancy (Non-Hodgkin's Lymphoma)	***02 (0.67%)***
Inadequate on repeated FNA	***47 (15.77%)***
TOTAL	***298 (100%)***

Table 7: Malignant Cytological Diagnosis

DIAGNOSIS	***NO. OF ASPIRATES***
Malignant Small Round Cell tumour	**03 (42.85%)**
Lymphoma	**02 (28.57%)**
Malignant Spindle Cell tumour	**01 (14.28%)**
Germ cell tumour	**01 (14.28%)**
TOTAL	**07 (100%)**

Table 8: Correlation between cytological and histopathological diagnosis:

FNA Cytology		***Histopathology***	
Diagnosis	**No. of Aspirates**	**Diagnosis**	**No. of cases**
TB Lymphadenitis	**01**	***Chronic non-specific lymphadenitis***	***01***
Fibroadenoma	**34**	**Fibroadenoma**	**32**
		Fibrocystic disease	***02***
Fibrocystic disease	**01**	***Fibroadenoma***	***01***
Gynaecomastia	**02**	**Gynaecomastia**	**02**
Cystic lesion	**13**	**Epidermal/ Sebaceous / Dermoid cyst**	**09**
		Ganglion cyst	**03**
		Thyroglossal cyst	**01**
Colloid goitre	**03**	**Colloid Goitre**	**01**
		Follicular Adenoma	***01***
		Lymphocytic thyroiditis	***01***
Lipoma	**02**	**Lipoma**	**02**
Inadequate smear on repeated FNA	**06**	**Reactive Lymphadenitis**	**01**
		Sebaceous cyst	**01**
		Non-Hodgkin's lymphoma	**01**
		Neurofibroma	**01**
		Normal histology	**02**
Malignant Small Round Cell Tumour	**01**	**Retinoblastoma**	**01**
Malignant Spindle Cell Tumour	**01**	**Synovial Sarcoma**	**01**
Total	**64**	**Total**	**64**

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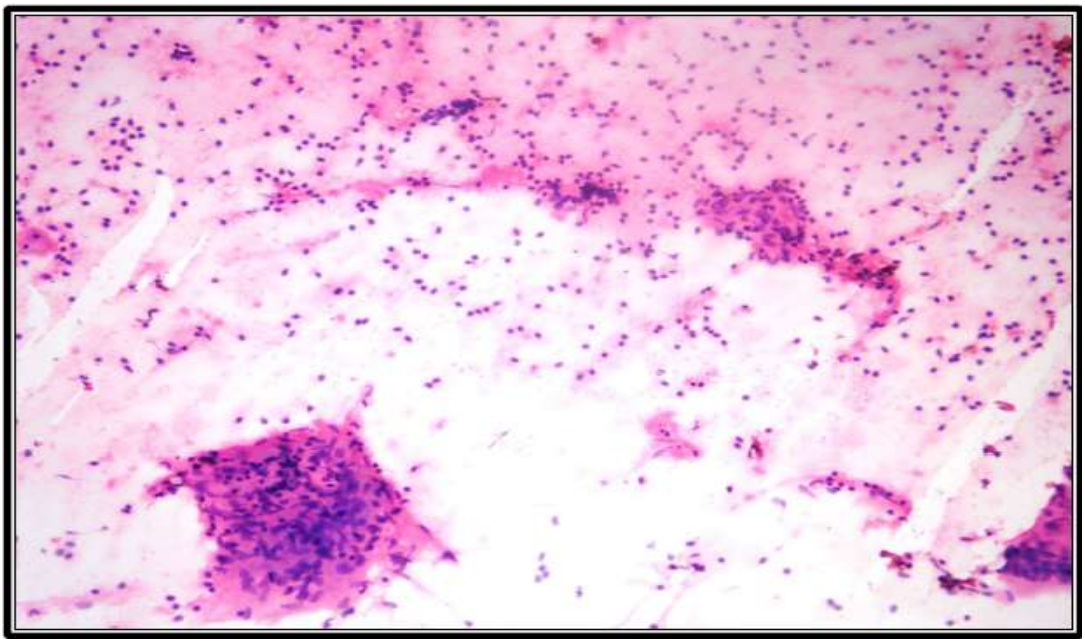

