A CLINICOPATHOLOGICAL STUDY OF OVARIAN TUMORS AND THE ROLE OF IMMUNOHISTOCHEMICAL PROLIFERATIVE MARKER Ki 67

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Department of Pathology,
Madurai Medical College and
Government Rajaji Hospital,
Madurai.

CERTIFICATE

This is to certify that the dissertation entitled " A CLINICOPATHOLOGICAL STUDY OF OVARIAN TUMORS AND THE ROLE OF IMMUNOHISTOCHEMICAL PROLIFERATIVE MARKER Ki 67 " submitted by Dr. R.Lavanya to the Faculty of Pathology, The Tamilnadu Dr. M.G.R. Medical university, Chennai in partial fulfilment of the requirement for the award of M.D. Degree in Pathology is a bonafide work carried out by her during the period 2009 - 2011 under my direct supervision and guidance.

Place: Madurai

Date:

Professor and Head,
Department of Pathology,
Madurai Medical College,
Madurai.

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CONTENTS

Introduction

INTRODUCTION

Like the everyform of cancer, early detection is what all about.. It can be prevented with testing and it can be beaten if caught early!

-Rod Stewart

The ovarian tumors are not a single entity, but a complex wide spectrum of neoplasms involving a variety of histological tissues, ranging from epithelial tissues, connective tissues, specialized hormone secreting cells to germinal and embryonal cells.[40]

The ovary is complex in its embryology, histology, steroidogenesis and has potential to develop malignancy[40]. Of all the gynecologic cancers, the ovarian malignancies represent the greatest challenge because the ovary gives rise to greater and larger variety of tumors than any other organ.A female's risk at birth of having ovarian tumor sometime in her life is 6-7%,of having ovarian cancer is almost 1.5% and dying from ovarian cancer is 1%[49]

The incidence of ovarian cancer ranks below only to the carcinoma of cervix.The ovarian tumors constitute about 5% of gynaecological admissions. About 75% of them are benign and 25% are malignant. In India, ovarian tumors account for 8% of all gynecological malignancies[43]

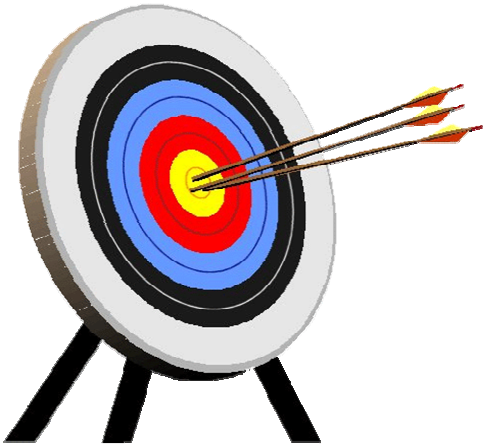
Different tumors tend to involve different age groups.They occur in perimenopausal and postmenopausal women, infrequently in children also. The risk of developing ovarian tumor peaks in the fifth decade of life[88.] The

ovarian tumors pose a special diagnostic and management problem in the postmenopausal women because of their late presentation , high risk of malignancy and poor prognostic outcome and in children pose a great challenge to the clinicians owing to the need of conservation of reproductive, endocrinal and menstrual function on one hand and malignant potential on the other.

Apart from primary tumors, ovaries are frequent site for metastatic involvement from organs like stomach, colon and breast

Signs and symptoms of ovarian cancer are frequently absent or subtle early on , or persist for several months before being recognized and diagnosed. More than 50% of patients are diagnosed in the advanced stage of the disease.

This study is undertaken to analyze the histopathological spectrum and clinical features and to emphasize the importance of immunohistochemical markers in accurate diagnosis and to investigate the biological significance of Ki 67 antigen expression in benign, borderline and malignant ovarian tumors.



Aims & objectives

AIMS AND OBJECTIVES

1. To study the incidence of ovarian tumors in our institution during 2009-2011.

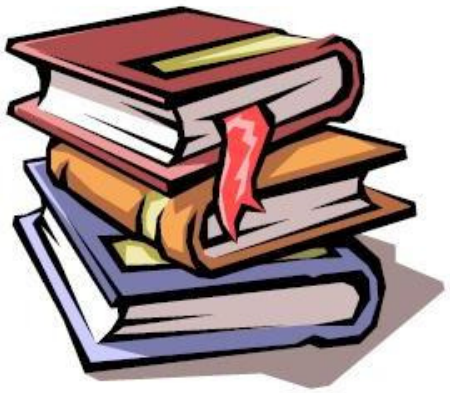
2. To study the age related occurrence and clinical presentation of various types of ovarian tumors.

