A COMPARATIVE STUDY ON CERVICAL LYMPH NODE PATHOLOGY

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CERTIFICATE

This is to certify that the dissertation titled "**A COMPARATIVE STUDY ON CERVICAL LYMPH NODE PATHOLOGY"** is the original work done by **Dr. N. SELVARAJ**, Post Graduate in Department of General Surgery, Madras Medical College, Government General Hospital, Chennai-3, to be submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai-32 towards the partial fulfillment of the requirement for the award of M.S. Degree in General Surgery, September 2006.

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CONTENTS

I- INTRODUCTION

Fine needle aspiration cytology is the study of cells obtained by a small gauge needle generally with a vacuum system provided by an airtight syringe. This technique has been in use for studying pathological lymph node enlargement since.

Lymph node enlargement may be due to a variety of underlying diseases both benign and malignant. The clinical examination may be inaccurate in differentiating benign from neoplastic enlargement of the lymph node.

Although surgical excision of a palpable peripheral lymph node is relatively simple it does require anesthesia, strict sterility and theatre time and it leaves behind a scar.

Fine needle aspiration cytology offers the advantages of an immediate, although not always specific diagnosis with little cost and trauma.

The primary purpose of fine needle aspiration biopsy of an abnormal peripheral lymph node is to decide on further course of treatment whether medical, surgical or observation. The alternatives are to just observe the patient, to carry out further investigations or try a course of conservative treatment for example with antibiotics. Obviously there are practical and psychological advantages if this decision can be made within a day.

The accuracy of diagnosis has improved considerably over the past few years. Therefore FNAC has got a definite role in the initial evaluation of all patients with peripheral lymphadenopathy.

The present study is being undertaken to evaluate its accuracy in the diagnosis of tuberculosis and malignancy of the cervical lymph nodes.

II – AIM AND OBJECTIVE

The purpose of the study is

1. To assess the usefulness of FNAC in the diagnosis of cervical lymph node enlargement.

2. To study the cytological features of common pathological conditions affecting the lymph nodes viz., tuberculosis, and lymphoma and secondary malignancy.

3. To evaluate the diagnostic accuracy of FNAC in cervical lymphadenopathy.

III – REVIEW OF LITERATURE

"Many observations have been made by morphologists and pathologists interested in normal and morbid cytology and its diagnostic possibilities. This impressive volume of work did not reach a stage of recognition for decades until finally its cumulative force strengthened by the impact of new contributions caused a break in the dam of inertia and scepticism that blocked its progressive course" – *Papanicolaou* (1883-1962)– the father of exfoliative cytology [3].

Kun[7] introduced needle aspiration in 1841. *Erichson* (1853) adopted this method of using an exploring needle to withdraw cells from tumors for cytological diagnosis. It was however, only after Papanicoloau's basic discovery in 1928 of the usefulness of exfoliated cells in the diagnosis of carcinoma that the cytological diagnosis of tumor became popular.

Fine needle aspiration of lymph nodes has been around for quite a long time. In 1904 *Greig* and *Gray*[4,5] isolated trypanosomes by aspirating lymph nodes in patients with sleeping sickness. The technique has subsequently been used to study both benign and malignant diseases.

However, the procedure did not gain wide acceptance in medicine at that time. In the 1930s, Memorial Sloan Kettering[2,7] rediscovered the utility of needle biopsy of head and neck masses. The use of large-bore needles at that time led to frequent complications, one of which was occasional seedling of the tumor along the biopsy tract. The frequent morbidity associated with this procedure prevented widespread acceptance of this technique in other centers of America. A resurgence of FNA occurred in the 1950s, led by physicians in Sweden. FNA was commonly used for cytologic examination of metastatic lesions in the neck with excellent results. Since then, FNA of solitary neck masses has become a well-accepted, safe, and cost-effective procedure in the diagnosis of neck masses.

Forkner (1927)[9], *Martin* and *Ellis* (1930)[8, 10, 11] and *Stewart* (1933) were the pioneers in using fine needle aspiration for lymph node enlargement. This procedure gradually gained momentum through the efforts of *Franzen*, *Zajicek*[6] and *Sodernstorm* in Sweden and now it has become an extremely well documented technique in the diagnosis of palpable/ localized masses.

In India the technique was first introduced at PGI, Chandigarh in the early seventies followed by AIIMS, New Delhi, in the mid seventies[8, 12].

The assumption that aspiration biopsy spreads malignancy appears theoretical rather than actual. *Zajicek* and *Engzell*[16] found no clinical evidence of tumor dissemination along the needle tract after a long follow-up of lymph node FNAC (1971).

ADVANTAGES OF FNAC[8,32]

(i) Office procedure – neither anaesthesia nor patient preparation required

(ii) Eliminates lengthy periods of "watchful waiting"

(iii) Safe and painless

(iv) Cost-effective [32]

(v) High Specificity

(vi) Readily repeatable [23]

(vii) Obviates (in many cases) the need for frozen sections[24]

Special studies like Electron Microscopy or ImmunoHistoChemistry can be used to establish a diagnosis on FNAC.

The emergence of the AIDS epidemic in recent years has greatly increased the number of the patients presenting with lymph node enlargement. The exclusion or confirmation of malignant lymphoma and other malignant processes by FNB is of great practical importance in these patients, since it may obviate the need for surgical excision.

As a rule, the cytological examination can decide whether the lymphadenopathy is due to reactive hyperplasia, malignant lymphoma, or metastatic malignancy. In the case of reactive hyperplasia, surgical excision

is not indicated, unless the subsequent course is atypical. Clinical follow-up is justified in all cases in view of the small but significant rate of false-negative cytological reports.

DIAGNOSTIC CRITERIAS

Diagnosis is made by examination with a scanning and low power microscope.

CRITERIA OF MALIGNANCY

- Cellularity
- Discohesion
- Monomorphism
- Anisonucleosis
- Nuclear membrane irregularity
- Loss of polarity

- Nuclear crowding and piling
- Indistinct cell borders
- Nuclear Cytoplasmic ratio alteration
- Clumped chromatin

CRITERIA OF BENIGN LESION:

- Relative paucity of cells
- Cohesion
- Polymorphism
- Nuclear membrane regularity
- Nuclei of same size
- Polarity
- Distinct cell borders

PATHOLOGY OF CERVICAL NODE

Cervical node involvement in malignancy is grouped as

Zone I includes submandibular and submental nodes.

Zones II to IV encompasses lymph nodes along the jugular vein region deep to the sternocleidomastoid muscle in the upper, mid, and lower neck.

Zone V contains nodes that lie posterior to the sternocleidomastoid muscle. These posterior neck nodes are commonly enlarged with viral infections (eg, mononucleosis) but can also be a site of metastasis for several head and neck cancers.

Zone VI lies between the carotid sheaths bilaterally and contains prelaryngeal and pretracheal nodes that drain the larynx and thyroid gland.

NEOPLASMS

Squamous cell carcinoma

Squamous cell carcinoma is the commonest type of primary carcinoma of the head and neck from the lip, tongue, oral cavity, larynx, etc

[22]. Well-differentiated squamous carcinoma has a tendency to undergo liquefactive degeneration. The aspirate may resemble pus but is more often clear and yellow with a mucoid, viscous consistency.

Extremely dense, globoid, kertinised anucleate cells and cells with bizarre shapes are virtually diagnostic of malignancy. Some authors also report that in squamous cell carcinoma of the head and neck, surgical biopsy prior to definitive surgery may adversely affect prognosis[22].

Nasopharyngeal carcinoma

Criteria for diagnosis (undifferentiated)

1. Undifferentiated malignant cells, single and in compact aggregates.
2. Scanty but well-differentiated eosinophilic cytoplasm.
3. Basaloid cells
4. Normal lymphoid cells in the background .

Nasopharyngeal carcinoma frequently presents to the cytologist as a lymph node metastasis in the neck without a known primary. Cytological recognition is important since the primary is often clinically occult.

Paraganglioma (carotid body and glomus jugulare tumours)

Criteria for diagnosis

1. Neoplastic cells single and in poorly cohesive clusters often with a vaguely follicular arrangement.

2. Abundant but poorly defined, pale cytoplasm with fine red granularity

3. Nuclei round to spindle with finely granular, evenly distributed nuclear chromatin; moderate anisokaryosis.

4. Samples heavily admixed with blood.

Granulomatous Adenitis:

Criteria for diagnosis

1. Histiocytes of epithelioid type forming cohesive clusters.

2. Multinucleated giant cells of Langerhan's type.

3. Epithelioid cells are quite characteristic of smears from lymph nodes. They have elongated nuclei, the shape of which can be described as resembling the 'sole of a shoe'.