Fig 1a. Microphotograph of FNA smears from tuberculous lymph node showing clusters of epithelioid cell granulomas, lymphocytes. (H&E 100x)

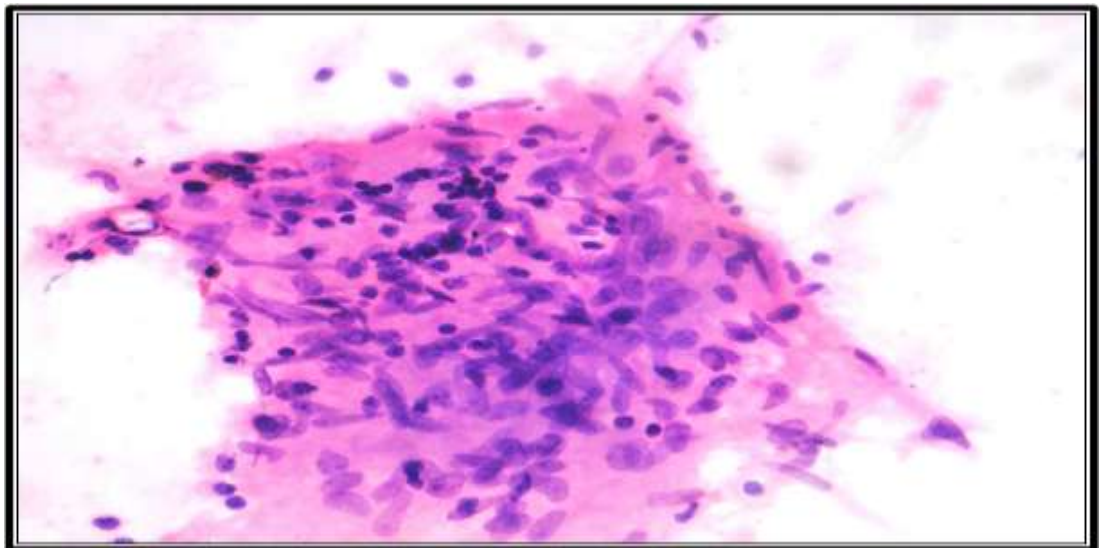

Fig.1b Microphotograph of FNA smears from tuberculous lymph node showing cluster of epithelioid Cells forming granuloma having elongated nuclei and abundant ill defined cytoplasm, lymphocytes. (H&E 400X)

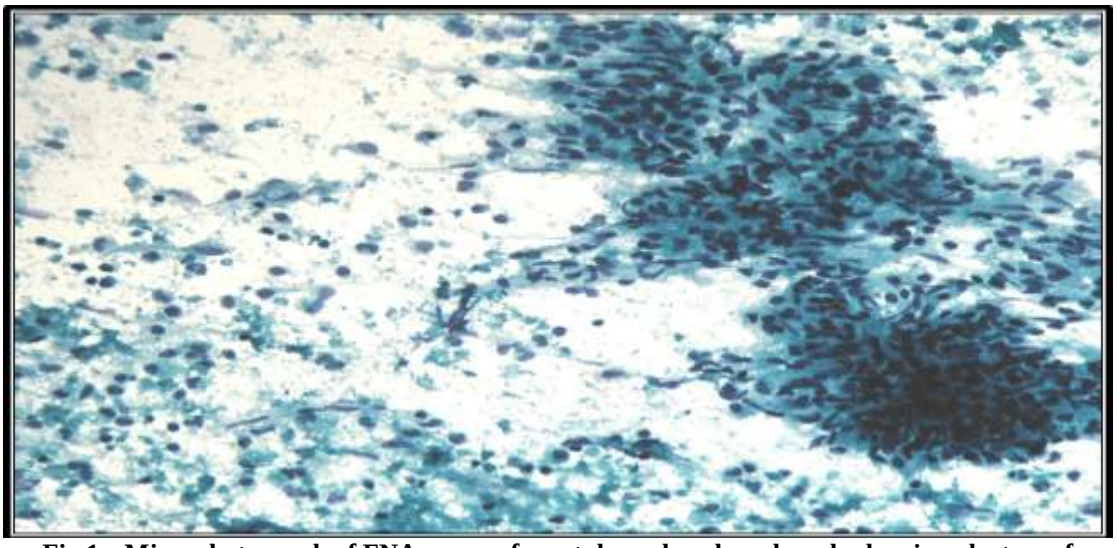

Fig 1c. Microphotograph of FNA smears from tuberculous lymph node showing clusters of Epithelioid cell granulomas, lymphocytes and caseous necrosis. (PAP 100X)

