UTILITY OF CLINICOCYTOLOGICAL STUDY IN DETECTING PRIMARY TUMOR IN PATIENTS PRESENTING WITH METASTATIC TUMOR

By

DR. MAMATHA.K

Dissertation submitted to the

BLDE University, Bijapur, Karnataka

In partial fulfillment of the requirements for the award of the degree of

DOCTOR OF MEDICINE

IN

PATHOLOGY

Under the Guidance of

DR. SUREKHA. U. ARAKERI MD

Professor, Department of Pathology

BLDE UNIVERSITY, SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, BIJAPUR, KARNATAKA.

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Date ;

Place : Bijapur

Dr. Surekha. U. Arakari M.D

Professor
Department of Pathology,
BLDEU Shri B.M.Patil Medical College, Hospital & RC, Bijapur, Karnataka

B.L.D.E UNIVERSITY'S

SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, BIJAPUR

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Date:

Place: Bijapur

Dr. B. R. Yelikar

Professor and H.O.D,
Department of Pathology,
BLDEU Shri B.M.Patil
Medical College, Hospital &
RC,Bijapur.

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Date:
Place: Bijapur

Dr. M. S. Biradar
Principal,
Department of Pathology,
BLDEU Shri B.M.Patil
Medical College, Hospital &
RC, Bijapur

,

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ACKNOWLEDGMENT

A line from Sanskrit Shlokha Says “Guru r brahma guru r vishnu gurudevo maheshwaraha, guru ssakshaat parabrahma tasmay shri gurave namaha” - meaning a teacher is next to god and without him knowledge is always incomplete

I wish to take this opportunity to express my indebtedness to my guide **Dr.Surekha. U.Arakeri**, Professor Department of Pathology, for her resolute guidance, precise approach, constructive criticism and meticulous supervision throughout the course of my work and preparation of manuscripts that have been a valuable part of my learning experience.

I express my sincere gratitude to **Dr. B.R.Yelikar,** Professor and Head, Department of Pathology for his valuable suggestions, indispensable guidance and critical appreciation in pursuit of this study.

I am forever grateful to Dr R.M.Potekar Prof, Dr.S.B.Hippargi Prof, Dr.Mahesh H. Karigoudar Prof, Dr.Girija Patil Assoc Prof ,Dr.Padmaja kulkarni Assoc Prof, Dr Prakash Patil Assoc Prof , Dr.Savitha Shettar Assos Prof, Dr AnirudhV.K Asst prof, , Dr.Vijayalaxmi S Patil Asst. Prof, Dr. Anita P Javalgi Asst prof, for their valuable help and guidance during my study.

My sincere thanks to all my batchmates and seniors who have helped and encouraged me during my work.

I am very grateful to all the non teaching staff of Department of Pathology, who have helped me during this work.

I also wish to thank Mrs.Vijaya Sorgavi for her valuable help in statistical analysis.

Last but not the least**,** My sincere gratitude to all my study subjects whose cooperation has contributed to this study.

Date: **Dr. Mamatha.K**

Place: Bijapur

ABSTRACT

BACKGROUND: About 5-10% of cancer patients clinically present as metastatic lesions in the absence of a discernable primary site. Diagnosis of primary site in patients presenting with metastatic tumors is a challenging task for the clinicians and cytopathologists. Localising the primary malignant tumor in metastatic lesions helps in more specific and effective treatment. However identification of primary site in patients presenting with metastatic tumor requires extensive and exhaustive investigations. If careful evaluation of clinical presentation of the disease is done and correlated with the cytological evaluation of the metastatic lesion, it provides better clue of the primary and helps in specific management of the lesion .

OBJECTIVES: To evaluate the utility of clinicocytological study in diagnosis of primary tumor in patients presenting with metastatic tumors.

METHODS : Patients presented with palpable or radiologically visible metastatic lesions for cytological evaluation and cytological specimen of metastatic effusions referred to the Department of pathology in BLDEU'S Shri B.M. Patil Medical College, Hospital and Research centre, Bijapur 1st September 2011 to 1st September 2013 were included

RESULTS: Out of 100 cases, in 64 cases metastatic site was lymph node and metastatic effusion was the presentation in 25 cases. Metastatic deposit in omentum, skin and soft tissue and liver was noted in 6, 4 and 1 case each respectively. Most of the cases were in the age group of 50-70 years. Mild male preponderance with male to female ratio of 1.1:1 was noted. Out of 64 lymphnode metastasis, Nasopharynx (34%) was the commonest primary site followed by breast(33%), tongue(11%), skin oesophagus(5%),oropharynx(3%), larynx(3%), lung(1.5%),parotid(1.5%),skin(1.5%)

and others(6.5%). Out of 16 ascitic fluid metastasis ovary was the primary site in 93% of cases. In metastatic pleural effusion, breast and lung was most common primary followed by nasopharynx and thyroid. Histopathological follow-up was available in 40 cases. On correlation of cytologically confirmed primaries, 32(86%) cases were concordant and 5(13%) cases were discordant. Whereas in 3 cases(1%) primary was unknown**.**

CONCLUSION: FNAC is a rapid, safe and cost effective technique in determining the primary site.Clinicocytological correlation has got high sensitivity,specificity and positive predictive value in determining the primary site. Thus thorough clinicocytological evaluation is effective diagnostic method to detect the primary tumor with cost effective diagnostic procedures.

KEY WORDS: Primary site, Metastatic lesion, Clinicocytological correlation

LIST OF ABBREVIATIONS USED

AFP	Alpha fetoprotein
β-HCG	Human chorionic gonadotrophin
CK	Cytokeratin
CT	Computed tomography
ER	Estrogen
HEGF	Human epidermal growth factor
MRI	Magnetic resonance imaging
PET SCAN	Positron emission tomography
PR	Progesterone
PSA	Prostatic specific antigen

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INTRODUCTION

About 5-10% patients clinically present as metastatic lesions in the absence of a discernable primary site.[1] Cancers of unknown primary origin represent a group of heterogeneous tumors that share a unique clinical features of early apparent metastatic diseases with no identifiable site of origin at the time of presentation.[1,2]

Diagnosis of primary site in patients presenting with metastatic tumors is a challenging task for the clinicians and cytopathologists. Localising the primary malignant tumor in metastatic lesions helps in more specific and effective treatment.[3]

However identification of primary site in patients presenting with metastatic tumor requires extensive and exhaustive investigations. Such a strategy costs the patient a longer hospital stay with the experience of painful and distressing investigations and it also leads to an unacceptable cost effectiveness ratio to the health care system.[3]

Commonest sites of metastasis are lymph node, liver, lung, ascitic fluid, pleural fluid and bone. Sometime the primary tumor rarely manifests itself, clinically due to either regression/slow growth rate. This results in biologically advanced tumor that acquires a metastatic clinical presentation.[3]

Most common symptoms of metastatic lesions are general deterioration and weight loss. Clinical presentation of metastatic lesions depend on the predominant site of metastatic involvement. The clinical presentation such as digestive symptoms, respiratory symptoms, liver enlargement, ascites, skin nodule, bone pains gives clue for the primary site of involvement.[3]

If careful evaluation of clinical presentation of the disease is done and correlated with the cytological evaluation of the metastatic lesion, it provides better clue of the primary and helps in specific management of the lesion.[4] Thus early detection and correct cytodiagnosis of metastatic tumors save the patient from invasive and costly diagnostic procedures and also, helps the surgeons to formulate the therapeutic strategy in treatable primary tumors.[1,3]

Hence the present study is undertaken to emphasize the role of cytological study and correlation of clinical presentation in evaluating the primary site of tumor in patients presenting with metastatic tumors .

OBJECTIVE OF THE STUDY

To evaluate the utility of clinicocytological study in diagnosis of primary tumor in patients presenting with metastatic tumors.

REVIEW OF LITERATURE

FNAC TECHNIQUE

Fine needle aspiration cytology (FNAC), a technique for obtaining cellular material for cytological examination has become a very important easy and fast diagnostic tool in pathology.[5]

FNAC is done by using a 21-gauge or smaller needle with 5, 10, or 20ml syringe either freehand or using special syringe holders. It is minimally invasive, rapid diagnostic procedure to obtain tissue samples, however histological architecture is not preserved as in histopathology. In 1900 papanicolaou smear, an exfoliative cytology was universally accepted and widely used method of cytological diagnosis. It was used primarily to detect precancerous and cancerous conditions which were not apparent clinically. However aspiration cytology was mainly used to determine the nature of clinically detectable tumors.[5]

Kun in 1847 described a new instrument for obtaining material for microscopic diagnosis of tumors. Obaseki DE et al[5] in their study quoted that Hayes Martin, a head and neck surgeon and James Ewing, the chief pathologist at the New York Memorial Hospital carried detailed and systematic study on FNAC in the late 1920. Their experience on FNAC study of 2500 tumors per year was documented by Fred Stewart, a histopathologist who enunciated the fundamental principles regarding philosophy of aspiration and emphasized the need for close clinical and pathological correlation. However, full confidence in FNAC procedure was never achieved and during this period, both in Great Britain and the USA there was a fierce controversy over the reliability and risks of open biopsy in surgical practice. Clinicians feared that

it would increase the risk of tumor spread. However, as their fears were laid to rest, the popularity of needle aspiration waned to such an extent that by the 1960s the technique was all but obsolete in the USA. Interest in the procedure was resurrected by Europeans in the mid 1950s. In contrast to Martin and Stewart who used thicker caliber 18 gauge needles, the European workers popularized the technique by employing thin needles 22 gauge and higher with an external diameter of 0.6mm or less. This technique today is known as FNAC.

Obaseki DE *et al*[5] in their study quoted that, workers such as Sixten, Franzen, Sordenstrom, and Torsten Lowhagen in collaboration with Joseph Zajicek from Stockholm Karolinska Radiumhemmet Hospital in Sweden applied the requisite scientific rigour to define precise diagnostic criteria in a variety of conditions. They thus provided a model for FNAC services for the rest of the world which was then a part of all sophisticated pathology departments. It was generally accepted as the initial diagnostic technique due to the advantages such as cost effectiveness, low risk as compared to surgical biopsy, readily repeatable and useful for multifocal lesions, with minimal physical and psychological discomfort for the patient, rapid reporting and bedside diagnosis of neoplastic, hyperplastic, and inflammatory masses.[5]

CARCINOMA OF UNKNOWN PRIMARY(CUP)

In most cancer patients, the organ in which the cancer initially developed is readily identifiable. However in a minority of patients with metastatic cancer however, the primary organ cannot be identified, despite an extensive work-up. These cases are termed as metastatic cancer of an unknown primary site.[6]

It constitutes about 5-10% of all cancers. It is regarded as the fourth most common cause of cancer deaths in both sexes. Median age of presentation in CUP is

60 years, with slightly higher prevalence in males. Natural history of patients with CUP is different than that of a patients with cancer of known primary site. These cancers of unknown primary sites are characterized by early dissemination and are unpredictable with regards to pattern of spread and overall aggressive nature.[6,7]

CUP is biologically differentiated by its progression of malignancy. CUP is thought to undergo type-2 progression means progression without a premalignant stage as opposed to type1 progression which progress from a premalignant stage.