Tuberculosis has to be ruled out whether necrosis is present or not. Caseous material appears granular and eosinophilic.

METASTATIC MALIGNANCY

Criteria for diagnosis

1. Foreign cells among normal/relative lymphoid cells.

2. Cytologic criteria of malignancy.

Problems in diagnosis

1. Representative sampling - small metastatic deposits in a reactive lymph node.

2. Benign epithelial, mesothelial or naevoid inclusions.

3. Necrosis or cystic change.

4. Malignant lymphoma.

5. Pseudoepithelial clustering of lymphoid cells or histiocytes in bloody smears.

Special situations

TESICULAR TUMOURS

FNAC findings of testicular tumour

Testicular tumors may be clinically occult and present with metastases

to pelvic, para-aortic or supraclavicular nodes. The cytological pattern of seminoma is characteristic. The tumor cells are mainly dissociated and are mixed with lymphocytes and epithelioid cells. They have large, rounded, vesicular nuclei and an evenly distributed nuclear chromatin. The cytoplasm is dispersed forming a ' tigroid ' background to the nuclei.

PAPILLARY CARCINOMA[35, 36, 39].

FNAC findings of papillary carcinoma

1. Cellular smears.
2. Syncytial aggregates and flat sheets of cells with a distinct ‘anatomical ’ border, nuclear crowding and overlapping.
3. Papillary tissue fragments with or without a fibrovascular core.
4. Enlarged, ovoid, pale nuclei, finely granular, powdery chromatin (pap).
5. Multiple distinct nucleoli; intranuclear cutoplasmic inclusions; nuclear grooves.
6. Dense cytoplasm, distinct cell borders (single cells).
7. Scanty, viscous, stringy colloid (‘Chewing gum colloid’).
8. Squamoid or histiocyte – like, “metaplastic” epithelial cells.
9. Psammoma bodies.

10. Macrophages and debries multinucleate giant cells and lymphocytes variable.

LYMPHOMA

The role of cytology in the diagnosis of lymphoma has become more clearly defined: it is to confirm a clinical suspicion of lymphoma or to exclude it with the highest possible confidence. A cytological diagnosis of NHL is confirmed by open biopsy and histological examination - especially to study the growth pattern - and by immune marker studies necessary for definitive diagnosis and subtyping. A negative cytological diagnosis needs to be supported by clinical observation.

Although FNA biopsy does not replace histological examination in the diagnosis of lymphoma, it is still of value in the management of these patients of the following reasons.

1. In a general practice situation, a cytological diagnosis suggests appropriate referral and further investigations without delay.

2. A representative node can be selected for surgical biopsy by FNB sampling of multiple nodes. The biggest or the most easily accessible node is not always the most suitable and may show only reactive change.

3. If a diagnosis or suspicion of lymphoma is known beforehand steps can be taken to ensure that the node is sent fresh to the laboratory without fixation, so that a complete immunhistochemical investigation can be carried out.

4. Saving time and avoids anaesthesia.

5. For staging purposes FNA biopsies in different sites may be performed.

6. Suspected recurrent or residual disease in patients with previously confirmed lymphoma can in most cases be diagnosed by FNB alone without the need for a formal biopsy. A change in the type of lymphoma will also usually be recognized.

HODGKIN'S DISEASE

Criteria for diagnosis.

1) Typical Reed-Sternberg cells or their mononuclear variants.

2) Atypical mononuclear cells ('Hodgkin cells')

3) Variable number of eosinophils, plasma cells and histiocytes

4) Background population of lymphocytes

5) Immunophenotype: 'classic' Hodgkin's disease: Reed-Sternberg cells, CD30, CD15; small lymphocytes pan T. lymphocyte predominant type: Reed-sternberg cells pan B, CD45, #MA; small lymphocytes pan B.

Subtyped as – Mixed cellularity, Lymphocyte predominant, Lymphocyte depleted, and Nodular Sclerosis.

Problems in diagnosis OF Hodgkin’s lymphoma

1. Poor biopsy yield
2. Reed-sternberg look-alike cells in other conditions.
3. Epitheloid histiocytes suggestive of granulomatous lymphadenitis.

NON – HODGKIN’S DISEASE

The working formulation classification, which identifies the lymphomas according to their grade and is therefore of prognostic and therapeutic significance is followed.

LOW GRADE

- Small lymphocytic
- Follicular small cleaved cell

- Follicular mixed small cleaved
- Large cell.

INTERMEDIATE GRADE

- Follicular predominantly large cell
- Diffuse small cleaved cell
- Diffuse mixed small and large cell
- Diffuse large cell

HIGH GRADE

- Large cell immunoblastic
- Lymphoblastic
- Small non-cleaved cell

Problems In Diagnosis Of Lymphoma

1. Suboptimal cytological preparations.

2. Variable pattern in one node.

3. Distinction from reactive lymphadenopathy .

4. Malignant Lymphoma with few neoplastic cells in a dominant population of reactive lymphoid cells, e.g. T-cell rich B lymphoma.

5. Small cell anaplastic carcinoma and other small cell tumors, particularly versus Malignant Lymphoma- mantle cell and lymphoblastic type.

6. Large cell undifferentiated carcinoma and melanoma versus large cell lymphoma, especially Malignant Lymphoma CD 30 positive.

7. Effects of chemotherapy and radiotherapy.

REACTIVE HYPERPLASIA

The reactive node

Criteria for diagnosis

1. A mixed population of lymphoid cells.

2. A predominance of small lymphocytes.

3. Centroblasts, centrocytes, immunoblasts and plasma cells in variable but 'logical' proportions.

4. Dendritic reticulum cells associated with centroblasts and centrocytes (representing germinal centres).

5. Scattered histiocytes with intracytoplasmic nuclear debris (tingible body macrophages).

6. Pale histiocytes, interdigitating cells, endothelial cells, eosinophils, neutrophils (variable).

It is the commonest change observed in enlarged nodes.

The characteristic features, which differentiate it from lymphoma, are

1.Mixed population of cells representing the whole range of transformation from small lymphocytes to immunoblasts and plasma cells.

2. A predominance of small, sometimes slightly larger 'stimulated' lymphocytes, which have small round nuclei and a characteristic chromatic pattern of large ill-defined condensations.

Problems in diagnosis

1. Follicular hyperplasia with large germinal centres

2. Follicular lymphoma.

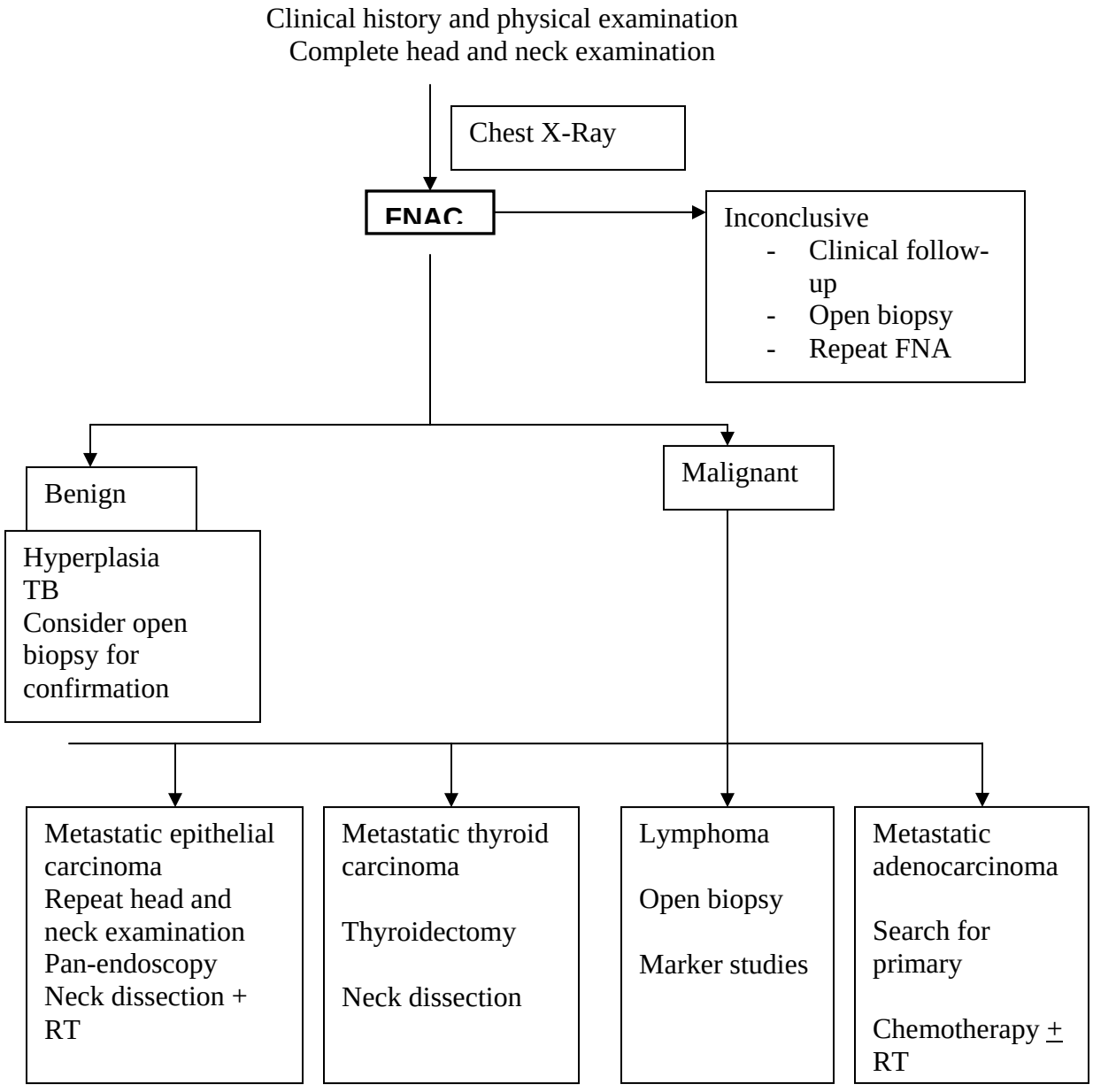
3. Paracortical hyperplasia with prominent immunoblastic and plasmacellular reaction.