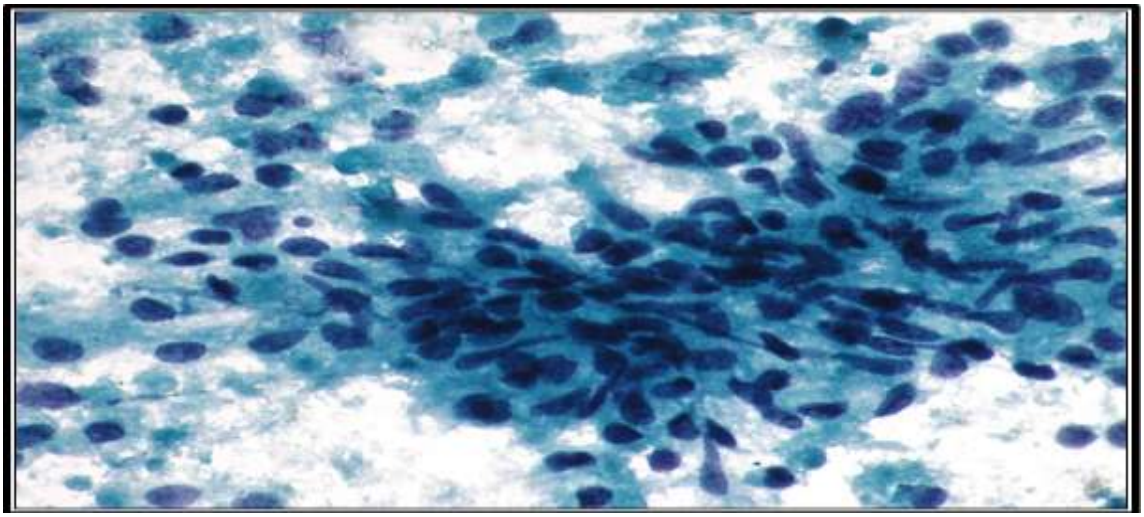

Fig 1d. Microphotograph of FNA smears from tuberculous lymph node showing cluster of epithelioid cells forming granuloma having elongated nuclei and abundant ill defined cytoplasm, lymphocytes and caseous necrosis. (PAP 400X)