Life expectancy in patients with CUP remains poor with median survival of 6-9 months. The factors associated with favourable prognosis are young age, tumors located in retroperitoneum and absence of liver metastasis.[8]

Categorization of CUP subtypes- Carcinomas in patients presenting with metastatic tumors are divided into 4 major subtypes based on light microscopic morphology such as well to moderately differentiated adenocarcinomas, undifferentiated carcinoma/ poorly differentiated adenocarcinoma, squamous cell carcinoma and undifferentiated neoplasms.[6,9]

Approximately 50% of all CUP patients fall in to well to moderately differentiated adenocarcinomas. Undifferentiated / poorly differentiated adenocarcinoma constitute 30%, squamous cell carcinomas and undifferentiated neoplasms constitute 15% and 5% respectively. Undifferentiated neoplasms are commonly divided into neuroendocrine tumors,germ cell tumors, embryonal carcinomas, lymphomas, sarcomas and melanomas.[6,10]

Precise natural history of this heterogeneous cluster of neoplasms cannot be established easily. Clinical course of CUP especially for patients with untreatable subsets differs from that of known primary tumors.[1] Early dissemination, clinical absence of primary tumor, unpredictable metastatic pattern, and aggressiveness constitute the fundamental characteristics of these tumors . However, CUP has several fundamental characteristics such as short history with symptoms and signs associated with metastatic sites, early dissemination in the absence of primary tumor, aggressive clinical course and occasionally an unpredictable metastatic pattern. Metastasis to multiple organs may be noted in many cases. Classification of patients with CUP into several clinicopathological subsets according to age, sex, clinical presentation, organ or site involvement and microscopic features helps oncologists to plan the investigations and decide appropriate therapeutic management.[6,11]

CYTOLOGICAL FEATURES IN PATIENTS PRESENTING WITH METASTATIC TUMORS

Cytology smears of metastatic squamous cell carcinoma show isolated cells/clusters of keratinizing malignant squamous cells with or without evidence of keratin formation.Cells have distinct cell borders, hyperchromatic nucleus with coarse chromatin. Eosinophilic keratinized cells are better appreciated by pap staining.[12]

Metastatic adenocarcinoma on cytology shows cells arranged in cohesive groups of various sizes. The cell groups are either arranged in ball like clusters, papillary fragments or acini with central lumina. Cells show eccentric nucleus with prominent nucleoli and evidence of mucin production in the form of cytoplasmic vacuolation.[6]

Metastatic poorly differenciated carcinomas on cytology show large pleomorphic cells in sheets and clusters with high nucleocytoplasmic ratio, prominent nucleoli and scant to moderate cytoplasm.[12]

Cytology smears from metastatic melanoma show large pleomorphic cells with prominent nucleoli and intracellular or extracellular melanin. The presence of fine, granular melanin pigment in the cytoplasm is helpful in identifying melanoma.[1,6]

Metastatic small cell carcinomas can be easily confused with small cell lymphoma on FNAC. Small cell carcinoma shows neoplastic cells in aggregates and flat sheets with high nucleocytoplasmic ratio.[1,6]

SEARCHING FOR ANATOMICAL LOCATION OF PRIMARY TUMORS

Identification of the occult primary in patients presenting with metastatic tumor is challenging task for clinicians. The argument in favor of pursuing the anatomical location of the primary is that localizing primary site results in more specific and effective treatment. In minority of CUP patients, primary site of origin can indeed be identified after extensive diagnostic evaluation, which require exhaustive investigations. Such strategy costs the patient longer hospital stay, with the experience of painful and distressing investigations.[1,13] This also leads to unacceptable cost-effectiveness ratio on health care system, although the practice of performing all available sophisticated tests on these patients in everyday clinical practice is not uncommon. Regarding the identification of treatable subgroups, careful evaluation of clinical presentation of the disease with an optimal re-evaluation of cytology and biopsy specimen provides better clue for primary site.[6] Thus the well-recognized clinicopathological subsets of treatable and potentially curable tumors can easily be

identified, and any histological misclassifications can be clarified. Such a strategy can lead to optional management of treatable tumors by collaboration and interaction between clinician and pathologist. Immunohistochemistry and in exceptional cases, molecular and cytogenetic studies also help in the diagnosis of primary site.[1]

Proposed Diagnostic Strategy

A reasonable diagnostic approach to CUP patients is to diagnose primary site with limited investigations without compromising clinically useful diagnostic efficacy. Based on the initial clinical presentation and cyto-histopathology report, the diagnostic strategy for a probable CUP can be planned.

The physical examination must be thorough and should include head and neck examination, thyroid and rectal examination. In females, thorough examination of breast and pelvis and in males, thorough examination of prostate and testicles will help to locate primary site.[1]

Chest radiography has always been a prerequisite for the diagnosis of CUP, however its usefulness in the differential diagnosis between primary and secondary diseases in lungs has been disputed .

Computed tomography is considered today one of the most valuable imaging tests in CUP cases. It has a clearly proven impact on diagnosis of CUP, providing an additional diagnostic accuracy of 20% in cases previously characterized as CUP . CT scan also helps for the evaluation of tumor mass and provides guidance to biopsy procedure.[1]

Briasoulis E and Pavlidis N[1] stated that most barium studies failed to contribute to the detection of the primary site and to the overall management of

patients. They also concluded that it is rarely used as a diagnostic method in determining primary site. Mammography has been proposed as a basic test in women with metastatic adenocarcinomas in axillary lymph nodes, but its sensitivity in this context was found to be low.[1]

Endoscopy should always be symptoms or signs oriented investigational procedures in CUP cases. In cases of cervical node involvement, ENT panendoscopy with fine-needle aspiration of lymph node has been proposed as the initial diagnostic approach. Fiber optic bronchoscopy is advisable in cases of clinically and radiologically suspected cases of tumors of lung as the occult primary and in cases of failure of radiography to differentiate primary and secondary tumor in the CUP setting . Proctoscopy and colposcopy seem to be of practical interest in cases of inguinal lymph node involvement.[1]

Investigations for the diagnosis of CUP

The standard diagnostic procedure proposed for the majority of these patients is to include the histopathologic review of biopsy material with the use of immunohistochemistry, complete blood cell count, routine biochemistry, fecal occult blood testing, urine testing, chest radiography, and computed tomography of abdomen and pelvis. It must be emphasized that immunohistochemistry staining for common leukocyte antigen, carcinoembryonic antigen, cytokeratin, and vimentin is considered today a routine pathology procedure for these tumors.[14] For the subgroups of the cervical node metastasis of squamous cell carcinomas, more specific initial investigational procedures are advisable which include ear, nose and throat panendoscopy and head and neck CT scanning. For metastatic axillary adenocarcinomas in females, mammography is recommended. Other recommended

optional investigations of high specificity are α-fetoprotein (AFP), β-human chorionic gonadotropin (β- HCG) and prostate-specific antigen (PSA) and other serum tumor markers in men to exclude extragonadal germ cell tumor or prostate cancer.[1,15]

Poorly differentiated carcinoma with midline distribution predominantly affects young male with average age being less than 50 years and it is rarely reported in females. It mainly involves mediastinal or retroperitoneal lymph nodes, and less frequently supraclavicular nodes, cervical nodes, or lung parenchyma. This tumor commonly shows features of extragonadal germ-cell tumors.[1]

Histologically, these metastatic tumors are characterised as undifferentiated or poorly differentiated carcinoma. These tumors show positivity for β human chorionic gonadotropin, α-fetoprotein, placental alkaline phosphatase, or octomer-binding transcription factor 4 with immunoperoxidase stains.Serum concentrations of β human chorionic gonadotropin or α-fetoprotein can be raised in as many as 20% of cases.[16]

Adenocarcinoma identified in isolated unilateral axillary lymph nodes without an obvious primary tumor is unique CUP subset, in which the most frequent primary is breast cancer. This subset has similar presentation and outcome as that of stage II breast cancer. Its true incidence seems to range from 0·12% to 0·67% of all diagnosed breast cancers. Women are exclusively affected with a mean age of 52 years and 66% of patients are postmenopausal women. Light microscopic examination of haematoxylin and eosin stained slides supplemented by immunohistochemistry marker study such as ER receptor, PR receptor, CK 7, CK20, mammaglobin protein expression, or HEGF 2 over expression can contribute to precise diagnosis.[1]

In a study done on systematic review of axillary nodal metastasis from carcinoma of unknown primary by Pentheroudakis G *et al*.[17] showed that, out of 689 patients, 358 (52%) patients had lymph node metastasis showing N2 or N3 status. Histologically, 83% of patients had ductal carcinoma, with ER receptor positivity in 43%. Out of 13 cases investigated for HEGF 2,only in four cases overexpression of HER 2 neu protein was noted. Out of 446 patients undergoing mastectomy, an occult breast primary tumor was identified histologically in 321 (72%) patients.

In a study of cervical lymph node metastases of squamous cell carcinoma from an unknown primary, done by Jereczek Fossa BA *et al.*[18] reported that metastatic squamous cell carcinoma in cervical lymph nodes constitutes to 5% of all head and neck cancers, with an annual incidence of 0·34 cases per 100 000 people. Squamous-cell carcinoma is the most common type of cervical node CUP, representing 75% of cases, and the most common clinical presentation is painless and unilateral cervical mass. Level II lymph nodes that is jugulodigastric or upper cervical lymph nodes are most frequently implicated amounting to 30–50% of patients.[19]

Panendoscopy with anaesthesia and flexible nasopharyngoscope and biopsy is recommended in evaluation of metastatic squmous cell carcinoma involving cervical lymph nodes. CT scan can detect the primary tumour of squamous-cell carcinoma in 22% of patients, MRI in 36%, and PET-CT in 28 to 57%. Patients with squamous-cell carcinoma involving inguinal nodes require careful clinical and endoscopic examination and biopsy of suspicious lesions in anal region, vulva, vagina, uterine cervix, penis or scrotum.[1]

Serous papillary peritoneal carcinomatosis has also been termed as primary peritoneal carcinoma. In a systematic review series of 579 patients of serous papillary peritoneal carcinoma of unknown primary tumor , noted that most prominent clinical presentation was pain abdomen, abdominal mass, ascites, and intestinal obstruction.[9,20]Ovarian tumors spread mainly to the peritoneal, mesenteric, and omental surfaces of the abdomen and pelvis. Psammoma bodies were noted on H and E section of serous papillary peritoneal carcinoma. Immunohistochemical expression of MUC16, oestrogen receptors, mesothelin, WT1 and KRT7 was noted in these cases with heightened serum MUC16 concentrations recorded in 70–90% of patients. Notably, an ovarian or peritoneal primary tumor might be occult in the presence of undifferentiated, non-papillary peritoneal deposits.[9]

Diffuse carcinomatosis of the peritoneal surfaces of non-papillary serous adenocarcinoma originates predominantly from tumors of the gastrointestinal tract, as well as from other hidden primary sites. Clinicians should suspect a gastrointestinal origin in patients with mucin-producing adenocarcinoma, often with signet ring cells.[9]

Patients with low-grade neuroendocrine tumors have typical morphology of well differentiated carcinoids of unknown primaries. Small-cell anaplastic carcinoma is clinically similar to small-cell lung cancer, whereas poorly differentiated large-cell neuroendocrine carcinomas of unknown primary can present at many sites and have an aggressive course. Morphology of neuroendocrine tumors established with haematoxylin and eosin stains can help in diagnosis. Immunohistochemistry markers such as chromogranin and synaptophysin are useful markers especially in poorly differenciated neuroendocrine tumor .[21]

According to the study of diagnostic and therapeutic management of cancer of unknown primary, done by Pavlidis N *et al*.,[22,24] incidence of metastatic visceral or skeletal CUP is 80%. Most commonly involved metastatic site was liver amounting to 40–50% followed by lymph nodes, lungs, bones and brain. Histological investigation of this subset mostly identifies adenocarcinoma of moderate-to-poor differentiation (64%), followed by undifferentiated (20%), neuroendocrine (9%), and squamous carcinomas (7%).