4. Prominent histiocytic component.

EVALUATION OF NECK NODES

Evaluation of a patient with a neck mass should always begin with a thorough history, followed by a complete head and neck examination. The entire mucosal surface of the upper aerodigestive tract requires special attention. If the physical examination does not explain the neck mass, a fine-needle aspiration (FNA) of the neck mass may be performed. If the mass is believed to be a metastatic lesion, a panendoscopy of the aerodigestive tract is warranted

Algorithm of the practical approach to cervical adenopathy



METHOD OF REPORT

Definition of Terminology

There is a difficulty when comparing results and techniques from different centers. For the purpose of the current study, we have defined several terms as follows

Adequate sample: Sample adequacy was a subjective judgement made by the histopathologist. A specimen was deemed adequate if the lesion was correctly sampled and if sufficient material was present for a diagnosis to be rendered.

Inadequate sample*:* An inadequate sample was one in which insufficient material was obtained for histologic diagnosis. This includes cases of sampling error, as well as cases in which the lesion was correctly sampled but the histopathologist was unable to render a diagnosis on the basis of the material supplied.

False-negative biopsy result: A biopsy result was considered to be false negative when the tissue sample was thought to be adequate but histologic diagnosis indicated benign disease when the final diagnosis was of malignancy.

False-positive biopsy result: A biopsy result was considered to be false positive when the tissue sample was thought to be adequate but histologic diagnosis indicated malignant disease when the final diagnosis was of benign disease.

DIAGNOSTIC PITFALLS[35]

1. Inexperience
2. Fibrosis
3. Necrosis
4. Difficulty in classification of neoplasm.

Chief causes of false negative diagnosis are still inexperience not only in interpretation but also in cytology techniques and slide preparation.

Geographic miss and lack of representative and sufficient material may be result of inept technique.

Small nodal metastases can be missed and very well differentiated squamous cell carcinoma can cause problems.

The size of the lymph node also influences the adequacy of the aspirate.

Satisfactory samples, both quantitatively and qualitatively, and unequivocal criteria of malignancy are prerequisites for positive diagnosis.

Fibrosis hinders the release of cells from the matrix and leads to false negative results.

If the patient has had radiotherapy, it may be difficult to locate a small recurrence in an area of post-radiation oedema and fibrosis

The distinction between an inflamed branchial cyst and a node metastasis of well-differentiated squamous cell carcinoma with liquefactive necrosis is a particular problem.

Limitations of FNA cytology in the exact diagnosis and subtyping of lymphoma. Conventional cell morphology is not sufficient and must be supplemented with panels of immune markers. Good results are obtained with immunohistological methods applied to cytocentrifuge prepratations of

lymph node aspirates.

Several of the reported studies in which the Kiel classification of non-Hodgking's lymphoma was applied to cytological preparations recorded an acceptable level of accuracy of both diagnosis and classification. However, as a rule histology is necessary - 'no meat, no treat' - to be able to determine the prognostically important growth pattern and also the cellular composition of the tissue section, which is not per se reflected in the aspirated cell sample.

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ACCURACY OF DIAGNOSIS

The accuracy of FNAC of lymph nodes in the diagnosis of metatstatic malignancy is influenced by factors such as the size and site of the node, fibrosis, previous irradiation and the number of punctures made. Adequate material can easily be obtained from nodes only a couple of millimetres in diameter in a cervical or supraclavicular position. Fibrosis in nodes sometimes makes it difficult to obtain sufficient material for diagnosis. It is a problem in nodular sclerosing Hodgkin's disease.

DIFFICULT SITUATIONS

When the mass lesion is hypervascular, sampling obtained by non-aspiration method.

Non-aspiration sampling with a 25-gauge needle is recommended[8]. *Zajdela* [8] recommended needle biopsy without aspiration based on the observation that the capillary pressure in a fine needle is sufficient to keep the scraped cells inside the lumen. In this technique a 25-23 gauge needle is held directly with the finger tips, is inserted into the target lesion and is moved back and forth in various directions within the lesions to an extent that depends on the cellularity and the vascularity of the tissue[8].

DIAGNOSTIC ACCURACY IN VARIOUS SERIES

Ashok saha et al [16] in their study of 140 cases of cervical lymph node aspiration in 1986 here reported 100% diagnostic accuracy for the diagnosis of metastatic squamous cell carcinoma. High specificity of 90 – 95% was reported for other metastatic malignancies and lymphoma.

Martelli G. Pilotti et al 1989[18] here analysed critically 266 cases of FNAC of superficial lymph nodes and reported an over all diagnostic accuracy of 95-100% for benign and malignant lesions.

Engzell.U. & Zajicek.J[6] presented the largest series of metastatic lymph nodes describing 1101 cases and reported a diagnostic accuracy of 90-95%.

References to Indian literature include the study of FNAC in the diagnosis of tuberculosis by Author *M. & Ali.M.A.* in 1985[17] who reported high specificity of 90-95%.

Series of 103 cases of Primary and Secondary lymph nodes ‘comparing FNAB with excision biopsy by *Anand Kumar et al* [14] 1994 obtaining histopathological correlation in 90% of cases.

In patients with lymphoma, tissue diagnosis is essential for treatment both at initial presentation[29] and at possible relapse. The value of cytologic examination in lymphoma is controversial. In specialized laboratories, the diagnostic accuracy of FNAC in lymphoma approaches 79%–90%[30, 31] . However, the required ancillary examination techniques, including immunocytochemistry, flow cytometry, cytogenetics, and molecular

genetics, are not universally available. In practice, the accuracy of FNAC in the assessment of lymphoma is approximately 20% less than its accuracy in carcinoma[32].

Fine needle aspiration is most sensitive at detecting anaplastic (almost 100%) and papillary (around 90%) carcinomas[33, 34]. Diagnosing metastatic or recurrent malignancy by FNAC generally has a high specificity and sensitivity[32].

Complications like hematoma, infarction of the node and sepsis were few and negligible1[3].

There are no reported malignancy following core biopsy of superficial lymph nodes[33], and there are only 12 reported cases in the literature following FNAC. In a large series of cutting-needle biopsies in the head and neck, *Southam et al*[34] found no cases of needle-track metastases after up to 7 years of follow-up.

However the concept of tumor dissemination along the needle track has been revived with the well-documented recent series of *Rousell et al* (92) who studies 10 cases of needle-tract tumor extension following intra-

abdominal node biopsy. The use of needles larger than ZIG, multiple passes and absence of normal parenchymal zone surrounding the malignant zone appear to increase the risk.