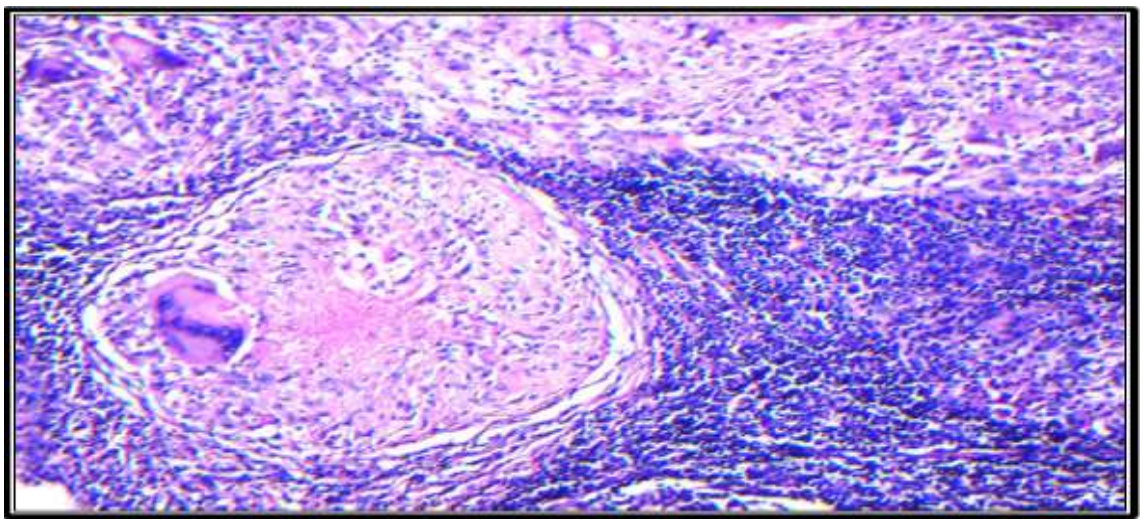

Fig 2a. Histologic section from a tuberculous lymph node showing well formed epithelioid cell granulomas, giant cells, caseous necrosis and lymphocytes. (H&E 100X)

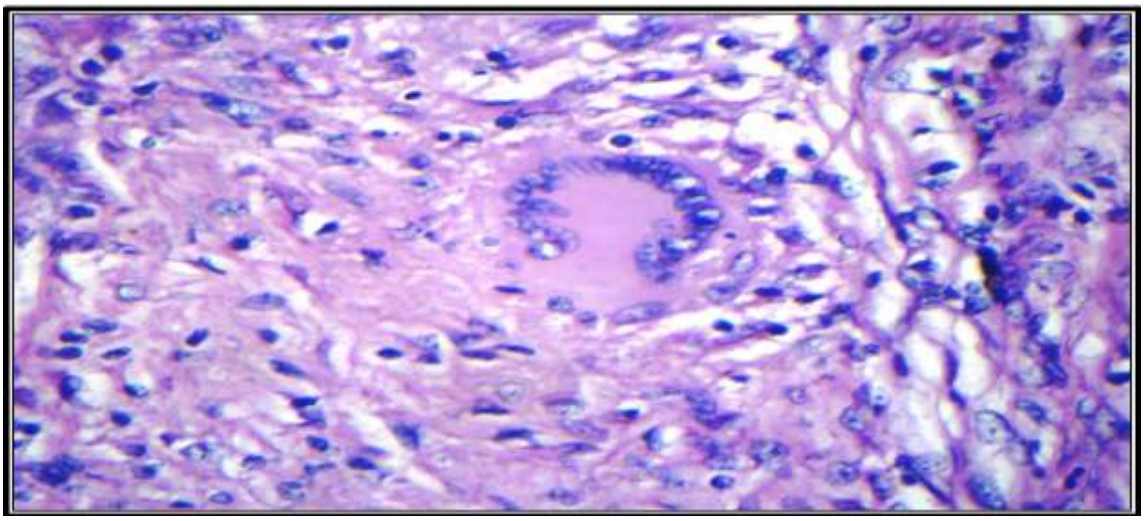

Fig 2b. Histologic section from a tuberculous lymph node showing epithelioid cells, Langhan's giant cell and lymphocytes. (H&E 400X)

