"CORRELATION BETWEEN FNAC AND HISTOPATHOLOGY IN THE DIAGNOSIS OF PALPABLE LESIONS OF HEAD AND NECK- A TERTIARY CARE HOSPITAL BASED OBSERVATIONAL STUDY"

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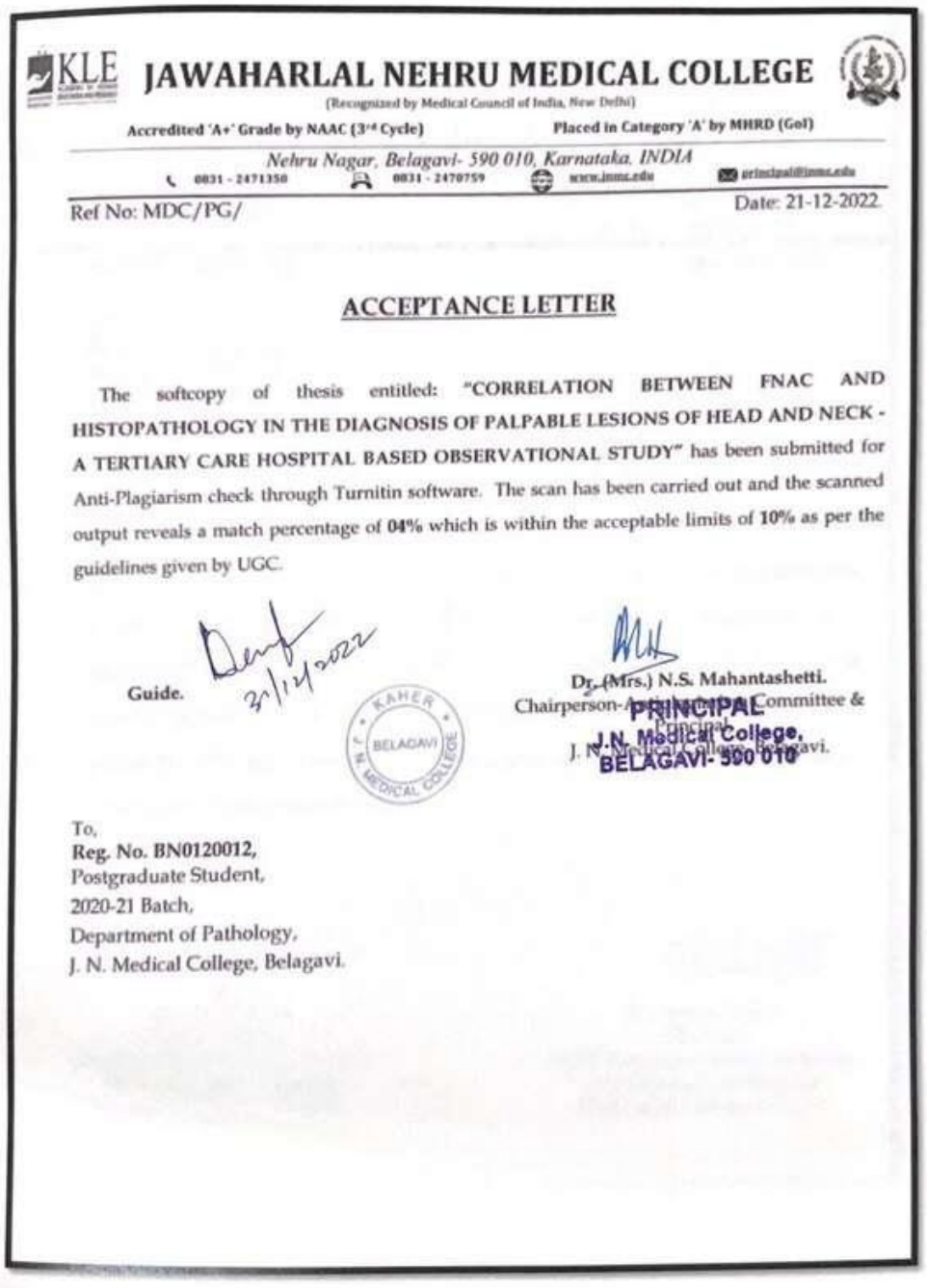

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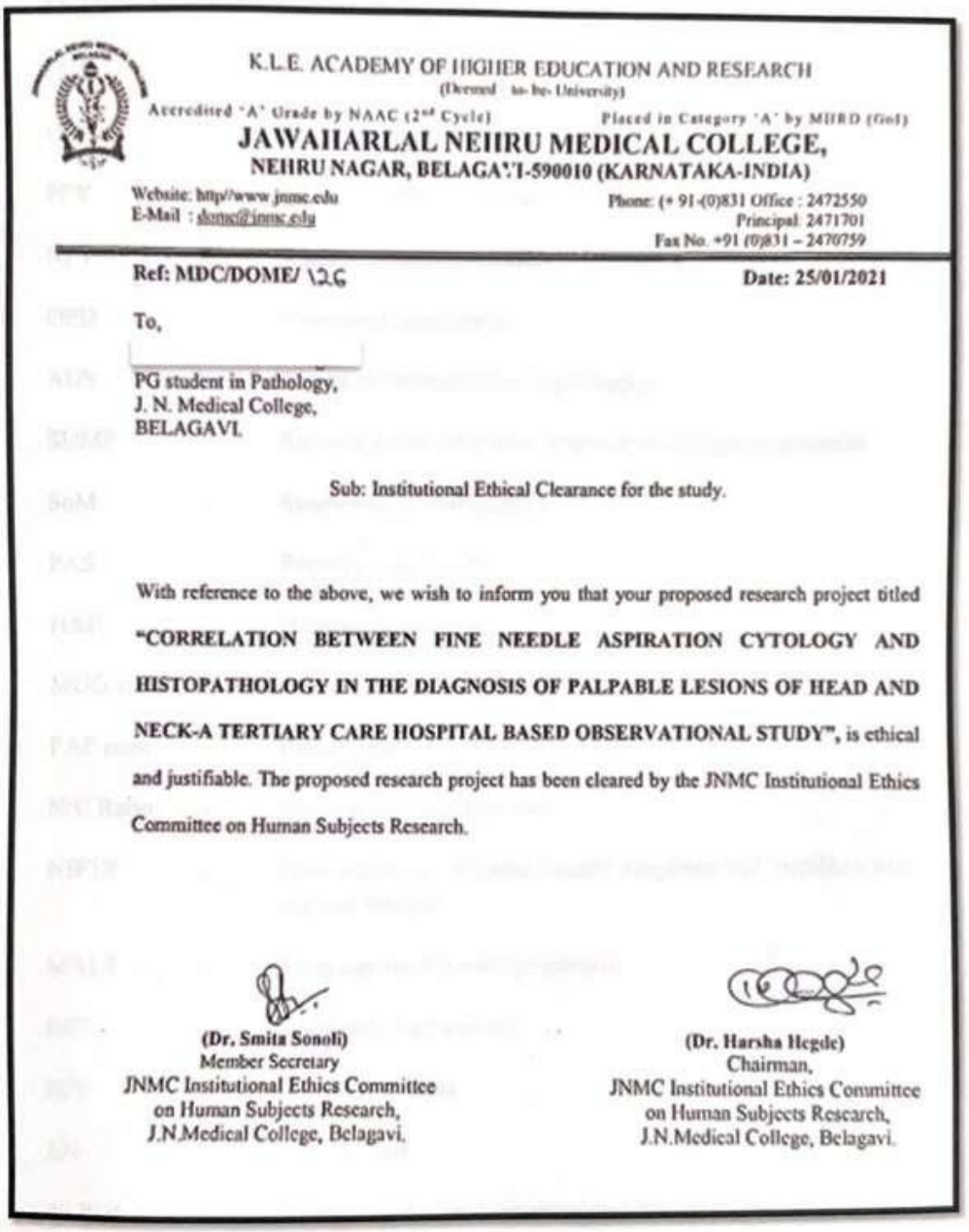

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To,

PG student in Pathology,
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Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"CORRELATION BETWEEN FINE NEEDLE ASPIRATION CYTOLOGY AND HISTOPATHOLOGY IN THE DIAGNOSIS OF PALPABLE LESIONS OF HEAD AND NECK-A TERTIARY CARE HOSPITAL BASED OBSERVATIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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LIST OF ABBREVIATIONS USED

FNAC	-	Fine needle aspiration cytology
FNA	-	Fine needle aspiration
HPE	-	Histopathological examination
PPV	-	Positive predictive value
NPV	-	Negative predictive value
OPD	-	Outpatient department
AUS	-	Atypia of undetermined significance
SUMP	-	Salivary gland neoplasm of uncertain malignant potential
SoM	-	Suspicious of malignancy
PAS	-	Periodic acid-Schiff
H&E	-	Hematoxylin and eosin
MGG stain	-	May Grunwald-Giemsa stain
PAP stain	-	Papanicolaou Stain
N:C Ratio	-	Nuclear: Cytoplasmic ratio
NIFTP	-	Non- invasive Follicular thyroid neoplasm with papillary like nuclear features
MALT	-	Marginal zone B-cell lymphoma
IHC	-	Immunohistochemistry
HPF	-	High power field
LN	-	Lymph node
NLPHL	-	Nodular lymphocyte predominant Hodgkin’s lymphoma
RS cell	-	Reed Sternberg cell
EBV	-	Epstein-Barr virus
CD	-	Cluster of differentiation

SCC	-	Squamous cell carcinoma
NSE	-	Neuron specific enolase
AFB	-	Acid fast bacilli
ZN stain	-	Ziehl -Neelsen stain
10% NBF	-	10% Neutral buffered formalin
NHL	-	Non-Hodgkin’s lymphoma
MRD	-	Medical records department
MNG	-	Multinodular goiter

SOFN- Suspicious of follicular neoplasm

ABSTRACT

BACKGROUND: Various masses can develop in the head and neck region which include growths, lumps or tumours that can arise from lymph nodes, thyroid – parathyroid glands, salivary glands and other cystic lesions like lipomas, dermoid cysts, thyroglossal cysts, skin malignancies, oral cavity lesions etc. For proper treatment of the lesion early recognition and categorization of the lesion is needed. Fine needle aspiration cytology (FNAC) is a cost effective, simple and quick method used to sample superficial lesions found in head and neck. Due to easy accessibility of the target site, minimally invasive nature of the procedure and great patient compliance it holds a lot of importance. The patient also finds these lesions cosmetically unacceptable. Based on the consultants request a thorough cytological and radiological investigation should be done to find the nature of the lesion.[1] FNA as a procedure is non-traumatic, avoids unnecessary anaesthetic complications and the requirement of open surgery. Thus aids in preventing unnecessary use of surgery in case of benign lesions and helps use conservative treatment for these lesions.[2] FNAC has proved to be one of the most valuable tests available in the initial assessment of such lesions. Thus allowing the clinician to take immediate and urgent treatment calls for the well-being of the patient.[3] Despite these various advantages and usefulness, it's been advised that FNAC cannot replace HPE since the biological material that is obtained on FNAC does not provide precise details of cellular architecture, and hence making HPE to be viewed as the gold standard for diagnosing a number of lesions[4].

OBJECTIVES: To find the correlation between Fine Needle Aspiration Cytology and Histopathology in the diagnosis of palpable head and neck lesions, to assess the

efficiency of FNAC as an first line diagnostic tool in patients with swellings of head and neck and to obtain organ wise statistical analysis of all head and neck lesions.

MATERIALS AND METHODS: In this observational study we have taken 46 swellings of Head and neck lesions of patients who underwent FNAC and HPE at our Institute over one year prospectively and two years retrospectively. The data is collected using a predesigned proforma .The information about the clinical parameters were obtained from the clinical records from MRD and Department of Pathology, Dr. Prabhakar Kore Charitable Hospital and MRC, Belagavi. The results of which were further analysed.

RESULTS: In our study which comprised of 46 cases 30% were males and 70% were females, giving a Male:Female Ratio of 1:2.33. Out of 46 lesions we observed a Concordance of 91.3% and Discordance of 8.7% on correlating cytological diagnosis with Histopathological diagnosis. The association between FNAC diagnosis and Histopathological diagnosis is statistically significant with p value < 0.005%. The sensitivity, specificity, positive predictive value and negative predictive value of FNAC as a diagnostic tool are 87.5%, 94.7%, 77.77% and 97.29% respectively.

CONCLUSION: FNAC is a safe and simple diagnostic modality for palpable head and neck lesions and has high accuracy and specificity. Despite the high sensitivity of FNAC, there are certain pitfalls due to the misleading diagnostic yield. FNAC and Histopathology should complement each other along with other newer diagnostic techniques for the diagnosis to be reliable and accurate for further management.

KEY WORDS: FNAC, Histopathology, thyroid, salivary gland, lymph node, head and neck

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INTRODUCTION

Various masses can develop in the head and neck region which include growths, lumps or tumors that can arise from lymph nodes, thyroid – parathyroid glands, salivary glands and other cystic lesions like lipomas, dermoid cysts, thyroglossal cysts, skin malignancies, oral cavity lesions etc. Face and neck having a rich blood –lymphatic supply, any malignant lesions here have a high chance of metastasizing to the brain due to its close proximity. Neck lymph nodes are the secondaries for multiple primary malignancies in the rest of the body and these being superficial structures in the neck, any metastasis to these nodes is immediately identified as swellings by the patient. Thus allowing early detection of any suspicious lesions.

The lesion should be identified and classified at an early stage for proper treatment. Fine needle aspiration cytology (FNAC) is a simple, quick, cost effective method used to sample superficial lesions found in head and neck . Since the target tissue can be easily accessed and the procedure being very minimally invasive with great patient compliance FNAC holds a lot of importance. The patient also finds these lesions cosmetically unacceptable. Based on the consultants request a thorough cytological and radiological investigation should be done to find the nature of the lesion.[1]

FNA as a procedure is non-traumatic, avoids unnecessary anesthetic complications and the requirement of open surgery. Thus aids in preventing unnecessary use of surgery in case of benign lesions and helps use conservative treatment for these lesions.[2]

In patients who present with a mass in the head and neck region or a recurrence after previous treatment, FNAC has proved to be one of the most valuable tests available in the initial assessment of such lesions. Thus allowing the clinician to take immediate and urgent treatment calls for the well-being of the patient.[3]

Despite these various advantages and usefulness, it's been advised that FNAC cannot replace HPE since the biological material that is obtained on FNAC does not provide precise details of cellular architecture, and hence making HPE to be viewed as the gold standard for diagnosing a number of lesions[4]

AIMS AND OBJECTIVE

1. To study the correlation between Fine Needle Aspiration Cytology and Histopathology in the diagnosis of palpable head and neck lesions.
2. To assess the efficiency of FNAC as a first line diagnostic tool in diagnosingswellings of head and neck.
3. To obtain organ wise statistical analysis of all head and neck lesions

REVIEW OF LITERATURE

FINE NEEDLE ASPIRATION CYTOLOGY:

The origin of FNAC was around the year l950. The concept of introducing a needle into abnormal tissue to retrieve cells and tissue fragments wasn't new. To diagnose cancer in the mid-nineteenth century, Kün (l847), Lebert (l85l) and Menetrier (l886) used needles to take tissue. Leyden (l883) retrieved pneumonic microorganisms by using the same technique. Clinicians were largely involved in the development of aspiration cytology along with exfoliative cytology. Bone marrow needling was a common practice in those times that led to the realization that such a simple technique did not require the intervention of expensive anesthesia and surgeons. In l927, Dudgeon and Patrick from UK,proposed that rapid microscopic diagnosis was possible just by needling of tumors. During the same time, Martin and Ellis in the USA were also promoting needle aspiration, even though the pathologists who were working with them initially said that a confident diagnosis could be made by obtaining tissue fragments through sectioning as well as smearing the samples. At around the same time, Martin and Ellis adopted thicker needles than those used today. General awareness in 'aspiration biopsy' took another 40 years to develop in the USA. l950s and l960s was the time when FNAC in Europe began to flourish. Thousands of cases were being studied each year by Söderström and Franzén in Sweden, Zajdela in France, Lopes Cardozo from Holland. Pathologists at the Radiumhemmet adopted this technique. As experience accumulated Sweden and countries like America, Europe, Asia and Australia came to study the technique, in the next few years. FNAC is now part of all departments of pathology.[5-17]

Advantages of FNAC

- It is a simple OPD technique

- Helps give quick diagnosis
- Economical
- Can access multiple sites
- Many ancillary tests can be done on the material obtained by FNAC

Limitations

- Cannot comment upon architecture
- Capsular and lympho-vascular invasions are not identified
- Differentiating in situ as opposed to invasive carcinoma is difficult
- Considerable training is needed for accurate diagnosis

Complications

- Hematoma
- Rupture of aneurysmal vessel
- Anaphylaxis
- Surgical emphysema
- Bowel perforation
- Infarction
- In cases where thick bore needle is used, needle tract seedling of cancer cells is possible.

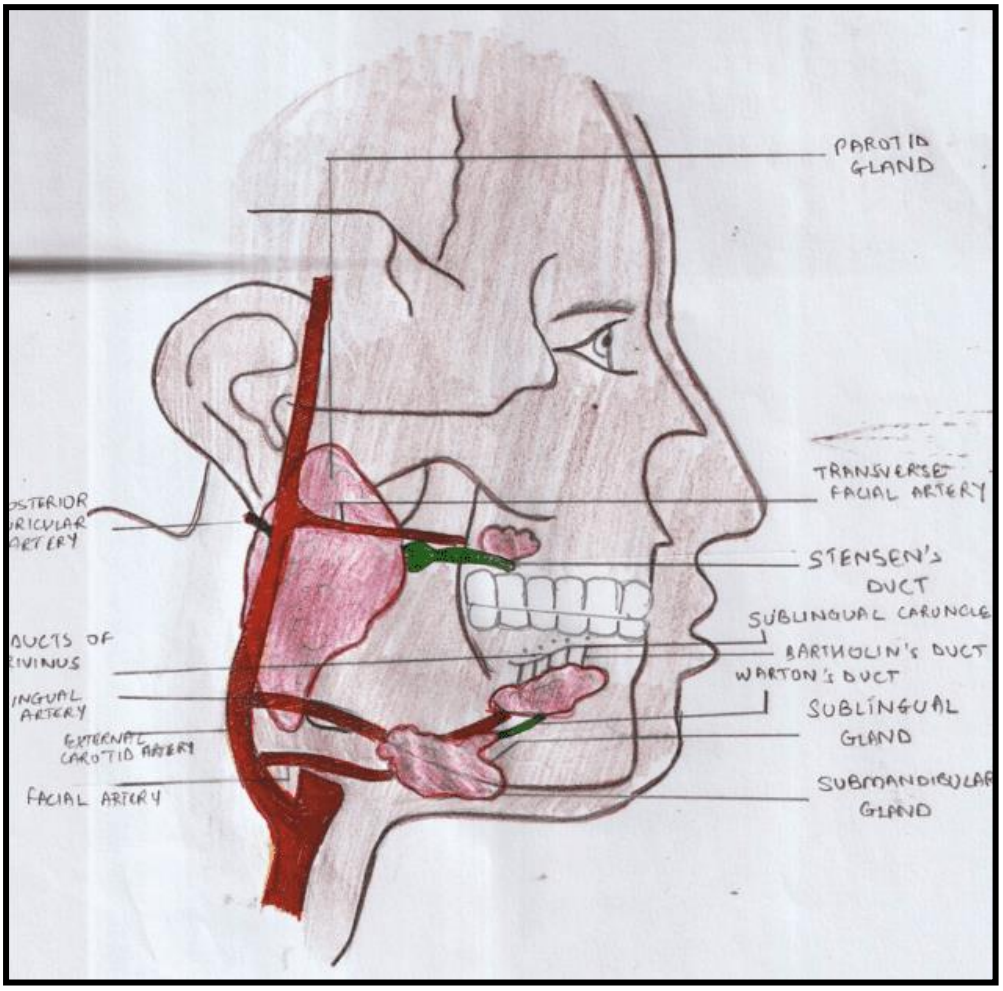
FNAC PREREQUISITES

It is advisable that the procedure should be performed by the cytopathologist himself/herself. A 22–23G needle is routinely used. The FNAC clinic should preferably be located as an OPD service. The room should have good source of light. Should include examination bed, basic equipments for FNAC, waste disposal baskets, rapid staining kit and small binocular microscope, sink with water connection and a cytotechnologist. Clinical history should be taken before starting the procedure. Chief complaints should be asked for. Preparation of the patient should include talking to the patient and ask about the swelling. Explain the procedure, purpose, complication and advantages of the procedure. Written consent should be taken. [18-20]

SALIVARY GLANDS

EMBRYOLOGY

The primitive oral cavity and pharynx are separated by the oropharyngeal membrane. Ectodermal derived structures develop external to the oropharyngeal membrane and endodermal arise internal to the membrane. The parotid gland is ectodermal in origin. Sublingual and submandibular glands are of ectodermal and endodermal origins respectively. A primitive epithelial bud forms each gland. The order of formation of glands is firstly the parotid glands, then the submandibular glands, and sublingual glands, and lastly by l0th week the minor salivary glands develop. Branching morphogenesis of the epithelium is the basis of development of salivary gland. By l6 weeks the intercalated and striated ducts are seen, and by the 20th to 24th weeks the acinar cells become prominent. Development of salivary glands continues up to 28 weeks. At birth the glands become functionally capable to secrete saliva. Although the parotid is the first gland to develop, it gets encapsulated last. The lymphatic system near the major salivary glands forms from the mesoderm just before the parotid gland gets encapsulated[21-23]



ANATOMY AND HISTOLOGY OF THESALIVARY GLAND

Salivary glands are the tubuloalveolar exocrine glands that develop from the oral mucosa.

There are two groups of salivary glands:

a. Major salivary glands: These consist of a pair of parotid glands, submandibular glands and sublingual salivary glands.

b. Minor salivary glands: There are large number of minor salivary glands in the mucosa of the oral cavity, nasal sinuses, larynx and bronchial tree.

Parotid gland: It is the largest salivary gland and weighs between 20 and 25 g. It is primarily a serous gland. The location of each parotid gland lies in the angle of

the mandible. Anatomically, the gland is circumscribed by the masseter muscle in the front, the external auditory canal in the middle and the styloid process, internal carotid artery, and the jugular vein in the back. The parotid gland's secretion enters the oral cavity near the upper second molar tooth via the Stensen's duct, which travels along the masseter muscle and then penetrates the buccinator muscle. Lymphoid tissue is incorporated into the parotid gland during embryological development; this may be the cause of origin of Warthin's tumour. The facial nerve and its branches cross between the two compartments where the superficial and deep parts of the gland are split. The majority of parotid gland tumors originate from the superficial lobe as superficial bulging, whereas those in its deeper lobe manifest as parapharyngeal swelling.[24]

Submandibular salivary gland: It is considerably smaller and lighter than the parotid gland. It weighs 7-8 g and is a seromucinous gland. It is situated in the submandibular triangle and is bordered superiorly by the mandible, posteriorly by digastricus -posterior belly, and anteriorly by the anterior belly of the digastricus. The gland has both superficial and deep lobes. The gland secretions pass through the Wharton's duct, which exits the mouth's floor posterior to the lower incisor tooth.[24]

Sublingual gland: With a weight of just 3 g, it is the smallest major salivary gland. This gland secretes mucin and is situated in the sublingual fossa. Its secretion travels through a number of excretory channels before emerging into the mouth cavity.[24]

HISTOLOGY

Secretory and ductal parts make up the main salivary gland. Acini that are bordered by cells of the serous, mucinous, or mixed (seromucinous) cell types make up the secretory portion. The triangle form of the cells has the broad end facing the basement membrane and the narrow end facing the luminal region. The individual cells have nuclei positioned basally and a basophilic granular cytoplasm. In acini, the cells are organized into lobules that are ringed by myoepithelial cells. The intercalated ducts and the acini opens a bigger excretory duct.[24]

ROLE OF FNA IN SALIVARY GLAND LESIONS

A correct diagnosis by FNAC may appear to be difficult due to the wide range of salivary gland disorders available. The goal of FNAC in combination with radiological and clinical data is to provide a primary evaluation based on which therapeutic calls might be taken.