CONTRAINDICATIONS FOR FNAC:

None

COMPLICATIONS

Hematoma

Sepsis

Tumor implantation along the needle track.

Serious complications have been reported following FNB or carotid body and glomus jugulare tumors. Confirmation by radiological investigation is therefore preferable before doing FNAC.

IV – MATERIALS AND METHODS

The cytological material for this study was obtained from 100 patients who presented to the general surgical department with cervical lymphadenopathy. The study period was between Jan-2005 and March - 2006. The patients were examined clinically after taking a detailed history,FNAC was done on the same day. Prior to performing the procedure the patient was always informed.

The equipments used

1. Spirit soaked cotton swab
2. 10 ml disposable syringe
3. 22 G disposable needle
4. 5 Glass slides
5. Jar with ether-alcohol fixative

PROCEDURE

Patient was made to lie on a table. The mass was localized and skin prepared with a spirit swab. No local anaesthesia was used. About 5 ml of air was aspirated into the syringe before the introduction of the needle into the mass, which was held between the finger and thumb of the other hand. This is to obtain a uniform distribution of aspiration material on the glass slide. The needle was introduced into the mass. Once the mass was entered the syringe was pulled to full suction and the needle advanced 3 to 5 times to various foci within the mass. With the continued suction, till fluid or cellular material was seen to enter the hub of the needle. Care was taken to ensure that the material was not

Aspirated into the syringe. Thereafter the plunger was released and the fall in suction allows it to return to the 5ml mark. This prevents the forceful dispersion of the aspirate into the cylinder of the syringe while the needle is being withdrawn. Following removal of the aspirated needle, gentle pressure was applied to the aspirated site for 1 – 2 minutes to prevent hematoma formation.

The needle contents were then expressed to glass slides by touching the needle to surface to prevent air-drying and a smear was made in a manner similar to that for a blood film. At least 5 smears were made, one was air-dried and the others were immediately placed in the ether-alcohol fixative.

MODIFICATIONS SUGGESTED INCLUDE

The use of a syringe holder that leaves one hand free to immobilise and feel the target lesion.Needle biopsy without aspiration on the basis that maintained negative pressure only increases the amount of blood aspirated.

Indirect smearing – If thin fluid is aspirated it is best processed by cytocentrifuge. Cell suspension is prepared by rinsing the aspirate containing needles in Hank's balanced salt solution, which is, then span in a cytocentrifuge. Smears of this type are particularly valuable in lymphoma.

The smears were stained with Eosin-Hematoxylin.

After the advent of supplementary techniques, the precision of cytologic diagnosis has improved vastly

These Include

ELECTRON MICROSCOPY

Helps in the unequivocal identification of cell type or differentiation and aids in sub-classification especially lymphoma.

SPECIAL STAINS

The use of PAS / Alcian blue for mucin in adenocarcinoma deposits . Congo red for amyloid (medullary carcinoma), formaldehyde induced fluorescence for melanin precursors are some of the examples.

IMMUNOHISTOCHEMISTRY

The increasing availability of monoclonal antisera to a variety of cell products which are specific to different cell lines is the most significant recent development in cytology. This is especially useful in differentiating anaplastic carcinoma and malignant lymphoma.

Immunohistochemistry is a method of detecting the presence of specific proteins in cells or tissues and consists of the following steps[21] :

1)primary antibody binds to specific antigen;

2) antibody-antigen complex is bound by a secondary, enzyme-conjugated, antibody;

3) in the presence of substrate and chromogen, the enzyme forms a colored deposit at the sites of antibody-antigen binding.

Tab: Immunohistochemical characterization of anaplastic tumours

Antibody against	**Nature of tumour**
Cytokeratin	Epithelial
Epithelial membrane antigen	Epithelial
Leucocyte common antigen	Lymphoid
Vimentin	Mesenchymal, lymphoid
Desmin	Muscle
Actin	Myoepithelial
Neuron-specific enolase	Neuroendocrine, neuronal
S100	Melanocyte, nerve sheath
Factor VIII	Endothelial
CD34 (QB end)	Endothelial

MICROBIOLOGY

Culture studies can be carried out from the aspirate material to establish a specific diagnosis e.g. in granulomatous adenitis.

MORPHOMETRY

Includes computer assisted image analysis, single cell micro-spectrophotometry and flow cytometry applied to FNA preparations. This is a good indicator of prognosis e.g. in lymphoma. It also helps in distinguishing between benign and malignant process.

V – OBSERVATION

A total of 100 patients were subjected to FNAC of cervical lymph nodes using a 22G needle on a 10 ml syringe. HPE correlation has obtained in 73 patients, since remaining 27 patients were diagnosed as non-specific lymphadenitis. They were treated with antibiotics and followed –up in the out patient department. The 73 patients were subjected to surgical excision routinely as part of the study or a part of radical dissection and HPE correlation obtained.

Break up of the cases according to the histology is given in the Table, which follow1: -

The size of the nodes, which were, sampled range from 1 – 6 cm. No complications occurred in the series. All inadequate and inconclusive aspirations were repeated.

METASTATIC LYMPHADENOPATHY

Of the 33 cases examined a total of 30 cases were positive while 3 were false negative. The diagnostic accuracy was 91%

The type was not specified in 4 smears and only a diagnostis of positive for malignant cells was given. Also the correlation was inaccurate in 2 cases where adenocarcinoma and squamous cell carcinoma were reported as anaplastic carcinoma.

Among the 3 false negatives, 2 cases on histopathological examination showed partial replacement of the nodes by malignant cell. The samples were therefore not representative. The otherone was a cystic metastasis from occult papillary carcinoma of thyroid reported as a benign cystic lesion.

LYMPHOMA

Of the 15 cases of lymphoma confirmed by histopathology, 8 cases were reported to be Non-Hodgkin's and 7 Hodgkin's disease.

FNAC was accurate in diagnosing 7 cases of Non-Hodgkin's. The false negative report was that of follicular lymphoma being reported as reactive hyperplasia because of the cellular pleomorphism.

6 cases of Hodgkin's were identified by FNAC and the false negative locked typical R-S cells. Sub-typing was accurate in 10 out of the 15 cases. High-grade lymphomas are readily recognized.

The overall diagnostic accuracy was 87%

TUBERCULOSIS

Of the 25 cases identified by histopathology correlation with FNAC was obtained in 22 cases. The diagnostic accuracy was 88%.

In 2 cases a non-specific diagnosis of granulomatous adenitis was reported.

Among the false negatives where a clinical suspicion was entertained (supplemented with positive Mantoux and history of exposure), two were reported as chronic non-specific adenitis and in one adequate smear could not be obtained due to the presence of necrosis.

BREAK – UP CASES ACCORDING TO HISTOLOGY

Disease	HPE +ve	FNAC +ve	%
Tuberculous Lymphadenitis	25	22	-
Malignant Disease	48	43	-
Lymphoma	15	13	87%
Metastatic adenocarcinoma	5	3	60%
Metastatic squamous cell Ca. (Primary known)	9	9	100%
Metastatic squamous cell Ca. (unknown primary)	6	6	100%
Metastatic thyroid carcinoma	6	5	83%
Metastatic Anaplastic carcinoma	7	7	100%
Reactive hyperplacia		27	

VI – DISCUSSION

FNAB is an effective way to diagnose the pathological process underlying lymphadenopathy.

The diagnostic accuracy in various series ranges from 85% to 100%. Diagnostic accuracy in this study was 88% for benign lesion and 89% for malignancy. It is comparable with various studies[25, 26, 27, 28].

The high rate of accuracy and its simplicity here resulted in FNAB occupying an important place in the initial evaluation of cervical lymphadenopathy. It is still not considered as an alternative to histopathological examination of the node. The extent to which therapeutic decisions can be made solely on the basis of FNAB alone is a moot point.

'An enlarged lymph node should never be excised as the first or even an early step in diagnosis' – Hayes Martin . This is especially true in the case of metastatic malignancy with unknown primary were in it may be detrimental for a number of reasons including-

- Local and possibly general spread of the disease.

- A false sense of security for the patient, who feels that the lump has been removed.

- Compromise of adequate radical dissection due to improperly placed incision.

- Wound infection delaying definitive surgery.

The advantage of FNAB lies in facilitating further work-up in the search of an occult primary tumor. The cytological patterns give clues to the site of the primary tumor.

Only when the primary cannot be found despite the evidence provided by FNAB and supplementary investigations and when this information is likely to be of therapeutic importance is a surgical excision of the node indicated.