In these patients with metastatic visceral or skeletal CUP, age, number of metastatic sites, lactate dehydrogenase concentration, performance status, and neuroendocrine differentiation are independent prognostic factors. Men presenting with blastic bone metastases and high serum concentrations of PSA have a better prognosis than do others in this subset and should be managed in the same way as patients with metastatic prostate cancer. In these favourable cases, immunohistochemical staining of tissue with PSA is mandatory. Patients with visceral metastases and a colon cancer IHC profile such as CK20 and homeobox protein CDX2 positivity and CK7 negativity has favourable prognosis.[22]

Histopathology is the cornerstone in the diagnostic procedure of CUP. A good biopsy specimen is of great importance, especially in cases of poorly differentiated tumors, and for the application of special pathology techniques that can improve the diagnosis of chemosensitive tumors which are subject to misdiagnosis. Identifying the primary site is not an easy task on conventional histopathology, especially in metastatic adenocarcinoma cases. Interestingly, a correct diagnosis of only 48% was achieved by pathologists when they were shown 100 metastatic adenocarcinomas of

known primary origin which were presented as unknowns with the provision of minimal essential clinical data. A higher accuracy was achieved for prostate, ovarian, and breast carcinomas, and a lower accuracy for the upper gastrointestinal tract, biliary tract, and pancreatic adenocarcinoma.[1,16]

Serum Tumor Markers

In males high-specificity tumor markers such as β-HCG, AFP, and PSA should always be tested to exclude treatable extragonadal germ cell tumors and prostate cancer which are amenable to endocrine treatment. In children, testing for urinary catecholamines can produce valuable diagnostic clues, as high urine levels of catecholamines are diagnostic of neuroblastoma.[1]

Immunohistochemistry is the most useful diagnostic tool and the central axis of the initial basic investigation, especially in cases of poorly differentiated carcinomas . Immunoperoxidase staining has now become widely available and can be reliably applied on routinely fixed paraffin-embedded biopsy materials. It uses specific monoclonal or polyclonal antibodies directed against a wide range of antigens specific membrane antigens, cytoskeleton proteins, secreted proteins, enzymes, hormonal receptors, and other cell elements. Immunocytochemistry can also be applied on cytological preparations in cases of malignant perfusions. Today, with the help of a wide range of immunohistochemistry markers, the misdiagnosis of other malignancies such as lymphomas, extragonadal germ cell tumors, malignant melanomas, and undifferentiated sarcomas as CUP is rather rare. Nevertheless, it should always be kept in mind that regardless of the relatively high specificity of several immunoperoxidase markers, false positive as well as false negative staining

may be expected. Differences in fixation techniques and in the kind of antigen used are responsible for the observed differences in sensitivity and specificity.[1]

Electron microscopy can be useful diagnostic tool in 15% of undifferentiated CUP offering an additional diagnostic accuracy in one-third of these cases . It is a well-reputed diagnostic method for the poorly differentiated neuroendocrine tumors and amelanotic melanomas recognizing core granules, electron-dense secretory granules, and premelanosomes.[23] It can also contribute to the diagnosis of dedifferentiated squamous cell tumors (desmosomes attached to tonofilaments), adenocarcinomas (acinar spaces, tight junctions, and microacini) and sarcomas (myofibrils, dilated rough endoplasmic reticulum, extracellular osteoid). Disadvantages of electron microscopy are the special handling procedure, the experienced personnel, and the expensive equipment required.

Molecular genetic and cytogenetic studies can offer today additional diagnostic information towards the identification of special tumor types that have specific genetic markers. Fluorescence in situ hybridization (FISH) using the chromosomal marker i(12p) , which is highly nonrandom for germ cell tumors, has been proven an excellent diagnostic tool in atypical extragonadal germ cell tumors presenting as undifferentiated CUP . Genetic analysis can also contribute to the diagnosis of a number of tumors with specific chromosomal aberrations, usually seen in soft tissue sarcomas and lymphomas. Nasopharyngeal undifferentiated carcinomas can be distinguished from dedifferentiated epidermoid tumors by detection of EBV genome with PCR analysis.[1]

MATERIALS AND METHODS

Source of data

Patients presented with palpable or radiologically visible metastatic lesions for cytological evaluation and cytological specimen of metastatic effusions referred to the Department of pathology in _____ Medical College, Hospital and Research centre, were included.

Study period: 1st September 2011 to 1st September 2013.

Methods of collection of data.

Thorough examination of the patients who were referred to the Department of pathology for cytological evaluation of metastatic lesions was done and also detailed clinical history was taken. Standard FNAC procedure was performed by using Cameco syringe pistol with 10ml disposable syringe and 23-22G needle and multiple smears were prepared. Also body fluids sent for cytological evaluation which were positive for malignancy were included in the study and detailed clinical history was taken. Smears fixed in absolute alcohol were stained with Haematoxylin and Eosin (H&E) and Papanicoloau stains while air dried smears were stained with May-grunwald Giemsa (MGG) stain. Immunohistochemistry markers study such as CK 7 and CK 20 was done wherever feasible.

Sample Size:

Overall prevalence rate of malignant tumors which clinically manifest as metastatic lesions is 7%.[2] At 95% confidence interval and 5% margin of error, the required sample size is calculated using the

Statistical formula $n = \frac{(1.96)^2 \, p \times q}{d^2}$

Where p : prevalence rate

d: margin of error

The calculated sample size is 100.

Hence, minimum of 100 cases were included in the study.

Statistical analysis:

1. Chi square test was applied to evaluate the efficacy of cytological study and clinical correlation in diagnosis of primary tumors in patients presenting with metastatic tumors.
2. Diagramatic representation of the data

Inclusion criteria: All patients clinically presented with metastatic tumors with palpable or radiologically visible lesions which are easily approachable were included.

Exclusion criteria: Patients presenting with metastatic lesions in Brain and lung were excluded.

RESULTS

Total number of cases studied for clinicocytological diagnosis of metastatic tumors from september 2011 to september 2013 were 100. Out of 100 cases, in 64 cases metastatic site was lymph node and metastatic effusion was the presentation in 25 cases. Metastatic deposit in omentum, skin and soft tissue and liver was noted in 6, 4 and 1 case each respectively.

TABLE -1.DISTRIBUTION OF SITES OF METASTATIC LESIONS

Sl.No	METASTATIC SITE	NUMBER OF CASES	PERCENTAGE(%)
1	**LYMPH NODE**	64	64
2	**ASCITIC FLUID**	16	16
3	**PLEURAL FLUID**	08	08
4	**OMENTAL DEPOSITS**	06	06
5	**SKIN AND SOFT TISSUE**	04	04
6	**PERICARDIAL FLUID**	01	01
7	**LIVER**	01	01
8	**TOTAL**	100	100

Lymph node was the commonest site of metastasis amounting to 64 % followed by ascitic fluid (16%) , pleural fluid (8%), omentum (6%), skin and soft tissue (4%) and others.

TABLE 2-AGE AND SEX DISTRIBUTION OF THE METASTATIC LESIONS

Sl.No	AGE IN YEARS	MALES	FEMALES	TOTAL	PERCENTAGE (%)
1	31-50	08	09	17	17
2	51-70	37	36	73	73
3	71-90	07	03	10	10
	TOTAL	52	48	100	100%

Maximum number of cases were in the age group of 50-70 years. Out of 100 cases , 52 were males and 48 were female patients.

Bar diagram showing Age and sex distribution

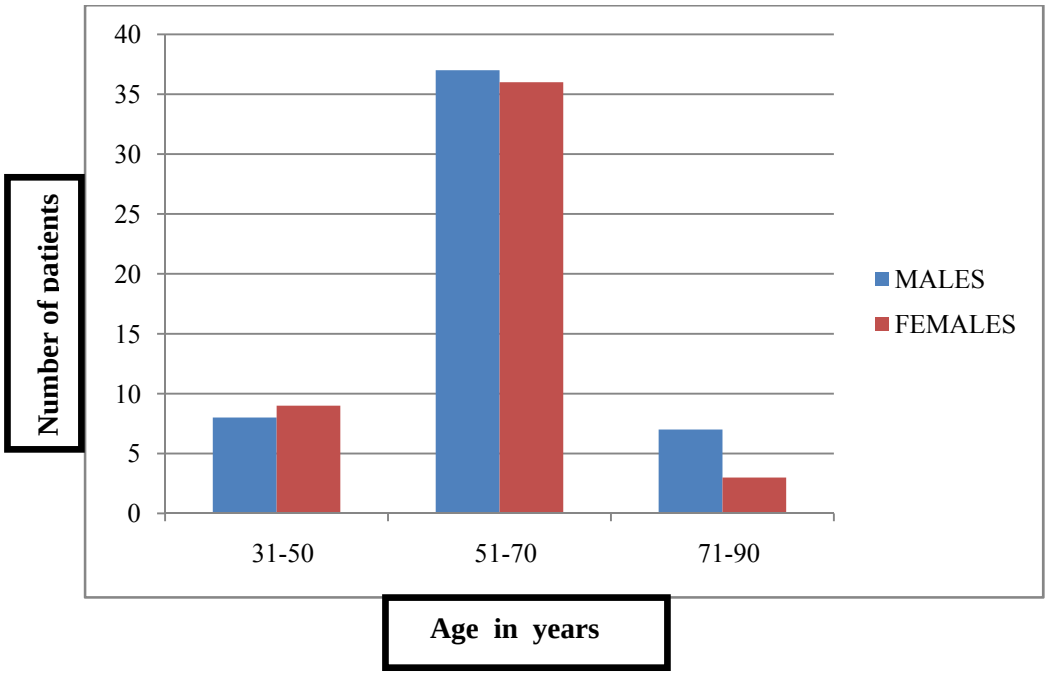

TABLE 3-DISTRIBUTION OF GROUP OF METASTATIC LYMPH NODES

(n=64)

Sl.No	GROUP OF LYMPH NODE	NUMBER OF CASES	PERCENTAGE %
1	CERVICAL LYMPH NODE	49	77
2	AXILLARY LYMPH NODE	12	18
3	INGUINAL LYMPH NODE	03	5
	TOTAL	64	100%

The commonest group of lymphnode was cervical group seen in 49 cases constituted to 77% of cases followed by axillary (18%) and inguinal group (5%) of lymphnodes .

TABLE 4-DISTRIBUTION OF PRIMARY SITES IN LYMPH NODE METASTAES (n=64)

Sl.No	PRIMARY SITE	NUMBER OF CASES	PERCENTAGE(%)
1	NASOPHARYNX	22	34
2	OROPHARYNX	02	3
3	LARYNX	02	3
4	BREAST	21	33
5	TONGUE	07	11
6	OESOPHAGUS	03	5
7	POORLY DIFFERENCIATED CARCINOMA NASOPHARYNX	02	3.5
8	POORLY DIFFERENCIATED CARCINOMA LARYNX	01	1.5
9	POORLY DIFFERENCIATED CARCINOMA / LYMPHOMA	01	1.5
10	LUNG	01	1.5
11	PAROTID	01	1.5
12	PERIANAL SKIN	01	1.5
	TOTAL	64	100%

Out of 64 lymphnode metastases, Nasopharynx was the commonest primary site amounting to 22 cases (34%) followed by breast 21 cases (33%) . In 7 cases (11%) tongue was the primary site and in 3 cases(5%) oesophagus. Oropharynx and larynx was primary in 2 cases each amounting to 3%. Primary from lung, parotid and perianal skin was noted in 1 case (1.5%) each.

TABLE 5-DISTRIBUTION OF PRIMARY SITES IN ASCITIC FLUID METASTASES (n=16)

Sl.No	PRIMARY SITE	NUMBER OF CASES	PERCENTAGE(%)
1	OVARY	15	93
2	OVARY/GIT/LUNG	01	7
	TOTAL	16	100%

Out of 16 ascitic fluid metastases ovary was the primary site in 15 cases amounting to 93% of cases.