COMPLICATIONS [33]

- Hemorrhage
- Facial nerve pain
- Infection
- Post-FNAC changes: Squamous metaplasia, infarction
- Inflammation

INDICATIONS

Any unexplained salivary gland lesion that occupies space is a candidate for FNAC. FNAC offers a trustworthy diagnosis that confirms the mass's salivary gland origin and provides details on the lesion's neoplastic or non-neoplastic nature. The FNAC diagnosis of the neoplastic lesion aids the surgeon in deciding whether to do

radical or superficial surgery. Incision biopsy may result in the creation of a fistula or a possible infection and facial nerve palsy and FNAC can stop this. Additionally, FNAC offers good specificity and sensitivity for confirming the presence of cancer.[25-34]

The Milan system for Reporting Salivary Gland Cytopathology: [35]

Diagnostic category	**Risk of malignancy (%)**	**Management**
I. Non-diagnostic	25	Clinical and radiologic correlation/repeat FNAC
II. Non-neoplastic	l0	Clinical follow-up and radiological correlation
III. Atypia of undetermined significance (AUS)	20	Repeat FNAC or surgery
IV. Neoplasm		
Neoplasm: Benign	<5	Surgery or clinical follow-up
Neoplasm: Salivary gland neoplasm of uncertain malignant potential (SUMP)	35	Surgery
V. Suspicious for malignancy (SoM)	60	Surgery
VI. Malignant	90	Surgery

World Health Organization Histologic Classification of Tumors of the Salivary Glands[36]

MALIGNANT TUMORS

Mucoepidermoid carcinoma
Adenoid cystic carcinoma
Adenocarcinoma, NOS
Polymorphous adenocarcinoma
Acinic cell carcinoma
Clear cell carcinoma
Basal cell adenocarcinoma
Intraductal carcinoma
Salivary duct carcinoma
Myoepithelial carcinoma
Epithelial-myoepithelial CA
Carcinoma ex pleomorphicadenoma
Secretory carcinoma
Sebaceous adenocarcinoma
Carcinosarcoma
Poorly differentiated carcinoma
Undifferentiated carcinoma
Large cell neuroendocrine CA
Small cell neuroendocrine CA
Lymphoepithelial carcinoma
Squamous cell carcinoma
Oncocytic carcinoma
Uncertain malignant potential
Sialoblastoma

BENIGN TUMORS

Pleomorphic adenoma
Myoepithelioma
Basal cell adenoma
Warthin tumor
Oncocytoma
Lymphadenoma
Cystadenoma
Sialadenoma papilliferum
Ductal papillomas
Sebaceous adenoma
Canalicular adenoma and other ductal adenomas

NONNEOPLASTIC EPITHELIAL LESIONS

Sclerosing polycystic adenosis
Nodular oncocytic hyperplasia
Lymphoepithelial sialadenitis
Intercalated duct hyperplasis

BENIGN SOFT-TISSUE LESIONS

Hemangioma
Lipoma/sialolipoma
Nodular fasciitis

HEMATOLYMPHOID TUMORS

Extranodal marginal zone lymphoma of MALT, lymphoma Sialadenitis, Sialolithiasis,Sialadenosis

NORMAL ASPIRATE [37]

The aspirate smear shows a heavily blood stained but scanty cellular aspirate. The acinar cells, resemble grapes in a bunch . The individual acinar cells form tightly packed tissue fragments delineated by a basement membrane and bound together by fibrovascular stroma. The individual acinar cells have finely vacuolated abundant bubbly cytoplasm. The nucleus is small round and is eccentrically placed at the base of the cell. The ductal epithelial cells are smaller and contain a dense cytoplasm. Their nuclei are round. Individual cells may be in tubules or small cohesive flat sheets. Occasionally background may show stripped nuclei of acinar cell . In the background adipose tissue, fibrous tissue which is loose and endothelial cells can be seen**.**

LESIONS OF SALIVARY GLAND

NON NEOPLASTIC/INFECTIOUS

- BRANCHIAL CYST
- ACUTE SIALADENITIS
- CHRONIC SIALADENITIS
- SIALADENOSIS
- RETENSION CYSTS

BENIGN

- PLEOMORPHIC ADENOMA
- BASAL CELL ADENOMA
- WARTHIN TUMOR
- ONCOCYTOMA
- MYOEPITHELIOMA

MALIGNANT

- MUCOEPIDERMOID CARCINOMA
    - LOW GRADE
    - INTERMEDIATE/HIGH GRADE
- ACINIC CELL CA
- ADENOID CYSTIC CA
- POLYMORPHOUS LOW GRADE CA
- SALIVARY DUCT CA
- EPITHELIAL MYOEPITHELIAL CA
- ADENOCARCINOMA OF NO SPECIAL TYPE
- METASTATIC MALIGNANCY

BRANCHIAL CYST

CYTOLOGY

The aspirate reveals a pus-like, gray-yellow fluid of variable thickness. Squamous epithelial cells and anucleate keratinized cells, mostly mature but some metaplastic are also seen in the smear. The background shows amorphous debris and inflammatory cells[38,39]

INFECTIOUS SIALADENITIS

CYTOLOGY

The aspirate is purulent and the smear contains varying amounts of inflammatory cells in acute sialadenitis. Occasionally chronic sialadenitis shows rare acinar and inflammatory cells, along with sparse tissue consisting of ductal epithelial cells are seen. Ductal epithelium showing squamous metaplastic changes and/or regenerating atypia are seen arranged in sheets. The background displays a fibrous stroma.[40]

CHRONIC SIALADENITIS

HISTOLOGY

Tissue shows large amount of acinar atrophy, fibrosis and lymphoplasmacytic inflammation. There may be periductal inflammation and be a little neutrophilic inflammatory reaction. Frequently lymphoid aggregates are seen. Due to atrophy the acini may totally disappear. Squamous cell and mucous cell metaplasia are two metaplastic alterations that can occur in the ductal epithelium. Salivary glands that are irritated frequently undergo oncocytic transformation. Saliva extravasation due to duct rupture may be accompanied by a granulomatous inflammatory reaction.[41]

SIALADENOSIS

CYTOLOGY

With the exception of an expanded acinar diameter and cytoplasmic modifications, the smear from the aspirate shows glands that appear generally normal under the microscope. The acinar diameter may be two to three times larger than predicted in part due to cellular hypertrophy. The acinar cells are enlarged and seem to be transparent or basophilic (honeycombed or vacuolated pattern). Inflammation is not present. If the illness doesn't get better, the parenchyma eventually atrophies and is replaced with fat. This lesion has been accurately diagnosed by FNA biopsy. [41-45]

MUCUS RETENTION CYST

CYTOLOGY

Although the aspirate shows mucous cells and squamous epithelium, the epithelium is made up of columnar cells which may show snouting. The stroma appears loose and edematous, and the cyst's epithelial basement membrane may appear thickened. Oncocytic and papillary changes of the epithelium are less

frequently seen, and they are known as reactive oncocytoid cysts and mucopapillary cysts respectively.[46-48]

PLEOMORPHIC ADENOMA (BENIGN MIXED TUMOR)

CYTOLOGY

The aspirate shows a variable cell density. The cells are arranged in sheets, clusters and singly with a fibrillary chondromyxoid ground material. There are many well-defied myoepithelial cells that are ovoid, plasmacytoid or spindle-shaped. Typical ovoid nuclei have a smooth nuclear membrane and bland, finely granular nuclear chromatin. [49-51]

HISTOLOGY

Tissue shows various myoepithelial/stromal and epithelial components that are combined in different ways to form the tumor. The spindled myoepithelial cells enter the chondromyxoid stroma from the ductal components. The individual tumor cells can have a number of morphologies, including oval, epithelioid, spindle-shaped, translucent and plasmacytoid. Squamous metaplasia and keratin pearls are commonly seen. Mucous cells, sebocytes and oncocytic cells are less frequently present. Stromal components that are chondromatous, lipomatous, myxoid or osseous are possibly found. Occasionally microliths, collagenous stellate fibrilliar structures and crystalloids loaded with tyrosine are also found. Presence of ductal atypia, extensive fibrosis and necrosis should require further samples to be assessed in order to rule out malignancy. A coincidental detection of intravascular tumor cells may result from either fine-needle aspiration or intraoperative trauma. [52,53]

MYOEPITHELIOMA

CYTOLOGY

The aspirate shows a variable stromal component and solitary cells as well as cells arranged in clusters. The individual neoplastic cells might appear spindled, epitheloid, or plasmacytoid and are normally bland in appearance. Cytoplasmic features vary between tumors.

HISTOLOGY

Tissue from myoepithelioma exhibits spindle, plasmacytoid, hyaline, epithelioid and transparent cell features. The tumor cells are in cords or nests pattern arrangement. Individual tumor cells are round-polygonal with centrally located nuclei and contain varied quantities of eosinophilic cytoplasm. There could be random ducts and intercellular microcystic spaces. The reticular variant of myoepithelioma is identified by net-like patterns of connected cell connections. Intracellular mucin and ring-shaped cells have both recently been identified. Occasionally, especially when it is the plasmacytoid variety, myoepitheliomas may not stain with any of the myoepithelial markers.[54-56]

MYOEPITHELIAL CARCINOMA

CYTOLOGY

The aspirate smears show a mixture of spindled, epithelioid and/or plasmacytoid cells arranged in small groups or large fragments. The individual cell nuclei can be round or oval, with variable cytoplasmic features[57]

HISTOLOGY

The malignant myoepithelial cells are arranged in disordered nodules with infiltrative boundaries. The tumour cells are arranged in reticular, trabecular and solid patterns. The stroma may show hyalinized or myxoid substance. The tumour may have pseudocyst development and necrosis. Spindle, plasmacytoid, epithelioid and clear cell morphological characteristics can all be seen in the individual tumour cells. There have also been descriptions of tumor cells having morphologies that are vacuolated or ring-like[58]

WARTHIN TUMOR (PAPILLARY CYSTADENOMA LYMPHOMATOSUM)

CYTOLOGY

The aspirate shows mucoid, murky fluid with a background of amorphous and granular debris. Bland oncocytic cells are seen arranged in cohesive, monolayered sheets. Many lymphoid cells are seen in the smear. [59-60]

HISTOLOGY

The tumors are made up of a mixture of papillary-cystic structures lined by oncocytic epithelial cells. The stroma contains lymphoid tissue with germinal centers. The inner columnar and outer cuboidal cells make up the epithelial component. There may be small foci of squamous, mucous, ciliated, and sebaceous cells. A granulomatous reaction with giant cells of the Langhans type may also be observed. It may be difficult to make a diagnosis when infarcted or metaplastic tumors show noticeable mucinous or squamous metaplasia and stromal response. [60-61]

BASAL CELL ADENOMA

CYTOLOGY

The aspirate smear shows numerous tiny basaloid epithelial cells. The tumor cells may be organized both singly and in multilayered clusters and occasionally show peripheral palisading. Individual tumor cells have scant cytoplasm and several bare nuclei. Nuclei is circular or oval and can appear dark. The chromatin is bland and granular in texture. Some tumors have a sparse fibrous stroma and hyaline material that is most likely from the basement membrane.[62-69]

HISTOLOGY

The tumor cells are arranged in solid, trabecular, tubular and membranous patterns. These basaloid cells have sparse cytoplasm, hazy cell boundaries, round to oval nuclei and they could have palisading on the periphery. Large cells with lighter staining nuclei in the centre may be visible in basaloid nests. [70-74]

ONCOCYTOMA

CYTOLOGY

The aspirate smear shows aggregates of oncocytic cells that are cohesive and multilayered .These individual cells have a small nuclei. [75-76]

HISTOLOGY

The oncocytes are characterized by abundant eosinophilic granular cytoplasm and centrally located vesicular nuclei with a single conspicuous nucleolus. Oncocytes are organised into sheets, nests, trabeculae and duct-like patterns and a thin fibrovascular stroma serves as the barrier between them. Both micro- and macrocysts can be seen. Occasionally, a condition known as clear cell oncocytoma occurs in which the entire tumour is made up of clear cells. Phosphotungstic acid haematoxylin

stains the tumour cells. Despite the fact that oncocytoma is typically conceived of as a tumour with a single cell type, some oncocytomas have a population of basal cells. The differences between an oncocytoma and a Warthin tumour include the absence of lymphoid stroma and papillary cystic architecture. [77-81]

ACINIC CELL CARCINOMA

CYTOLOGY

The aspirate smear shows a clean background with lots of cell material. Cells are primarily arranged in clusters, with a sparse, undetectable fibrovascular stroma. The individual tumor cells have cytoplasm that is abundant, delicate, finely vacuolated and occasionally thick like oncocytes .The nucleus is rounded, medium-sized and contains bland chromatin with mild to moderate anisokaryosis. A lot of stripped nuclei are seen in the background.[82,83]

HISTOLOGY

Acinar and ductal cells are seen having solid, microcystic and follicular patterns of arrangement. These tumor cells have varying vacuolated, clear, oncocytic and hobnail characteristics. If the papillary cystic component is present it shows macrocystic spaces with papillary proliferations. There is a noticeable lymphoid infiltration seen. The acinar cells are large and polygonal. They have a spherical, eccentric nuclei and basophilic granular cytoplasm. The granules produce a positive periodic acid-Schiff(PAS) reaction focally and is diastase-resistant , but this test is not always required for diagnosis. Mitoses are rarely visible in acinic cell carcinomas. Low-/intermediate-grade cancers include necrosis and show substantial pleomorphism. Aggressive behavior of this tumor is linked to the occurrence of neural invasion and stromal hyalinization.[84-89]

MUCOEPIDERMOID CARCINOMA

CYTOLOGY

The aspirate smear shows a characteristic low cellularity and a "dirty" background consisting of mucus and debris. Epithelial cells are arranged in sheets and clusters that are cohesive. Individual tumor cells have a bland nuclei with large nucleoli. The background mucus contains tiny streams of cells .Intermediate cells are seen in the smear. Smear also shows a few mucin secreting cells. [90-93]

HISTOLOGY

Tumor has a varied composition of intermediate, squamoid and mucin-producing cells show a cystic and solid growth arrangement. Extreme keratinization is uncommon. Variants that are oncocytic, clear-cell and sclerosing have been identified. The uncommon oncocytic variant consists mostly of polygonal/columnar oncocytic cells, with a few to no squamoid cells and scattered mucocytes. Dense hyalinizing fibrosis is a feature of the sclerosing variant. Solid pattern tends to have a predominance of intermediate and squamoid cells with a delicate transition between these two parts. Low-grade tumor is well circumscribed and cystic with abundant mucous cells. Nuclear atypia, necrosis, an elevated mitotic rate and perineural, lymphovascular, or bone invasion are all characteristics of high-grade tumor. The diagnosis of high-grade tumor requires at least focal intracellular mucin positivity. [94-96]

POLYMORPHOUS LOW-GRADE ADENOCARCINOMA

CYTOLOGY

The aspirate shows cells that are arranged singly, in clusters and in tissue fragments. They can be seen forming a trabecular (pseudopapillary) pattern when they adhere to threads of fibrovascular stroma. Hyaline stromal globules are frequently found in the background. Small basaloid or somewhat bigger ductal epithelium or metaplastic squamous cells are seen. Individual cell nuclei are ovoid, whitish, somewhat expanded and uniform. [97-99]

HISTOLOGY

Tumor is typically submucosal in location and not capsulated. Cytological uniformity, histological diversity and an infiltrative growth pattern characterize the tumor. Individual neoplastic cells are round in shape. They have a sporadic nucleoli and bland, barely hyperchromatic oval nuclei. In high-grade transformation, necrosis is evident. The primary architectural types of include papillary-cystic, solid, lobular, trabecular, microcystic or cribriform (as in adenoid cystic cancer), and lobular. It is possible to see foci of oncocytic, clear, squamous or mucous cells. The stroma may be hyalinized or mucinous. There is a frequent neuronal involvement seen.[100]

EPITHELIAL – MYOEPITHELIAL CARCINOMA CYTOLOGY

The aspirate shows cells that are arranged in tissue fragments, clusters or alone in a smear. Tissue fragments are arranged in a trabecular or a pseudopapillary pattern. The background may show clearly visible hyaline stromal globules. Some tumors exhibit a population that is clearly biphasic. Less cohesive myoepithelial (clear) cells have a fragile cytoplasm which is pale, and the nucleus shows atypia with increase in

size. Presence of stripped off nuclei is common in the smear. Epithelial cells are smaller, homogeneous and are primarily seen in close clusters[101-105]

HISTOLOGY

The tumor displays a multinodular pattern. Tumor cells have a biphasic or bilayered arrangement. The inner luminal layer consists of small ductal cells with a dense eosinophilic cytoplasm and the outer layer consists of polygonal myoepithelial cells with a clear cytoplasm. This is the characteristic feature of the tumor. Necrosis may be present occassionally. Perineural invasion is commonly seen. [106-108]

ADENOID CYSTIC CARCINOMA

CYTOLOGY

The aspirate smear is highly cellular and contains cells arranged both singly and in clusters. The background shows variously sized hyaline spherical globules with tumor cells that are adhering to them. The hyaline stroma is seen in the smear as finger-like cords along with fragments of cellular tissue. Individual tumor cells have a characteristic scanty cytoplasm, high N:C ratio and nuclear sculpting or bare nuclei. The nucleus is homogeneous, hyperchromatic, spherical or oval and has coarse nuclear chromatin. Tumors with poor differentiation may not have hyaline stromal material.[109-110]

HISTOLOGY

Tumor can present as tubular and cribriform structures with variable solid components. Nests of tumor cells containing sharply punched out spaces filled with basophilic matrix is the most recognizable architectural form of cribriform pattern. The tubular pattern is composed of bilayered tubules with true lumin. The nuclei of tumour cells are frequently small, angulated and hyperchromatic, with scant

cytoplasm. The solid pattern of tumor made up of epithelial or myoepithelial components. It is typical to have perineural invasion[111,112]

SALIVARY DUCT CARCINOMA

CYTOLOGY

The aspirate smear shows malignant epithelial cells arranged singly or grouped together. The cytoplasm of the individual tumor cells is squamoid, voluminous and occasionally oncocyte-like. There are no obvious stromal components visible. The background is dirty and shows necrotic material. [113-117]

HISTOLOGY

Tumor with its cribriform and Roman bridge-like features, massive ducts with comedo necrosis and other characteristics bears a striking resemblance to high-grade variant of ductal carcinoma of the breast. Tumor cells are usually apocrine and oncocytoid type. The individual tumor cells are characterized by abundant cytoplasm and a large pleomorphic nuclei with coarse chromatin and a prominent nucleoli. [118]

ADENOCARCINOMA OF NO SPECIAL TYPE

CYTOLOGY

The aspirate smear shows cells having some glandular differentiation (microglandular pattern). The individual tumor cell nuclei show features of malignancy . Intracellular and/or extracellular mucin is seen. There are no characteristic features that would indicate a particular entity[119]

HISTOLOGY

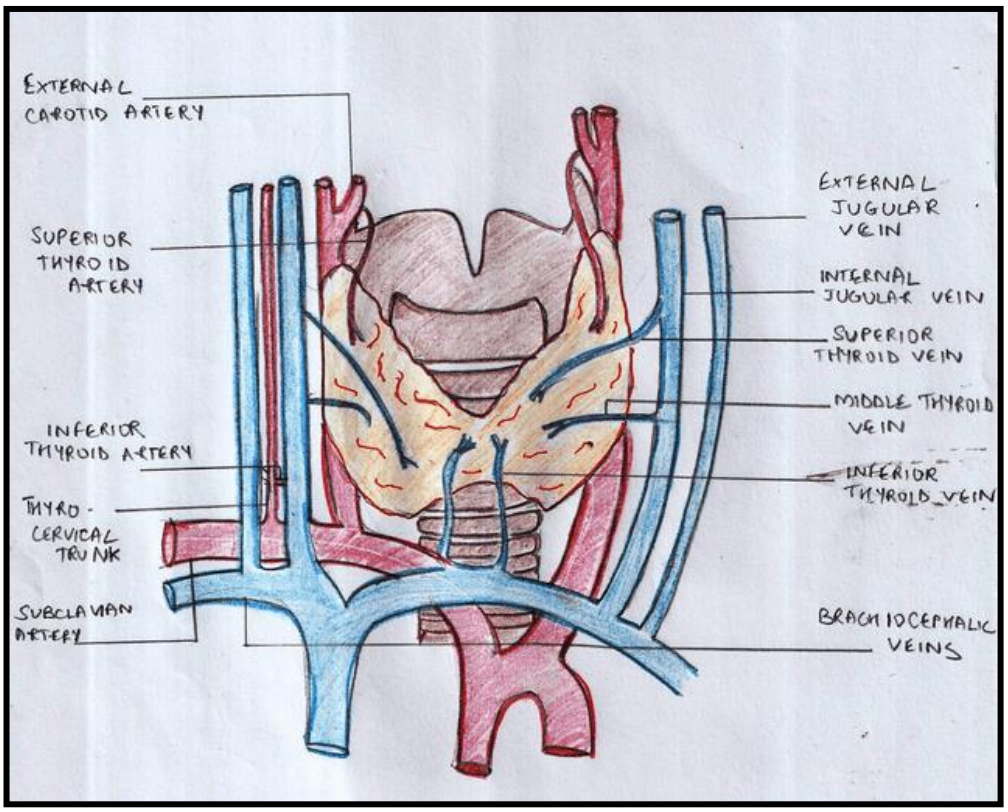
Ductal or glandular proliferations of cells, with or without cystic development, are seen in tumours. Cells are arranged in many different patterns, such as little nests, cords or big islands with connective tissue in between them. There is a thick, dense

cellular stroma. The individual tumour cells can have morphologies such as cuboidal, columnar, polygonal, transparent, mucinous, oncocytoid, and/or plasmacytoid. Compared to high-grade tumours, low- and intermediate-grade tumours frequently have ductal and glandular features. [120]

THYROID GLAND

EMBRYOLOGY

Both medial and paired lateral diverticulum contribute to the development of the thyroid gland. The medial diverticulum gives rise to the isthmus, thyroglossal duct and each central lobe. It forms as a midline diverticulum extending from the floor of the pharynx and base of tongue in the fourth week of development. It then migrates caudally during development and solidifies. The thyroglossal duct disappears gradually. The pyramidal lobe is a remnant of the thyroglossal duct. Ectopic thyroid tissue may develop along the thyroid anlage's complete line of normal descent if it fails to migrate normally. Sinus tracts along the thyroglossal duct may develop as a result of this. The fourth/ fifth pharyngeal pouches give rise to; the ultimobranchial bodies, which in turn give rise to C cells. Before becoming part of the growing thyroid gland, the C cell progenitors migrate to the ultimobranchial bodies. [121-125]



ANATOMY AND HISTOLOGY

The larynx and trachea are located behind the bilobed thyroid gland, located in the middle of the neck. The thyroid gland contains 2 lobes and an isthmus which is at the level of the cricoid cartilage. Occasionally the pyramidal lobe is present. The typical gland weighs between l5 and 30 g. Vasculature includes the superior and inferior thyroid arteries. Veins empty into the brachycephalic, internal and anterior jugular veins. The isthmus, has an abundant supply of lymphatic vessels and are close to the venous drainage system. The major draining nodes include those in the immediate pericapsular region, the recurrent laryngeal nerve chain,the pretracheal, paratracheal and prelaryngeal areas, the internal jugular chain, and the retropharyngeal and retroesophageal areas. Thyroid's "sentinel node," the Delphian

lymph node, is located right above the isthmus. The lobules, which are formed from groups of 20 to 30 follicles. The follicles vary in size, with a diameter between 200 and 300 m. Follicle contains thyroglobulin and a periodic acid-Schiff positive colloid. The size and form of the follicular cells vary according on their functional state. Flattened follicular cells are thought to be relatively dormant, whereas columnar follicular cells are thought to be functionally active. The nucleus is typically composed of a single tiny nucleolus and is spherical to oval in shape with slightly uneven curves. Oncocytes, Askanazy cells, Hürthle cells or oxyphil cells, are terms used for follicular cells with a profusion of granular eosinophilic cytoplasm. Numerous mitochondria are a characteristic of oncocytic cells. [126-132]

INDICATIONS OF FNAC:[133]

1. To differentiate between benign solitary thyroid nodules and malignant ones
2. To identify inflammatory/autoimmune lesions from nodular goiter
3. To confirm and categorize clinically obvious thyroid malignancy that may need preoperative palliative treatment, as for lymphomas and metastatic malignancies where surgery is not indicated
4. Evaluation of lesions with a diameter of 1–l.5 cm and having features suspicious of malignancy that are detected by imaging.
5. To perform ancillary tests/prognostic parameters

COMPLICATIONS

Local hemorrhage: It is the most common complication and is a localized hemorrhage which heals spontaneously within few days. Rarely, there is a large hematoma compressing the air way tract in non coagulopathic disorder. Radioisotope

scan should always be done before FNAC as its character may be altered following hemorrhage.

Vasovagal reaction: Rarely patient may feel dizzy and fall down due to vasovagal reaction.