PROBLEMS IN THE DIAGNOSIS OF METASTATIC NODES

Representative sampling – small metastatic deposits in a reactive node is the main cause of false negative report and may be missed even by repeated aspirations.

Benign epithelial inclusions of salivary gland origin and thyroid gland origin in cervical nodes have been observed. Although a rare occurrence this possibility should be kept in mind when only a few epithelial cells without obvious malignant features are found in aspirates.

If an aspirate consists of necrotic material it may be difficult to decide whether it represents caseous necrosis or tumor necrosis. Reaspiration should be done from the periphery of the node and examined for cells. Squamous cell carcinoma is particularly proven to undergo liquefactive necrosis.

There is a risk of mistaking cystic metastasis of a well-differentiated squamous cell carcinoma for a branchial cyst. Cystic nodes in the neck may also represent metastases from papillary carcinoma of thyroid.

Follicle cell centre lymphoma (a type of Non-Hodgkin's lymphoma) may resemble metastasis of small cell anaplastic carcinoma. Also large cell lymphoma can be difficult to distinguish from large cell anaplastic

carcinoma without recourse to immunocytochemistry or electron microscopy.

LYMPHOMA

Diagnostic sensitivity has been found to be lower for lymphoma than for metastatic Malignancy. For a diagnosis of lymphoma to be of clinical practical value it must identify good and bad prognostic subgroups and therefore subtype according to one of the current classifications. Cytology is not reliable in this respect.

PROBLEMS IN DIAGNOSIS OF HODGKIN'S DISEASE

Poor biopsy field is a problem in the nodular sclerosis subtype. Use of Rotex screen needle may be necessary to obtain sufficient material.

Reed-Sternberg look alike cells may be present in other conditions like infectious mononucleosis and angioimmunoblastic lymphadenopathy.

The most difficult differential diagnosis is T-immunoblastic lymphoma in which both the giant cells and background of predominantly small T cells

may be very similar to Hodgkin's. Finally an occasional example of large malignant cells with multilobated nuclei in a background of reactive lymphoid cells, representing malignant cells of metastatic carcinoma which were misdiagnosed as Hodgkin's lymphoma.

Clusters of epitheloid histiocytes are sometimes seen in smears of Hodgkin's and Non-Hodgkin's and could suggest granulomatous adenitis. The lymphoid cells must always be carefully scrutinised in lymph node smears containing epitheloid cells.

PROBLEMS IN THE DIAGNOSIS OF NON-HODGKIN'S LYMPHOMA

Cytological subtyping requires experience and expert smear preparation. Smears of a cell suspension prepared in a cytocentrifuge and very helpful in the diagnosis and classification and are better suited for immune marker studies.

Smears may be mistaken for reactive lymphadenopathy unless close attention is paid to the finer cytological details.

Pseudoglandular clusters may simulate small cell anaplastic or adenocarcinoma. This problem occurs in follicular lymphomas. Immuno peroxidase staining for cytokeratin and panleucocyte marker can solve the problem of distinguishing between lymphoma and small cell carcinoma.

GRANULOMATOUS LYMPHADENITIS

The commonest cause in our set-up is tuberculosis. As seen in this series, tuberculosis can be diagnosed with a reasonable degree of accuracy.

The material aspirated can be used for identifying acid fast bacilli with Ziehl-Nielsen stain and for microbiological culture.

TABLE 1 – AGE DISTRIBUTION

Age group	Benign	Malignant	Total
0-10	1		1
11-20	15	4	19
21-30	21	7	28
31-40	11	11	22
41-50	1	12	13
51-60	2	10	12
61-70	-	4	4
>70	1		1