TABLE 6-DISTRIBUTION OF PRIMARY SITES IN PLEURAL FLUID METASTASES (n=8)

Sl.No	PRIMARY SITE	NUMBER OF CASES	PERCENTAGE(%)
1	BREAST	03	37.5
2	LUNG	03	37.5
3	NASOPHARYNX	01	12.5
4	THYROID	01	12.5
	TOTAL	8	100%

In metastatic pleural effusion, breast (37.5%) and lung (37.5%) was primary in 3 cases each. Nasopharynx and thyroid was primary in one case each.

One case of metastasis to pericardial fluid was noted and the primary was diagnosed as carcinoma lung after clinicocytological correlation.

TABLE-7 DISTRIBUTION OF PRIMARY SITES IN OMENTAL METASTASES (n=6)

Sl.No	PRIMARY SITE	NUMBER OF CASES	PERCENTAGE(%)
1	STOMACH	03	50
2	OVARY	02	33
3	COLON	01	17
	TOTAL	6	100%

In omental metastases, out of 6 cases, commonest primary was from stomach(50%) followed by ovary(33%) and colon(17%).

TABLE 8-DISTRIBUTION OF PRIMARY SITES IN OTHER ORGAN METASTASES, (n=5)

Sl.No	METASTATIC SITE	PRIMARY SITE	NUMBER OF CASES	PERCENTAGE %
1	SKIN AND SOFT TISSUE	LIVER	02	40
		POORLY DIFFERENCIATED CARCINOMA FROM LUNG	01	20
		UNKNOWN	01	20
2	LIVER	GIT/GALL BLADDER	01	20
	TOTAL		05	100

In other organ metastases, skin and soft tissue constituted 4 cases and one case of liver in which suggested primary was from GIT/gall bladder. Out of 4 cases of skin and soft tissue metastases, primary was from liver in 2cases, followed by lung in one case and in 1 case primary was unknown.

TABLE-9. CLINICAL PRESENTATION IN METASTATIC TUMORS

CLINICAL PRESENTATION	NUMBER OF CASES	PERCENTAGE(%)
Hoarseness of voice, cough and difficulty in swallowing	40	40
General deterioration and weight loss	35	35
Digestive symptoms	15	15
ascites	12	12

In our study, hoarseness of voice, cough, difficulty in swallowing was the commonest clinical presentation followed by general deterioration, weight loss and digestive symptoms and ascites

TABLE 10- ANALYSIS OF DISCREPANCIES BETWEEN CLINICOCYTOLOGICAL AND HISTOPATHOLOGICAL DIAGNOSIS OF PRIMARY SITE (n=40)

Clinicocytological diagnosis of primary	Number of cases	Histopathological Diagnosis of primary	Number of cases
Invasive ductal carcinoma Breast	10	Invasive ductal carcinoma Breast	10
Adenocarcinoma ovary	07	Adenocarcinoma ovary	07
Squamous cell carcinoma Nasopharynx	05	Squamous cell carcinoma Nasopharynx	05
Poorly differenciated carcinoma nasopharynx	02	Lymphoma	02
Squamous cell carcinoma Tongue	03	Squamous cell carcinoma Tongue	03
Adenocarcinoma Lung	02	Adenocarcinoma Lung	02
Adenocarcinoma stomach	02	Adenocarcinoma stomach	02
Squamous cell carcinoma larynx	02	Squamous cell carcinoma larynx	02
Poorly differenciated carcinoma larynx	01	Lymphoma	01
Malignant Melanoma Ski	01	Malignant Melanoma Skin	01
Poorly differenciated carcinoma from female genital tract	01	Small cell carcinoma Cervix	01
Adenocarcinoma Ca colon/gall bladder	01	Hepatocellular carcinoma	01
Unknown	03	Unknown	03
TOTAL	40		40

Histopathological follow-up was available in 40 cases. On correlation of cytologically confirmed primaries, 32(86%) cases were concordant and 5(13%) cases were discordant. Whereas in 3(1%) cases primary was unknown**.**

TABLE-11 STASTICAL ANALYSIS OF HISTOPATHOLOGICALLY CONFIRMED CASES OF PRIMARY SITES.

Clinicocytological diagnosis of primary site	**Histopathological diagnosis of primary site**		
	Positive	**Negative**	**Total**
Positive	32	0	32
Negative	05	3	08
Total	37	3	40

Sensitivity-86%

Specificity-100%

Positive predictive value-100%

Negative predictive value-37%

Stastical analysis of cases with histopathological follow up showed that clinicocytological correlation has got high specificity (100%), sensitivity(86%) and high positive predictive value(100%).

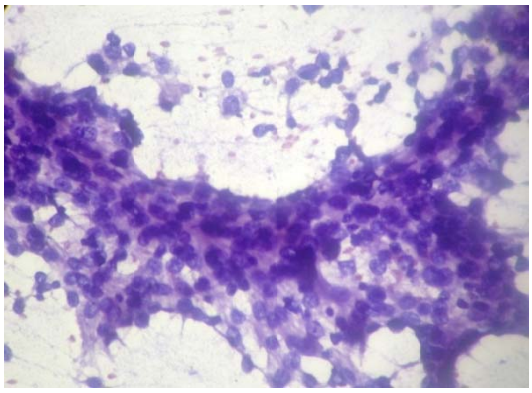

Fig1-MGG stain 40x Photomicrograph of metastatic squamous cell carcinoma in lymph node on cytology.

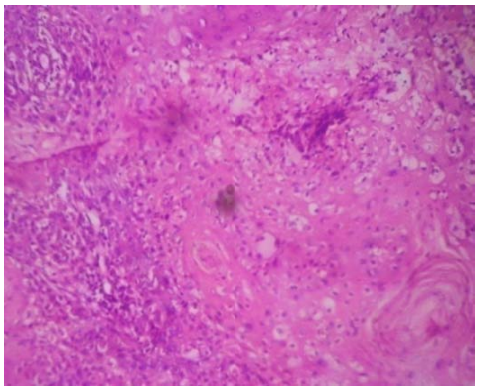

Fig2-H&E stain 10x HPR Photomicrograph of primary Squamous cell carcinoma nasopharynx

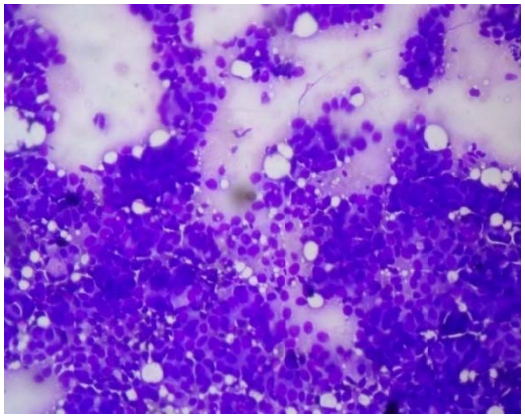

Fig3-MGG stain 10x.Photomicrograph metastatic adenocarcinoma in ascitic fluid

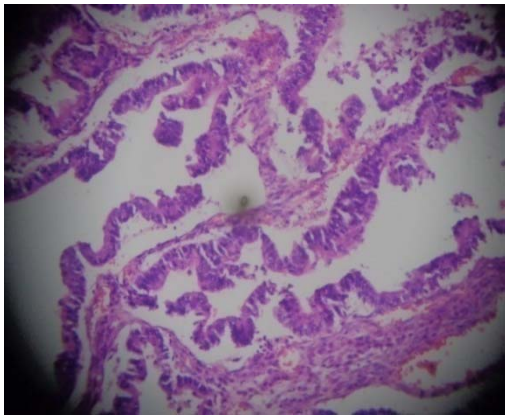

Fig4-H&E stain 10x.HPR photomicrograph of mucinous adenocarcinoma of ovary

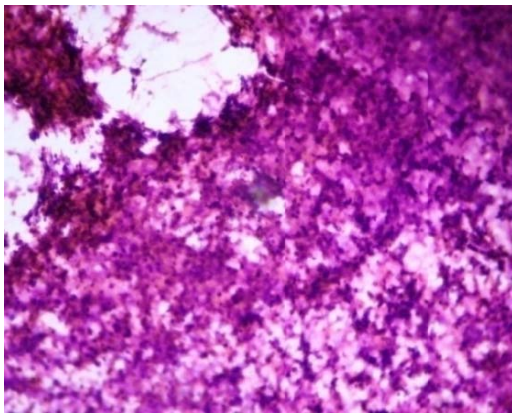

Fig5-H & E stain (20x)Photomicrograph of metastatic malignant melanoma in lymph node on cytology

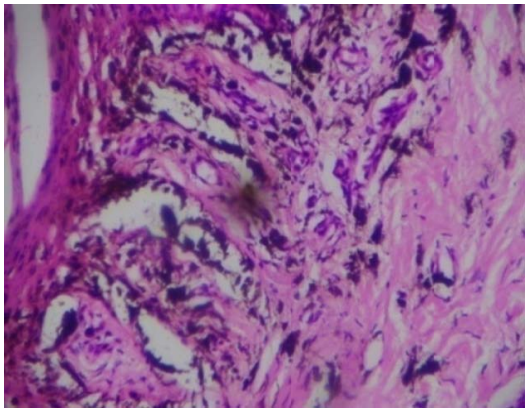

Fig6-H&E stain (10x)HPR Photomicrograph of primary malignant melanoma of skin

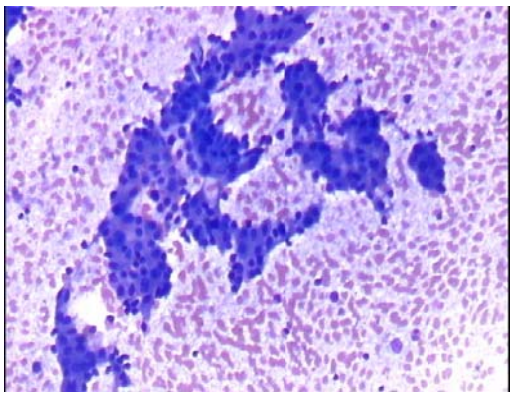

Fig 7-MGG stain.20x.Photomicrograph of metastatic carcinoma breast in lymph node

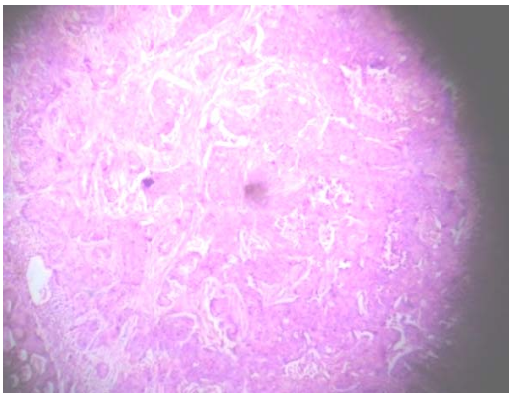

Fig 8-H&E stain 10x.HPR Photomicrograph of primary ductal carcinoma of breast

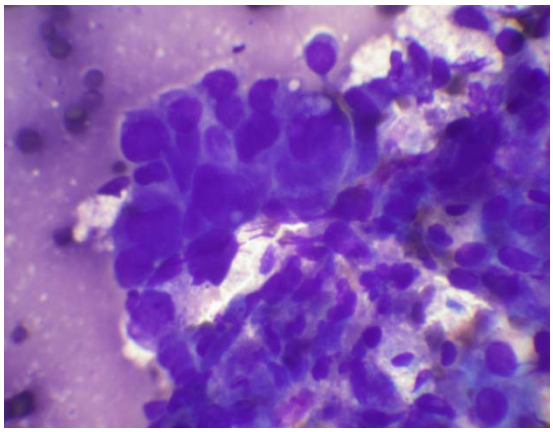

Fig9-MGG stain 10x.Photomicrograph of FNAC liver

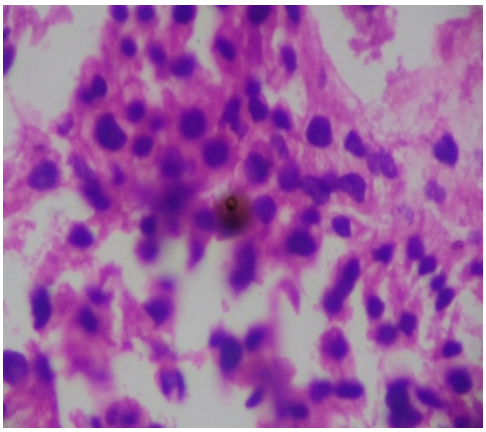

Fig10-H&E stain 10x.HPR Photomicrograph of Primary hepatocellular carcinoma

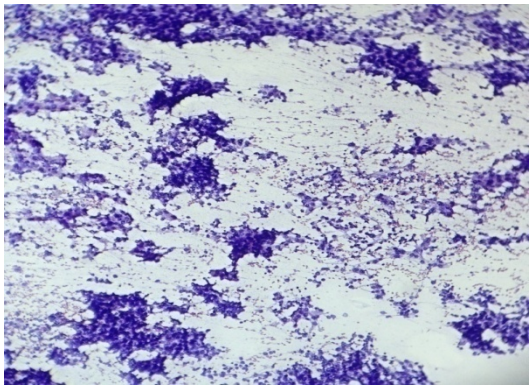

Fig11-MGG stain 10x.Photomicrograph of metastasis to soft tissue in inguinal region