Recurrent laryngeal nerve injury: Is a rare complication of FNAC of thyroid gland. About one to two days after FNAC procedure the patient may present with transient dysphonia and dysphagia recovers within few months[134-141]

A SATISFACTORY SAMPLE

Sample from a benign thyroid nodule is said to be adequate if minimum six clusters of benign cells on at least two slides obtained from two needle passes are obtained.[142]

The revised 20l7 Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)

Diagnostic category	ROM (NIFTP considered as cancer)	ROM(NIFTP not considered as cancer)	Management options
1. Non diagnostic/ unsatisfactory	5-l0	5-l0	Correlate with clinical/radiological findings Consider repeat FNA
2. Benign	0-3	0-3	Surveillance and follow up
3. AUS or follicular lesion of undermined significance	6-l8	l0-30	Correlate with clinical/radiological findings Consider repeat FNA Consider molecular testing
4. Follicular neoplasm/Follicular carcinoma	l0-40	25-40	Consider molecular testing Lobectomy
5. Suspicious for malignancy	45-60	50-75	Total thyroidectomy/Lobectomy

Diagnostic category	ROM (NIFTP considered as cancer)	ROM(NIFTP not considered as cancer)	Management options
6. Malignant	94-96	97-99	Total thyroidectomy/Lobectomy

NODULAR GOITER

CYTOLOGY

The aspirate smear shows thick or thin colloid in abundance with follicular cells. The follicular cells are organized singly, in monolayered sheets or in loose cohesive clusters. Individual follicular cells have fragile cytoplasm, are involutional, hyperplastic and oxyphilic. There are hemosiderin laden macrophages (foam cells) present in the background. The background may also show blood and cell debris.[143]

HISTOLOGY

Tissue shows nodules having a variety of appearances. Some are very cellular and hyperplastic, while others are mostly made up of oncocytic (Hürthle) cells. Some nodules are composed of enormous follicles with flattened lining epithelium. A group of small active follicles at one pole (so-called Sanderson polsters) may be present in some dilated follicles. There may be papillary projections facing the cystic follicle's lumen. Within a nodule of big dilated follicles, follicular cells may be observed in well-defined solid or microfollicular clusters. Stroma may occasionally show variable amount of chronic inflammatory infiltrate suggesting the coexistence of chronic thyroiditis. [144]

CYSTIC NODULES

CYTOLOGY

The aspirate smears reveal scanty, degenerating follicular epithelium and hemosiderin laden macrophages. Background may show a brownish, colloid-like fluid with altered blood[145-147]

ACUTE SUPPURATIVE THYROIDITIS

CYTOLOGY

The aspirate smear showsa good number ofneutrophils, necrotic debris and cells. There may be intracellular microorganisms (often Gram-positive cocci) present. Occasionally seen organisms include mycobacteria, viruses, aspergillus, etc. Culture and sensitivity can be done on the cytologically obtained tissue.[148]

HISTOLOGY

Sections studied show neutrophils, microabscesses and prominent tissue necrosis. The could be associated fungal elements seen.

GRAVES' DISEASE (PRIMARY HYPERPLASIA)

CYTOLOGY

The aspirate smear shows a colloid-free bloody background with moderate to high cellularity. Follicular cells are arranged in monolayered sheets, follicular or ring structures. The individual tumor cells show moderate amounts of pale, cobweb-like cytoplasm with larger marginal vacuoles giving the characteristic appearance of fire flares[149-150]

HISTOLOGY

The lining of follicles show obvious papillary infoldings and are highly hyperplastic. The lining epithelium of the follicles contain columnar cells. These

columnar cells have a basally positioned normochromatic or hyperchromatic nuclei and transparent, microvacuolated basophilic or amphophilic cytoplasm. The colloid shows noticeable scalloping and is pale and finely vacuolated. In the stroma, lymphoid tissue clusters with germinal centre development can be seen[144,151,152]

HASHIMOTO'S THYROIDITIS/LYMPHOCYTIC THYROIDITIS

CYTOLOGY

The aspirate smear shows lymphoid cells superimposed over follicular cells. Lymphoid and plasma cells are seen in the background. Lympho-histiocytic collections are also seen in the smear. Variable amount of oxyphillic (Hurthle cell/ Askanazy cell) change is present wherein cells arranged singly or in aggregates show gray blue abundant finely granular cytoplasm. Background multinucleate giant cells and epithelioid cells may also be seen in 40% cases[153-158]

HISTOLOGY

The two main characteristics of this lesion are oxyphilic change of the follicular epithelium and lymphocytic infiltration of the stroma. Within and around the lobules, lymphoid tissue is seen, and this tissue displays sizeable follicles with distinct germinal centres. T lymphocytes out number B cells. Intrafollicular multinucleated giant cells, plasma cells, histiocytes, and other cells are also seen. There are a lot of dilated lymphatic vessels, which produce the recognisable "cracking spaces." Though some thyroid follicles exhibit regenerative hyperplasia, the majority of them are atrophic. Oncocytic (Hürthle) cells of varying sizes line the follicles, and their nuclei either display enlargement and hyperchromasia or an optically clear appearance[159-163]

DE QUERVAIN'S THYROIDITIS (SUBACUTETHYROIDITIS; GRANULOMATOUS THYROIDITIS)

CYTOLOGY

The aspirate smear contains large Multinucleate giant cells having numerous nuclei and phagocytosed colloid. Also Granulomatous aggregates of epithelioid cells with degenerating follicular cells, neutrophils, lymphocytes and macrophages are seen in the smear. Paravacuolar granules are seen in these degenerating follicular cells. The smear background is dirty consisting of cell debris and colloid.[155,164-165]

HISTOLOGY

There are granulomas with foreign body giant cells and distinct zones of inflammation. These granulomas typically surround the follicles and the multinucleated giant cells engulf the colloid (the majority of which are histiocytic in origin). Caseation necrosis is missing and the granulomas are not particularly noticeable. Patchy fibrosis is also present in some areas. The same gland may exhibit many phases of the same process.[166]

FOLLICULAR NEOPLASMS

CYTOLOGY

The aspirate smear shows moderate to high cellularity with a bloody, usually colloid-free background. Clusters of follicular cells are seen forming microacinar

pattern and they contain a central colloid filled lumen, these represent the microfollicles. Cells show nuclear crowding and overlapping. [167-173]

FOLLICULAR ADENOMA

HISTOLOGY

A benign encapsulated tumour known as a follicular adenoma lacks the nuclear characteristics of the papillary family of neoplasms and exhibits signs of follicular cell differentiation but no signs of invasion from capsular, vascular or any other type. A notably thin capsule that is both grossly and microscopically complete surrounds this lesion. The architecture and cytology of the adjacent normal gland, which typically exhibits compression symptoms, is different from the involved adenoma. Tumor cells are arranged in different patterns, including normofollicular (simple), macrofollicular (colloid), microfollicular (foetal), and solid/trabecular (embryonal) , which can be seen alone or in combination[174-179]

FOLLICULAR CARCINOMA

HISTOLOGY

Tumor structure can range from well-formed follicles to a solid growth pattern. There may be cribriform regions, trabecular structures or poorly developed follicles sometimes present all three at once. The tumour could consist of spindle cells or it could have obvious glomeruloid structures. The presence of cytoplasmic clear changes can be widespread or localized. There are no psammoma bodies and very little squamous metaplasia seen. According to the Turin proposal, tumours with a

primarily solid/trabecular/nesting pattern of growth should be thoroughly examined for mitoses and necrosis in order to rule out the diagnosis of poorly differentiated carcinoma.[180-181]

Follicular Carcinoma Subtypes include:

Minimally invasive - Encapsulated, with capsular invasion only (no vascularinvasion)

Encapsulated angioinvasive

- With limited vascular invasion (l–3 vessels, with or without capsular invasion)
- With extensive vascular invasion (≥4 vessels, with or without capsular invasion)

Widely invasive - Extensive invasion (macro and microscopically evident), Multinodular growth, no obvious tumor capsule

POORLY DIFFERENTIATED THYROID CARCINOMA

CYTOLOGY

The aspirate shows a hypercellular smear with cells arranged singly or in a solid, trabecular and insular pattern. Individual tumor cells are oval, they have a hyperchromatic nuclei and a granular cytoplasm with occasional intranuclear cytoplasmic inclusions and/or grooves[182-186]

HISTOLOGY

Tissue from insular carcinoma is characterized by a nested, or "insular," pattern of growth, a solid to microfollicular organization, small homogeneous tumor

cells, fluctuating mitotic activity and fresh necrotic tissue. These insular nests are bounded by thin fibrovascular septa, and are separated from tumour cell nests by clefts. The individual tumor cells have a round hyperchromatic nuclei, vague nucleoli, and little pleomorphism. In some cases, the chromatin is black, the nuclei have irregular, "raisin-like," convoluted characteristics. Some poorly differentiated cases lack the traditional characteristics of "insular" carcinoma and instead have a trabecular pattern with bigger, more pleomorphic nuclei with comedo-like necrosis. Vascular infiltration is also seen frequently. Infiltration of the extrathyroidal tissue is frequently seen. Some poorly differentiated carcinomas are composed of Hürthle (oncocytic) cells. Clear cells foci, mucinous differentiation and signet ring or rhabdoid features can also be seen occassionally.[186-189]

PAPILLARY CARCINOMA

CYTOLOGY

The aspirate shows tumor cells arranged in the form of flat sheets and fibrovascular core containing papillary tissue fragments. Individual tumor cells contain an ovoid,enlarged , granular pale nuclei with intranuclear cytoplasmic inclusions, nuclear grooves and finely granular, powdery chromatin. The cell boundaries and the cytoplasm of individual cells are well defined. Nuclear overlapping and crowding are seen. 'Metaplastic' epithelial cells that are squamoid or histiocyte like in appearance are also seen. The background shows scanty, viscous and stringy (like chewing gum) colloid in varying amounts. There are various numbers of Psammoma bodies visible in the background smear. Lymphocytes, multinucleate large cells, macrophages, and debris (evidence of cystic degeneration) are also seen.[190-194]

HISTOLOGY

True papillae occur in a typical papillary carcinoma. With a central fibrovascular core and a single or stratified lining of cuboidal cells, some of which may exhibit hobnail characteristics, the papillae are typically complex, branching, and randomly oriented. Lymphocytes, foamy macrophages, hemosiderin, or adipose tissue may be present in the stroma. The stroma can also be edematous or hyaline in appearance. These papillae are almost usually connected to follicular development. The follicles frequently have tubular shapes, are branched, and have uneven shapes.

The cells have characteristic nuclear features consisting of

1. Ground-glass nuclei, which are optically transparent with an overlapping nature. The nuclear membrane appears thickened and shows nucleolus.
2. Cytoplasmic invaginations known as nuclear pseudoinclusions, which resemble clearly defined, spherical, acidophilic vacuoles that are attached to the nuclear membrane are seen.
3. Nuclear ridges are typically seen and are oriented along the longest nuclear axis. These are an expression of nuclear membrane infoldings.[195-203]

Variants of papillary carcinoma

- Follicular (and macrofollicular encapsulated) variants
- Oncocytic variant,
- Warthin tumor-like variant,
- Cribriform-morular variant,
- Adenoid cystic variant,
- Variant with fasciitis-like stroma,
- High-grade variants: tall cell, columnar, diffuse sclerosing and solid/trabecular variants.

HYALINIZING TRABECULAR TUMOR CYTOLOGY

The aspirate smear shows oval or polyhedral cells that are organized singly, in small clusters or in parallel arrays. Individual tumor cells have moderate to abundant cytoplasm and low nuclear cytoplasmic ratios. In some focal binucleate forms, the nuclei may be eccentrically positioned. Around hyaline material, cohesive aggregates of cells are seen to be radially directed. Occasionally Papillary carcinoma mimicking nuclear grooves and inclusions are visible in the smears. Giant lysosomes known as intracytoplasmic "yellow bodies" have also been seen[204-206]

HISTOLOGY

The lesion has a noticeable trabecular pattern and a hyaline appearance. The latter is found both in the extracellular space and the cytoplasm of the tumor cells. Depending on whether the trabeculae are straight or curved, organoid forms can emerge. The so-called cytoplasmic yellow body, which is a circular, 2-5 m, pale yellow cytoplasmic inclusion body in a paranuclear site with a refractile quality and observable both in tissue sections and in FNA smear, is another distinguishing (but not specific) morphologic hallmark of this tumor.[207]

MEDULLARY CARCINOMA

CYTOLOGY

The aspirate smear is highly cellular with some cells clustered and others scattered in a bloody background. These tumor cells show different patterns like Plasmacytoid, small cell or spindle cell pattern. Plasmacytoid/triangular cells with an eccentric nuclei. Smear can show cells with an ovoid nuclei, high N:C ratio in dense clusters. Elongated pale nuclei are seen in the spindle cell variant. Nuclei shows binucleate and multinucleate forms, are large, dispersed and show moderate

anisonucleosis. Nuclear chromatin in each individual cell is stippled ('neuroendocrine'). The background shows amyloid material, which is amorphous and pink or violet, is present in varying amounts[208-218]

HISTOLOGY

Tumor shows a solid proliferation of round to polygonal cells with granular amphophilic cytoplasm and medium-sized nucleus, separated by a highly vascular stroma, hyalinized collagen and amyloid. The various growth patterns can be trabecular, glandular (tubular and follicular), carcinoid-like, paraganglioma-like, or pseudopapillary. The stroma can be edematous, ossified, hemorrhagic or sparse. There may be an extensive amyloid deposition present or none at all. There might be true psammoma bodies present. There may occasionally be a significant neutrophil infiltration seen. The tumour cells may have odd characteristics such as being spindle-shaped, oncocytic, squamoid, or plasmacytoid (due to nuclear peripheralization). Other unusual varieties of medullary carcinoma include a true papillary form, a clear cell variant, a small cell type resembling the homonymous lung tumor, another small cell type with features resembling neuroblastoma, and a pigmented (melanin-producing) variant.[219-226]

ANAPLASTIC CARCINOMA

CYTOLOGY

The aspirate smear shows highly pleomorphic malignant. The individual tumor cells show a variety of shapes and are mixed with spindle and giant cells. Tumor cell nuclei may be bizzare with macronucleoli, coarse chromatin and irregular nuclear membranes. Frequent, abnormal mitoses is seen[164,208-210]

HISTOLOGY

There are two main types that occasionally coexist. The first tumor is undifferentiated because it lacks papillae, trabeculae or even follicles, yet it has an obvious epithelial look visually and immunohistochemically. This pattern is known as the squamoid pattern. The second category consists of spindle cell and giant cell, two patterns that are combined and classified as sarcomatoid patterns. These tumours may closely mimic a wide range of soft tissue sarcomas because they exhibit a fascicular or storiform pattern of growth, significant neutrophilic infiltration, substantial vascularization and differentiation into bone, cartilage and skeletal muscle. There may be multinucleated large cells that resemble osteoclasts. Anaplastic carcinomas always contain a significant number of tumor-associated macrophages.[227-231]

LYMPHOMA

CYTOLOGY

Lymphomas involve thyroid mostly secondarily and rarely primarily. Most thyroid lymphomas are of B-cell lineage (MALT type). In high-grade lymphomas show large, abnormal blastic type of lymphoid cells are seen. Low- grade lymphomas show a mixed cell population. [164]

HISTOLOGY

Majority cases are of diffuse large B-cell type. Focally sclerosis is present. The second largest category is that of a diffuse or a nodular (follicular) pattern of growth of the low-grade lymphomas composed of small or “intermediate” lymphocytes. Many exhibit focal plasmacytoid features and a few are composed of signet ring cells. Both of these major thyroid lymphoma types belong to the MALT-typecategory (“marginal zone B-cell lymphoma). This is supported by the fact that large cell lymphomas often show an associated low-grade MALT-type component

and that some show a marginal zone distribution of the tumor cells. An important diagnostic finding is the packing of follicular lumina by lymphoid cells ("lymphoepithelial lesions"). True follicular lymphomasof the thyroid are very rare and most of them contain lymphoepithelial lesions similar to those seen in MALT-type lymphomas. The most common is always associated with extrathyroidal disease. [232,233]

PARATHYROID GLANDS

EMBRYOLOGY [234-244]

Thickenings seen on the branchial pouch are the first noticeable traces of parathyroid glands at 5 to 6 weeks of development. The fourth brachial pouch forms the parathyroid IV glands (superior pair) and the ultimobrachial body. The final location of Parathyroid IV are persistent which is close to the cricothyroid junction where the inferior thyroid artery is seen crossing the recurrent laryngeal nerve. The inferior parathyroids (termed parathyroid III), are obtained from the third pouch together with the thymus. In case the parathyroid III fails to separate from the thymus, it may appear in the lower neck situated within the tongue, within the anterior mediastinum or very rarely may be located in the posterior mediastinum. The parathyroid III may be situated cephalic to parathyroid IV as a result of its early separation from the thymus and thus, parathyroid III may appear anywhere along the path from the angle of the jaw upto the pericardium.

ANATOMY [234-244]

Adults mostly have four parathyroid glands; however, l3% of people have more than four, and 3% have just three. The length, width, and thickness of a normal parathyroid gland range from 4 to 6 x 2 to 4 x l to 2 mm respectively. The glands weigh 60 mg. The inferior thyroid artery and recurrent laryngeal nerve meet l cm

apart from where the superior parathyroid glands (IV) are most frequently located. Rarely, glands can be found wholly inside the thyroid gland and sometimes seen along the thyroid parenchyma. The superior parathyroids can also infrequently be seen in the retropharyngeal, retroesophageal, or carotid sheath spaces. The anatomy of the inferior parathyroids (III) and that of the superior parathyroids is significantly different. The branches of the superior thyroid artery (parathyroid IV) and inferior thyroid artery (parathyroid III) provide the parathyroid glands' vascular supply . The superior thyroid vein is responsible for venous drainage of the upper glands, whereas the lateral or inferior thyroid vein is responsible for venous drainage of the lower glands. The pretracheal, paratracheal, retropharyngeal, and inferior deep cervical nodes are where lymphatic drainage from a subcapsular plexus enters the body. The principal cells, good number of oncocytes and transitional oncocytes make up the parathyroid parenchymal cells. Frequently the chief cells contain a rounded, centrally positioned nuclei with sharp nuclear membranes and coarse chromatin. The cytoplasm is clear or vacuolated and has a very slight eosinophilic tint. Plasma membranes in primary cells are generally well defined when they are at rest and become more tortuous when their functional activity increases. Secretory granules and mitochondria are seen in chief cells. Oncocytes are larger, measuring l2 m in diameter, and their cytoplasm is heavily eosinophilic and granular, the nuclei are often bigger and more vesicular. Transitional oncocytes are smaller, less eosinophilic and contain fewer mitochondria. At puberty, oncocytes first develop, and their numbers rise as people age. The cytoplasm of parathyroid cells turns clear with well-defined borders when they manufacture too much glycogen. Mature adipocytes, arteries and connective tissue are all present in the gland's stroma. The amount of stromal adipose is limited until adolescence, despite the fact that it frequently shows up in a normal adult

parathyroid gland. The chief cells contain cytoplasm that is focally vacuolated and a relatively small hyperchromatic nuclei. Eosinophilic cytoplasm is widely distributed in oncocytes.

PARATHYROID ADENOMA

CYTOLOGY

Many a times enlarged parathyroid glands have been subjected to FNA as clinically suspected solitary thyroid nodule. Typically, the aspirate smears of parathyroid tissue contain numerous bare nuclei as well as tiny cell sheets of cells that occasionally form acinar or follicular structures. Occasionally a few small aggregates of dense, colloid-like material may be seen. The individual cells are small with a rounded nuclei and have a hyperchromatic nuclei with coarse chromatin. Anisonucleosis is prevalent among the dispersed cells. The smear may also show big atypical bare nuclei. Individual tumor cells show a granular cytoplasm which may contain massive metachromatic granules. It could be challenging to distinguish this from thyroid follicular epithelium. Typically, thyroid-derived cells are smaller than other cell types. IHC is helpful in differential diagnosis. [245-247]

HISTOLOGY[245-247]

Tissue from most adenomas are made up mainly of chief cells, which, if present, are larger than nonneoplastic chief cells. The individual cell nuclei are spherical and slightly larger than those of normal cells and have a discrete nucleoli that are located central to somewhat basally. Oncocytic cells can be found in varying amounts either as nodular aggregates or focally admixed with chief cells. Oncocytic cells can make up the entirety of certain adenomas referred to as Oxyphilic or Oncocytic adenomas. The cells are arranged in sheets, cords, nests, or glandular

structures. There may be eosinophilic colloid-like material in glandular forms. Adenomas contain morphological evidence of mitosis typically l per l0 HPF. There have been reports of up to 4 mitoses per l0 HPF. No atypical mitoses are found. Only around 50% of cases have a rim of nonneoplastic parathyroid tissue which is useful in distinguishing between hyperplasia and an adenoma.

Variants

- **Oncocytic (oxyphilic) adenoma:** The aspirate smear shows cells that are large with a lot of eosinophilic and granular cytoplasm. They have a hyperchromatic nucleus. Occasionally Multinucleated cells or large atypical nuclei may be seen.
- **Lipoadenoma**: Is referred to as parathyroid hamartoma. It is a rare encapsulated neoplasm having parenchymal and stromal fat cell growth. Due to the amount of stromal fat, it is frequently mistaken for a normal parathyroid gland. Frequently fibrotic or myxoid-altered regions in stromal fat are present.
- **Atypical adenoma:** Parathyroid tumour displays symptoms that are suspicious for parathyroid cancer but missing definite indicators of the disease. Atypical histologic characteristics can include capsular abnormalities without surrounding soft tissue invasion, angioinvasion, soft tissue invasion, growth characteristics that are concerning but not diagnostic of invasion, increased mitotic activity upto 5 per l0 HPF, absence of abnormal mitoses, intralesional fibrotic bands, trabecular growth and spindle-shaped nuclei.
- **Double (multiple) adenomas**: Double adenomas can be diagnosed if there are two swollen, hypercellular parathyroid glands, confirmation during surgery that the remaining parathyroid glands are healthy and/or have been biopsy-proven to be histologically healthy, absence of MEN or familial HPT in the family, permanent treatment of hypercalcemia after removal of swollen glands and

possibly the most conclusive criterion, but one that needs years of monitoring, includes measuring serum calcium and parathyroid hormone levels. The diagnosis of two adenomas can be established if the above requirements are satisfied. True double parathyroid adenomas are rare.

LYMPH NODES

HISTOLOGY AND ANATOMY[248-252]

The head and neck contains an extensive network of lymphatic system comprising of nearly more than 300 nodes with their channels. These lymphatic chains on the left and right have lateralized orientation and do not have a direct communication, except if a pathology is present. The left side nodes, either drain through the jugulo-subclavian into the vasculature or directly into the thoracic duct.

The right side nodes drain directly into the lymphatic duct. Most of the structures on one side drain into nodes of the same side, except for anatomically midline structures namely the nasopharynx, base of the tongue, pharyngeal wall, soft palate, and larynx. The neck lymph nodes are divided into groups based on different levels.