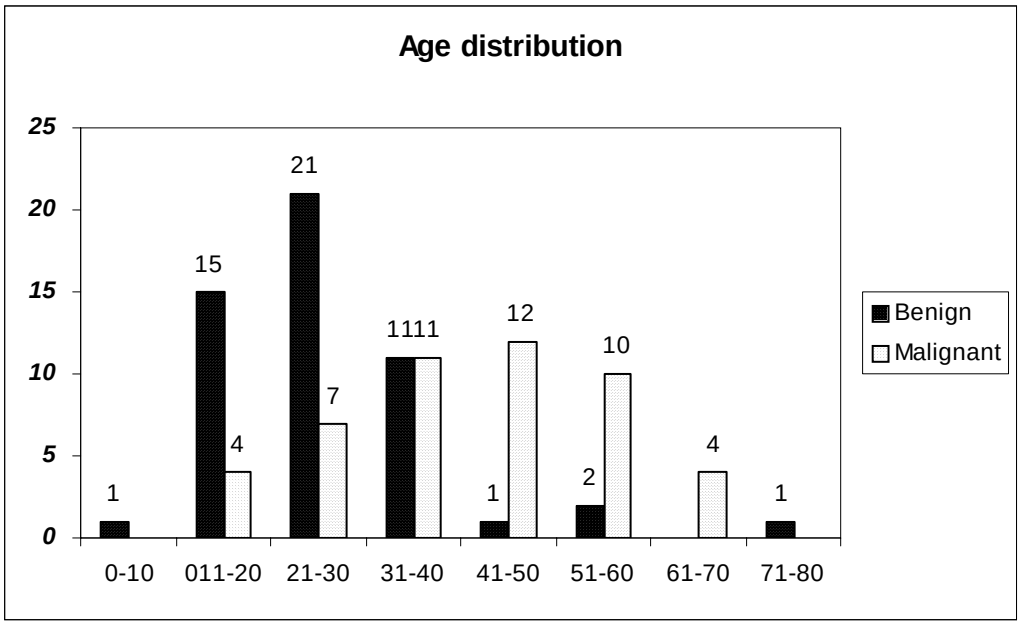


TABLE 2 – SEX DISTRIBUTION

Sex	Number
Male	57
Female	43

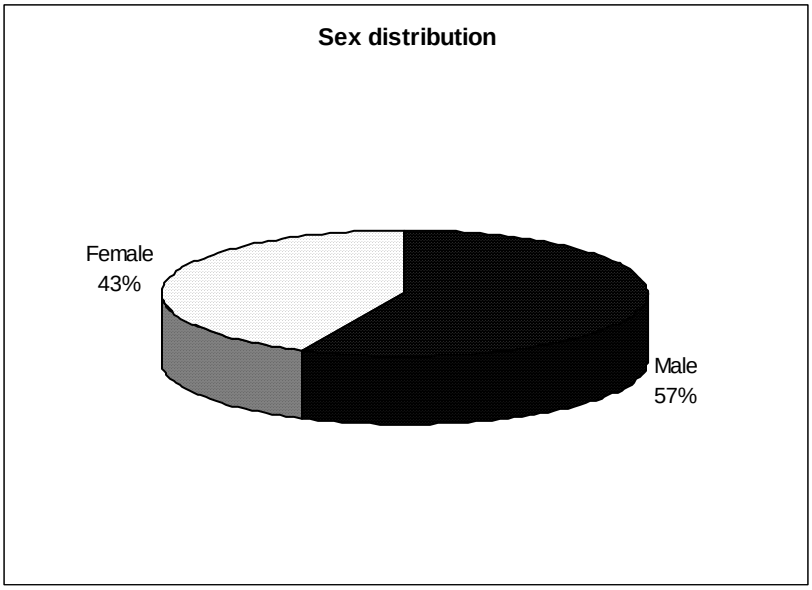


TABLE 3 – DURATION OF SYMPTOMS

Duration (in months)	Number
< 3 months	50
3 – 6 months	45
> 6 months	5

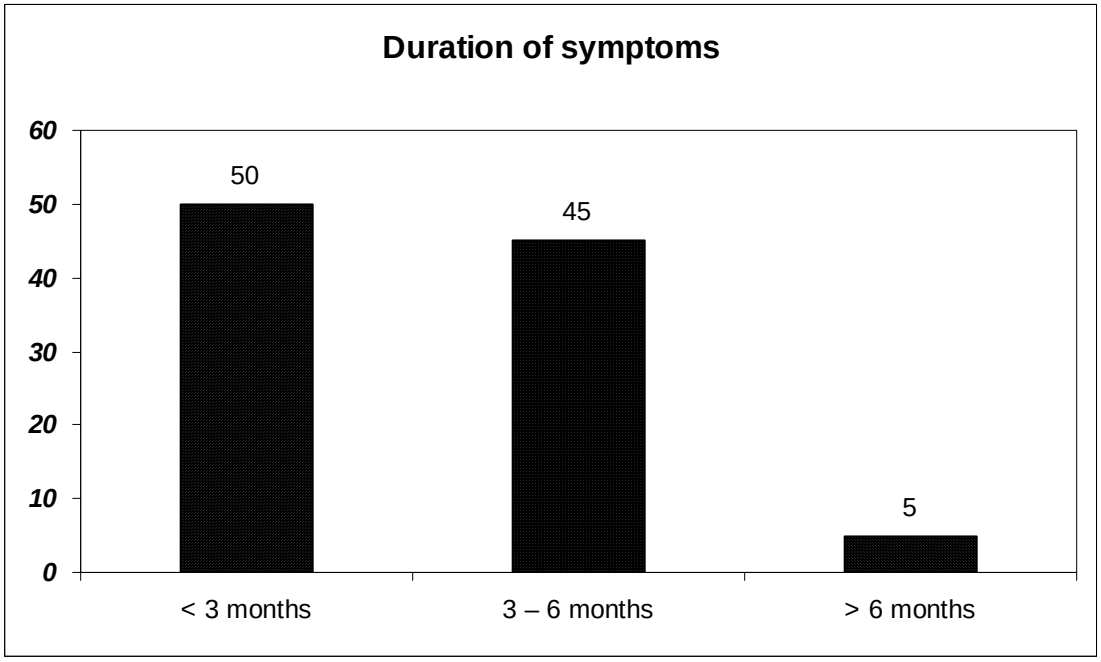


TABLE 4 – MATTED NODES IN TB ADENITIS

Present	**7**
Absent	**18**

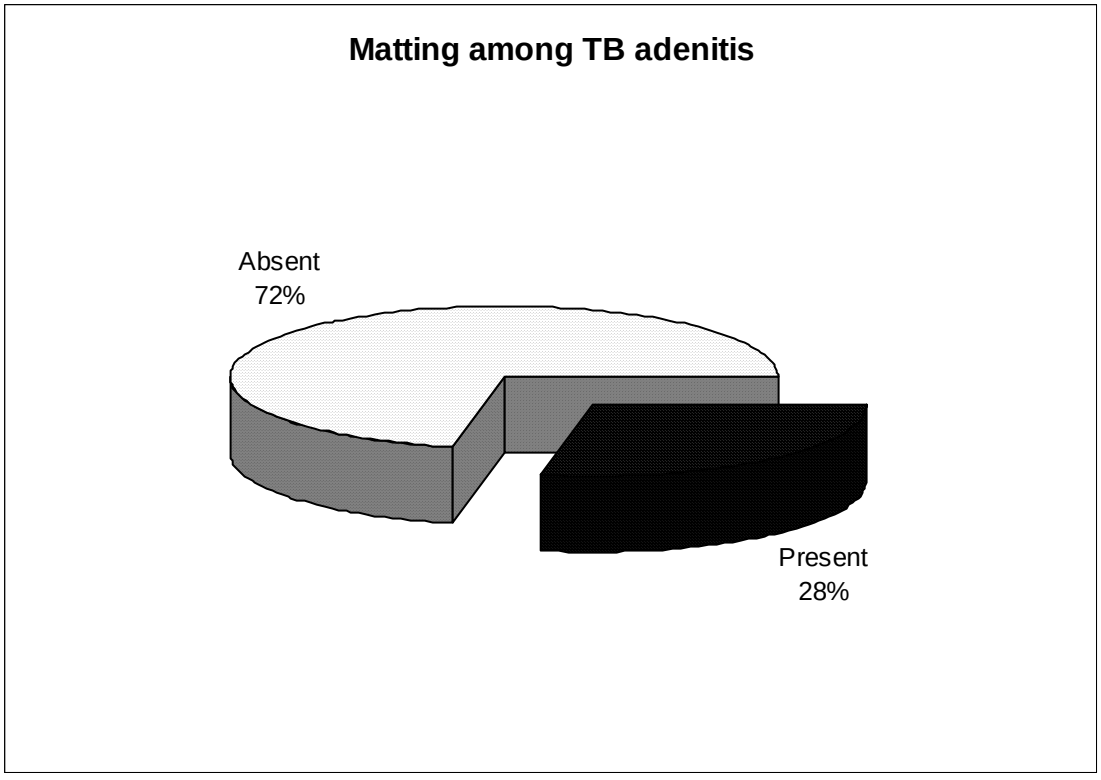
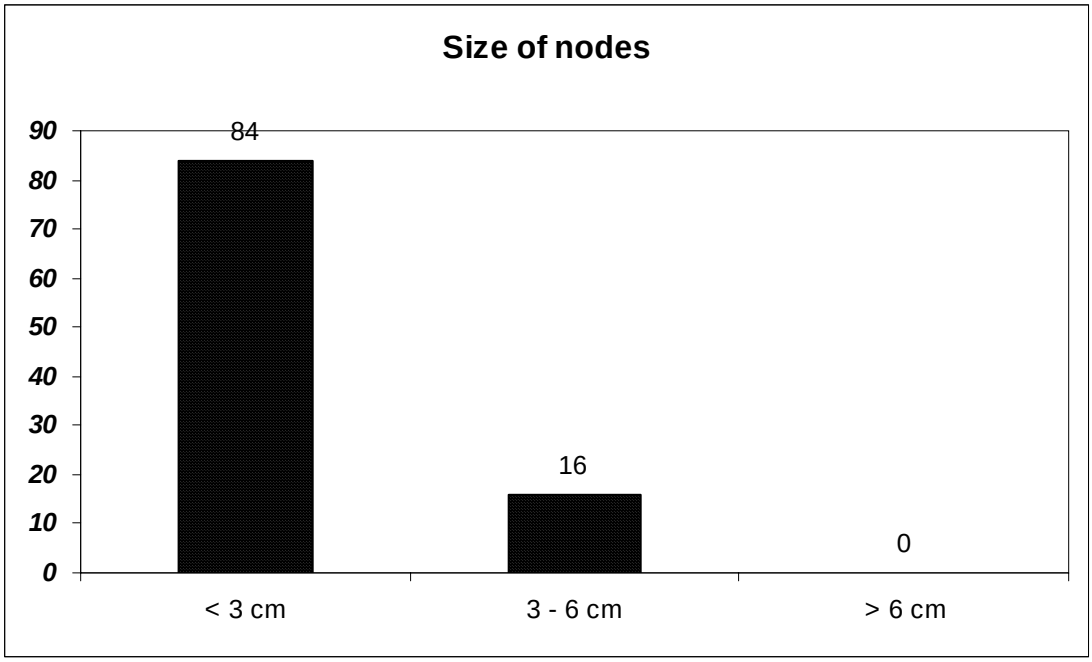