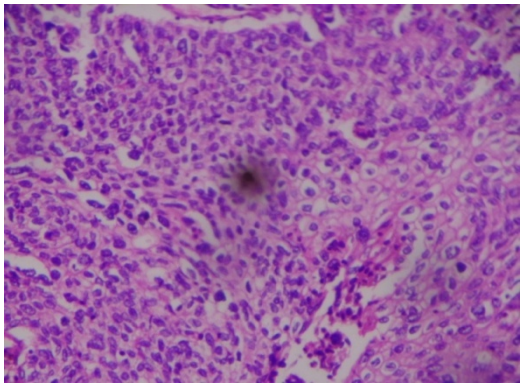

Fig12-H&E stain 10x.HPR Photomicrograph of primary squamous cell carcinoma cervix

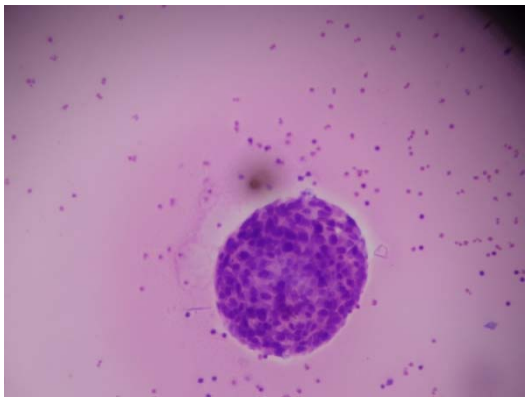

Fig 13 –H & E stain 10x.Photomicrograph of metastatic adenocarcinoma in pleural fluid

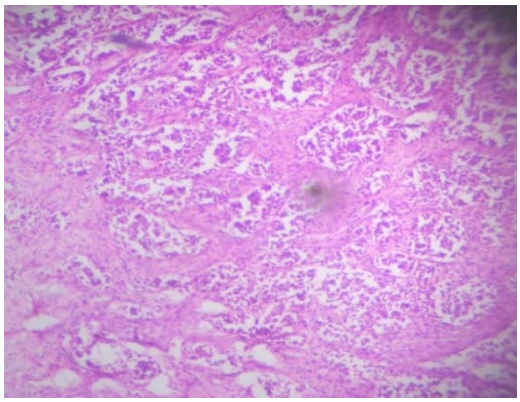

Fig 14-H & E stain. HPR Photomicrograph showing primary invasive ductal carcinoma of breast

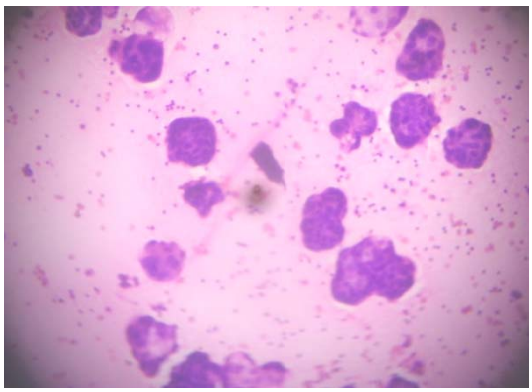

Fig 15- H & E stain.10x.photomicrograph showing metastatic adenocarcinoma in pericardial fluid

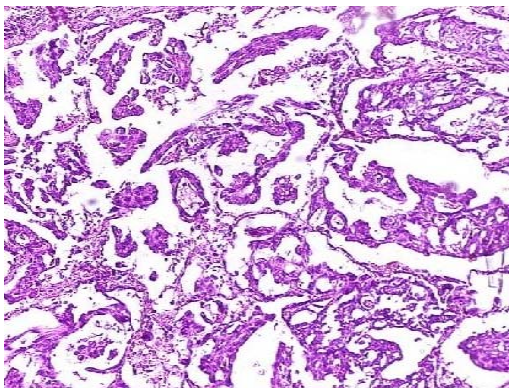

Fig 16-H & E stain.20x.HPR Photomicrograph showing primary adenocarcinoma lung

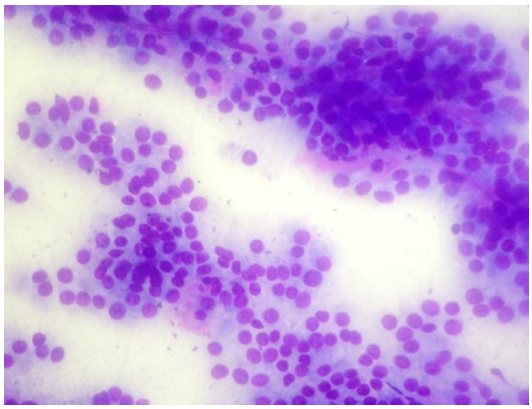

Fig 17- H&E stain.20x.Photomicrograph of metastatic deposits in anterior chest wall swelling

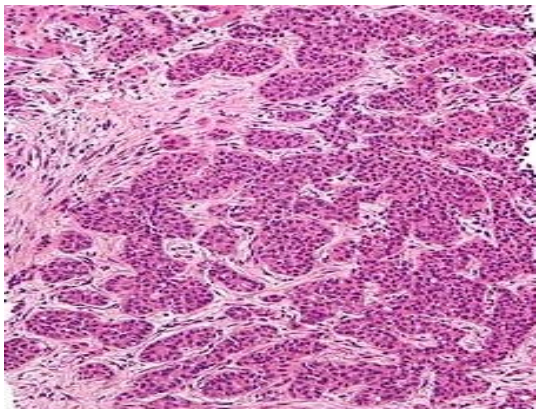

Fig 18-H & E stain.20x.HPR Photomicrograph showing primary hepatocellular carcinoma