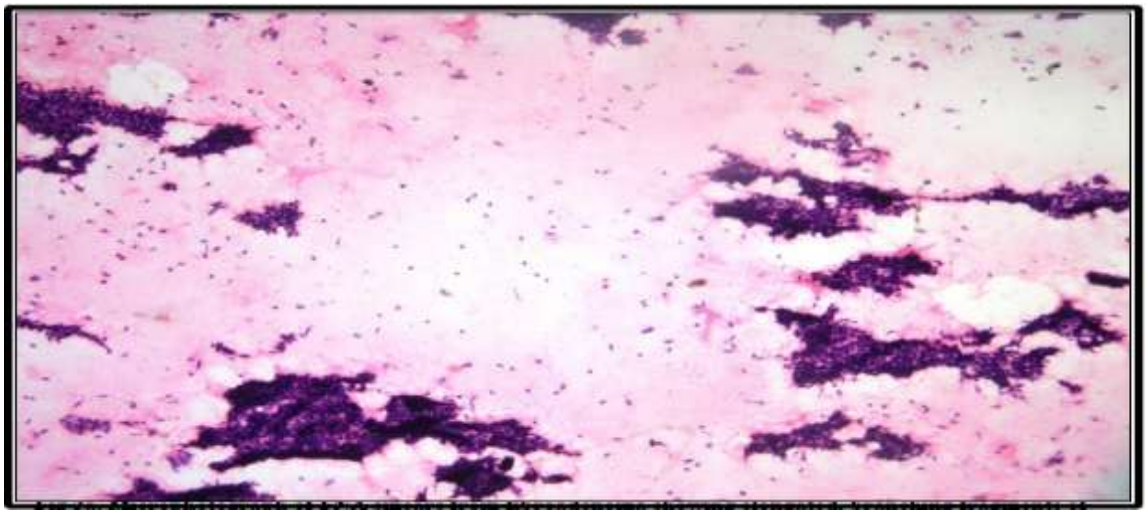

Fig 3a. Microphotograph of FNA smears from fibroadenoma showing elongated, branching fragments of ductal epithelium , numerous single bare bipolar nuclei in the background of Fibromyxoid stroma. (H&E 100X)

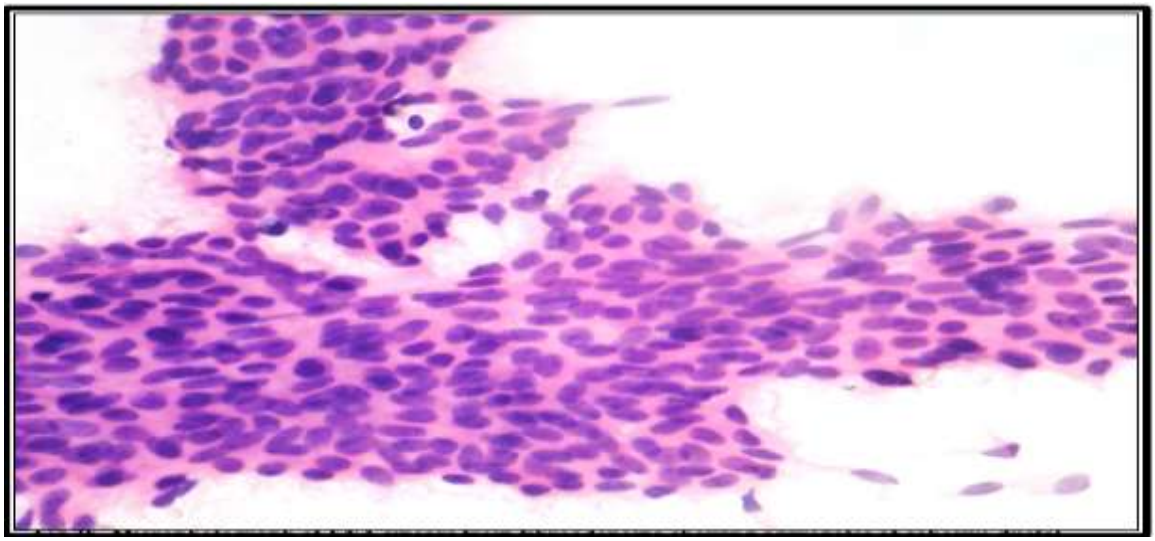

Fig 3b. Microphotograph of FNA smears from fibroadenoma showing aggregates of cohesive ductal epithelial cells , few bare bipolar nuclei. (H&E 400X)