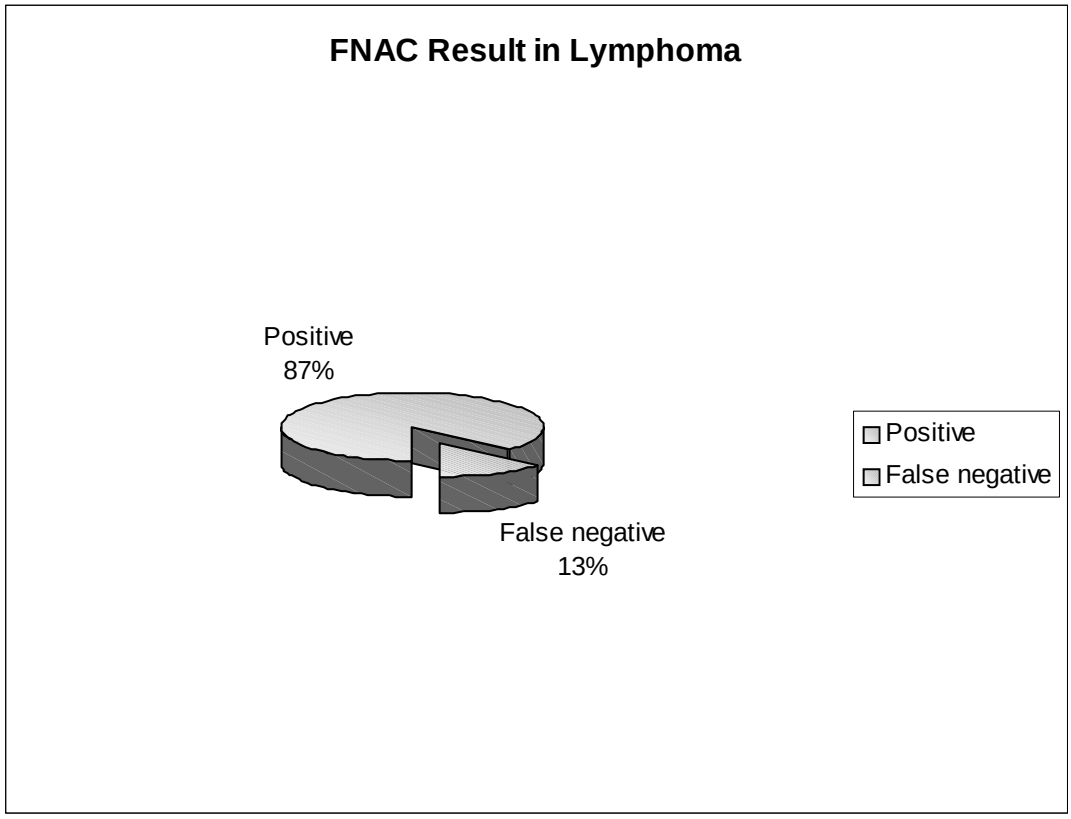
TABLE 5 – SIZE OF THE LYMPH NODES

< 3 cm	**84**
3 - 6 cm	**16**
> 6 cm	**0**



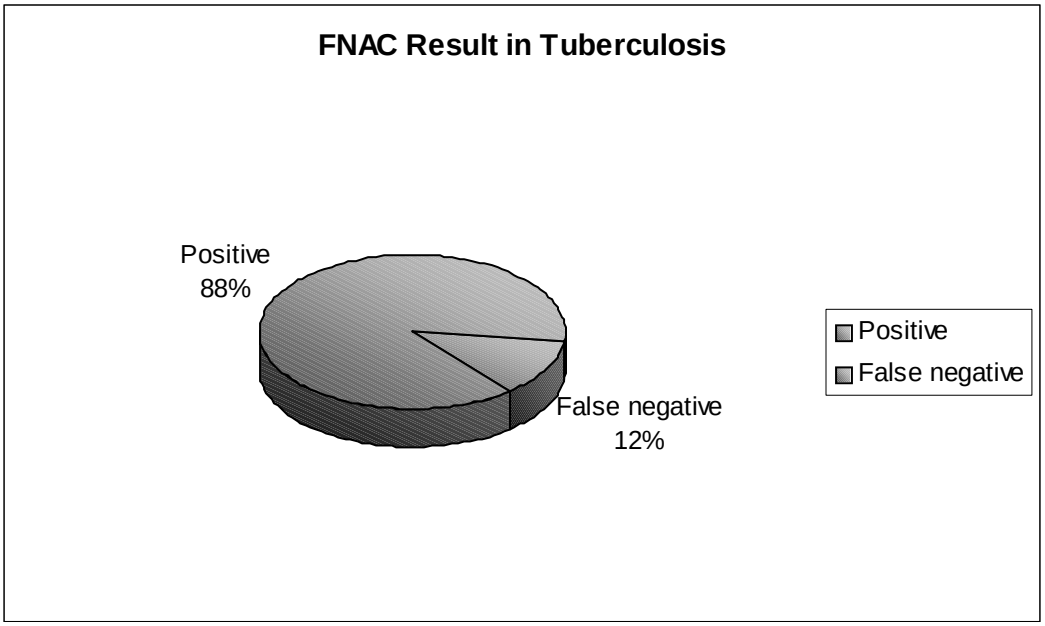
Tab 6. FNAC RESULT IN LYMPHOMA

Cytology + ve	HPE + ve
13	15



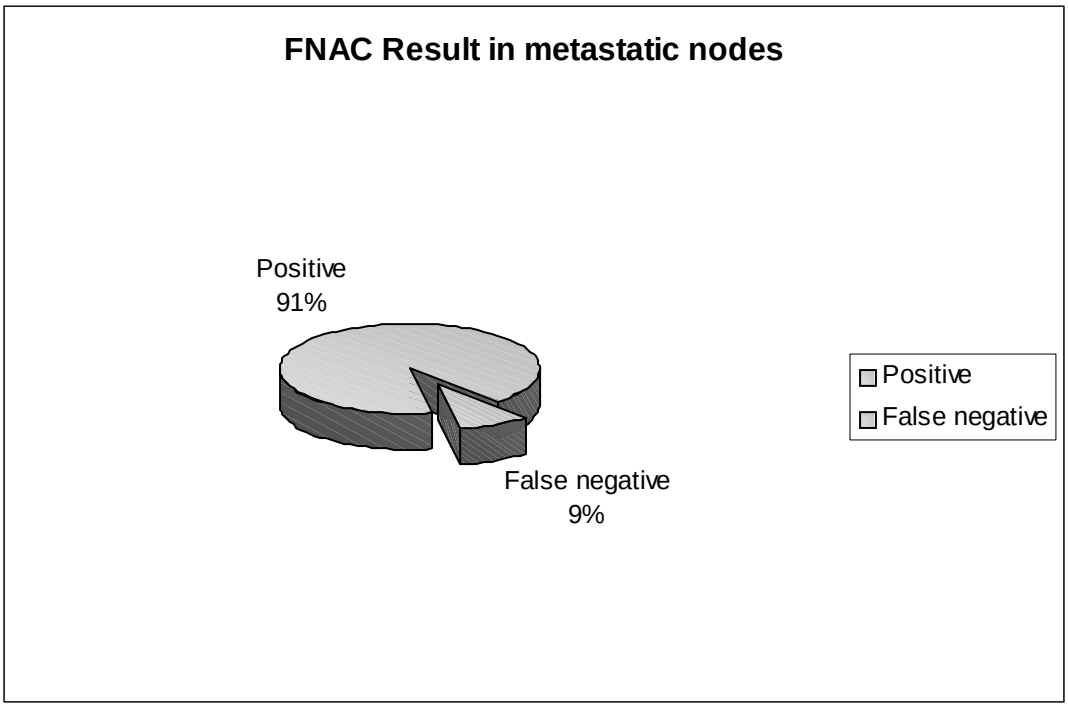
Tab 7. FNAC RESULT IN TUBERCULOSIS

FNAC + ve	HPE +ve
22	25



TAB 8. FNAC RESULT IN METASTATIC LYMPHADENOPATHY

FNAC +ve	HPE +ve
30	33



VII – CONCLUSION

Fine needle aspiration forms one of the most important investigations in the initial evaluation of cervical adenopathy.

It is a very simple, uncomplicated outpatient procedure that offers a rapid and specific diagnosis with little trauma and is very cost-effective [32]. One of its major advantages is the early confirmation of a malignant disease facilitating institution of immediate treatment.

It cannot be over emphasized that fine- needle aspiration is always part of the workup and not the final diagnosis. If the findings do not correlate with the clinical suspicion weight is given to the clinical picture and diagnostic work-up appropriate for the suspected disease is performed.

It should be borne in mind that a negative result on the fine-needle aspiration does not rule out malignancy. Proper use of fine needle aspiration requires close communication between an experienced cytologist and surgeon. This series demonstrates that fine needle aspiration is a safe accurate and valuable tool in the evaluation of cervical adenopathy.

The two fundamental requirements on which the success of FNA depends are representativeness of the sample and high quality of the preparation. It is true that increasing use of more sophisticated techniques here improved the potential to make precise specific diagnoses. But the two pre-requisites mentioned above will always remain the sine qua non.