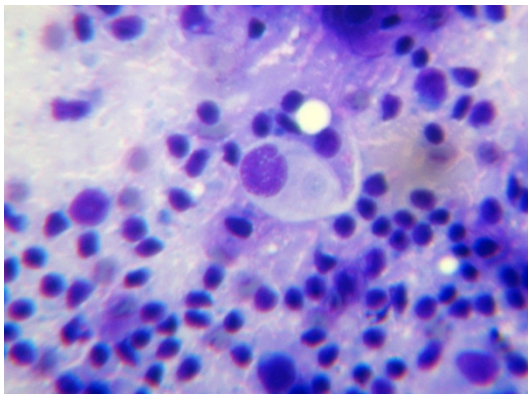

Fig 19-MGG stain.10x. Photomicrograph showing poorly differenciated carcinoma

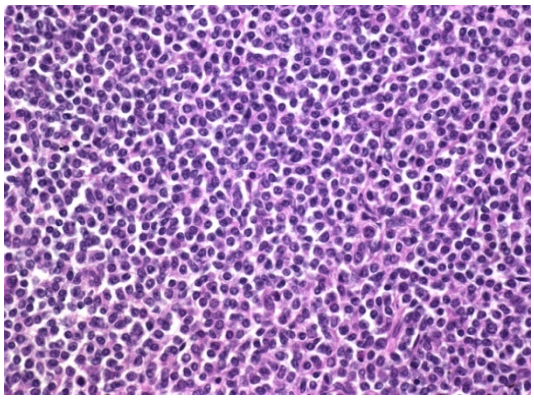

Fig -20.H & E stain.HPR Photomicrograph showing lymphoma

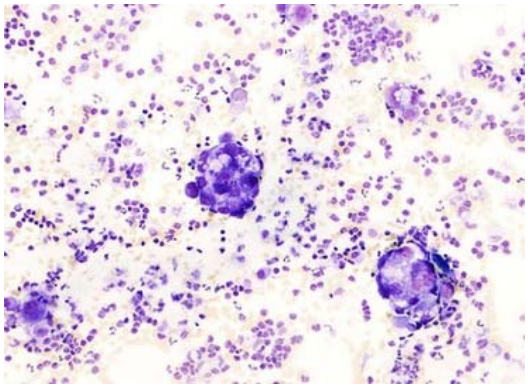

Fig 21-MGG stain.Photomicrograph showing metastatic adenocarcinoma in omentum

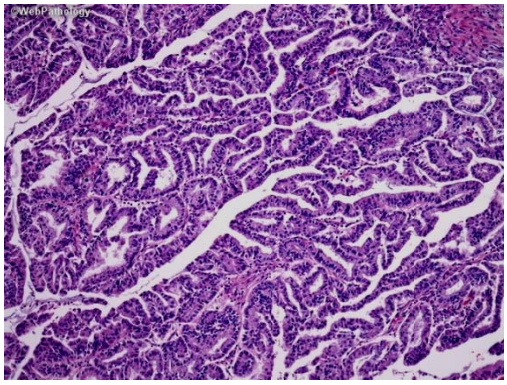

Fig -22.H & E stain.HPR photomicrograph showing primary adenocarcinoma stomach

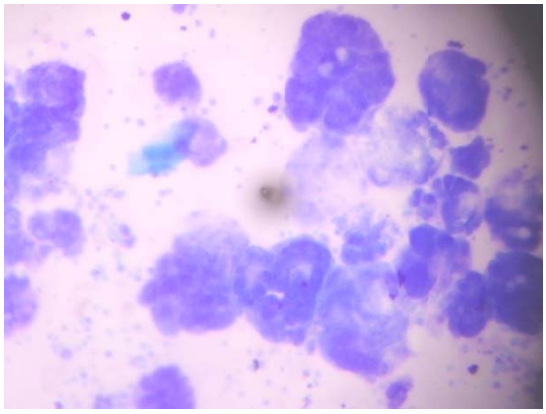

Fig 23-MGG stain.Photomicrograph showing metastatic adenocarcinoma in omentum

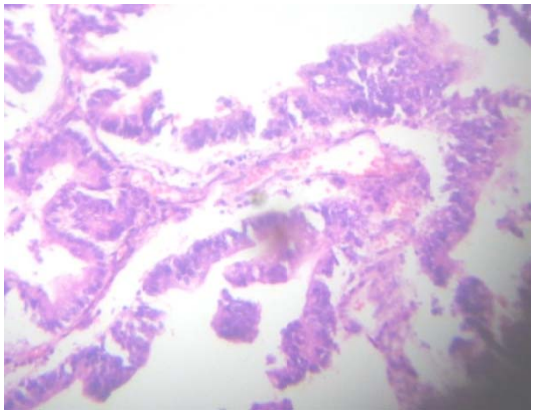

Fig -24.H & E stain.HPR photomicrograph showing primary adenocarcinoma ovary

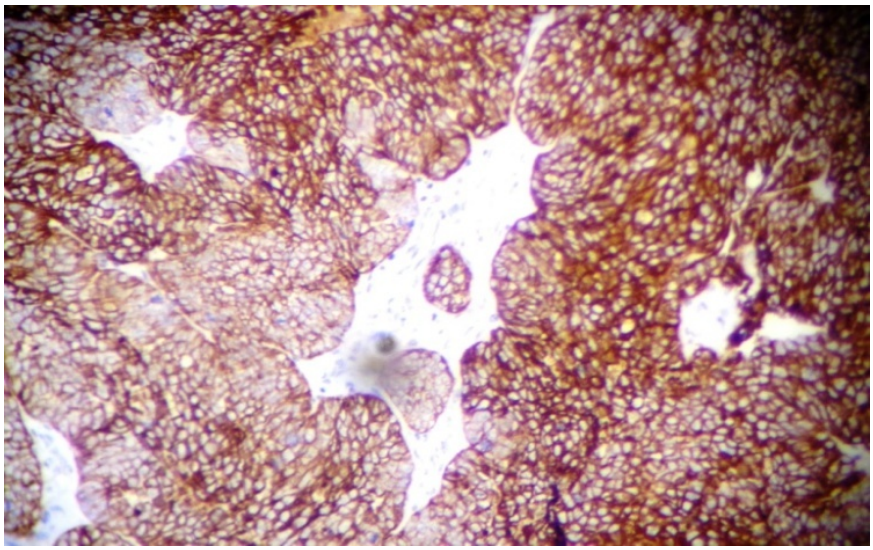

Fig-25 Omental metastasis from adenocarcinoma ovary CK- 7 positivity

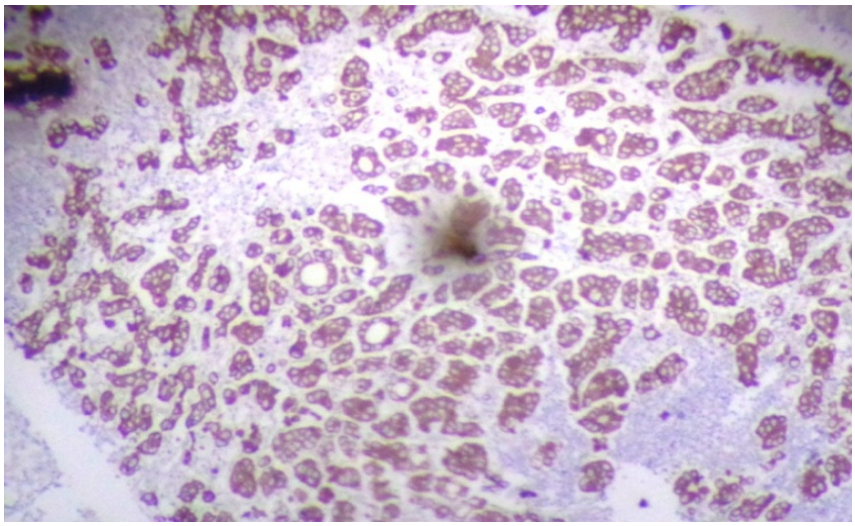

Fig-26 Lymph node metastasis from invasive ductal carcinoma breast. CK-7 positivity

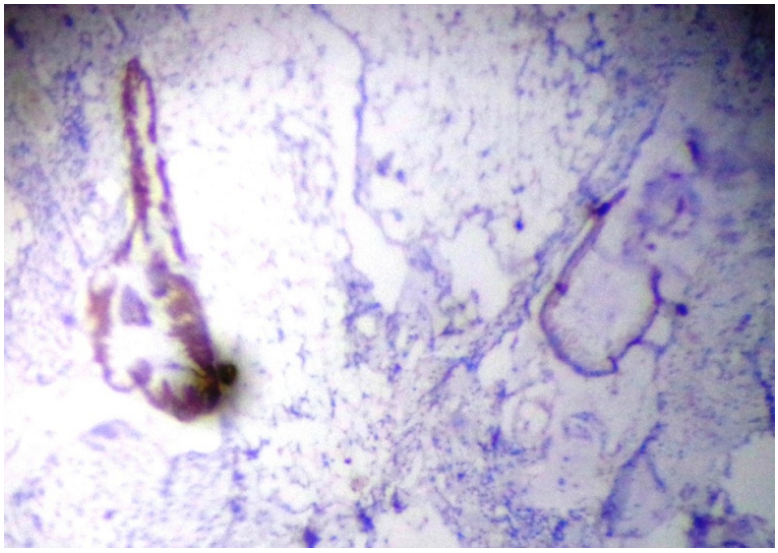

Fig- 27. Omental metastasis from adenocarcinoma stomach. CK-20 positivity

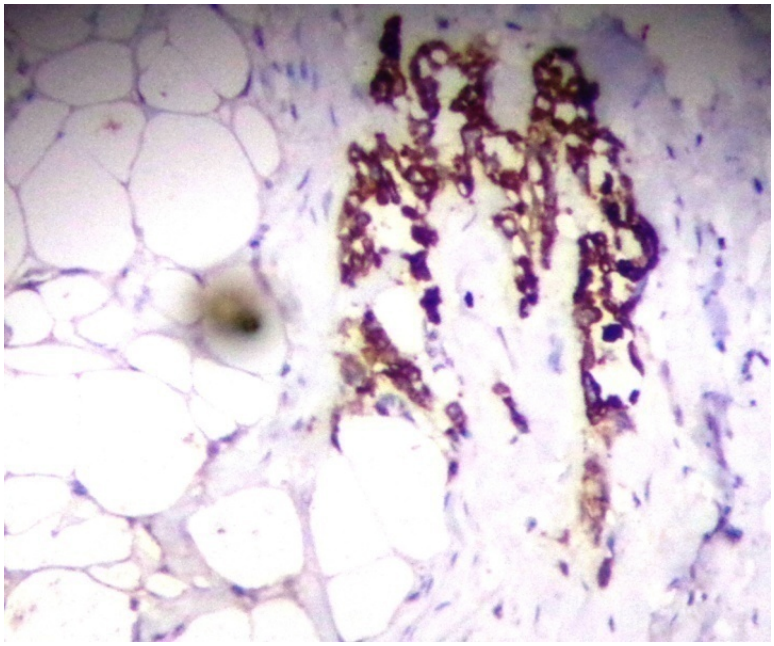

Fig-28. Omental metastasis from Carcinoma colon. CK-20 positivity

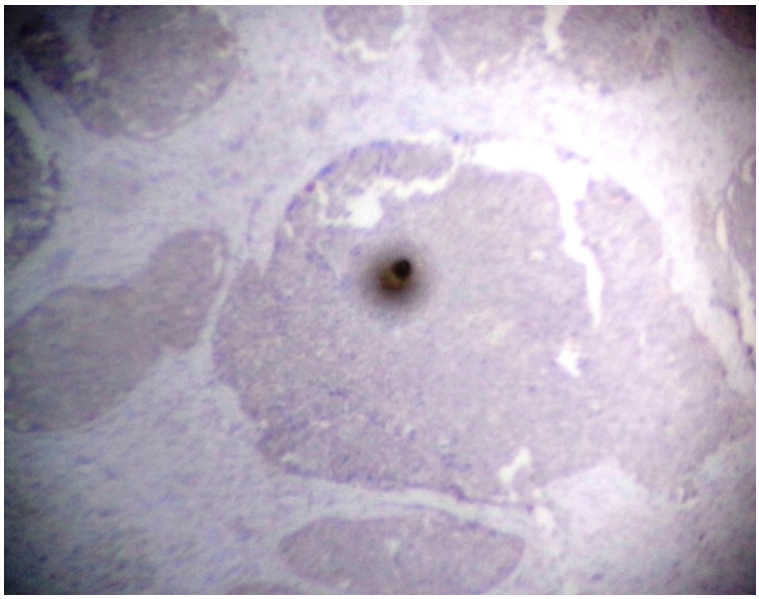

Fig-29. Omental metastasis from carcinoma ovary. CK-20 positivity.

DISCUSSION

Malignant tumors metastatize commonly to lymph nodes and other organs like liver,ascitic fluid, pleural fluid, bones and skin.[1] Early detection and correct cytodiagnosis of metastatic tumors saves the patient from invasive and costly diagnostic procedures and also, helps the surgeons to formulate the therapeutic strategy in treatable primary tumors.[1,3,28]

Hence in this study an attempt was made to provide primary site by careful evaluation of clinical presentation of the disease by correlating with the cytological findings of the metastatic tumor.

In this study we received total 100 cases for cytological examination. Out of which, lymph nodes constituted the major group amounting to 64 % followed by ascitic fluid(16%) , pleural fluid (8%) , omentum (6%) and others(6%). We observed that lymph nodes were the commonest site of metastasis in 64 cases(64%) similar findings were noted in study done by Ahmad *et al.*[29] in which,out of 155 cases , 67% of cases showed lymph node as the metastatic site followed by bone (10%), liver (8.8%) and skin (8.2%).

In Briasoulis and Nicholas P[1] study, lymph nodes were the major group of metastatic site amounting to 62% followed by liver,lung, bone and pleura.

In our study, maximum number of metastatic lesions were seen in the age group of 50-70 years amounting to 73%. Our findings correlated with the findings of studies done by Ahmad *et al.*[29] and Briasoulis *et al*.[1]

Cervical group of lymph nodes constituted the major group in 50 cases (80%), these findings correlated with findings of studies done by Sinha *et al.,*[4] Ahmed *et al.*[24] and Briasoulis *et al*.[1]

In our study maximum number of primary sites for metastatic lesions were pharynx, larynx and oral cavity amounting to 40%. Similar findings were noted in a study done by Ahmad *et al.*[29] (32%) and Sinha *et al*.[4] (40%).

Sears and Hajdu[30], reported that the most common primary tumor in ascitic fluid metastasis was ovary (32%) followed by breast (15%) and lymphoreticular system (7%). In our study ovary was the commonest primary site in ascitic fluid metastasis amounting to 93% of cases followed by GIT and lung in 7% of cases which is comparable with the study done by Sears and Hajdu.[30]

Clinicocytological correlation of 8 cases of pleural fluid metastasis showed breast and lung as the commonest primary each constituting 38% cases followed by thyroid and nasopharynx. These findings were comparable to study done by sears and Hajdu[30] and Khan *et al*.[31] in which carcinoma breast (24%) was the most common primary, followed by lung(19%) and lymphoreticular system (16%).

Out of 100 metastatic lesions we observed that adenocarcinoma was the predominant type of tumor in 51% of cases followed by squamous cell carcinoma in 40%, poorly differenciated carcinoma in (4%) and others constituted 6%.Similar findings have been reported in studies done by Didolkar MS *et al.*[32], Briasoulis E and Nicholas Pavlidis.[1]

In the present study we noted that the clinical presentation in cases of metastatic tumor depends on the predominant site of metastatic involvement.

In Briasoulis *et al.*[1], general deterioration and weight loss were the common symptoms in most of the patients, followed by digestive symptoms, respiratory symptoms, enlargement of liver and ascites.

In our study, hoarseness of voice, cough, difficulty in swallowing was the commonest clinical presentation followed by general deterioration, weight loss and digestive symptoms and ascites

In 40 cases (40%) histopathological follow-up was available. On correlation with histopathology, 32 cases (86 %) were concordant and 5 cases(13%) were discordant.

In one case of liver malignancy, differential diagnosis given on cytology was metastasis from GIT and gall bladder, but cell block study showed features of multifocal hepatocellular carcinoma.