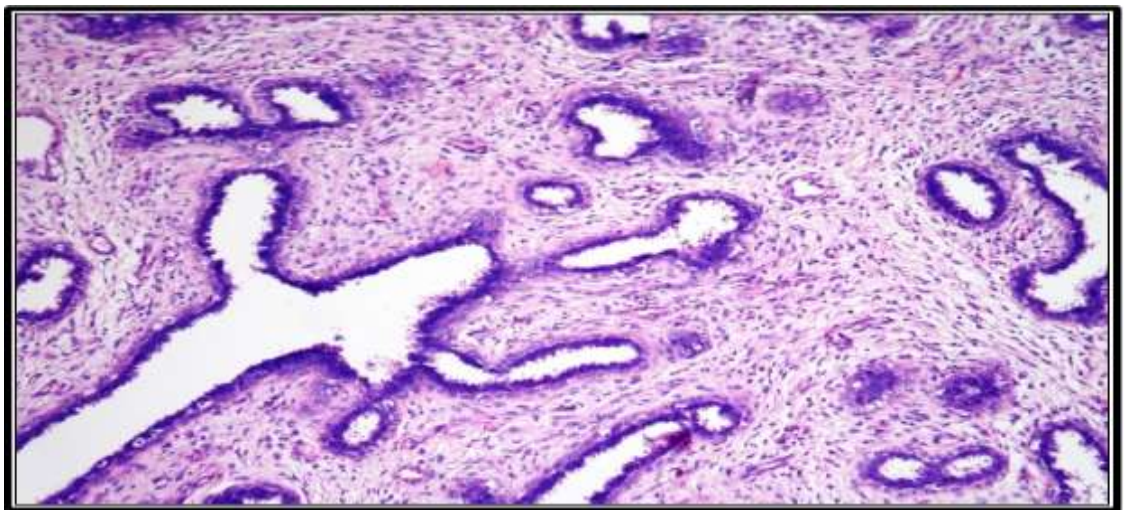

Fig 4a.Histologic section from fibroadenoma showing proliferation of glandular and stromal elements. (H&E 100X)

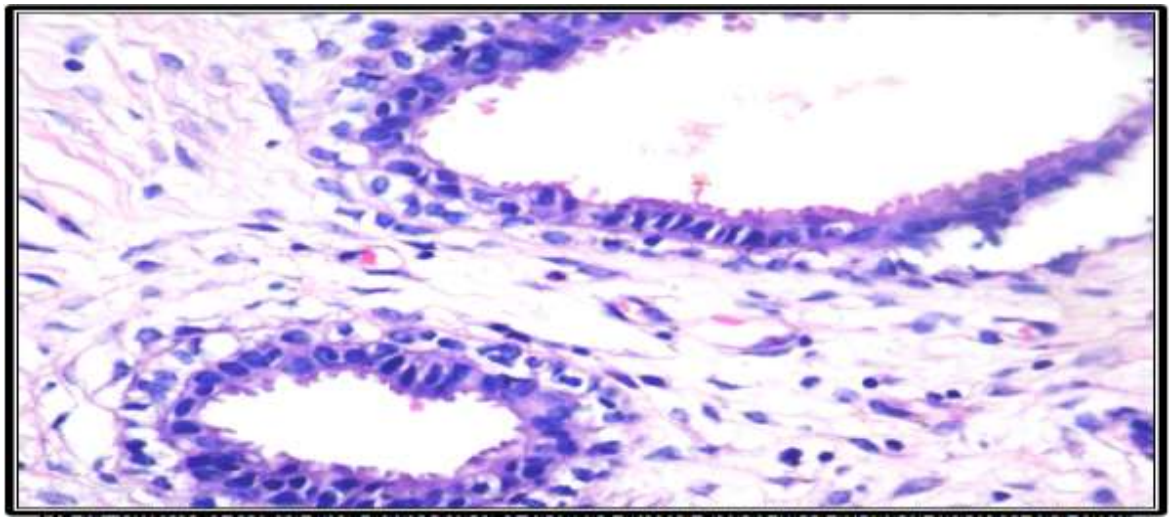

Fig 4b. Histologic section from fibroadenoma showing dilated glands lined by inner cuboidal and outer myoepithelial layer and the stroma is fibrocollagenous. (H&E 400X)