These levels are given as;

Level Ia: Submental Group

Level Ib: Submandibular Group

Level II: Upper Jugular Group

Level III: Middle Jugular Group

Level IVa: Lower Jugular Group

Level IVb: Medial Supraclavicular Group

Level Va and Vb: Posterior Triangle Group

Level Vc: Lateral Supraclavicular Group

Level VI: Anterior Compartment Group

Level VIa

Level VIb

Level VII: Prevertebral Group

Level VIIa: Retropharyngeal Nodes

Level VIIb: Retrostyloid Nodes

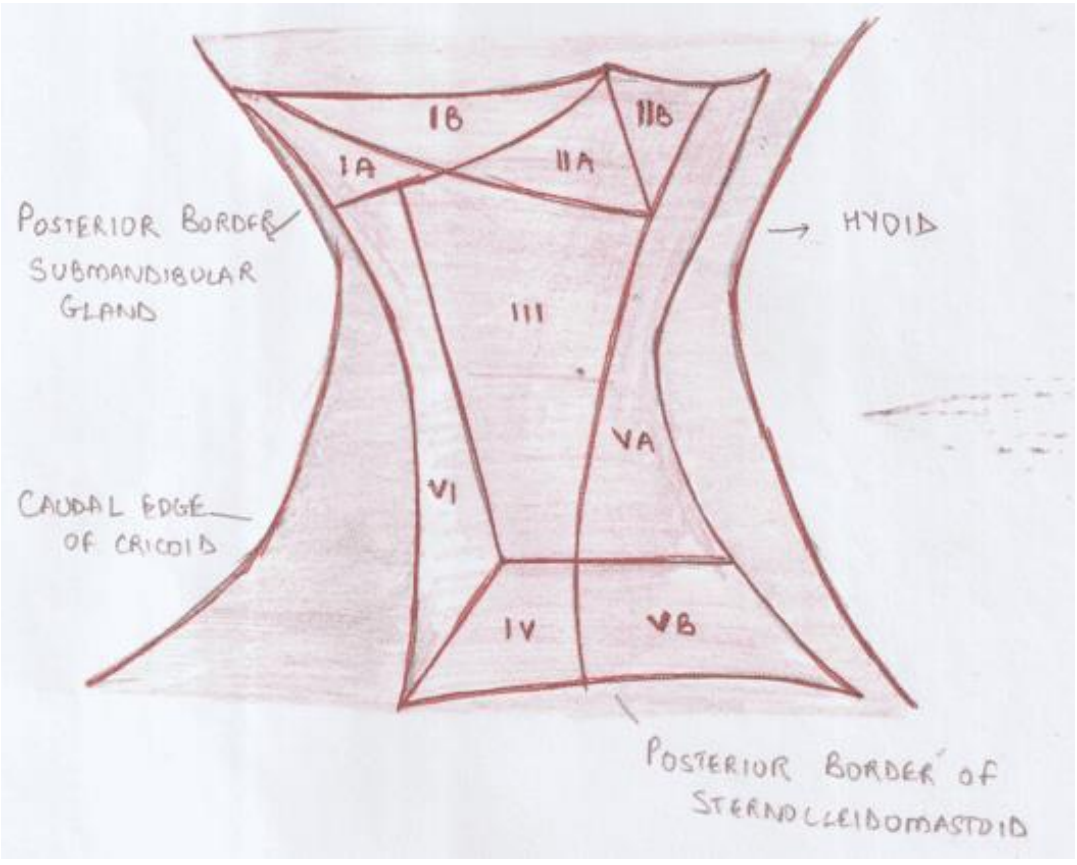
Level VIII: Parotid Group

Level IX: Buccofacial group

Level X: Posterior Group

Level Xa: Retroauricular and Subauricular Nodes

Level Xb: Occipital Nodes



A little bean-shaped well encapsulated structure called a lymph node is found in the neck, axilla, inguinal area, body cavity, and along lymphatic channels. The collagenous capsule of the LN capsule's fibrous trabeculae split the lymph node into a number of incomplete compartments. The convex side of the lymph node is where the afferent lymph veins enter to create a subcapsular sinus. From the subcapsular sinus, lymph passes down the trabeculae until it reaches the medulla. The medullary sinuses, which are wide, interconnected lymphatic passages, are abundant in number. The concave hilum is where the efferent lymphatic vessels emerge. They then drain into the proximal lymph nodes and finally into the thoracic duct.

Anatomically, the lymph node is divided into three regions: cortex, paracortex and medulla.

Cortex: The cortex, which is made up of a substantial number of lymphocytes, is found in the lymph node's subcapsular outer convex region. Primary and secondary lymphoid nodules are the two different types of lymphoid nodules visible here. In response to the antigenic stimulation, secondary lymphoid nodules form. A lighter germinal centre is surrounded by the darkly pigmented Mantle zone. B lymphocytes that are actively dividing are present in the germinal centre. On exposure to antigens, resting B cells first differentiate into centroblasts, then into centrocytes, which move from the dark zone to the apical zone of the germinal centre. Finally, immunoblasts that move to the medullary cords and undergo plasma cell differentiation are formed. The Mantle zone cells are resting B lymphocytes.

Paracortex: Is situated in between the cortex and medulla. T lymphocytes remain here.

Medulla: It consists of medullary cords that encircle large, convoluted lymphatic sinuses. Lymphocytes, plasma cells, and macrophages are tightly packed together to form these medullary cords. When leaving the lymph node, lymphocytes from the cortex go into the medullary sinuses and efferent lymphatic vessels.

NORMAL LYMPH NODE PARTSFRAMEWORK

Capsule, Fibrous trabeculae, Reticulin network

CORTICAL AREA

- Lymphoid follicles: Primary, Secondary
- Germinal centers: B cells, Centroblasts: dark zones, Centrocytes: light zones, T cells: small, inactivated, Tingible-body macrophages, Dendritic reticulum cells
- Mantle zone: memory B cells
- Marginal zone: monocytoid cells

PARACORTICAL AREA

- T cells: Small inactivated and Large immunoblasts

MEDULLARY AREA

Plasmablasts, Plasma cells

LYMPHATIC SINUSES

Marginal, Cortical, Medullary

BLOOD VESSELS

Arteries, Veins, Capillaries, High endothelial postcapillary venule

NORMAL ASPIRATE OF A LYMPH NODE

The aspirate smear shows a polymorphous population of mature lymphocytes, Centrocytes, Centroblasts, Immunoblasts, Plasma cells, Polymorphs, Eosinophils, Mast cells and Tingible body macrophages. Background can also show lymphoglandular bodies.

INDICATIONS FOR FINE NEEDLE ASPIRATION OF LYMPH NODES

1. To establish the cause of lymphadenopathy
2. To stage lymphoid or non-lymphoid malignancy
3. To monitor recurrence malignancies

COMMON PATHOLOGIES ENCOUNTERED IN LYMPH NODE

- Reactive lymphoid hyperplasia
- Infections
- Bacterial , Fungal , viral and parasites
    - Necrosis
    - Acute inflammation
    - Granulomatous inflammation
- Metastatic malignant tumors
- Lymphomas
    - Non-Hodgkin's lymphomas
    - Hodgkin's lymphoma

REACTIVE HYPERPLASIA

CYTOLOGY

The aspirate smear shows a mixed population of lymphoid cells comprising predominantly of small lymphocytes, Centroblasts, centrocytes, immunoblasts and plasma cells. The small lymphocytes have a small round nuclei and ill defined

condensed chromatin. Smear also shows Dendritic reticulum cells associated with centroblasts and centrocytes (derived from germinal centers). In the background Tingible body macrophages are also seen. Variable number of pale histiocytes, interdigitating cells, endothelial cells, eosinophils, neutrophils may be seen in the smear. [253,254]

HISTOLOGY

In Follicular Type Hyperplasia, reactive follicles show variation in their size and shape .Their borders are sharply defined and a mantle zone of small lymphocytes are frequently organized circumferentially. This gives an onion-skin design, occasionally centered on one the follicle's pole, which corresponds to the area of antigenic stimulation. The follicles are made up of a combination of small and large lymphoid cells having an elongated and cleaved nuclei. Pigment laden macrophagescreating the appearance of a starry sky are seen. Between the follicles, there is distinctly different lymphoid tissue as compared to the follicles' own. It is made up of a variety of small lymphocytes, large lymphoid cells, postcapillary venules and sometimes a prominent component of mature plasma cells.[255,256]

Other patterns of hyperplasia include:

Interfollicular/ paracortical, Diffuse, Sinus, Mixed.

GRANULOMATOUS LYMPHADENITIS

CYTOLOGY

The aspirate smearshows a characteristic finding of cohesive clusters of epithelioid type histiocytes. These epitheloid cells have a boomerang or ‘’sole of shoe’’ shaped nuclei. Nucleus has pale, with finely granular chromatin and the cytoplasm is pale with indistinct borders. Multinucleated giant cells usually of

Langhans type are seen in the smear occassionally. Necrosis and suppuration is infrequently present in the smear.[24]

HODGKINS LYMPHOMA

World Health Organization's classification of Hodgkin's lymphoma

- Classical Hodgkin's lymphoma
- Nodular sclerosis Hodgkin lymphoma
- Lymphocyte-rich Hodgkin lymphoma
- Mixed cellularity Hodgkin lymphoma
- Lymphocyte-depleted Hodgkin lymphoma
- Nodular lymphocyte predominant Hodgkin's lymphoma

CYTOLOGY

In Classical Hodgkin's Lymphoma the aspirate smear shows a Polymorphic population of cells containing Mature lymphocytes, eosinophils, plasma cells and immunoblasts. Classical Reed–Sternberg cells which are large, with a binucleated nucleus and a prominent nucleoli are seen. In the mononuclear variant a single nucleus with other features of RS cell is seen. Lymphocyte and histiocyte (L & H) cell/popcorn cell may be seen in Lymphocyte predominant type of Hodgkin's Lymphoma. Ill formed epithelioid cell granulomas may be present in the background. Scattered elongated cells are seen in nodular sclerosing variety. Lymphohistiocytic tangle is usually absent in the smear[24]

HISTOLOGY

CLASSICAL HODGKIN'S LYMPHOMA

The classic Reed-Sternberg cell is a large (20–50 m in diameter or more) weakly acidophilic cell that can be found in all subtypes of conventional Hodgkin

lymphoma (although not in NLPHL).This cell has abundant amphophilic cytoplasm which may be granular or homogenous. The cell appears binucleated or multinucleated. The nuclear membrane is well defined and thick. The nucleus shows vesicular chromatin and contains a huge, round, extremely acidophilic central nucleolus encircled by a transparent halo. The two nuclear lobes of the Reed-Sternberg cell face one another ("mirror image"), giving rise to "owl eye" look. When there is multilobation, then its appearance has been compared to an "egg basket."

Variants suggestive but not diagnostic of Hodgkin's Lymphoma are Mononuclear variants of RS cell, multilobated anaplastic type, Mummifed and Popcorn type.

NODULAR SCLEROSIS

Tissue shows broad bands of bifringent collagen separating the lymphoid tissue into well-defined nodules. These fibrous bands are seen around blood vessels when viewed with polarized light. A variant of Reed-Sternberg cell known as lacunar cells may be seen. This cell type is large (40–50 m), has a multilobulated nuclei with complex infoldings, transparent cytoplasm and a smaller-sized nucleoli compared to the conventional RS Cell . These cells have "frail" cytoplasm that has been drawn back in close proximity to the nuclear membrane, giving the impression that nuclei are floating in a "lacuna." This is the outcome of a formalin-induced artifact and is absent in tissues that have been fixed in B5 or Zenker solution. These lacunar cells can occasionally cluster, especially around the necrotic areas. Cases of nodular sclerosis Hodgkin lymphoma showing prominence of this feature have been referred to as the syncytial, sarcomatoid or sarcomatous variant.[257]

MIXED CELLULARITY

Tissue shows eosinophils, plasma cells and atypical mononuclear cells intermingled with the classic Reed-Sternberg cells. Focal fibrosis may be minor or nonexistent, however necrosis may be present. This kind typically affects the head and neck region more frequently and can be related to Hodgkin's EBV infection.[258]

LYMPHOCYTE RICH

The Reed-Sternberg cells distributed against a nodular (most frequently) or diffuse backdrop, primarily made up of small B lymphocytes, characterize the lymphocyte-rich type (in contrast to other T-cell backdrop Types of Classical Hodgkin lymphoma).

LYMPHOCYTE DEPLETED

Less than 5% of all Hodgkin lymphoma patients belong to the lymphocyte-depleted category, which includes the "diffuse fibrosis" and "reticular" morphological subtypes . The subtype of diffuse fibrosis shows fewer lymphocytes and other cells as a result of extensive collagen deposition. The reticular subtype is distinguished by an abundance of Reed–Sternberg cells among atypical mononuclear cells and others**.** [259]

NON HODGKINS LYMPHOMA [24]

DIAGNOSIS	**CYTOMORPHOLOGY**	**IMMUNOPHENOTYPING**	**MOLECULAR GENETICS**
Small lymphocytic	The aspirate smear shows cells having a small round regular nucleus. The nuclear chromatin is coarsely clumped and no nucleoli is seen.	Positive for: CD5, CD23, CDl9, CD 20 Co-expression of CD 5 and CD 23, Negative for: CD10	Trisomy 12; 13q deletion
MCL	The aspirate smear shows cells that are small with an irregular nuclear contour. The nuclear	Positive for: CD5,CDl9+, CD 20+, Paraffin section: Cyclin Dl, FMC7	t(ll:l4); (BCLl gene

DIAGNOSIS	CYTOMORPHOLOGY	IMMUNOPHENOTYPING	MOLECULAR GENETICS
	chromatin is fine and nucleolus is inconspicuous.	Negative for: CDl0, CD23	rearrangement)
Follicular	The aspirated smear studied shows a mixture of cleaved and non-cleaved small and large cells.	Positive for: Surface Ig, CDl0, CDl9, CD20, Bcl2, Bcl6 Negative for: CD5	t(l4:l8) and BCL2 gene rearrangement
Lympho-plasmacytic	The aspirate smear shows lymphocytes, plasma cells and plasmacytoid cells. Intracytoplasmic PAS positive inclusion bodies are also seen.	Positive: Cytoplasmic immunoglobulin, CO I9. CD20. CD22. CD 79a, CD 38 Negative: CD 5, 23, CD l0	
Marginal zone	The aspirate smear shows a heterogeneous population of small centrocyte like cells, plasma cells, plasmacytoid cells and Monocytoid B cells with pale cytoplasm.	Positive: Surface Ig , CD l9,CD 20 Negative: CD5, CDl0, CD23	
Hairy cell leukemia	The aspirate smear shows cells with multiple villi on their surface.	Positive: CDl03, CDllc+, CD25+ Negative: CDl0, CD3, CD5	
Plasmacytoma / multiple myeloma	The aspirate smear shows immature and mature looking plasma cells.	Positive: CD38+, CDl38+ Negative: CDl0, CD3, CD5,CD23	
Precursor B lymphoblastic	The aspirate smear shows small to medium sized cells with a scanty basophilic cytoplasm. The nuclear chromatin is condensed and contains a	Positive: Tdt, CDl0, CDl9, CD20 Negative: Surface Ig	t(l;9), t(9:22

DIAGNOSIS	CYTOMORPHOLOGY	IMMUNOPHENOTYPING	MOLECULAR GENETICS
	small inconspicuous nucleoli.		
Burkitt's	The aspirate smear shows medium sized cells with cytoplasm that is deep basophilic and vacuolated. The nuclear chromatin is coarse with multiple prominent nucleoli. The background shows a typical Starry sky.	Surface Ig +, CD5-, CD23 -, CDl0+, CD l9 +, 20 +, Ki67index is more than 85%	t(8:l4), t(8:22). Rearrangement of c-MYC gene
Diffuse large B cell	The aspirate smear shows monomorphic large cells which are two to three times the size of mature lymphocytes. These cells contain a prominent nucleoli and basophilic cytoplasm.	Positive: Surface Ig +/-, CDl0+/- , CD l9, 20 Negative: CD5 (90%) Ki 67 index less than 90	
T-lymphoblastic	The aspirate smear shows cells that are small with a scanty basophilic cytoplasm. The nucleus contains condensed chromatin and a smallinconspicuous nucleoli.	Positive: TdT, CD3, CD7, CD4+/-, CD8	
Peripheral T cell	The aspirate smear shows medium to large sized cells. Individual tumor cells contain a pleomorphic nucleus and a prominent nucleoli. Nuclear margin shows marked irregularity with	Positive: CD3, CD7 and CD4/CD8	

DIAGNOSIS	CYTOMORPHOLOGY	IMMUNOPHENOTYPING	MOLECULAR GENETICS
	deep notching and convolution.		
Anaplastic large cell	The aspirate smear shows large cells many of which have multilobated nuclei -"Hallmark" cells -Doughnut cells	Positive: CD30 (Ki-l), EMA, ALK Negative: CD45 +/-,CD3 +/-	t (2:5), causing fusion of ALK and NPM

METASTASIS TO LYMPH NODE [24]

Metastatic carcinoma from primaries in the head and neck and metastatic melanoma are the most commonly found cancers in neck nodes. Among these metastatic SCC from a primary head and neck tumor is the most common.

Squamous cell carcinoma: The aspirate smear from the metastatic SCC in lymph node often shows features of cystic degeneration and yields turbid fluid on aspiration. The smears show polyhedral squamoid cells a large hyperchromatic, pleomorphic nuclei. Cells with an orangeophilic cytoplasm indicating intracellular keratin is seen on PAP stain. A good number of tadpole and fiber cells are also seen in the smear. Based on the presence of only mature squamous cells it may be difficult to make a definite diagnosis.

Adenocarcinoma: The aspirate smear of adenocarcinoma shows loose clusters of cells showing a glandular arrangement. The individual tumor cells show moderate amount of vacuolated cytoplasm and a central to eccentric nuclei having a prominent nucleoli. Mucinous material may be seen in the background.

Small cell carcinoma: The aspirate smear shows predominantly discrete cells and occasional small loose clusters of cells. The individual cells are small with a scanty cytoplasm and having a round mildly pleomorphic hyperchromatic nuclei. The

nucleus shows condensed chromatin with an indistinct or absent nuceoli. A characteristic feature seen is nuclear molding. These tumors are positive for NSE and synaptophysin.

Germ cell tumor: The aspirate smear shows a foamy vacuolated background and tigroid appearance. The individual cells are predominantly discrete, round and have a central large nuclei. Nuclear chromatin is fine with a single prominent nucleoli. The individual tumor cell morphology along with the typical background may help in the diagnosis of metastatic dysgerminoma or seminoma. Cells of endodermal sinus tumor show highly pleomorphic features and a large prominent nucleoli.

Sarcoma: These may also metastasize in the lymph node and 2 to 5% of patients can develop nodal metastases. The differential diagnosis of metastatic round cell sarcomas in the lymph node includes NHL, undifferentiated carcinoma or neuroblastoma. Metastatic spindle cell sarcoma is relatively easy to diagnosis and the differential diagnosis of metastatic sarcoma having spindle-cell morphology includes melanoma and spindle cell carcinoma.

Others

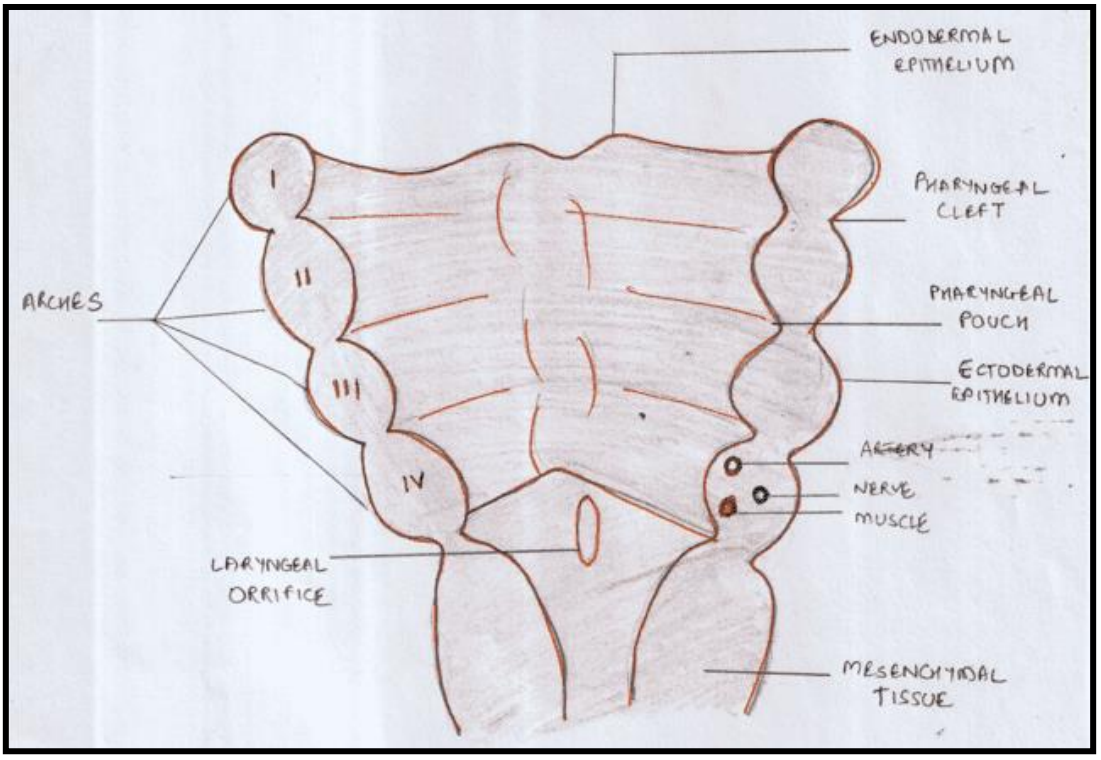
A number of other malignancies such as melanoma, renal cell carcinoma, carcinoid, etc. may also show metastasize in the lymph node. Cytological features and thorough clinical history are helpful in their diagnosis. In difficult situations IHC may be also helpful.

MISCELLANEOUS LESIONS

- **ODONTOGENIC CYSTS**
    - ODONTOGENIC KERATOCYSTS
- **JAW LESIONS**

- AMELOBLASTOMA

- **PARAGANLION TUMORS**
    - PARAGANGLIOMA
- **CYSTS AND CYST- LIKE LESIONS**
    - EPIDERMAL/PILAR/ DERMOID CYST
    - RANULA
    - THYROGLOSSAL DUCT CYST
    - BRACHIAL CLEFT CYST
- **OTHERS**
    - LIPOMA
    - HEMANGIOMA
    - CYSTIC LYMPHANGIOMA
    - NEUROFIBROMA/ NEUROLEMOMA



ODOTOGENIC KERATOCYSTS

CYTOLOGY

The aspirate smears show plenty of squamous cells containing abundant eosinophillic cytoplasm and a benign nucleus. The background is dirty and shows keratinous debris, multinucleated giant cells and mild inflammation

HISTOLOGY

Histology reveals a fibrous wall that is not inflammatory and is lined by a regular epithelium that is just 5-8 cell layers thick and devoid of rete ridges. An obvious granular cell layer and orthokeratinization are visible on the surface. The keratin surface is thick and lamellated. The nuclei of the basal cells are flat or cuboidal. Focal areas may be non-keratinized or parakeratinized, although they only make up a small portion of the lining and are frequently accompanied by inflammation.

AMELOBLASTOMA

CYTOLOGY

The aspirate smears studied shows cell clusters that are compact and cohesive. The individual cells are basaloid , having a increased N:C ratio. The nucleus shows fine powdery chromatin with small peripheral inconspicuous nucleoli.

HISTOLOGY

The most prevalent kind is the follicular type, which resembles the enamel organ's epithelial component within a fibrous stroma. The peripheral cells are columnar to cuboidal (like ameloblasts), with a hyperchromatic nuclei grouped in a palisading pattern with reverse polarity. The central core has loosely placed angular cells that frequently undergo cystic change, which is similar to stellate reticulum. The plexiform variant of these conditions is the most prevalent. It consists of anastomosing strands of ameloblastoma with a subtle stellate reticulum and cyst-like stromal degeneration. There are also acanthomatous, granular, and basaloid histologic forms. The desmoplastic ameloblastoma is composed of cuboidal to flat peripheral cells with central spindle-shaped cells and dense collagen**.**

PARAGANGLIOMA

CYTOLOGY

The aspirate smears shows tumor cells arranged in irregular clusters. The individual tumor cells show a finely granular eosinophilic cytoplasm and occasional intracytoplasmic pigment. The nuclei may show mild to moderate pleomorphism , binucleation and intranuclear pseudoinclusions.

HISTOLOGY

Sections studied show different patterns of tumor cell arrangement. The most prevailing pattern consists of epitheloid chief cells arranged in a Zellballen pattern and are separated by prominent fibrovascular stroma. The trabecular pattern of arrangement shows ribbons or cords of epitheloid cells separated by fibrous bands. Pseudorosette, angioma like, spindled and sclerosing are other tumor patterns seen. The individual chief cells are round ,oval to polygonal and contain abundant eosinophilic cytoplasm. Occasional giant multinucleated cells may be present.

RANULA

HISTOLOGY

A simple ranula is a mucin-containing pseudocyst that may be focally lined by squamous, cuboidal, or columnar epithelium. A plunging ranula is a pool of mucin surrounded by fibrous tissue and inflammatory cells (often histiocytes), without an epithelial lining. For the purpose of recognising extravasated mucin, mucicarmine staining or periodic acid Schiff (PAS) with diastase may be useful.

THYROGLOSSAL CYST

CYTOLOGY

The aspirate smear shows inflammatory cells and debris that are mixed with mature squamous tissue. Sometimes, thyroid follicular epithelium is seen in the smear.

HISTOLOGY

Thyroid follicles and mucous glands may be visible in the wall of the cyst. Cyst wall is lined by benign epithelium that is typically respiratory or squamous in nature. The cyst lining might be obliterated by severe granulomatous inflammation,

abscess, and the reaction with cholesterol granulomas. Rarely, malignancy may develop (most commonly papillary thyroid cancer).