Another case where discordance noted was in skin and soft tissue metastasis, On cytology differential diagnosis was given as poorly differenciated carcinoma or lymphoma but histopathologically showed features of small cell carcinoma of cervix.

Other 2 cases where discordance was noted were, 2 cases of cervical LN metastasis , on cytology poorly differenciated carcinoma nasopharynx was given but histologically it was confirmed as lymphoma.

One more case of discordance was in upper cervical LN metastasis, on cytology primary given was from larynx but histopathologically proved as lymphoma.

Ahmed *et al.*[29] conducted a study on Fine needle aspiration cytology (FNAC) of 171 metastatic lesions with special reference to clinicopathological analysis of primary site in patients of epithelial and non-epethelial tumors. Out of 171 metastatic lesions, 155cases (90.6%) were diagnosed by fine needle aspiration cytology alone and 16cases (9.4%) by histopathology. The most frequent site of metastasis in their study was lymphnode accounting to 115 cases with cervical group of lymphnodes being the most common group of lymphnode. The oropharynx including the oral cavity and pharyngolarynx was the most common primary site accounting to 55 cases (32.2%).They concluded that 90.6% of the metastatic lesions were diagnosed by FNAC, which was rapid, safe and cost effective technique in determining the primary site.

Sinha *et al.*[4] conducted study on aspiration cytodiagnosis of metastatic lesions with special reference to primary sites in 104 metastatic tumors. In their study lymphnodes were the commonest site of metastasis, accounting to 80 cases followed by bone accounting to 10 cases & remaining 14 cases were presented with metastatic lesions in liver, skin, soft tissue and pleura. In cervical and left supra clavicular lymph nodes, 60% of the primaries were from upper aerodigestive tract, lung & thyroid. Malignancies from gastrointestinaltract, gall bladder, and breast, and ovary, external and internal genetalia metastatised predominantly to left supraclavicular, axillary, inguinal nodes, liver and bones.

Our study also showed lymph node as the commonest site of metastasis and nasopharynx including oral cavity as the commonest primary. These findings were similar to Ahmed *et al*.[29] and Sinha *et al*.[4] study.

In a study conducted by Briasoullias E and Nicholas P[1] on cancer of unknown primary origin in 2114 patients with metastatic tumour of unknown origin, most of the patients (60%) have more than two sites affected at presentation with lymphnodes being the commonest site of metastasis followed by liver, lung, bone and pleura. They noted that clinical presentation in cases of carcinoma of unknown primary depends on the predominant site of metastatic involvement. General deterioration and weight loss were the common symptoms in most of the patients, followed by digestive symptoms, respiratory symptoms, enlargement of liver, ascites, skin nodule, bone pains depending on the sites of metastatic involvemement. Thus they concluded that a thorough clinicopathological evaluation is recommended to detect the primary tumor with limited diagnostic procedures.

Didolkar *et al*.[32] conducted study on metastatic carcinoma from occult primary A study of 254 patients .Most common site of metastasis was lung followed by cervical lymph node, bone and liver. However in our study cervical lymph node was the commonest site of metastasis. Adenocarcinoma was the commonest type morphologically followed by undifferentiated and squamous cell carcinoma in their study. Frequently the patients had multiple presenting signs and symptoms. The most common clinical presentation were in the form of pulmonary or pleural metastasis followed by cervical lymphadenopathy and weight loss.

In the present study, majority of the patients presented with hoarseness of voice, cough and difficulty in swallowing, followed by general deterioration, weight loss, digestive symptoms and ascites. These findings were comparable with the findings of studies done by Briasoullias E and Nicholas P[1] and Didolkar *et al*.[32]

CONCLUSION

FNAC is a rapid, safe and cost effective technique in determining the primary site. Clinicocytological correlation has got high sensitivity,specificity and positive predictive value in determining the primary site. Thus thorough clinicocytological evaluation is effective diagnostic method to detect the primary tumor with cost effective diagnostic procedures.

SUMMARY

In the present study total 100 cases were received from September 2011 to september 2013 for cytological evaluation in the Department of pathology _____Medical College.

Patients presented with palpable or radiologically visible metastatic lesions for cytological evaluation and cytological specimen of metastatic effusions were included in the study.

Thorough examination of the patients and detailed clinical history was taken. Standard FNAC procedure was performed. Smears fixed in absolute alcohol were stained with Haematoxylin and Eosin (H&E) and Papanicoloau stains, while air dried smears were stained with May-grunwald Giemsa (MGG) stain.

Out of 100 cases, in 64 cases metastatic site was lymph node and metastatic effusion was the presentation in 25 cases. Metastatic deposit in omentum, skin and soft tissue and liver was noted in 6, 4 and 1 case each respectively.

Most of the cases were in the age group of 50-70 years. Mild male preponderance with male to female ratio of 1.1:1 was noted.

Out of 64 lymphnode metastasis, Nasopharynx was the commonest primary site followed by breast, tongue, oesophagus , oropharynx , larynx, lung, parotid and perianal skin.

Out of 16 ascitic fluid metastasis ovary was the primary site in 93% of cases. In metastatic pleural effusion, breast and lung was most common primary followed by nasopharynx and thyroid.

Histopathological follow-up was available in 40 cases. On correlation of cytologically confirmed primaries, 32(86%) cases were concordant and 5(13%) cases were discordant.Whereas in 3 cases(1%) primary was unknown**.**

Stastical analysis of cases with histopathological follow up showed that clinicocytological correlation has got high specificity(100%), sensitivity(86%) and high positive predictive value(100%).Thus FNAC is a rapid, safe and cost effective technique in determining the primary site. Thus thorough clinicocytological evaluation is effective diagnostic method to detect the primary tumor with cost effective diagnostic procedures.

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ANNEXURES

RESEARCH INFORMED CONSENT FORM

TITLE OF THE PROJECT : UTILITY OF CLINICOCYTOLOGICAL STUDY IN DETECTING PRIMARY TUMOR IN PATIENTS PRESENTING WITH METASTATIC TUMOR.

PRINCIPAL INVESTIGATOR :

P.G.GUIDE :

PURPOSE OF RESEARCH:

I have been informed that this study is done to know the efficacy of cytological study in diagnosis of metastatic tumors.

PROCEDURE

I understand that I will undergo detailed clinical history, thorough clinical examination and after which fine needle aspiration cytology will be performed and subjected to cytological examination.

RISK AND DISCOMFORTS:

I understand that, I may experience some pain and discomforts during the examination of the lesion or during FNAC. This is mainly the result of my condition

and procedures of this study are not expected to exaggerate these feelings which are associated with usual course of treatment.

BENEFITS:

I understand that my participation in the study will have no direct benefit to me other than the potential benefit of the treatment.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulations of the hospital. If the data is used for publications the identity of patient will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw from the study at any time.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me during the study I will get medical treatment but no further compensations.

I have read and fully understood this consent form. Therefore I agree to participate in the present study.

_____ _____

Participant / Guardian Date:

_____ _____

Signature of Witness Date:

I have explained the patient the purpose of the study, the procedure required and possible risk and benefit to the best of my ability in the vernacular language.

_____ _____

Investigator / P.G. Date:

_____ _____

Witness to Signature Date

PROFORMA

NAME	:	OP/IP No.	:
AGE	:		
SEX	:	D.O.A	:
RELIGION	:	D.O.D	:
OCCUPATION	:		
RESIDENCE	:		
Presenting Complaints	:		
Past history	:		
Personal history	:		
Family history	:		
Treatment history	:		

General physical examination:

Pallor	present/absent
Icterus	present/absent
Clubbing	present/absent
Lymphedenopathy	present/absent
Edema	present/absent
Built	poor/average/well

VITALS: PR: RR:

BP: TEMPERATURE:

WEIGHT:

EXAMINATION OF METASTATIC LESIONS:

Inspection:

Number :

Site :

Size :

Margins :

Others :

Palpation:

SYSTEMIC EXAMINATION:

Cardiovascular system

Respiratory system:

Per Abdomen:

Central nervous system:

Examination of Breast, Thyroid, Genitourinary system:

Clinical Diagnosis:

INVESTIGATIONS:

Haematological investigations:

Biochemical Investigations:

Radiological Investigations:

Cytology: Site:

Adequacy:

Cellular features:

Impression on Cytology:

Histopathological Diagnosis:

Special investigations (wherever required):

Cytochemical Staining

Immunohistochemistry

Tumor marker assay

ETHICAL CLEARANCE CERTIFICATE

MASTER CHART

Sl.No	Patient name	Age	Sex	IP/OP No	FNAC site	Clinical correlation
1	Anasuya	65	F	2301	Axillary lymph node	general deterioration ,weight loss
2	Bagappa	66	M	2483	supraclavicular lymph node	swelling in the neck
3	Sidramappa	75	M	2435	Pleural fluid	cough,breathlessness,change in voice
4	Siddavamma	58	F	2764	Axillary lymph node	general deterioration ,weight loss
5	Pattanshetty	65	M	2874	cervical Lymph node	cough,breathlessness,change in voice
6	Gurubai	45	F	3245	Ascitic Fluid	Distension of abdomen
7	Kamalabai	35	F	4563	Pleural fluid	cough , breathlessness
8	Basamma	60	F	3647	swelling illiac fossa(left)	swelling in inguinal region
9	Hameedabegum	65	F	3890	Pleural fluid	cough , breathlessness
10	Shivalingappa	65	M	3125	cervical Lymph node	cough,breathlessness,change in voice
11	Sumangala	42	F	4572	Ascitic Fluid	Distension of abdomen
12	Rudrappa	62	M	4123	cervical Lymph node	cough,breathlessness,change in voice
13	Neelamma	65	F	4234	Liver	pain abdomen, weight loss
14	Siddanagouda patil	52	M	4354	Pleural fluid	cough , breathlessness
15	Apparubi	45	F	4456	cervical Lymph node	cough,breathlessness,change in voice
16	Parvati	88	F	4567	Ascitic Fluid	Distension of abdomen
17	Shivappagouda	75	M	4565	cervical Lymph node	cough,breathlessness,change in voice
18	Basanna	65	M	5123	cervical Lymph node	cough,breathlessness,change in voice
19	Iranna	72	M	5234	Pleural fluid	breathlessness, cough
20	Vittal	60	M	5345	cervical Lymph node	cough,breathlessness,change in voice
21	Neelamma patil	50	F	5456	Ascitic Fluid	Distension of abdomen
22	Mahadevamma	52	F	5675	Axillary lymph node	general deterioration ,weight loss
23	Komarappa	70	M	5678	cervical Lymph node	cough,breathlessness,change in voice