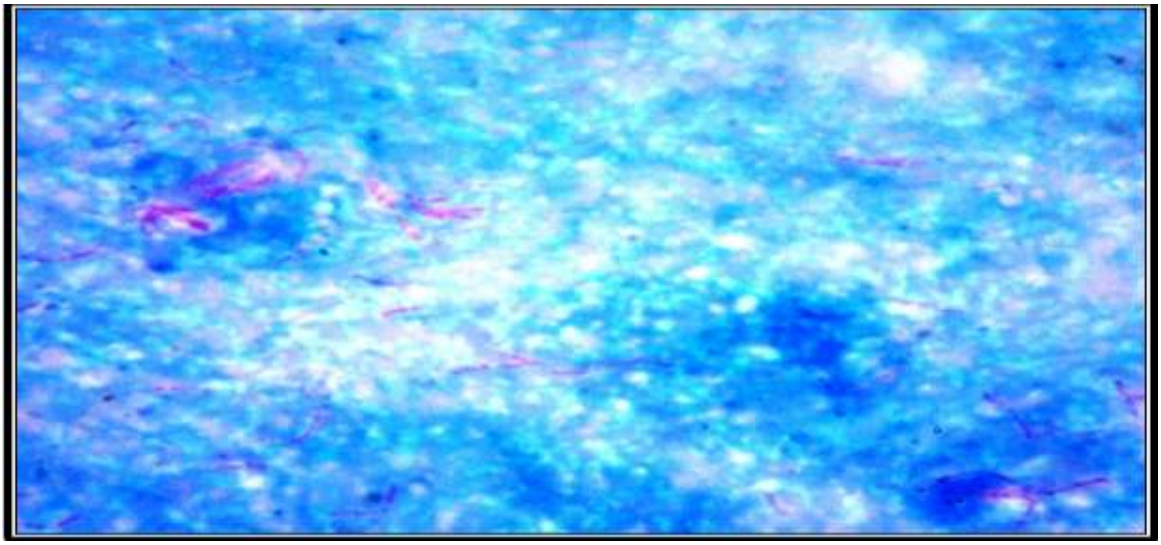

Fig 5. Microphotograph of FNA smears from tuberculous lymphnode showing acid fast bacilli. (Ziehl Neelsen stain under oil immersion).

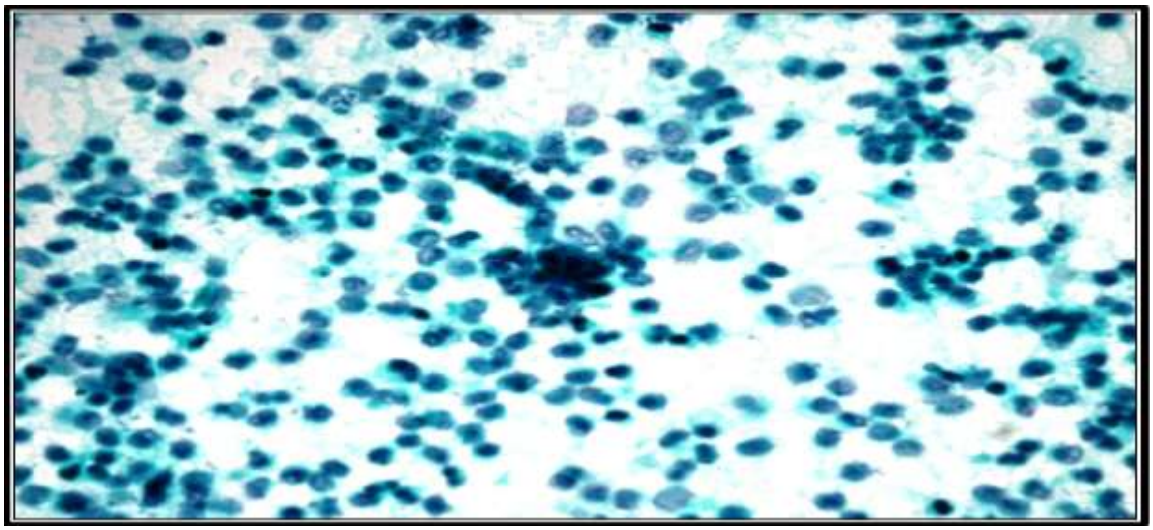

Figure 6 a. Microphotograph of FNA smears from eyeball tumour showing malignant small round tumour cells with hyperchromatic nuclei and scant cytoplasm, occasional rosette formation. (PAP 100X)