BRACHIAL CLEFT CYST

CYTOLOGY

The aspirate smear shows neutrophils, lymphocytes, and debris admixed with mature squamous cells, including degenerate forms.

HISTOLOGY

Branchial cleft cysts typically have a unilocular structure. 90% of the time, stratified squamous epithelium lines them, and less frequently, respiratory epithelium. Both epithelial types occasionally have goblet cells and transitional zones. Keratin debris are present throughout the lumen. The wall contains lymphoid tissue with germinal centres. Branchial cleft cysts do not or seldom develop carcinoma. In individuals older than 40 years, suspected branchial cleft cysts with cytological atypia should raise the potential of metastatic cancer from the oropharynx.

LIPOMA

CYTOLOGY

The aspirate smear shows fragments of mature adipose tissue. Few single fat cells and fat droplets are also seen. The individual fat cells are large, have abundant empty cytoplasm and a small often eccentric dark nucleus.

HISTOLOGY

Sections studied show nests of mature adipocytes separated by thin fibrous septa.

HEMANGIOMA

CYTOLOGY

The aspirate is hemorrhagic. Smear shows few strands of endothelial cells with pale, syncytial cytoplasm and pale spindle nuclei. Background may show mucinophages, hemosiderin laden macrophages and fibroblasts if thrombosis has occurred.

HISTOLOGY

Capillary Hemangioma: Sections studied show thin walled capillaries and a scanty stroma .

Cavernous Hemangioma: Sections studied show a sharply delineated mass that is not capsulate. A connective tissue stroma separates large cavernous vascular spaces.

CYSTIC LYMPHANGIOMA

CYTOLOGY

The aspirate smear shows only lymphoid cells containing mainly small lymphocytes in varying numbers against a plasmaceous background.

HISTOLOGY

Capillary Hemangioma: Sections studied show spaces lined by endothelium that can be differentiated from capillaries by absence of erythrocytes or by lymphatic endothelial markers(VEGFR-3, LYVE-l).

Cavernous Hemangioma: Sections studied show endothelium lined large massive dilated spaces that are separated by connective tissue stroma. The stroma shows lymphoid aggregates.

NEUROFIBROMA/NEUROLEMOMA

CYTOLOGY

The aspirate smear shows variable cellularity. Background contains fibrillary substance and myxoid or collagenous material. The individual cell nuclei tend to be long, slender and have pointed ends. Nuclear palisading may be seen in the smear.

HISTOLOGY

Sections studied show spindle cells arranged loosely and randomly in a myxoid to collagenous stroma .Individual spindle cells show wavy nuclei and inconspicuous cytoplasm. There are typical collagen bundles also visible showing a shredded carrots appearance**.**

EPIDERMAL/PILAR/DERMOID CYSTS

CYTOLOGY

Cytological analysis cannot distinguish between these three cysts. The aspiratefrequently produces a thick, oily, foul-smelling substance. Smear shows debris that includes some nucleated squamous epithelial cells and anucleate squames of cells. Inflammatory cells and large foreign body cells are seen in the background.

HISTOLOGY

Epidermal/Epidermoid/Infundibular cyst: Sections studied show cyst lining composed of stratified squamous epithelium with a granular layer and lacks normal skin appendages.The contents of the cyst are keratin flakes /anucleate squames of cells.

Pilar/Trichelemmal cyst: Commonly found on the scalp. Sections studied shows a cyst lining composed of stratified squamous epithelium and has a palisaded outer layer. The keratin is dense, laminated and eosinophilic. Granular layer is absent. Sebaceous glands may be seen.

Dermoid cyst: Sections studied show cyst lining showing stratified squamous epithelium containing normal skin appendages. The cyst contents are made up of keratin flakes and hair shafts

METHODOLOGY

The present study aims to correlate FNAC with Histopathology in palpable head and neck lesions. Study was conducted on patients who presented with superficially palpable head and neck lesions in Medicine, Surgical, Dermatology departments at KLES Dr. Prabhakar Kore Charitable Hospital and MRC, Belagavi. The study is undertaken from 1st January 202l-3lst December 202l and was approved by J.N. Medical College Institutional Ethics Committee for human subjects research. After obtaining permission from the hospital authorities, the participants will be briefed about the study and informed consent was taken from the prospective cases. The data is collected using a predesigned proforma .The information about the clinical parameters were obtained from the clinical records from MRD and Department of Pathology, Dr. Prabhakar Kore Charitable Hospital and MRC, Belagavi. FNAC was performed on 46 patients with head and neck lumps and also underwent surgical excision, the results of which were further analyzed.

METHOD OF ASPIRATION CYTOLOGY:

The same technique of FNAC that was described by Franzen, Zajicek and their colleagues is used in Our present study.

Firstly patient history was taken and a clinical diagnosis was made after proper local and systemic examination. A written consent was then taken after explaining the FNAC procedure to the patient in their vernacular language. Smears were then made.

BASIC EQUIPMENTS:

1. l0-20 ml disposable plastic syringe.
2. 22-25 gauge, 30-50mm long disposable needle.
3. Clean dry glass slides.
4. Fixative- 95% ethyl alcohol in a sterile container.
5. Aseptic solution, cotton swabs.
6. Stains- following stains were used to stain the smears
    a. Papinoculaou Stain,
    b. Giemsa Stain,
    c. Hematoxylin & Eosin Stain and
    d. Ziehl-Neelsen Stain.

PROCEDURE:

Positioning of the patient: Patient was positioned in such a way as to allow adequate palpation of the swelling depending on the site of aspiration.

Patients were kept in supine position for aspirating thyroid swellings. To make the gland more prominent a pillow was placed under the neck.

For supraclavicular lymph node aspiration, the patient was examined in sitting position.

In cases of cervical lymph node enlargement, the patient was asked to be in supine position and to turn the head away from the lesion, in order to make the nodule prominent.

In case of aspiration of salivary gland lesions, the swelling was made more prominent by instructing to the patient to be in supine position and face the opposite side.

THE PROCEDURE OF FNAC:

1. Wear gloves and use a cotton swab soaked in antiseptic solution to clean the area.
2. Feel the site of aspiration after fixing the swelling with one hand.
3. Insert a 22-25 gauge needle with a l0ml disposable syringe attached to it.
4. Negative pressure was then applied.
5. While applying negative pressure the needle was moved through and fro inside the swelling. Negative pressure was later released while keeping the needle inside the target tissue.
6. Needle was withdrawn.
7. Air was drawn into the syringe after detaching the needle.
8. Sample was blown onto the clean glass slide by again attaching the needle to the syringe.
9. Smears were prepared- Some smears were air dried to stain with MGG stain. Other smears were fixed in 95% ethyl alcohol for PAP and H&E Stains.
10. Aspirated smears were stained for Giemsa, PAP and H&E stains. ZN stain for AFB was performed whenever required.

The received post-operative surgical specimens were fixed in l0% NBF and subjected to gross examination, processing, paraffin embedding, section cutting and staining by H&E Stain.

All the smears were examined systemically as follows:

- Cellularity: Scant/Adequate/ Rich.
- Background of smear- presence of inflammatory cells, blood, necrosis.
- Detailed study of morphology of cell population.

All the Tissue sections were examined as follows:

- Cell arrangement
- Cell morphology- cytoplasm, nucleus, chromatin, nucleolus
- Stroma

PHOTOS

Figure 1: Tissue section lymph node showing Langhan's giant cell [H&E stain x400]

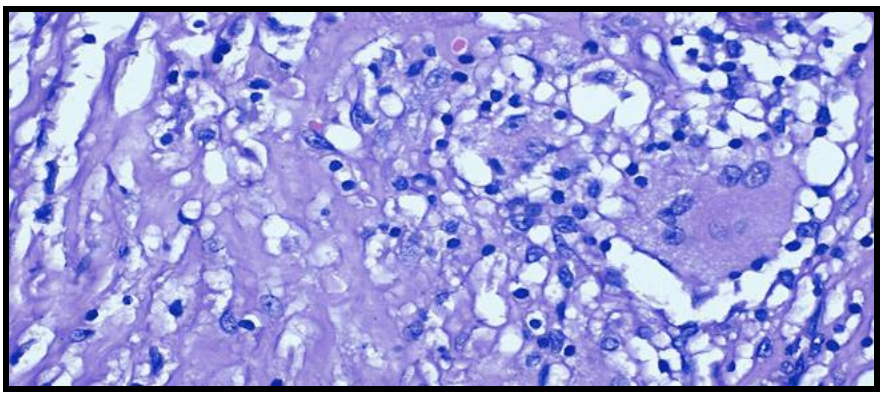


Figure 2: Smear lymph node showing well formed granuloma [MGG stain x400]

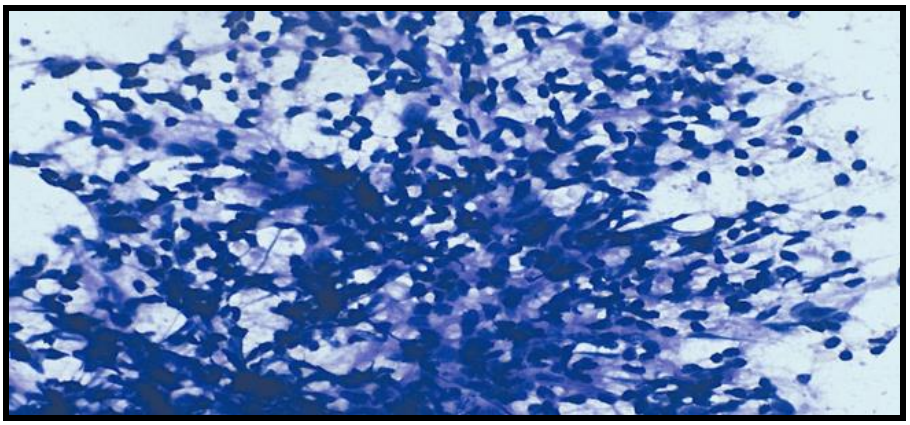


Figure 3: Tissue section lymph node showing caseation necrosis and granulomas with Langhan's giant cells [H&E x200]

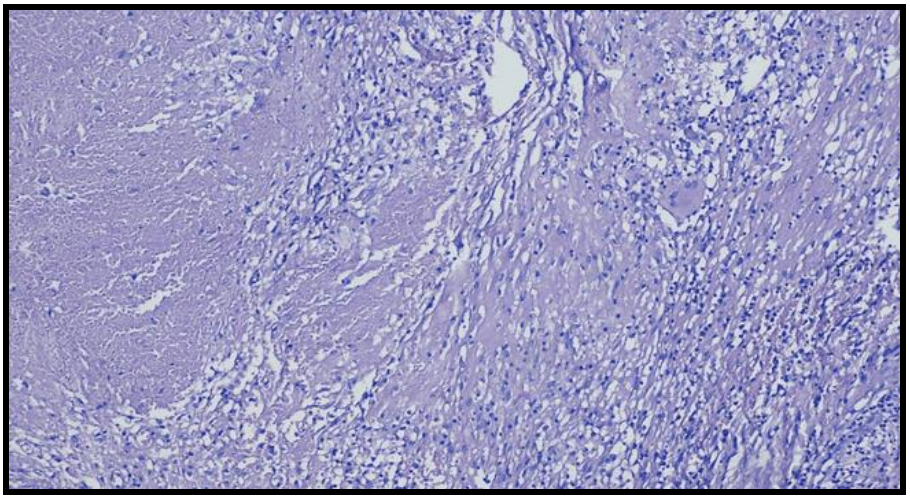


Figure 4: Smear from reactive lymph node showing polymorphous lymphoid cells and tingible body macrophage [MGG stain x 400]

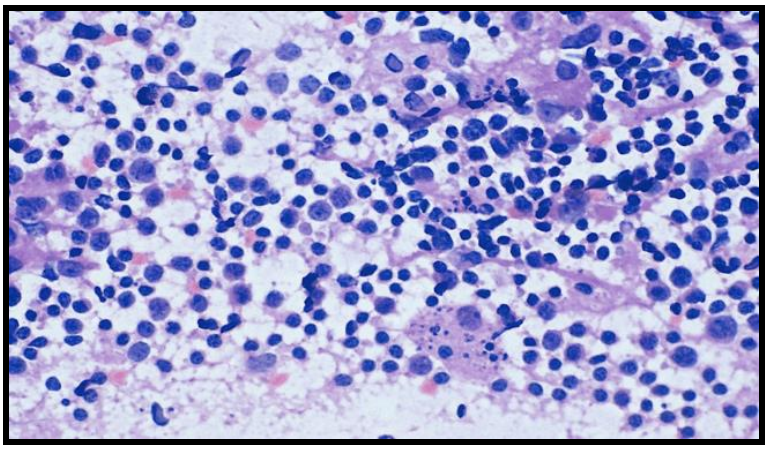


Figure 5: Tissue section from reactive lymph node showing hyperplastic lymphoid follicles [H&E stain x200]

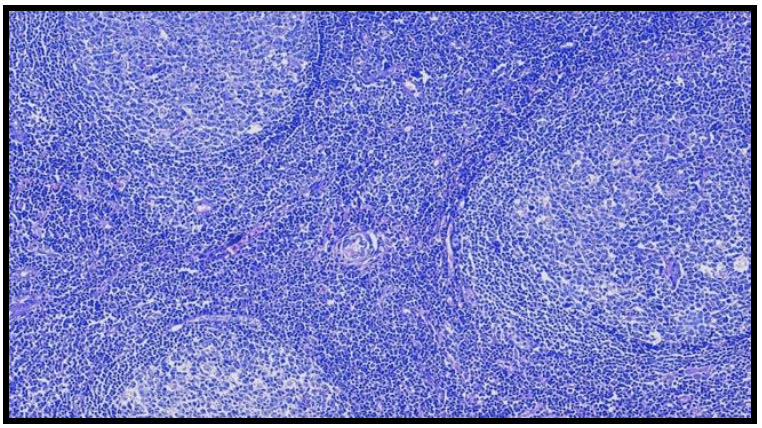


Figure 6: Smear from lymph node showing features of Hodgkin's lymphoma with binucleate RS like cell [MGG stain x400]

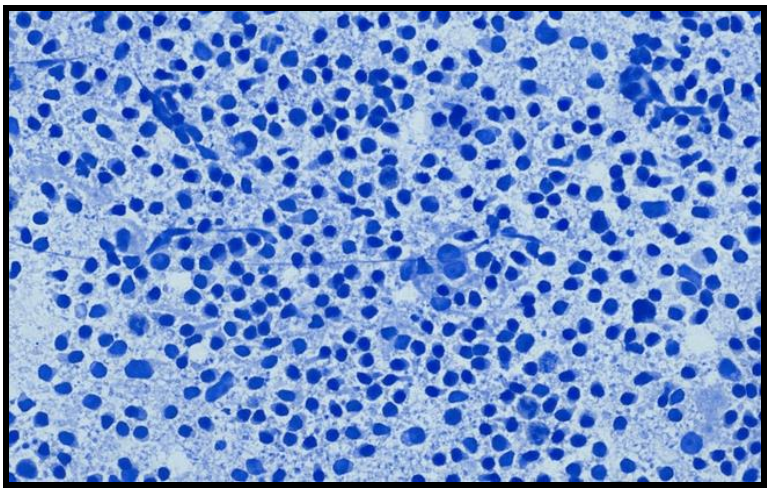


Figure 7: Tissue section from lymph node showing features of non-specific Sinus Histiocytosis [H&E X200]

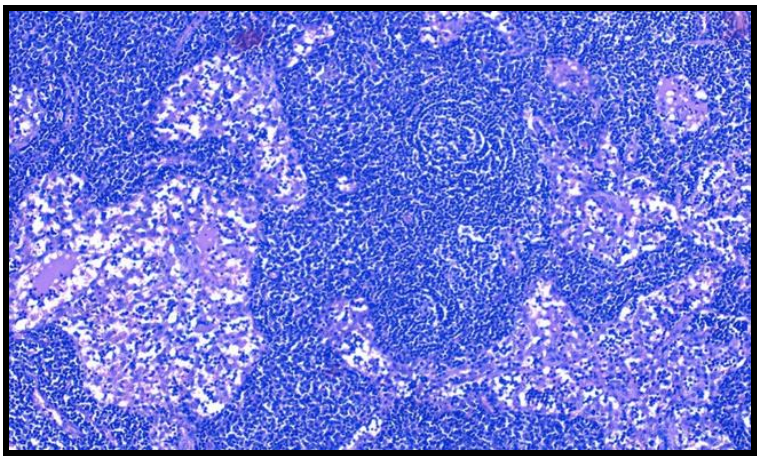


Figure 8: Smear from lymph node showing features of Non Hodgkin's lymphoma [MGG stain x400]

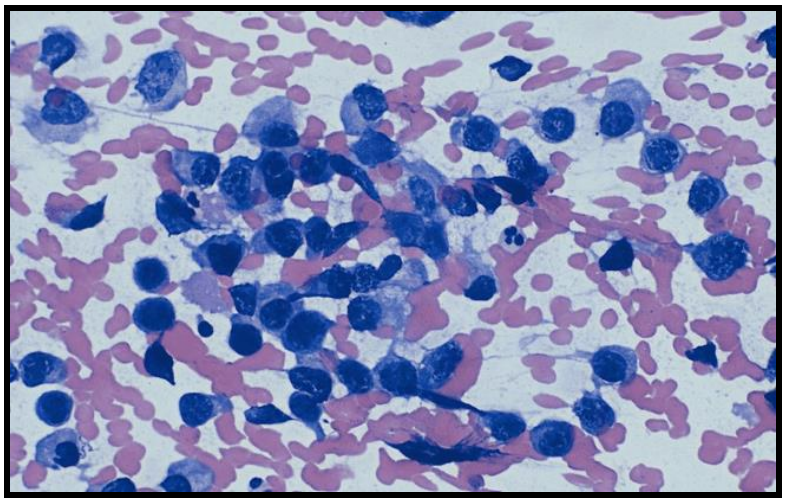


Figure 9: Tissue section from lymph node showing features of Burkitt's lymphoma [H&E X100]

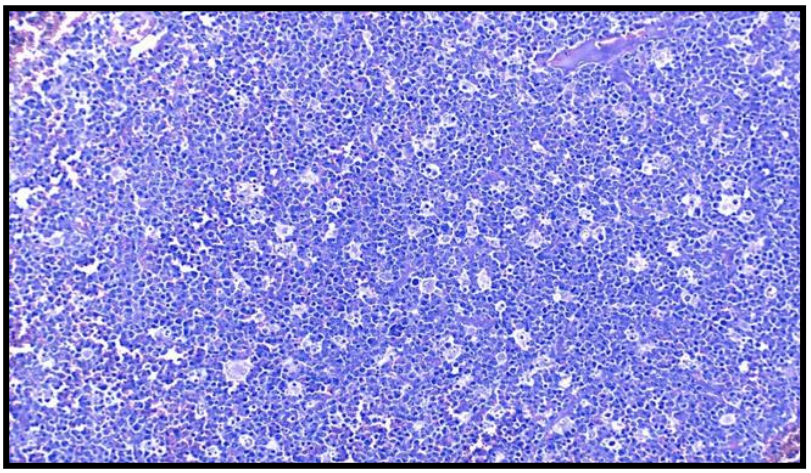


Figure 10: Smear from salivary gland showing features of Pleomorphic adenoma

[MGG stain x100]

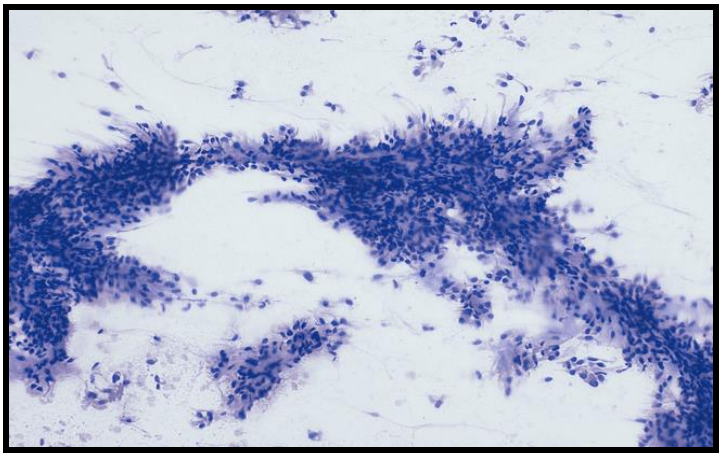


Figure 11: Tissue section from salivary gland showing features of Pleomorphic adenoma [H&E stain x100]

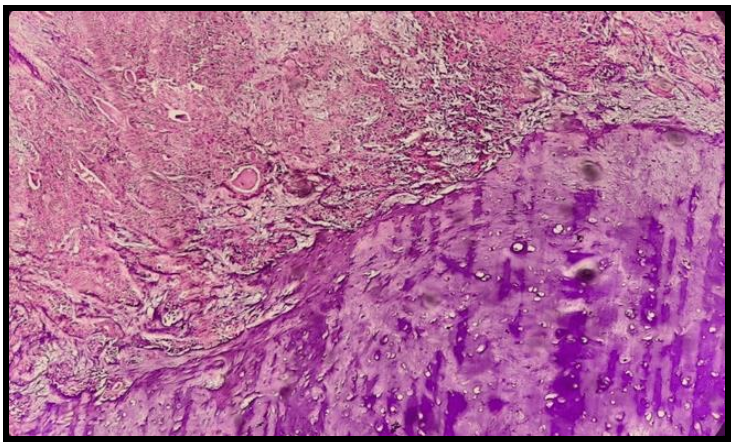


Figure 12: Smear from parotid gland showing features of Mucoepidermoid carcinoma [PAP stain x100]

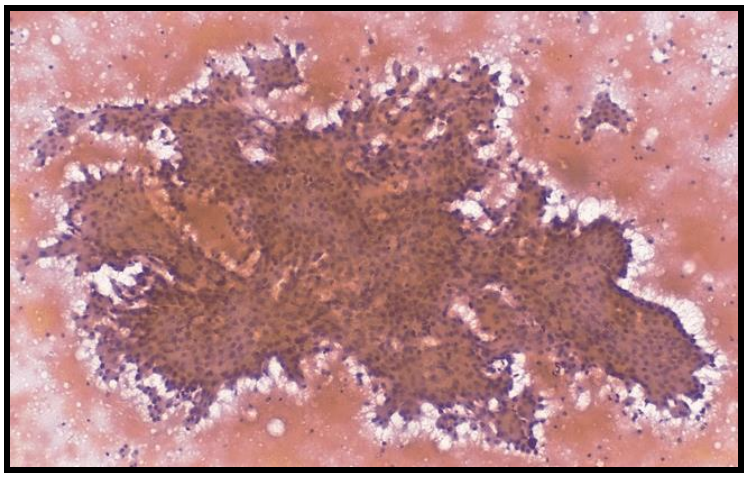


Figure 13: Smear from parotid gland showing features of Mucoepidermoid carcinoma [PAP stain x400]

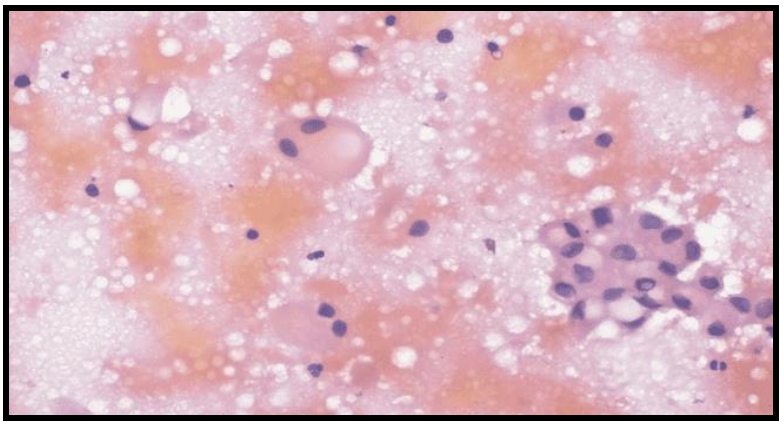


Figure 14: Tissue section from salivary gland lesion showing features of Mucoepidermoid Carcinoma [H&E stain x200]