Sl.No	Patient name	Age	Sex	IP/OP No	FNAC site	Clinical correlation
24	Ramu Bandivaddar	50	M	6787	Submandibular lymph node	cough,breathlessness,change in voice
25	Gangabai Natikar	70	F	6212	Inguinal lymphnode	swelling in inguinal region
26	Rachappa	55	M	6231	cervical Lymph node	cough,breathlessness,change in voice
27	sudramappa	76	M	4287	Postauricular lymphnode	cough,breathlessness,change in voice
28	Bhimappa	70	M	4682	cervical Lymph node	cough,breathlessness,change in voice
29	Kheeru	51	M	5172	cervical Lymph node	cough,breathlessness,change in voice
30	Krishna	65	M	6382	Postauricular lymphnode	swelling in the neck
31	Siddappa	78	M	5139	cervical Lymph node	general deterioration ,weight loss
32	Putlibai	58	F	2739	USG guided omentum	weight loss and pain abdomen
33	Dundabai	65	F	24536	Ascitic Fluid	Distension of abdomen
34	Dundappa Aewati	60	M	9876	Pericardial lymph node	cough , breathlessness
35	Krishnappa.S	70	M	9123	cervical Lymph node	cough,breathlessness,change in voice
36	Dyavamma	62	F	9231	Pleural fluid	cough , breathlessness
37	Laxmanna	60	M	9234	cervical Lymph node	general deterioration ,weight loss
38	Shivappa patil	76	M	9432	Jugulodigastric lymphnode	general deterioration ,weight loss
39	Padmavati Patil	62	F	6534	supraclavicular lymph node	general deterioration ,weight loss
40	Mahadevi	55	F	7654	cervical Lymph node	general deterioration ,weight loss
41	Rudrappa	46	M	4673	Pleural fluid	cough , breathlessness
42	Sharanappa	50	M	25346	Pleural fluid	cough , breathlessness
43	Ramesh Pyati	48	M	6435	cervical Lymph node	cough,breathlessness,change in voice
44	Danamma Maranur	60	F	29873	USG guided omentum	pain abdomen, weight loss
45	Hanumantaraya	60	M	5463	cervical Lymph node	cough,breathlessness,change in voice
46	Basappa	56	M	4676	cervical Lymph node	cough,breathlessness,change in voice
47	Channareddy	65	M	5364	cervical Lymph node	cough,breathlessness,change in voice
48	Renukabai	60	F	3452	Axillary lymph node	general deterioration ,weight loss

Sl.No	Patient name	Age	Sex	IP/OP No	FNAC site	Clinical correlation
49	Rajshekar	56	M	3444	cervical Lymph node	cough,breathlessness,change in voice
50	madamma	70	F	2683	Axillary lymph node	general deterioration ,weight loss
51	Dyamavva	62	F	4825	cervical Lymph node	cough,breathlessness,change in voice
52	M.M.Katti	59	M	5132	cervical Lymph node	swelling in the neck
53	Basanna	65	M	3894	cervical Lymph node	cough,breathlessness,change in voice
54	Sulasha Koujalagi	75	F	3365	Axillary lymph node	general deterioration ,weight loss
55	Lagumappa	62	M	4427	cervical Lymph node	cough,breathlessness,change in voice
56	Hanumavva	56	F	2351	Ascitic Fluid	Abdominal distension
57	kallappa	58	M	5421	Jugulodigastric lymphnode	general deterioration ,weight loss
58	Noor Jahaan	60	F	3980	Ascitic Fluid	Distension of abdomen
59	Mahadevappa	54	M	1627	cervical Lymph node	cough , breathlessness
60	Shivalingamma	59	F	1872	supraclavicular lymph node	general deterioration ,weight loss
61	Haji	60	M	1982	cervical Lymph node	difficuty in swallowing,weight loss
62	Neelakantappa	40	M	1092	Chest wall swelling	weight loss
63	Mahadevi	50	F	2793	Axillary lymph node	general deterioration ,weight loss
64	Sanganna	50	M	2903	cervical Lymph node	general deterioration ,weight loss
65	Shivaleelamma	60	F	2789	Gluteal region swelling	weight loss
66	Hanumavva	55	F	3780	supraclavicular lymph node	general deterioration ,weight loss
67	Yallamma	60	F	4788	USG guided omentum	weight loss and pain abdomen
68	Shantabai	80	F	4563	supraclavicular lymph node	general deterioration ,weight loss
69	Shantamma	50	F	3721	USG guided omentum	weight loss and pain abdomen

Sl.No	Patient name	Age	Sex	IP/OP No	FNAC site	Clinical correlation
70	Mysunsaab	60	M	4289	cervical Lymph node	cough,breathlessness,change in voice
71	Yallappa	59	M	56281	Chest wall swelling	weight loss
72	Neelamma	50	F	5321	Ascitic Fluid	Abdominal distension
73	Hanumantappa	64	M	4276	USG guided omentum	weight loss
74	Gangawwa	62	F	3726	Axillary lymph node	general deterioration ,weight loss
75	Gurubai	45	F	3528	Ascitic Fluid	Abdominal distension
76	chand Bi	62	F	3240	Axillary lymph node	general deterioration ,weight loss
77	Bashasaab	55	M	2580	USG guided omentum	pain abdomen and dyspepsia
78	Basappa	60	M	3690	cervical Lymph node	general deterioration ,weight loss
79	Rachawwa	50	F	4168	Ascitic Fluid	Abdominal distension
80	Renukabai	60	F	3692	Ascitic Fluid	Abdominal distension
81	Reshmabegum	65	F	3628	Ascitic Fluid	Abdominal distension
82	Mahantappa	59	M	4271	cervical Lymph node	cough,breathlessness,change in voice
83	Basavva	68	F	2791	Ascitic Fluid	Abdominal distension
84	Putlibai Chavan	60	F	3692	Inguinal lymphnode	weight loss
85	Shivlingappa	60	M	5632	Right jugular lymphnode	cough,breathlessness,change in voice
86	Suresh	36	M	2681	Chest wall swelling	weight loss
87	Padmavati Patil	52	F	3792	Axillary lymph node	general deterioration ,weight loss
88	Saabu	60	M	3189	Submandibular lymph node	weight loss
89	Laalbee	70	M	3681	cervical Lymph node	general deterioration
90	Basavrajappa	50	M	1429	cervical Lymph node	cough,breathlessness,change in voice
91	Sidramappa	60	M	1593	cervical Lymph node	weight loss
92	Bhagamma Ajor	75	F	1490	cervical Lymph node	cough,breathlessness,change in voice
93	Subhash	55	M	2671	Submandibular lymph node	weight loss

Sl.No	Patient name	Age	Sex	IP/OP No	FNAC site	Clinical correlation
94	Gurubasamma	62	F	3762	Ascitic Fluid	weight loss and pain abdomen
95	Sangavva	65	F	3809	Ascitic Fluid	Abdominal distension
96	shivanandappa	48	M	4178	cervical Lymph node	weight loss
97	Parvati	64	F	3892	Ascitic Fluid	Abdominal distension
98	Huligawwa	55	F	4185	supraclavicular lymph node	general deterioration ,weight loss
99	madamma	55	F	48720	Axillary lymph node	general deterioration ,weight loss
100	Ramachandrappa	65	M	3790	cervical Lymph node	cough,breathlessness,change in voice

Radiology and other investigation	Primary on cytology	Primary on histopathology n=40
mammography	Carcinoma Breast	Carcinoma Breast
CT Thorax	carcinoma Lung	
Indirect laryngoscopy	Carcinoma Nasopharynx	Carcinoma Nasopharynx
mammography	Carcinoma breast	
Indirect laryngoscopy	Carcinoma Nasopharynx	Carcinoma Nasopharynx
CT abdomen and pelvis	Carcinoma Ovary	Carcinoma Ovary
mammography	Breast carcinoma	
-	poorly diff Ca from female genital tract	Small cell carcinoma cervix
mammography	Breast Carcinoma	
Indirect laryngoscopy	Carcinoma nasopharynx	Carcinoma Nasopharynx
CT abdomen and pelvis	Carcinoma ovary	Carcinoma Ovary
Indirect laryngoscopy	Carcinoma Nasopharynx	Carcinoma Nasopharynx
CT abdomen and pelvis,AFP	GIT/ gall bladder	Hepatocellular carcinoma
CT Thorax	Carcinoma lung	Carcinoma lung
Indirect laryngoscopy	Carcinoma Nasopharynx	
CT abdomen and pelvis	Carcinoma Ovary	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Indirect laryngoscopy	Carcinoma Nasopharynx	
-	Anaplastic ca thyroid	
Indirect laryngoscopy	Carcinoma Nasopharynx	Carcinoma Nasopharynx
CT abdomen and pelvis	Carcinoma Ovary	Carcinoma Ovary
-	Carcinoma Breast	
Indirect laryngoscopy	carcinoma larynx	carcinoma larynx

Radiology and other investigation	Primary on cytology	Primary on histopathology n=40
Indirect laryngoscopy	Carcinoma Nasopharynx	
-	Malignant melanoma	Malignant melanoma
Indirect laryngoscopy	Carcinoma Nasopharynx	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Indirect laryngoscopy	Carcinoma Nasopharynx	
-	Parotid gland tumor	
-	Carcinoma Tongue	Carcinoma Tongue
Upper GI endoscopy	Carcinoma stomach	Carcinoma stomach
CT abdomen and pelvis	Carcinoma Ovary	Carcinoma Ovary
CT Thorax	Carcinoma lung	Carcinoma lung
Indirect laryngoscopy	Carcinoma larynx	Carcinoma larynx
-	Carcinoma Breast	
-	Carcinoma Tongue	
-	Carcinoma Tongue	
-	Carcinoma Breast	Carcinoma Breast
mammography	Carcinoma Breast	Carcinoma Breast
CT Thorax	Carcinoma lung	
-	carcinoma lung	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Colonoscopy	GIT	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Indirect laryngoscopy	Carcinoma Nasopharynx	
-	Carcinoma Breast	Carcinoma Breast

Radiology and other investigation	Primary on cytology	Primary on histopathology n=40
Indirect laryngoscopy	Carcinoma Nasopharynx	
-	Carcinoma Breast	
Indirect laryngoscopy	Carcinoma Nasopharynx	
-	unknown	unknown
-	mets poorly diff ca from larynx	Lymphoma
mammography	Carcinoma Breast	Carcinoma Breast
-	metastatic poorly diff ca from nasopharynx	Lymphoma
CT abdomen and pelvis	Carcinoma Ovary	
-	Carcinoma Tongue	Carcinoma Tongue
CT abdomen and pelvis	Carcinoma Ovary	Carcinoma Ovary
-	metastatic poorly diff ca from nasopharynx	Lymphoma
-	Carcinoma Breast	Carcinoma Breast
Indirect laryngoscopy	ca oropharynx	
-	mets poorly diff ca	
-	Carcinoma Breast	
-	Carcinoma Tongue	
-	unknown	unknown
mammography	Carcinoma Breast	Carcinoma Breast
CT abdomen and pelvis	Carcinoma Ovary	Carcinoma Ovary
mammography	Carcinoma Breast	
CT abdomen and pelvis	Carcinoma Ovary	Carcinoma Ovary

Radiology and other investigation	Primary on cytology	Primary on histopathology n=40
Indirect laryngoscopy	Carcinoma Nasopharynx	
CT abdomen	mets hepatocellular ca	
Ultrasound abdomen and pelvis	Carcinoma Ovary	
Upper GI endoscopy	carcinoma stomach	
-	Carcinoma Breast	Carcinoma Breast
CT abdomen and pelvis	Carcinoma Ovary	
-	Carcinoma Breast	Carcinoma Breast
Upper GI endoscopy	carcinoma stomach	carcinoma stomach
-	Carcinoma Tongue	Carcinoma Tongue
CT abdomen and pelvis	Carcinoma Ovary	
CT abdomen and pelvis	Carcinoma Ovary	
Ultrasound abdomen and pelvis	Carcinoma Ovary	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Ultrasound abdomen and pelvis	Carcinoma Ovary	
-	SCC Skin of leg	
Indirect laryngoscopy	Carcinoma Nasopharynx	
-	mets poorly diff ca	
-	Carcinoma Breast	Carcinoma Breast
-	unknown	unknown
-	Carcinoma Tongue	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Endoscopy	Carcinoma oesophagus	
Indirect laryngoscopy	Carcinoma Nasopharynx	
Endoscopy	Carcinoma oesophagus	

Radiology and other investigation	Primary on cytology	Primary on histopathology n=40
Ultrasound abdomen and pelvis	Carcinoma Ovary	
Ultrasound abdomen and pelvis	Carcinoma Ovary	
Endoscopy	Carcinoma oesophagus	
Ultrasound abdomen and pelvis	Carcinoma Ovary	
mammography	Carcinoma Breast	
-	Carcinoma Breast	
Indirect laryngoscopy	Carcinoma Nasopharynx	