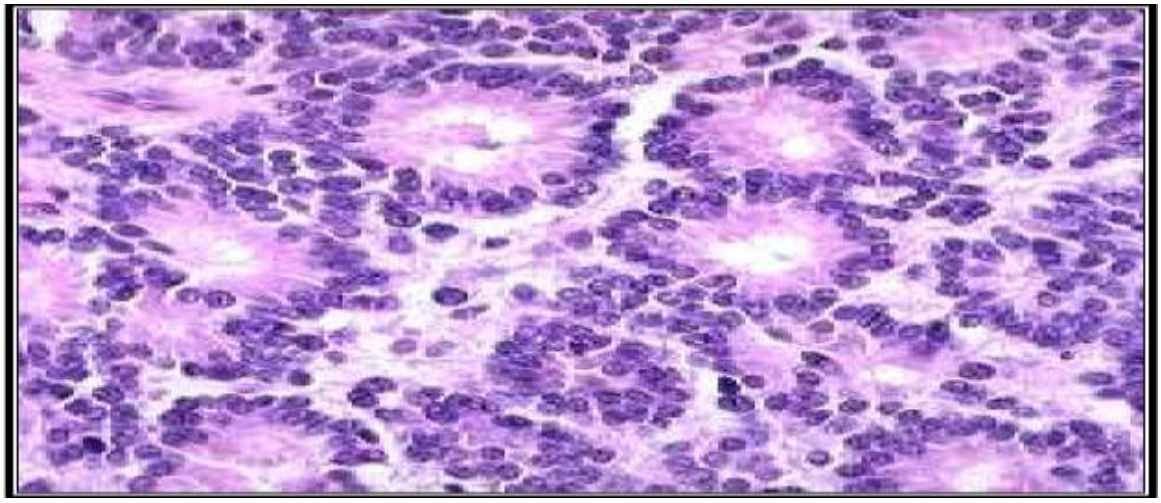

Fig 6 b. Histologic section from eyeball tumour showing malignant small round tumour cells with hyperchromatic nuclei and scant cytoplasm and rosette formation. (H&E 100X)

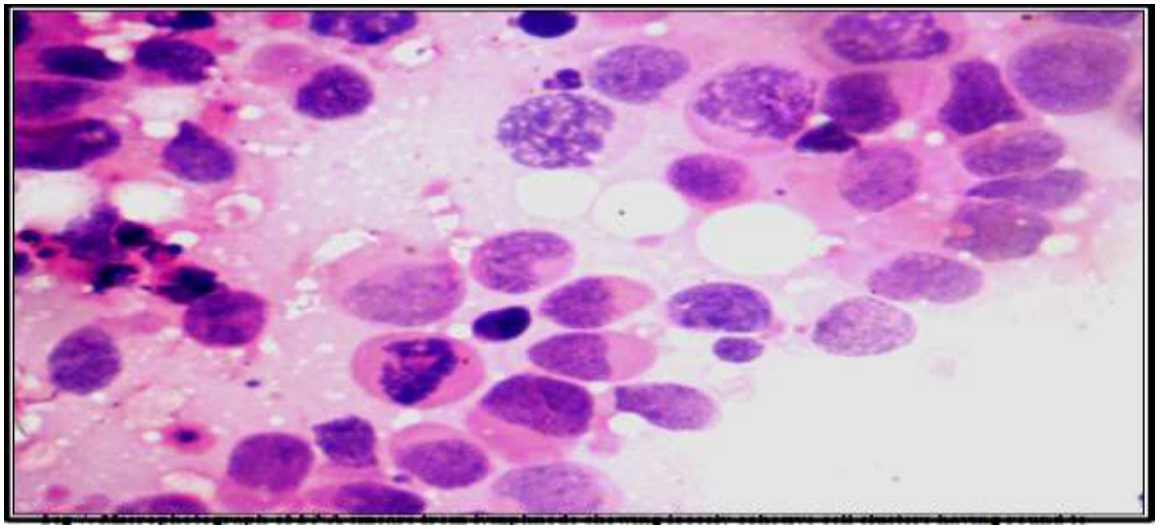

Fig 7. Microphotograph of FNA smears from lymphnode showing loosely cohesive cell clusters having round to oval , central to eccentric nuclei, irregular nuclear margins, coarse chromatin and moderate eosinophilic cytoplasm with brisk mitotic activity. (H&E 400X)