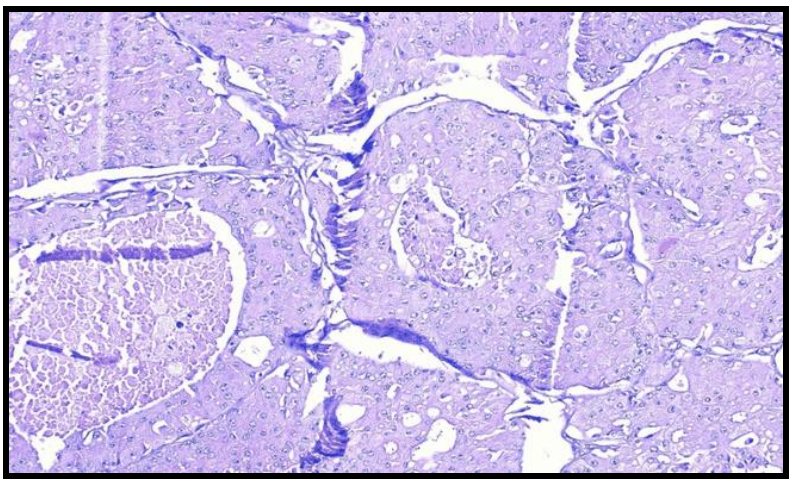


Figure 15: Smear from lipoma showing adipocytes [PAP stain x400]

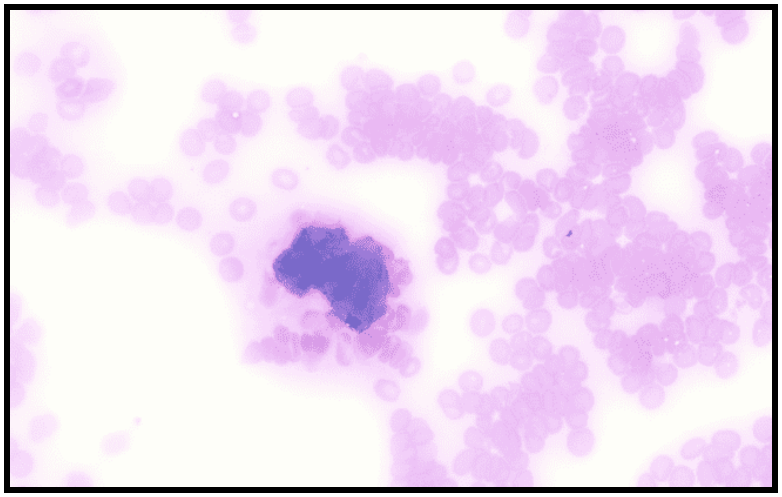


Figure 16: Tissue section showing features of lipoma [H&E stain x200]

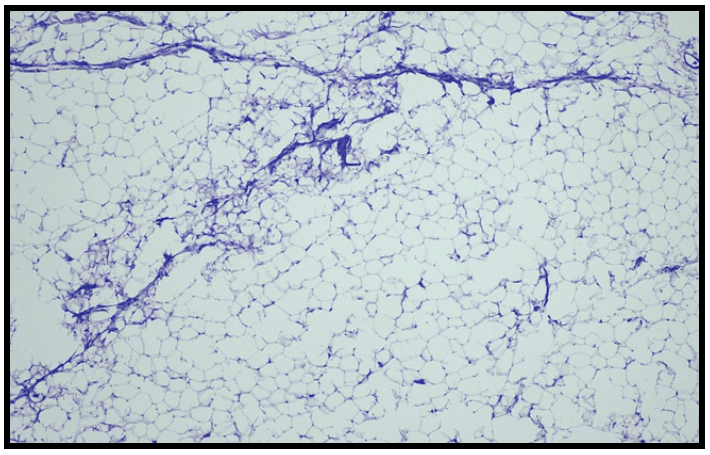


Figure 17: Smear showing features of Spindle cell lesion [Giemsa stain x100]

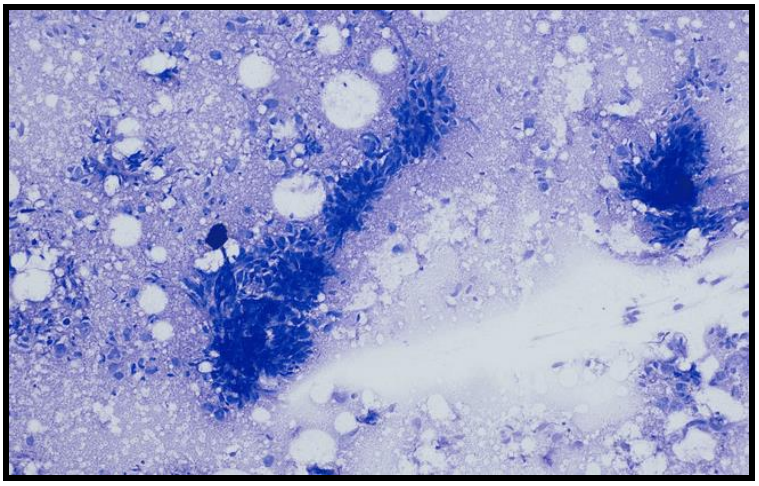


Figure 18: Tissue section showing Spindle cell lesion [H&E stain x50]

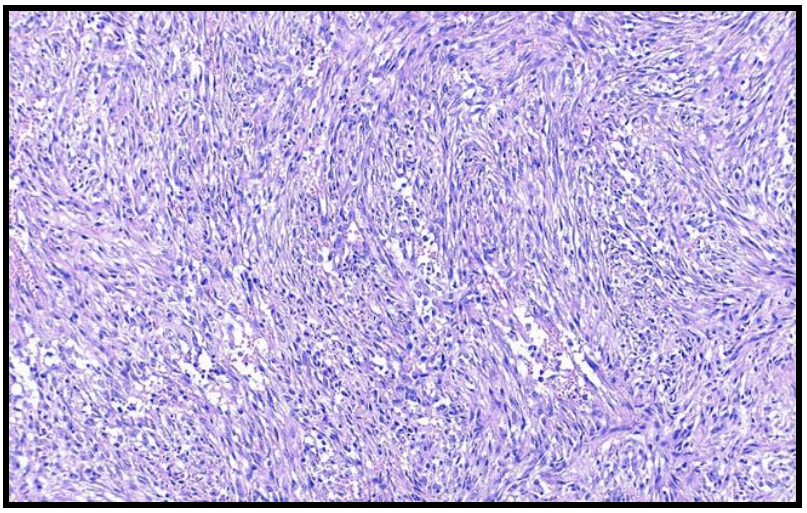


Figure 19: Tissue section showing Spindle cell lesion [H&E stain x100]

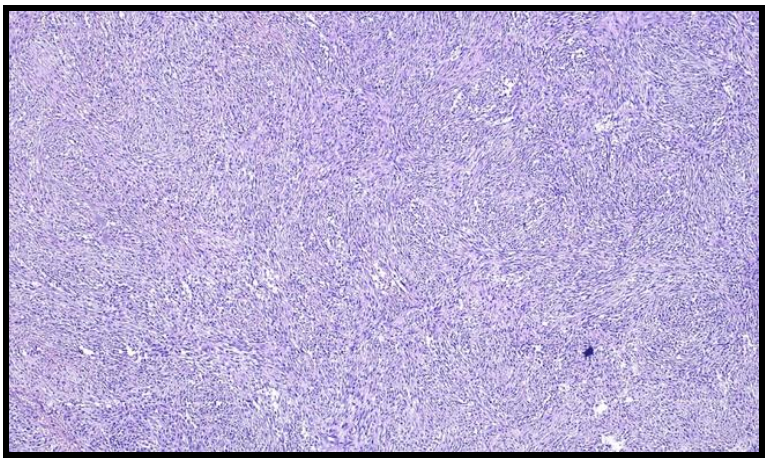


Figure 20: Smear showing an Acute suppurative lesion [H&E stain x400]

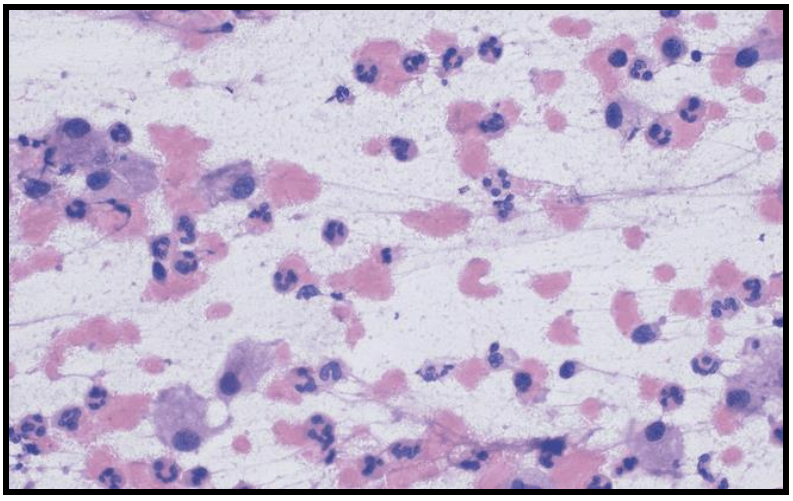
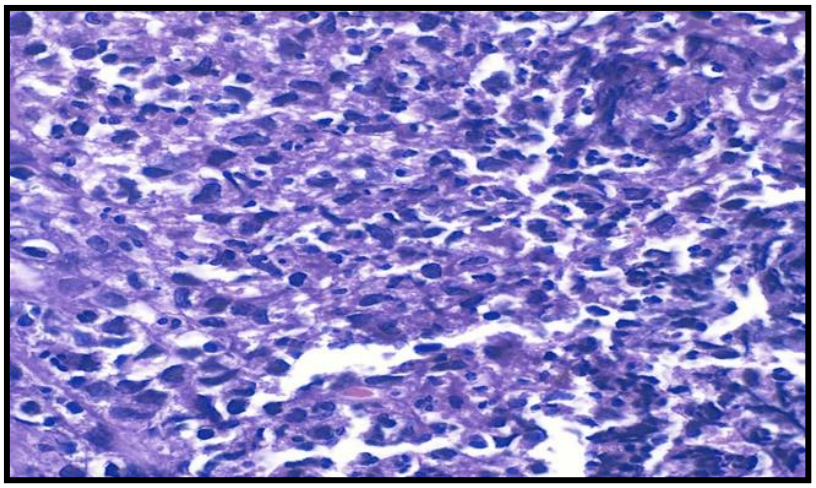


Figure 21: Tissue section showing an Acute suppurative lesion showing Acute inflammatory infiltrate [H&E stain x400]

Figure 22:  **Smear shows**

aspirate from colloid nodule [H&E stain x400]

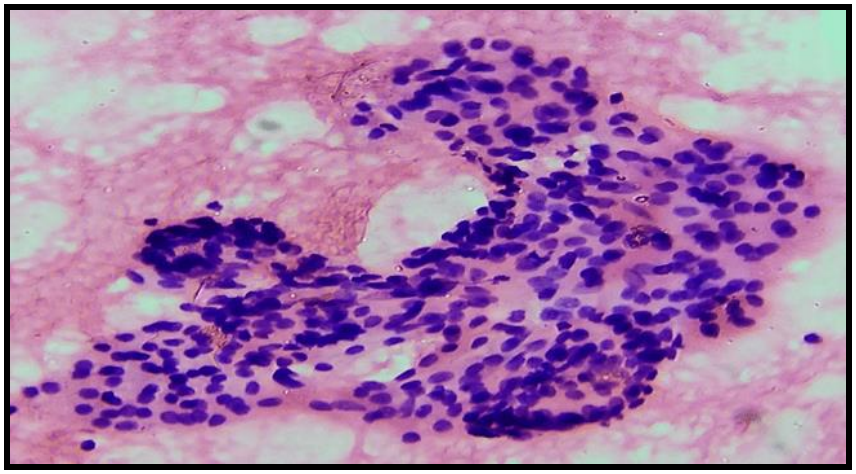


Figure 23: Tissue section from Multinodular goiter showing hemosiderin laden macrophages [H&E stain x400]

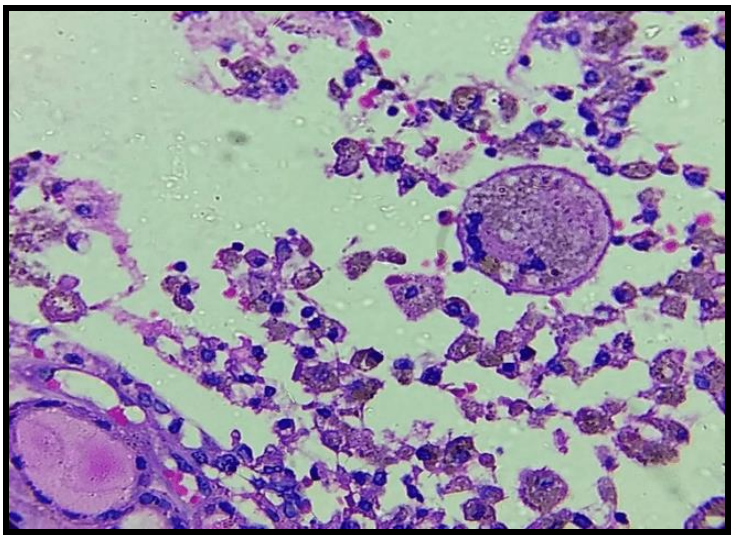


Figure 24: Tissue section shows Multinodular Goitre showing cystic degeneration [H&E stain x400]

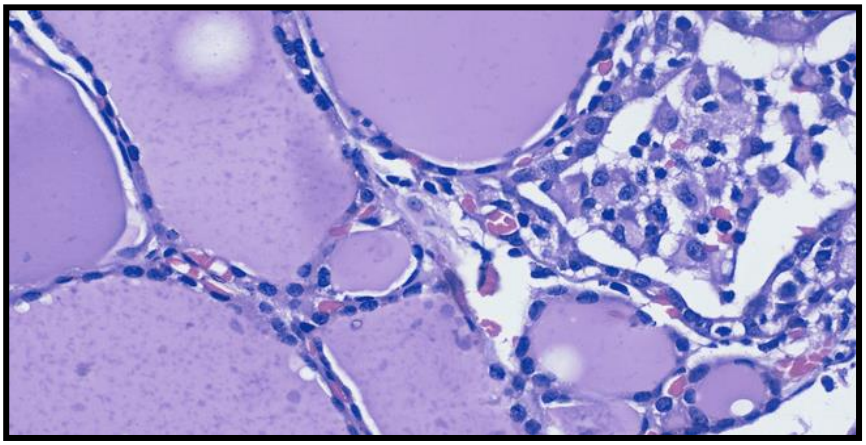


Figure 25: Tissue section shows Multinodular Goitre [H&E stain x200]

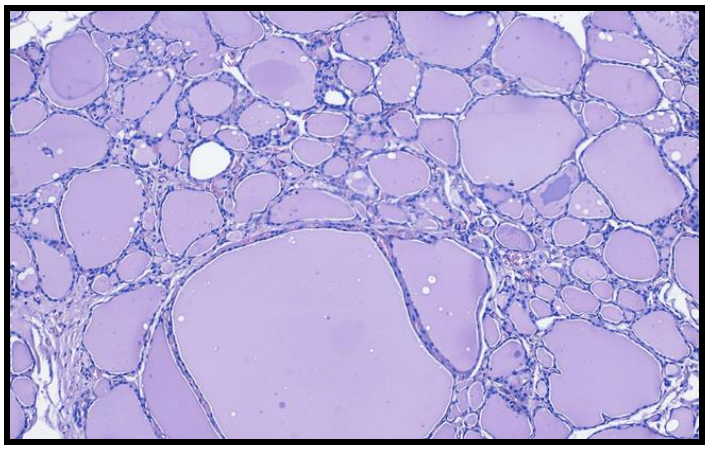


Figure 26: Tissue section from Follicular Carcinoma thyroid showing capsular invasion [H&E stain x200]

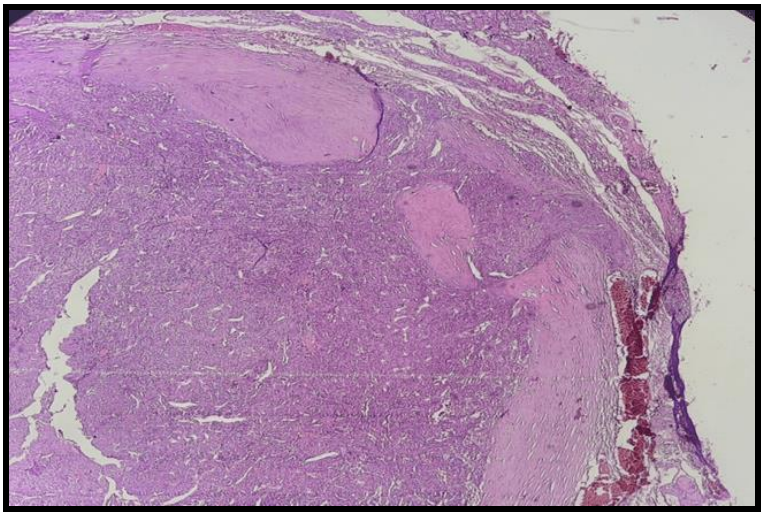


Figure 27: Smear from Follicular Adenoma [MGG stain x400]

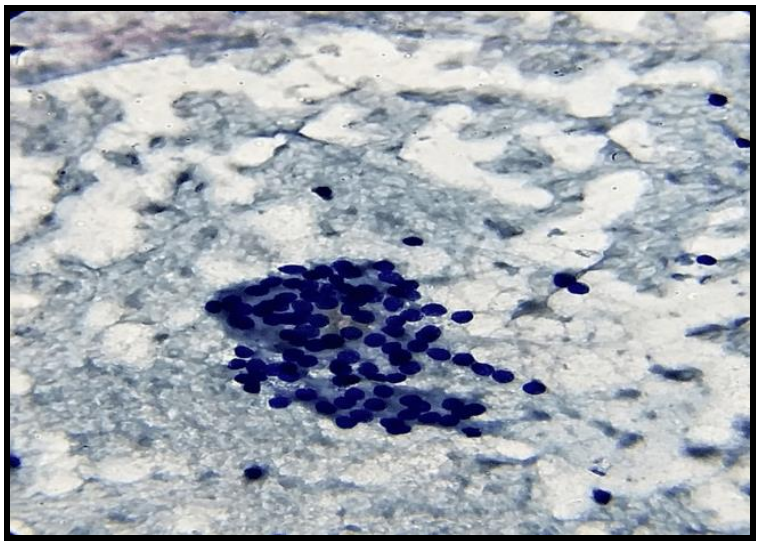


Figure 28: Tissue section from Follicular Adenoma [H&E X40]

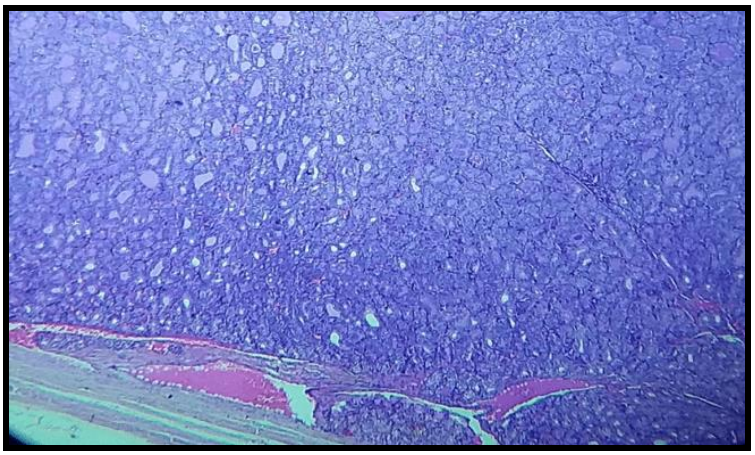


Figure 29: Section from Follicular Adenoma Thyroid [H&E stain x400]

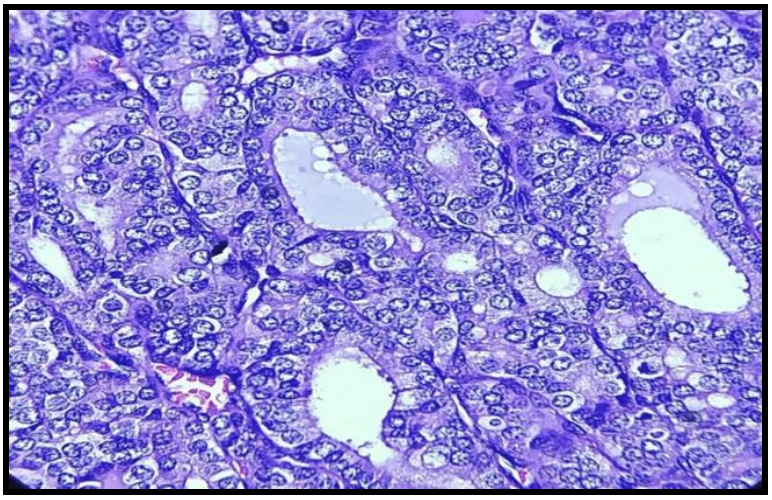


Figure 30: Smear from Papillary carcinoma thyroid [H&E stain x400]

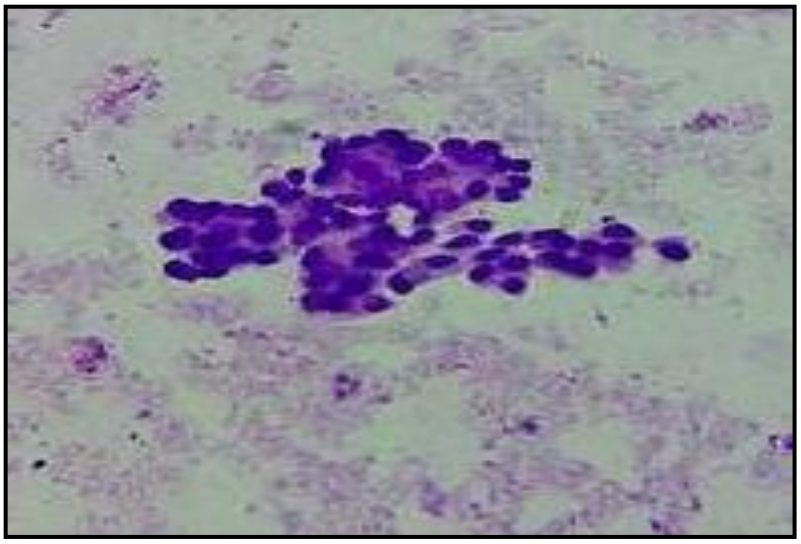


Figure 31: Tissue section showing Papillary Carcinoma thyroid [H&E stain x200

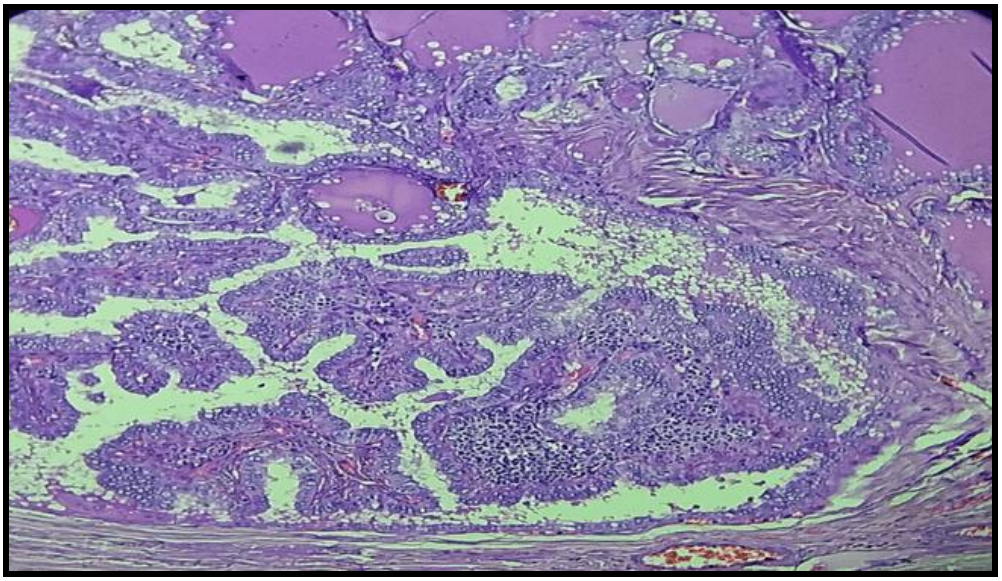
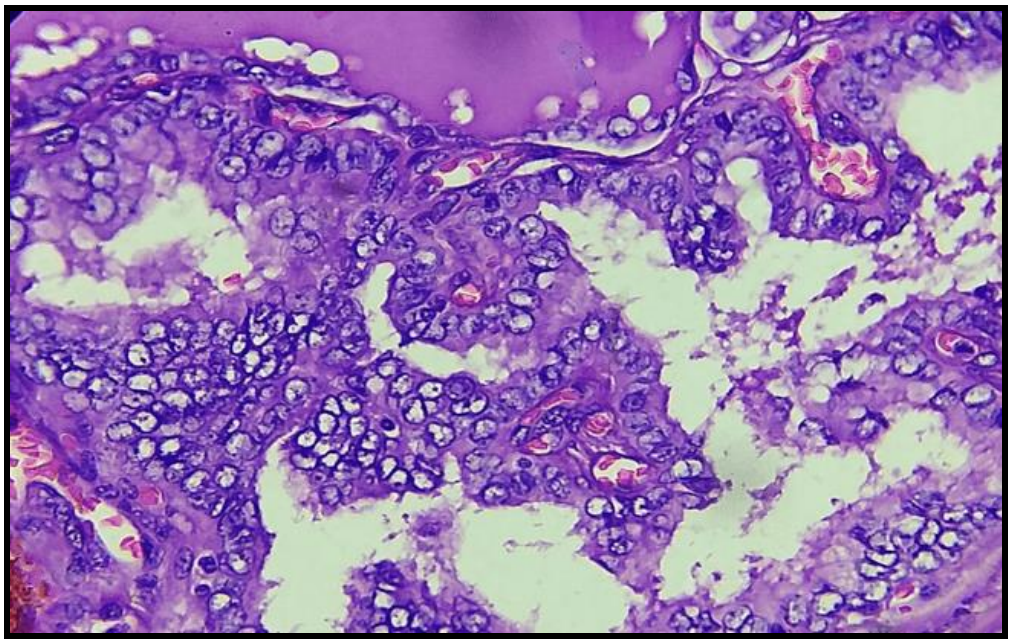