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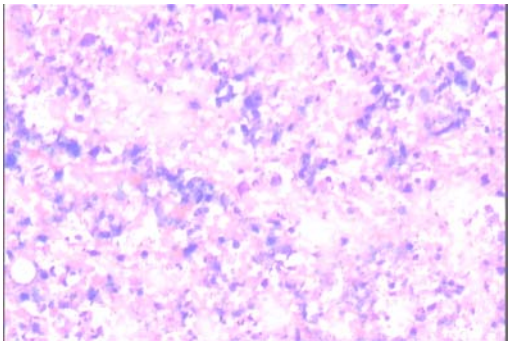
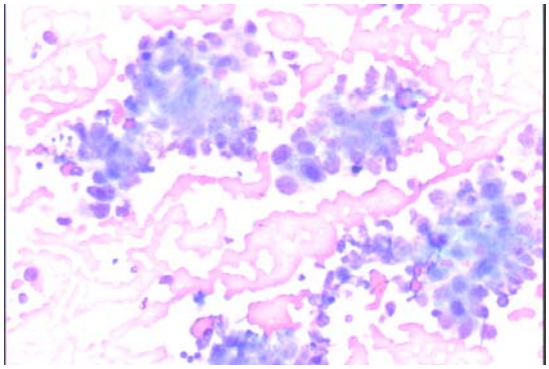
MASTER CHART

COLOUR PLATE I - FNAC

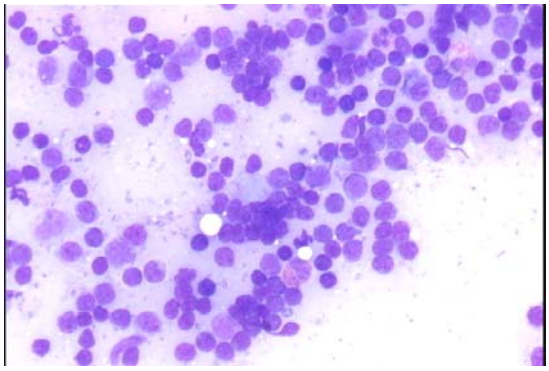
FNAC OF
METASTATIC SQUAMOUS CELL CARCINOMA



FNAC OF METESTATIC ADENOCARCINOMA

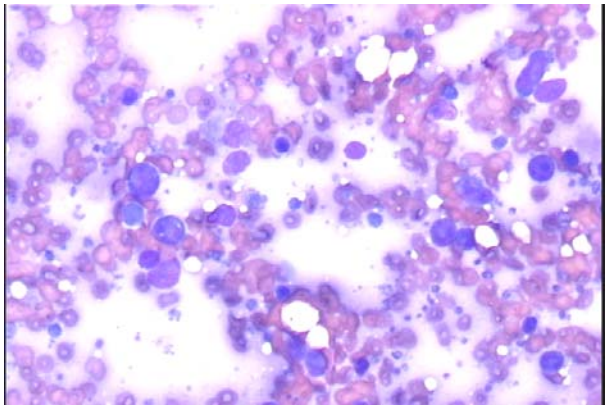


FNAC OF HODGKIN'S DISEASE

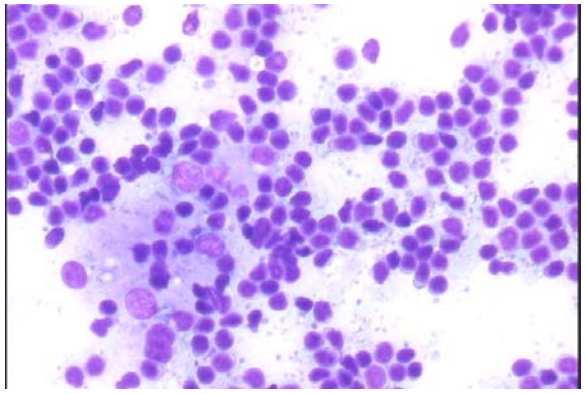


COLOUR PLATE II -FNAC

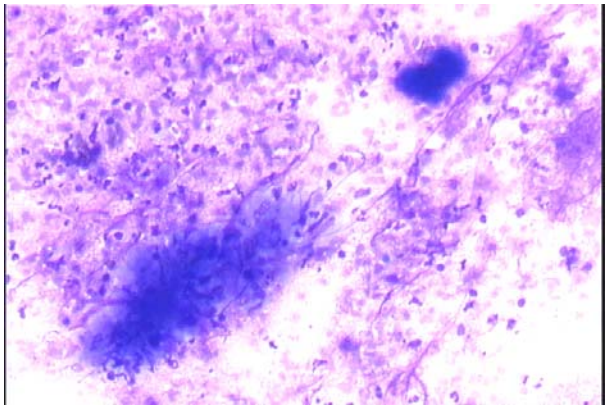
FNAC OF NON-HODGKIN'S DISEASE



FNAC OF FOLLICULAR HYPERPLACIA

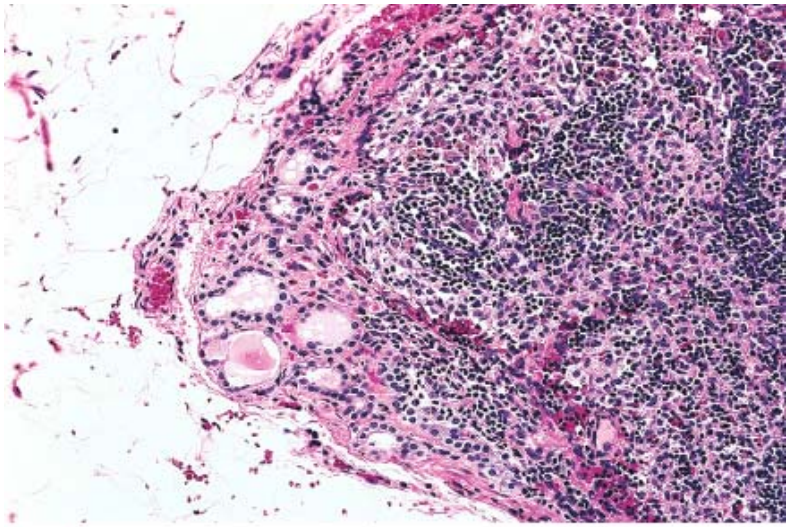


FNAC OF TUBERCULOUS ADENITIS

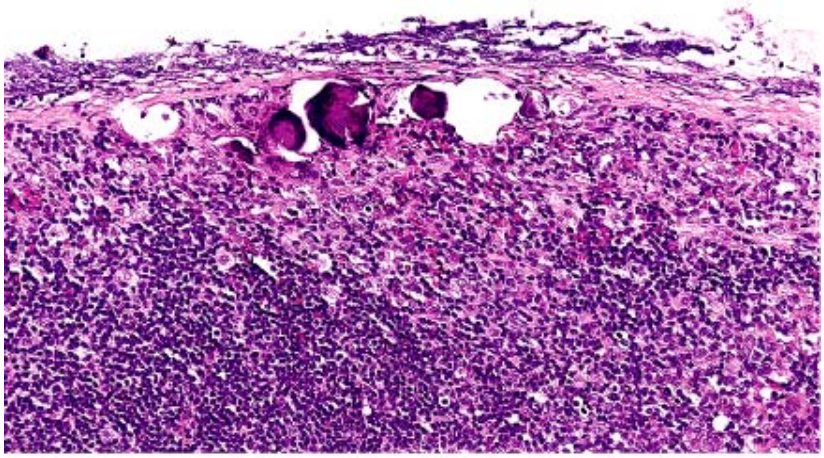


COLOUR PLATE III -HPE

ECTOPIC THYROID FOLLICLES IN LYMPH NODE.

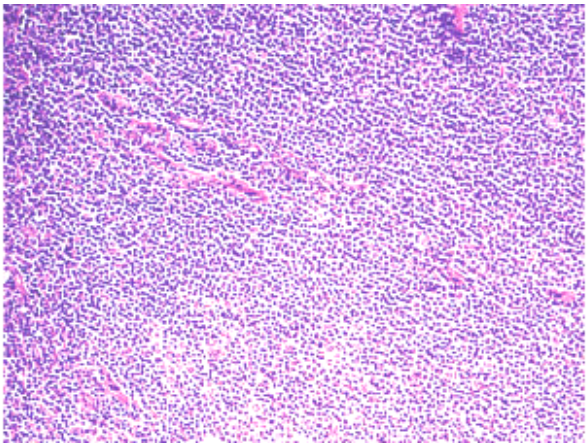


PSAMMOMA BODY BENEATH THE CAPSULE OF LYMPHNODE

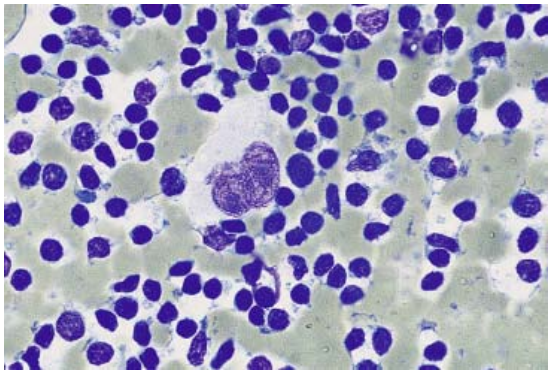


COLOUR PLATE IV - HPE

HODGKIN'S DISEASE – LYMPHOCYTE PREDOMINANT



HODGKIN'S DISEASE – REEDSTERNBERG CELLS



HODGKIN'S DISEASE – NODULARSCLEROSIS