Figure 32: Tissue section from Papillary Carcinoma thyroid showing Orphan Annie eye nuclei with nuclear grooves, intranuclear cytoplasmic inclusions, nuclear crowding and nuclear overlapping. [H&E stain x400]

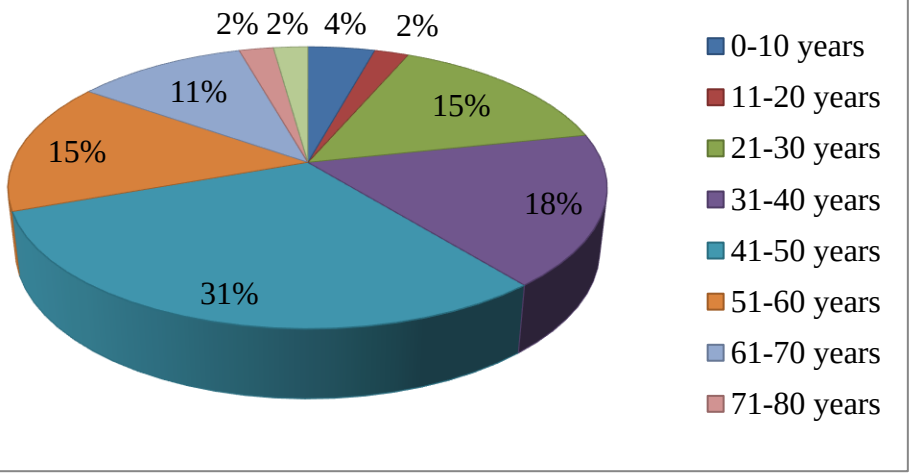


RESULTS

Graph 1 shows the distribution of participants based on their age. 31% of the participants belonged to the 41-50 years age group, followed by 18% in the 31-40

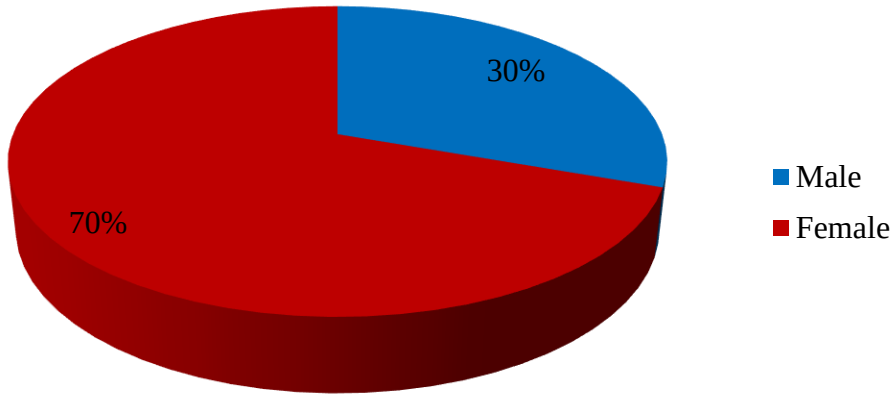
year age group. 11-20, 71-80 and 81-90 years were the least in the present study with 2% participants in each of the categories**.**

Graph 1: Distribution of participants based on age



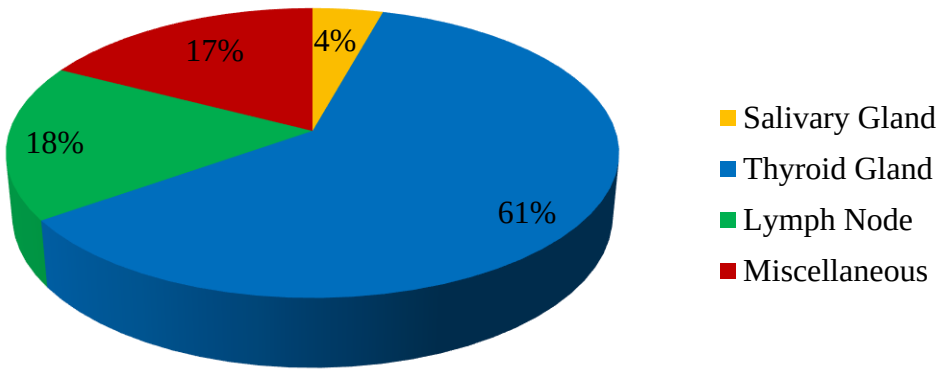
Graph 2 illustrates the distribution of participants based on their gender. Majority (70%) of the participants were females while only 30% were males.

Graph 2: Distribution of participants based on gender



Graph 3 depicts the distribution of participants based on the origin or the site of the lesion. The most common site of the lesion was the thyroid gland (61%), followed by 18% of lymph node lesions, 17% of miscellaneous and 4% salivary gland lesions.

Graph 3: Distribution of participants based on the origin/ site of lesion



Thyroid lesions

Table 1: Correlation between Cytological and Histopathological diagnosis in 28 Thyroid lesions

FNAC Diagnosis	No. of cases%	Histopathological Diagnosis	
		Benign	**Malignant**
l)Non diagnostic/Unsatisfactory	-	-	-
2)Benign	20(71.4%)		
(A)Colloid nodule	2	1-Adenomatous nodule 1-Colloid nodule with lymphocytic thyroiditis	-
(B)Colloid Goitre	13	2- Follicular Adenoma 10-MNG 1-MNG with lymphocytic Thyroiditis	-
(C)Colloid Goitre with cystic degeneration	5	4- MNG with cystic degeneration 1-MNG with Hashimoto's thyroiditis	-
3)AUS	-	-	-
4) Follicular Neoplasm/Suspicious of Follicular Neoplasm	5(17.8%)	2-Follicular Neoplasm 2-Follicular Neoplasm with lymphocytic thyroiditis	1-Follicular Carcinoma
5) Suspicious of malignancy	1(3.5%)	l-Multinodular Goitre	-
6)Malignant	2(7.14%)		
(A) Papillary Carcinoma	2	-	2- Papillary Carcinoma
Total	28	25	3

Table 1 shows Correlation between Cytological and Histopathological diagnosis in 28 Thyroid lesions. On cytology 20 lesions were reported as Benign Non-neoplastic and were consistent on histopathology. Two colloid nodules on FNAC were given as Adenomatous nodule and Colloid nodule with lymphocytic thyroiditis

on histopathology. Out of the 13 Colloid Goiter on cytology, 10 were reported as Multinodular goiter, 2 as Follicular adenoma and 1 as Multinodular Goitre with Hashimoto's thyroiditis. Four out of 5 lesions given as Colloid Goitre with cystic degeneration on cytology were consistent on histopathology and 1 was reported as Multinodular Goitre with Hashimoto's thyroiditis on HPE.

Out of 5 lesions reported as Follicular Neoplasm/Suspicious of Follicular Neoplasm on FNAC, 2 were confirmed on histopathology while 2 were given as Follicular neoplasm with lymphocytic thyroiditis and 1 was reported as Follicular Carcinoma.

One lesion given as Suspicious for malignancy on FNAC was reported as Multinodular Goitre on Histopathology. Two Papillary Carcinomas on FNAC were further confirmed on histopathology.

Thus showing a Concordance of 92.8% and Discordance of 7.1%.

Table 2: Correlation between Cytological and Histopathological diagnosis in 28 Thyroid lesions

Cytology Diagnosis	Histopathological Diagnosis

		Concordance		Discordance	
		No.	**%**	**No.**	**%**
Benign lesions	25	24	96	1	4
Malignant lesions	3	2	66.6	1	33.4
Total	28	26	92.8%	2	7.1%

Lymph node lesions

Table 3: Correlation between Cytological and Histopathological diagnosis in 8 lymph Node lesions

FNAC Diagnosis	No. of cases%	Histopathological Diagnosis				
		Benign			Malignant	
Benign	**4(50%)**	**Reactive Hyperplasia**	**Granuloma-tous lesion**	**Other inflammatory lesion**	**Lymphoma**	**Metastasis**
Reactive Hyperplasia	2(25%)	2				
Granuloma-tous lesion	2(25%)		Likely of Tubercular origin-1		Hodgkin's lymphoma-1	
Other inflammatory pathology						
Malignant	4(50%)	-	-			
lymphoma	3(75%)			Non-specific Sinus Histiocytosis-1	Burkitt's lymphoma-1 lymphoma-1	
Metastasis	l(25%)					Metastasis from Squamous cell carcinoma-1
Total	8	8	-			

Table 3 shows Correlation between Cytological and Histopathological diagnosis in 8 lymph Node lesions. Four out of 8 lesions were given as benign on cytology and consisted of 2 hyperplastic and 2 granulomatous lesions. The 2 lymph nodes reported as Reactive hyperplasia on FNAC were consistent on histopathology. Out of the 2 Granulomatous lesions on cytology, 1 was reported as Granulomatous

lesion possibly of tubercular origin and the other was Hodgkin's lymphoma on HPE. Thus showing a discordance of 25% and concordance of 75%.

Of the 4 lesions reported as malignant on FNAC, 3 were reported as lymphoma and 1 was reported as Metastasis to lymph node. Out of the 3 lesions given as lymphoma on cytology, 1 turned out to be non specific Sinus Histiocytosis and other 2 were consistent with lymphoma on HPE. Thus showing a discordance of 25% and concordance of 75%.

Table 4: Correlation between Cytological and Histopathological diagnosis in 8 lymph Node lesions

Cytology Diagnosis		**Histopathological Diagnosis**			
		Concordance		**Discordance**	
		No.	**%**	**No.**	**%**
Benign lesions	4	3	75	1	25
Malignant lesions	4	3	75	1	25
Total	8	6	75%	2	25%

Salivary gland lesions

Table 5: Correlation between Cytological and Histopathological diagnosis in 2 salivary gland lesions

FNAC Diagnosis	**No. of cases%**	**Histopathological Diagnosis**	
		Benign	**Malignant**
Benign Neoplastic	1 (50%)		
(A) **Pleomorphic Adenoma**	1	Pleomorphic Adenoma – 1	-
Malignant	1 (50%)		
(A) **Mucoepidermoid Carcinoma**	1	-	Mucoepidermoid Carcinoma- 1
Total	2	1	1

Table 5 shows Correlation between Cytological and Histopathological diagnosis in 2 salivary gland lesions. One lesion was given as benign Pleomorphic adenoma and the other was reported as malignant Mucoepidermoid carcinoma on FNAC and were consistent on HPE.Thus giving a Concordance of 100%.

Table 6: Correlation between Cytological and Histopathological diagnosis in 2 salivary gland lesions

Cytology Diagnosis		Histopathological Diagnosis			
		Concordance		Discordance	
		No.	%	No.	%
Benign Salivary gland lesions	1	1	100	-	-
Malignant Salivary gland lesions	1	1	100	-	-
Total	2	2	100		

Miscellaneous lesions

Table 7: Correlation between Cytological and Histopathological diagnosis in 8 Miscellaneous lesions

FNAC Diagnosis	No. of cases%	Histopathological Diagnosis	
Benign		**Benign**	**Malignant**
(A)lipoma	3	lipoma-3	-
(B)Acute Suppurative lesion	4	Acute Suppurative lesion-4	-
(C)Spindle cell lesion	1	leiomyoma Cutis -1	-
Malignant	-	-	-
Total	8	8	-

Table 7 shows Correlation between Cytological and Histopathological diagnosis in 8 Miscellaneous lesions. All 8 lesions were reported as benign on FNAC. Three lesions given as lipoma on cytology were confirmed on histopathology. Four lesions reported as Acute Suppurative lesions were consistent on histopathology. One lesion reported as Spindle cell lesion on FNAC was give as leiomyoma cutis on histopathology.Thus showing a concordance of 100%.

Table 8: Correlation between Cytological and Histopathological diagnosis in 8 Miscellaneous lesions

Cytology Diagnosis		Histopathological Diagnosis			
		Concordance		Discordance	
		No.	%	No.	%
Benign lesions	8	8	100	-	-
Malignant lesions	-	-	-	-	-
Total	8	8	100		

Statistical analysis

A true positive (TP) is a malignant FNA diagnosis of a lesion confirmed to be malignant on HPE.

A false positive (FP) is a malignant FNA diagnosis showed to be benign on HPE.

A true negative (TN) is a benign FNA diagnosis from a lesion confirmed to be benign on HPE.

A false negative (FN) is a benign FNA diagnosis showed to be malignant on HPE.

Sensitivity= TP / (TP+FN).

Specificity= TN / (TN+FP).

Positive predictive value= TP / (TP+FP).

Negative predictive value= TN / (TN+FN).

Accuracy= (TP+ TN) / (TP + FP+TN+FN)

Table 9: Association between FNAC and Histopathological diagnosis.

Test Result (FNAC)	No. of cases	Gold Standard (Histopathology)		Total
		Malignant(TP)	Non malignant(TN)	
Malignant(FP)	9	7	2	9
Non Malignant(FN)	37	1	36	37
Total	46	8	38	46
Fischer Exact Test: p value is <0.005%				

Table 9 shows the Association among FNAC and Histopathological diagnosis to be statistically significant with p value < 0.005%.

Table l0 gives The Correlation of FNAC with Histopathology. Most of the cases were true negatives, followed by true positives, false positives and the least were false negative diagnosis based on the cytology.

Table l0: Correlation of FNAC with Histopathology

		Histopathological Diagnosis				
		TP	**FP**	**TN**	**FN**	**Total**
Cytological Diagnosis	Pleomorphic adenoma	0 (0)	0 (0)	1 (2.2)	0 (0)	1 (2.2)
	Colloid goiter	0 (0)	0 (0)	19 (41.3)	0 (0)	19 (41.3)
	Reactive hyperplasia	1 (2.2)	0 (0)	2 (4.3)	0 (0)	3 (6.5)
	Granulomatous lymphadenitis	0 (0)	0 (0)	1 (2.2)	l (2.2)	2 (4.3)
	SOFN	0 (0)	0 (0)	2 (4.3)	0 (0)	2 (4.3)
	Suspicious of Hodgkins lymphoma	0 (0)	1(2.2)	0 (0)	0 (0)	1 (2.2)
	Spindle cell lesion	0 (0)	0 (0)	1 (2.2)	0 (0)	1 (2.2)
	Poorly differentiated neoplasm, likely lymphoma	2 (4.3)	0 (0)	0 (0)	0 (0)	2 (4.3)
	Acute supurative lesion	0 (0)	0 (0)	3 (6.5)	0 (0)	3 (6.5)
	Lipoma	0 (0)	0 (0)	4 (8.7)	0 (0)	4 (8.7)
	Hurthle cell adenoma	0 (0)	0 (0)	1 (2.2)	0 (0)	1 (2.2)
	Mucoepidermoid carcinoma	1 (2.2)	0 (0)	0 (0)	0 (0)	1 (2.2)
	Multinodular goiter	0 (0)	0 (0)	1 (2.2)	0 (0)	1 (2.2)
	Suspicious of thyroid malignancy	0 (0)	1(2.2)	0 (0)	0 (0)	1 (2.2)

		Histopathological Diagnosis				
		TP	**FP**	**TN**	**FN**	**Total**
	Thyroid malignancy	2 (4.3)	0 (0)	0 (0)	0 (0)	2 (4.3)
	Follicular neoplasm	1 (2.2)	0 (0)	1 (2.2)	0 (0)	2 (4.3)

Table11 shows the diagnostic accuracy of FNAC in Our study. Accordingly, it can be seen that, the sensitivity of the test is 87.5%, specificity is 94.7%, PPV is 77.77%, NPV is 97.29%, false negative and false positive error rates are 12.5% and 5.26%, respectively.

Table 11: Diagnostic accuracy of FNAC

Parameters	**Percentage**
Sensitivity	87.50%
Specificity	94.70%
Positive Predictive value	77.77%
Negative Predictive value	97.29%
False Negative error rate	12.50%
False Positive error rate	5.26%

DISCUSSION

The present study was conducted from 1st January 202l - 31st December 2021 with the aim to correlate FNAC with Histopathology in the diagnosis of palpable head and neck lesions in 46 cases and to assess the efficacy of FNAC as a diagnostic tool.

Out of 46 cases, Our study included 30% males and 70% females, giving a M:F Ratio of 1:2.33. Thus showing a prevalence of these lesions amongst females. Our findings are in concordance with the other similar studies shown in table 12.

Table 12: Comparison of M:F Ratio in other similar studies.

Study	Cases	M:F Ratio
Present study	46	1:2.33
Tilak et al.[260]	55	1:2.4
Solanki et al.[261]	100	1:1.32
Sharma et al.[262]	71	l:1.5
Rajbhandari et al.[263]	64	1:1.6

In a study conducted by Schwarz et al.[264] shows M:F Ratio of 1.43:1. In their study, thyroid lesions were excluded but they were included in Our study. Since thyroid swellings are more commonly found amongst females, the occurrence of head-neck lesions is greater amongst them.

In the present study maximum aspirates were from Thyroid (61%), followed by Lymph node (18%), Miscellaneous (17%) and Salivary glands (4%). Similar observation was done by Muddegowda et al.[265] and Rathod et al.[266] as shown in Table 13. Thus the incidence of head and neck lesions was higher amongst females in our study because thyroid swellings are more common amongst females.

Table 13: Percentage of site involved in different studies

Study	Cases	Thyroid Gland	Lymph node	Miscellaneous	Salivary Gland
Present study	46	61%	18%	17%	4%

Muddegowda et al[265]	100	60%	22%	8%	10%
Rathod et al.[266]	200	52%	28.50%	4%	11%

In Our study, the age of patients with head and neck swellings ranged from 4months to 81yrs. This is in concordance with a similar study done by Bhansali et al.[267] wherein peak incidence was found in the 5th decade of life as shown in Table 14.

Table l4: Common age group in different studies

Study	Number of cases	Observation
In the present study	46	Maximum number of patients belonged to the 5th decade of life followed by 4th and 2nd decade
Bhansali et al.[267]	l982	Peak incidence was found in the 5th decade of life.

In our study among the 46 lesions, 38 (82.6%) were benign and 8 (17.4%) were malignant. Comparison with a similar study done by Yogita Singh et al.[268] and other studies done by Kanu OO et al[269] and Popat V et al[270] also showed more number of benign cases as shown in table 15.

Table 15: Different studies and their Percentage of Benign and Malignant lesions.

Study	Cases	Benign lesion %	Malignant lesions %
Present study	46	82.6%	17.4%
Yogita Singh et al[268]	186	89.2%	10.8%
Kanu O O et al[269]	225	63.3%	36.7%
Popat V et al[270]	103	67%	33%

Thyroid lesions

Thyroid enlargement is a common condition. India is known to have the biggest goiter belt. In the present study a total of 28 (60.8%) thyroid aspirates were obtained. Among this colloid goiter turned out to be most commonly diagnosed lesion among 21 (45.6%) aspirates. This is in concordance with the studies done by Abrari AS et al[27l],Tilak et al[260] , Fernandes H et al[272] and Rahman et al.[273]

In Our study sensitivity and specificity were 100% and 96% respectively. PPV and NPV were 75% and 100% respectively. Results were comparable to studies done by; Handa et al.[274], Arun Sengupta et al.[275] and Sharma R et al.[276] as shown in table l6.

Table l6: Accuracy of FNAC in diagnosing Thyroid lesions

Study	Sensitivity	Specificity	PPV	NPV	ACCURACY

Present study	100%	96%	75%	100%	96.4%
Handa et al.[274]	97%	100%	100%	98.75%	-
Sengupta et al.[275]	90%	100%	100%	98.75%	98.88%
Sharma R et al.[276]	84%	100%	-	-	96%

Lymph node

Lymphadenopathy is seen in illnesses such as tuberculosis, reactive hyperplasia of lymph node, lymphoma, metastasis, etc. It is a clinical expression of local or systemic diseases and serves as a brilliant clue to the underlying disease.

Out of 8 LN lesions, 4 were benign and 4 were malignant on HPE. Reactive hyperplasia was the most frequent diagnosis followed by lymphoma and tuberculosis. A similar study done by Sudershan et al.[277] showed Tubercular lymphadenitis to be the most common lesion, they stated it to be due to Tuberculosis being an endemic condition in India. Fewer cases of tuberculosis and more of lymphomas in our study could be due to lesser routine surgeries planned because ongoing Covid pandemic and more of emergency biopsies done for Cancer. Among 4 lesions that were given as benign on cytology, 2 were hyperplastic and 2 granulomatous lesions. The 2 lymph nodes reported as Reactive hyperplasia on FNAC were consistent on histopathology giving 2 True Negatives. Out of the 2 Granulomatous lesions on cytology, 1 was reported as Granulomatous lesion likely of tubercular origin and the other was Hodgkin's lymphoma on HPE, thus giving 1 True Negative and 1 False Negative. In case of granulomatous disorders, the possible cause is extensive and the use of FNAC along with other ancillary tests (microbiological, immunohistochemical, radiological, biochemical and special staining techniques) is useful for obtaining a specific diagnosis. Granulomas are seen in both Hodgkins and Non-Hodgkins lymphoma, mostly T cell lymphoma and frequently lymph nodes having metastatic carcinoma may also depict features of granuloma. A study done by Khurana et al[278] stressed over the problems experienced in

approaching a definite diagnosis of malignant neoplasm that imitates or occurs in association with granulomas. Granulomatous inflammation occurring in lymph nodes in case of carcinoma is a known phenomenon[279-283].This could be the reason for the False Negative result in the present study. Our study showed a discordance of 25% and concordance of 75% on correlating FNAC with HP.

Of the 4 lesions reported as malignant on FNAC, 3 were reported as lymphoma and 1 was reported as Metastasis to lymph node. Out of the 3 lesions given as lymphoma on cytology, 2 were consistent on HPE while 1 turned out to be Sinus Histiocytosis. Thus giving 2 True Positives and 1 False Positive. In an article published by Manjari Kishore et al[284] they said that the presence of large pleomorphic histiocytes which resemble large multinucleated cells can imitate cells of anaplastic large cell lymphoma .This can explain the False positive result in Our study. One lesion was given as metastatic SCC on HPE similar to study done by Sudershan et al[277] that said that SCC was the most common metastasis to LN in head and neck region. Thus showing a discordance of 25% and concordance of 75%.

We could achieve a sensitivity, specificity, PPV, NPV and diagnostic accuracy of our study is 75%. This is similar to studies done by Rajbhandari et al[263]

Table l7: Comparison of Accuracy of FNAC in diagnosing lymph Node lesions

Study	Sensitivity	Specificity	Accuracy
Our Study	75%	75%	75%
Rajbhandari et al.[263]	82.7%	96%	88.76%

Salivary gland

The main role of FNAC in salivary gland lesions is to either determine if a mass is inflammatory / reactive and benign/ malignant or if possible to provide a definite diagnosis. A good surgical approach can be planned based on the preoperative information. Due to the coinciding morphologic patterns in many benign and malignant neoplasms, FNAC of salivary glands is one of the most diagnostically difficult areas in cytopathology.

In our study out of 2 salivary gland lesions, 1 lesion was given as benign Pleomorphic adenoma and the other was reported as malignant Mucoepidermoid carcinoma on FNAC and were consistent on HPE, thus giving 1 True Negative and 1 true Positive . No False positive or False Negatives were seen. The sensitivity, specificity, PPV and NPV was 100%. The diagnostic accuracy was l00%. Thus giving a Concordance of l00%. In a similar studies done by Sudershan et al [277] Fernandes et al[272] and Rahman et al[273] showed similar results as shown in table 18.

Table 18: Comparison of present study with similar studies.

Study		Observation
Our Study	46	The salivary gland lesion diagnosis on FNAC was consistent on HPE. No FP or FN were seen.The sensitivity, specificity, PPV,NPV and diagnostic accuracy was 100%.
Sudershan et al [277]	15	The most common benign lesion was Pleomorphic adenoma and Mucoepidermoid carcinoma was the most common malignant lesion and overall diagnostic accuracy of FNAC was 100%.
Rahman et al[273]	32	Pleomorphic adenoma was the commonest benign lesion and

		Mucoepidermoid carcinoma was the commonest malignant lesion.

Miscellaneous

In the present study among 8 miscellaneous lesions, all were reported as benign on FNAC. Acute suppurative lesion constituted the maximum number of lesions followed by lipoma and lastly spindle cell lesion. This is similar to study done by Bhagat et al[285]. Three lesions given as lipoma on cytology were confirmed on histopathology. Four lesions reported as Acute Suppurative lesions were consistent on histopathology. One lesion reported as Spindle cell lesion on FNAC was give as leiomyoma cutis on histopathology. Thus showing a concordance of l00%.The sensitivity, specificity and accuracy in detecting these lesions is l00%. This is comparable to other similar studies shown in table 19.

Table 19: Comparison of Diagnostic accuracy of FNAC in diagnosing miscellaneous lesion.

Study	Cases	Sensitivity	Specificity	PPV	NPV	Accuracy
Present study	46	100%	100%	100%	100%	100%
Mudassar Ahmed et al.[286]	100	-	-	-	-	100%
Sudershan et al.[277]	100	-	-	-	-	100%

In the present study on evaluating the overall diagnostic accuracy of FNAC in the diagnosis of palpable head and neck lesions, we found the sensitivity, specificity, PPV, NPV and Accuracy were comparable to other similar studies.

Table 20: Comparison of Diagnostic accuracy of FNAC with other studies.

Study	Cases	Sensitivity	Specificity	PPV	NPV	Accuracy
Present study	46	87.50%	94.70%	77.7%	97.2%	93.4%
Rajbhandari M et al.[263]	64	86%	97%	-	-	87.4%
Tandon et al.[287]	30 studies; 3459 cases	89.6%	96.5%	96.2%	90.3%	93%
Sudershan K. et al.[277]	l00	90.476%	98.73%	95%	97.5%	-
Tilak et al.[260]	55	90.9%	93.2%	-	-	92.%

CONCLUSION

In conclusion the results of our study are consistent with current published data. FNAC is a safe and simple investigative test and Our study showed that FNAC has a high accuracy and specificity. It has great importance in identifying benign lesions like Colloid goiter, lipoma, TB lymph node, etc.

It is a useful preoperative diagnostic tool particularly in developing countries. It aids in reducing the amount of investigative surgeries in patients with head and neck lumps. Chances of complications like infection and hemorrhage are nil. Surgical resection and HPE is needed for intermediate and suspicious lesions.

Despite the high sensitivity of FNAC, there are few drawbacks due to the misleading diagnostic yield. In case of reactive swellings of lymph nodes and other cystic swellings of head and neck, the diagnosis have to done on the basis of both adequate amount of cellularity and clinical history of the patient.

Different newer diagnostic modes should go hand in hand with each other along with FNAC and HP for reliable diagnosis and accurate management.

SUMMARY

This Observational study from 1st January 202l to 31st December 2021 was comprised of 46 FNACs of swellings from head and neck region along with their Histopathological correlation.

Among the total number of 46 patients we got a 1:2.33 M:F Ratio.

In Our study maximum of 31% of the participants belonged to the 41-50 years age group, followed by 18% in 31-40 year age group. 11-20, 71-80 and 81-90 years were the least in the present study with 2% participants in each of the categories.

In the present study out of 46 lesions, the most common site of the lesion was the thyroid gland (61%,), followed by 18% of lymph node lesions, 17% of miscellaneous and 4% salivary gland lesions. Thyroid gland was the most common aspirated organ in Our study.

On cytology 20 lesions were reported as Benign Non- neoplastic and were consistent on histopathology. Two colloid nodules on FNAC were given as Adenomatous nodule and Colloid nodule with lymphocytic thyroiditis on histopathology.

Out of the 13 Colloid Goiter on cytology, 10 were reported as Multinodular goiter, 2 as Follicular adenoma and 1 as Multinodular Goitre with Hashimoto's thyroiditis. Four out of 5 Colloid Goitre with cystic degeneration on cytology were

consistent on histopathology and 1 was reported as Multinodular Goitre with Hashimoto's thyroiditis on HPE.

Out of 5 lesions reported as Follicular Neoplasm/Suspicious of Follicular Neoplasm on FNAC, 2 were confirmed on histopathology while 2 were given as Follicular neoplasm with lymphocytic thyroiditis and 1 was reported as Follicular Carcinoma.

One lesion given as Suspicious for malignancy on FNAC was reported as Multinodular Goitre on Histopathology. Two Papillary Carcinomas on FNAC were further confirmed on histopathology. We observed a Concordance of 92.8% and Discordance of 7.l%.

Out of 46 lesions, 8 were lymph node lesions. Four out of 8 lesions were given as benign on cytology and consisted of 2 hyperplastic and 2 granulomatous lesions. The 2 lymph nodes reported as Reactive hyperplasia on FNAC were consistent on histopathology. Out of the 2 Granulomatous lesions on cytology, 1 was reported as Granulomatous lesion (likely of tubercular origin) and the other was Hodgkin's lymphoma on HPE. Thus showing a discordance of 25% and concordance of 75%.

Of the 4 lesions reported as malignant on FNAC, 3 were reported as lymphoma and 1 was reported as Metastasis to lymph node. Out of the 3 lesions given as lymphoma on cytology, 1 turned out to be Sinus Histiocytosis and other 2 were consistent with lymphoma on HPE. Thus showing a discordance of 25% and concordance of 75%.

Salivary gland lesions comprised 2 cases out of 46 lesions . One lesion was given as benign Pleomorphic adenoma and the other was reported as malignant Mucoepidermoid carcinoma on FNAC and were consistent on HPE. Thus giving a Concordance of l00%.

Among 8 miscellaneous lesions, all were reported as benign on FNAC. Three lesions given as lipoma on cytology were confirmed on histopathology. Four lesions reported as Acute Suppurative lesions were consistent on histopathology. One lesion reported as Spindle cell lesion on FNAC was give as leiomyoma cutis on histopathology. Thus showing a concordance of 100%.

On correlating FNAC with HPE, we observed most of the cases were true negatives, followed by true positives, false positives and the least were false negative.

The association between FNAC and HP diagnosis is observed to be statistically significant with p value < 0.005%.

The diagnostic accuracy of FNAC in Our study showed, sensitivity of 87.5%, specificity 94.7%, positive predictive value 77.77%, negative predictive value 97.29%.

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ANNEXURE I: STAINING PROCEDURES

(I) PAPANICOLAOU STAIN

PREPARATION

1) HARRIS HEMATOXYLIN

a) Hematoxylin – 5grams

b) Aluminium sulphate- 100grams

c) Ethyl alcohol – 50cc

d) Distilled water- 1000cc

e) Mercuric oxide -2.5grams

f) Dissolve Hematoxylin in alcohol and add ammonium sulphate to water in pyrex beaker and heat to boiling point. Add Hematoxylin solution and bring to full boil once more. Swirl quickly until a black purple colour appears, plunge beaker into cold water to cool rapidly. When cold filter into dark bottle. This is used as stock Harris Hematoxylin, to be aged not less than 2 weeks before using. To prepare hematoxylin for staining add 4cc of glacial acetic acid per 100cc of stock Harris Hematoxylin.

2) OG -6 (Osmium Green -6)

First prepare a 10% aqueous stock solution of Orange – G using distilled water. OG-6 stain is prepared as follows:

a) 95% ethyl alcohol -950cc.

b) Orange G (10% stock solution)- 50cc

c) Phosphotungstic Acid – 0.15 grams.

3) EA – 65: First prepare 10% aqueous stock solution of light green SF, yellowish Bismark brown and eosin yellow (water and alcohol soluble). Then prepare three alcoholic stock solutions as follows:

i. Light Green SF- 0.05% solution in 95% alcohol.

ii. Yellowish Bismark Brown- 0.5% solution in 95% alcohol

iii. Eosin Yellow-0.5% solution in 95% alcohol

EA – 65 stains is prepared as follows:

1) Alcoholic stock solution A- 180cc.

2) Alcoholic stock solution B- 40cc.

3) Alcoholic stock solution C- 180cc.

4) Phosphotungstic Acid- 2.4 grams.

Filter and store in brown bottle.

PROCEDURE:

1.Fix the smears in 95% alcohol for 30mins.

2. Bring the smears to 80% alcohol- 1min

3. Bring the smears to 70% alcohol- 1min

4. Bring the smears to 50% alcohol- 1min

5. Wash the smears in running tap water- 2-3mins

6. Stain with Harris Hematoxylin- 45sec

7. Wash in running tap water till purple tinge goes.

8. Bring the smears to 50% alcohol- 1min

9. Bring the smears to 70% alcohol (with 1% Ammonia- 1min)

10. Bring the smears to 80% alcohol- 1min

11. Bring the smears to 95% alcohol- 1min

12. Bring the smears to 95% alcohol- 1min

13. Stain with Orange G- 6- 2 1/2mins

14. Bring the smears to 95% alcohol- 1min

15. Bring the smears to 95% alcohol- 1min

16. Stain with EA- 65- 5mins

17. Bring the smears to 95% alcohol- 1min

18. Bring the smears to 95% alcohol- 1min

19. Bring the smears to absolute alcohol- 1min

20. Bring the smears to absolute alcohol- 1min

21. Air dry/ warm the smears

22. Clear in xylene- 2times and mount with DPX

(II) HEMATOXYLIN AND EOSIN

1. Fix the smears in 90% alcohol
2. Water wash – 1minute
3. Keep in Harris Hematoxylin – 1 minute
4. Blueing in lithium carbonate- 1minute
5. Water wash – 1 minute
6. Eosin – 1 dip
7. Acid alcohol- 1 dip
8. Dry and mount with DPX.

(III) MAY- GRUNWALD'S STAIN: PROCEDURE

PREPARATION OF STAINS:

Preparation of May – Grunwald's stain:

1) 0.3 grams of powdered dye is weighed out and transferred to a conical flask of 200-250 ml capacity.
2) 100 ml of methanol is added and the mixture is warmed to 50^{o} C.
3) The flask is then allowed to cool to room temperature and is shaken several times during the day.
4) After standing for 24hrs the solution is filtered . It is then ready for use.(No ripening is required).

Preparation of Giemsa stain: 1gram of Giemsa powder is dissolved in 54ml Glycerol. Mixed in 84ml of methanol and filtered.

STAINING TECHNIQUES:

Smears fixed in methanol for 10min are stained as follows

1) 1.May- Grunwald's stain is diluted with an equal part of phosphate buffer (or Tap water)
2. Giemsa stain is diluted with 9 parts of phosphate buffer
3. Pour diluted MG Stain on smear- Wait for 5min
4. Remove stain by tilting the slide.
5. Pour diluted Giemsa stain on smear & wait for 10mins.
6. Wash with phosphate buffer- pH- 6.8
7. Air dry the smear and mount with DPX.

(IV) ZEIL- NEELSON'S STAIN FOR AFB

Purpose: To demonstrate acid fast bacilli in smears.

Method: Procedure –

1) Air dried smears are used

2) Put Carbol Fushin for 7min (filter paper, flame it)

3) Wash in water

4) Differentiate in 20% sulphuric acid till pink colour goes

5) Counter stain with methylene blue for 2min

6) Wash in water

7) Clear and mount with DPX

(V) HEMATOXYLIN & EOSIN STAINING FOR TISSUE SECTIONS

PROCEDURE-

1. Deparaffinize with Xylene – 5 minutes.
2. Deparaffinize with Xylene – 5 minutes
3. Absolute alcohol- 5 min
4. Absolute alcohol- 5 min
5. Wash in water (hydration).
6. Stain with Hematoxylin- 3-5 min.
8. Wash in water.
9. Differentiate in 1% acid alcohol- 1 dip.
10. Wash in water.
11. Blueing with saturated solution of lithium carbonate- 2-3 min.
12. Rinse in water.
13. Stain with 1% Eosin- 1min.
14. Wash with tap water.
15. Dehydrate with absolute alcohol.
16. Clear with Xylene and mount with DPX.

ANNEXURE II: PROFORMA

PATIENT HISTORY

Name : Age :

IP no. :

Brief clinical history :

EXAMINATION FINDINGS

- SITE
- SIDE
- SIZE
- SKIN CHANGES
- OTHERS INVESTIGATIONS
- FNAC:

CLINICAL DIAGNOSIS:

HISTOPATHOLOGICAL DIAGNOSIS:

1. Hematoxyline and Eosin staining

ANNEXURE III: INFORMED CONSENT

Purpose of the study: You are being asked to enroll in this study as you are eligible for participation in this study. The purpose of this study is to determine the correlation between Fine Needle Aspiration Cytology and histopathology in diagnosis of palpable lesions of head and neck.

Procedure: During this study, you will be asked questions regarding history and background and you are supposed to answer to the best of your knowledge. The principal investigator of the study is **Dr.** under the guidance of **Dr.**

If you agree to enroll yourself in this study, you will be interviewed regarding your present, past and family history and your clinical manifestations.

Risks and benefits: There are no risks involved in taking part in this study and benefit is we will be able to know a better way to diagnose palpable head and neck lesions which is essential for providing appropriate treatment.

Alternatives: Taking part in this study is voluntary. You may choose not to take part in this study or if you decide to take part now, you can later change your mind and withdraw from the study. The study doctor or sponsor may terminate your participation in this study anytime.

Privacy and confidentiality: All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study will be published but your identity will be confidential in any publication. No information about you or information provided by you during research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Financial incentives for participation: You will not be paid / offered any gift /incentives for participating in this study.

Authorization to publish results: The results of this study would be forwarded to the KAHER, Belagavi as a part of requirement towards the completion of MD degree, review and publishing.

CONSENT STATEMENT

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any legal rights by signing this form. My signature below indicates that I

have read, or it has been read to me, this entire consent form and have had all my questions answered.

In case of the queries during the study or in future you may contact following person.

Principal Investigator :

Guide :

Name of the participant:

(signature/thumbprint)

Name of the witness : (signature)

Name of the investigator: (signature)

Date:

Phone no:

Address:

ANNEXURE IV: KEY TO MASTERCHART

1. SERIAL NUMBER
2. IP. NUMBER
3. NAME
4. AGE
5. SEX
    a. Male - M
    b. Female - F
6. ORGAN
    a. Thyroid gland - TG

b. Salivary Gland - SG

c. Lymph Node - LN

d. Miscellaneous - Misc

7. CYTOLOGY DIAGNOSIS

    a. Pleomorphic adenoma- PA

    b. Colloid Goitre- CG

    c. Multinodular Goitre-MNG

    d. Reactive Hyperplasia- RH

    e. Follicular Adenoma- FA

    f. Follicular Neoplasm- FoN

    g. Papillary Carcinoma Thyroid-PCT

    h. Follicular Carcinoma Thyroid-FCT

    i. Metastasis- Mets

8. HISTOPATHOLOGICAL DIAGNOSIS

9. NATURE ON CYTOLOGY-

    a. Benign- BN

    b. Malignant- MN

10. NATURE ON HISTOPATHOLOGICAL EXAMINATION

11. CONSISTENT/ NON CONSISTENT-C/ NC

12. TRUE POSITIVE- TP

13. FALSE POSITIVE-FP

14. TRUE NEGATIVE- TN

15. FALSE NEGATIVE-FN

ANNEXURE V: MASTER CHART

SR NO.	IP/OP NUMBER	PATIENT NAME	AGE	SEX	ORGAN	CYTOLOGY DIAGNOSIS	HISTOPATHOLOGY DIAGNOSIS	NATURE ON CYTOLOGY	NATURE ON HPE	C /NC	TP	FP	TN	FN
1	1109461	MAHESH NAGAPPA PUJARI	43Y	M	SG	PA	PA	BN	BN	C			TN	
2	1107387	MAHADEVI SADEPPA TAVAGAD	42Y	F	TG	CG	FA	BN	BN	NC			TN	
3	1059239	JYOTI PARASHRAM CHOGULE	37Y	F	LN	RH	RH	BN	BN	C			TN	
4	1117857	YASH PRASHANT MESTA	15Y	M	LN	GRANULOMATOUS LYMPHADENITIS	HODGKINS LYMPHOMA	BN	MN	NC				FN
5	1117113	LUIZA INAS LOBO	50Y	F	TG	CG	MNG	BN	BN	C			TN	

6	1118177	TANUJA RAMESH BETASUR	33Y	F	TG	CG	MNG	BN	BN	C			TN	
7	1060777	LALITA SHANTARAM NAIK	62Y	F	TG	COLLOID NODULE WITH CYSTIC CHANGE	MNG WITH CYSTIC DEGENERATION	BN	BN	C			TN	
8	1070633	SHEETAL NITIN SHINDE	39Y	F	TG	SUSPICIOUS OF FoN	FA	BN	BN	C			TN	
9	1070213	SUMAN SURESH KHATAWAKAR	57Y	F	TG	SUSPICIOUS OF FoN	FA WITH LYMPHOCYTIC THYROIDITIS	BN	BN	C			TN	
10	1066691	VENKAPPA APPANNA YARAGUDRI	81Y	M	LN	SUSPICIOUS OF HODGKINS LYMPHOMA	SINUS HISTIOCYTOSIS	MN	BN	NC		FP		
11	1066874	KUMAR SAMBAPPA SARVI	49Y	M	LN	GRANULOMATOUS LYMPHADENITIS	CASSEATING GRANULOMATOUS LYMPHADENITIS	BN	BN	C			TN	

							Favouring TB ORIGIN							
12	1112556	YALLAPPA BASALINGAPPA WALIKAR	54Y	M	TG	CG	COLLOID NODULE WITH LYMPHOCITIC THYROIDITIS	BN	BN	C			TN	
13	1110340	LAKAMMA HANAMANTAPPA NANDIHAL	66Y	F	TG	CG	MNG	BN	BN	C			TN	
14	1112039	TEJASHREE ANNAPPA MALI	23Y	F	Misc	SPINDLE CELL LESION	SPINDLE CELL LESION-LEIOMYOMA	BN	BN	C			TN	
15	1119286	SANGEETA SUBASH TARIHAL	37Y	F	TG	CG WITH CYSTIC DEGENERATION	MNG WITH CYSTIC DEGENERATION	BN	BN	C			TN	
16	1124594	SHEELA RAMACHANDRA ASODE	42Y	F	LN	POORLY DIFFERENTIATED NEOPLASM MOST LIKELY LYMPHOMA	POORLY DIFFERENTIATED NEOPLASM- BURKITTS/ PLASMA CELL NEOPLASM	MN	MN	C	TP			

17	1124737	KUMAR SHANKAREPPA DHAVALESHWAR	28Y	M	Misc	ACUTE SUPPURATIVE LESION	ACUTE SUPPURATIVE LESION	BN	BN	C			TN	
18	1105924	SUMAN SOMANATH BENAKE	49Y	F	TG	CG	MNG	BN	BN	C			TN	
19	1110720	MANISHA GANAPATI KODU PATIL	38Y	F	Misc	LIPOMA	LIPOMA	BN	BN	C			TN	
20	1109622	ROOPA MAHESH BASETTI	28Y	F	TG	HURTHLE CELL ADENOMA	MNG	BN	BN	NC			TN	
21	1035435	SHANTAVVA MAHANTAPPA HALIYAL	68Y	F	SG	MUCOEPIDERMOID CARCINOMA-MILAN CLASSIFICATION IV A	MUCOEPIDERMOID CARCINOMA	MN	MN	C	TP			

22	1035325	ROOPA PARSHURAM KITTUR	28Y	F	TG	MNG	FA	BN	BN	NC			TN	
23	1034223	ANITA PATIL	38Y	F	TG	CG WITH CYSTIC DEGENERATION	MNG WITH CYSTIC DEGENERATION	BN	BN	C			TN	
24	1080695	DHANAKKA SHIVALINGAPPA DODAMANI	44Y	F	Misc	LIPOMA	LIPOMA	BN	BN	C			TN	
25	1083009	MONAPPA LAXMAN BELGUNDKAR	41Y	M	TG	CG WITH CYSTIC DEGENERATION	HASHIMOTOS THYROIDITIS WITH MNG	BN	BN	C			TN	
26	1043705	PRAVEEN MAHANTESH HUBBALLI	9Y	M	LN	RH	RH	BN	BN	C			TN	
27	1042381	MAHANANDA RACHAPPA	30Y	F	TG	SUSPICIOUS OF THYROID	MNG	MN	BN	NC		FP		

		MANGASULI				MALIGNANCY								
28	1040800	KAMALAVA YAMANAPPA VALARAMATI	43Y	F	TG	CG	MNG	BN	BN	C			TN	
29	1039652	DRAKSHAYANI MALLAPPA KALASHETTI	50Y	F	TG	CG,	MNG	BN	BN	C			TN	
30	1038785	SHANKRAMMA SOMASHEKHARAYYA HIREMATA	45Y	F	Misc	LIPOMA	FIBROLIPOMA	BN	BN	C			TN	
31	1043853	B/O SHREYA PRAMOD PATIL	4MONTH	M	Misc	ACUTE SUPPURATIVE LESION	ACUTE SUPPURATIVE LESION	BN	BN	C			TN	
32	1047497	MEGHA SANJAY MELAVANKI	26Y	F	Misc	ACUTE SUPPURATIVE LESION	ACUTE SUPPURATIVE LESION	BN	BN	C			TN	

33	1034227	GHULAPPA PANDAPPA CHANDARAGI	45Y	M	Misc	LIPOMA	LIPOMA	BN	BN	C			TN	
34	1049949	SANGEETA CHANDRASHE KAR T.	42Y	F	TG	THYROID MALIGNANCY-PCT, BETHESDA CATEGORY IV	PCT	MN	MN	C	TP			
35	1049316	YALLAPPA LAKMAN HIDAKAL	73Y	M	LN	FEATURES ARE THAT OF LYMPHOMA	FEATURES ARE THAT OF LYMPHOMA	MN	MN	C	TP			
36	1033655	ROOPASHRI SURESH BHENDE	34Y	F	TG	CG	COLLOID NODULE	BN	BN	C			TN	
37	4933430	POOJA MARUTI MALADKAR	24Y	F	TG	CG	MNG	BN	BN	C			TN	
38	5958962	PRABHAKAR BHIMAPPA	70Y	M	TG	THYROID MALIGNANCY-	PAPILLARY CA THYROID	MN	MN	C	TP			

		MUNDINMANI				D/D FCT/ PCT								
39	5446432	MASABI FAKRUDDIN GADAD	57Y	F	TG	CG	MNG	BN	BN	C			TN	
40	957306	AMBUJA SHIVASHANKAR GANIGER	57Y	F	TG	CG	HASHIMOTOS THYROIDITIS WITH MNG	BN	BN	C			TN	
41	5128333	GANGAVVA SHANKAR SHIRUR	45Y	F	TG	CG	MNG	BN	BN	C			TN	
42	4552148	JAHEERABI ABDUL SHAIKH	58Y	F	TG	FoN	FA WITH LYMPHOCYTIC THYROIDITIS	BN	BN	C			TN	
43	941309	BHIMASEN MAHADEVAPPA KOKARE	60Y	M	TG	CG WITH CYSTIC DEGENERATION	MNG WITH CYSTIC DEGENERATION	BN	BN	C			TN	
44	5089453	KOSUMARY SIMON D	68Y	F	TG	CG	MNG	BN	BN	C			TN	

		SOUZA												
45	5770106	GANGAVVA SOMU PIJARI	37Y	F	TG	FoN	FCT	MN	MN	C	TP			
46	6088715	SHANKARARAO ANANDRAO NALAVADE	55Y	M	LN	METASTASIS TO LN	METASTATIC MODERATELY DIFFERENTIATED SQUAMOUS CELL CARCINOMA	MN	MN	C	TP			