3. To classify ovarian tumors based on gross and histopathological features and categorizing them into benign, borderline and malignant tumors.

4. To apply special stains like Reticulin, Periodic Acid Stain (PAS) in selected cases for differentiation of tumors.

5. Application of immunohistochemical markers in selected cases for final diagnosis.

6. To analyze the role of immunohistochemical proliferative marker Ki 67 in selected cases.



Review of literature

REVIEW OF LITERATURE

Historical aspects

A historical account of the ovary should begin with Herophilus of Chalcedon, a great anatomist of Alexandrian school of the fourth century B.C "Hemophilus must be regarded as the first anatomist to describe the mammalian ovaries. He called it "female testis".

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FEMALE GENITAL TRACT

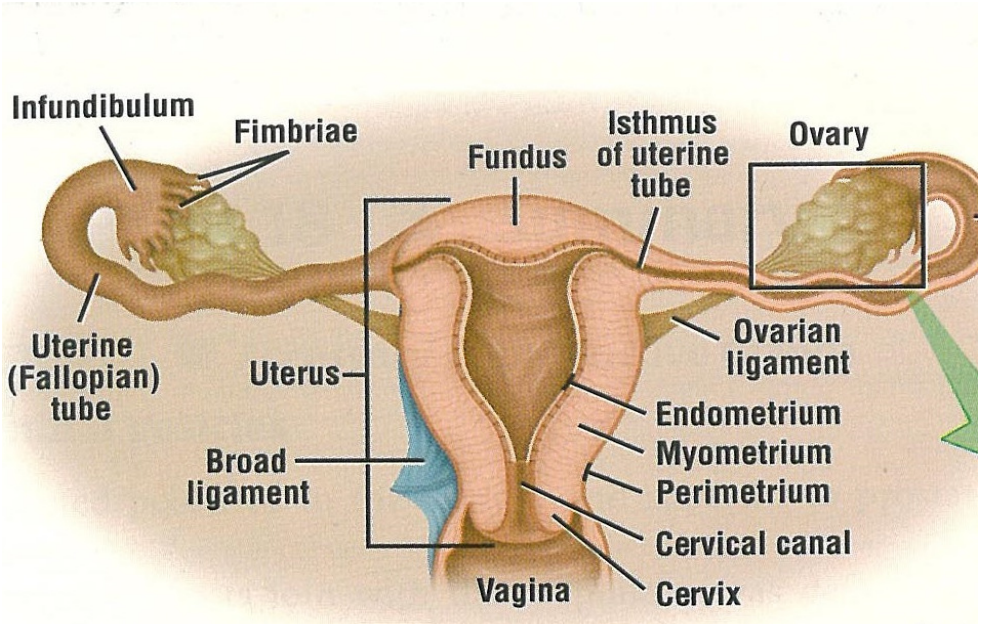


Fig.1

ANATOMY OF OVARY

Ovary develops from the genital ridge by 5th week of gestation and oogonia develops by mid gestation.

The ovaries which are the site of oogenesis are paired organs lying on either side of the uterus adjacent to the lateral wall of the pelvis(Fig1).[100]

During active reproductive life, ovaries measure about 4x2.5x1cm in dimension. The ovary is divided into cortex and medulla. Follicles in varying stages of maturation are found within the outer cortex[89].These are numerous in infants and young adults, where they are estimated to total about 4,00,000 but the number progressively decreases with age and follicles disappear by menopause. [105]

With each menstrual cycle, one follicle develops into a graffian follicle, which is transformed into a corpus luteum following ovulation.

The medulla of the ovary consists a loosely arranged mesenchymal tissue and contains remants of both wolffian duct (rete ovarii) and small clusters of round to polygonal, epithelioid cells around vessels and nesves. The ovaries are also endocrine organs producing the hormones oestrogen and progesterone.

HISTOLOGY

Numerous ovarian follicles are seen in various stages of development in the stroma of cortex. Primordial follicles contain the immature small primary oocyte which gradually increases in size and develop into primary, secondary and mature follicles(Fig 2).

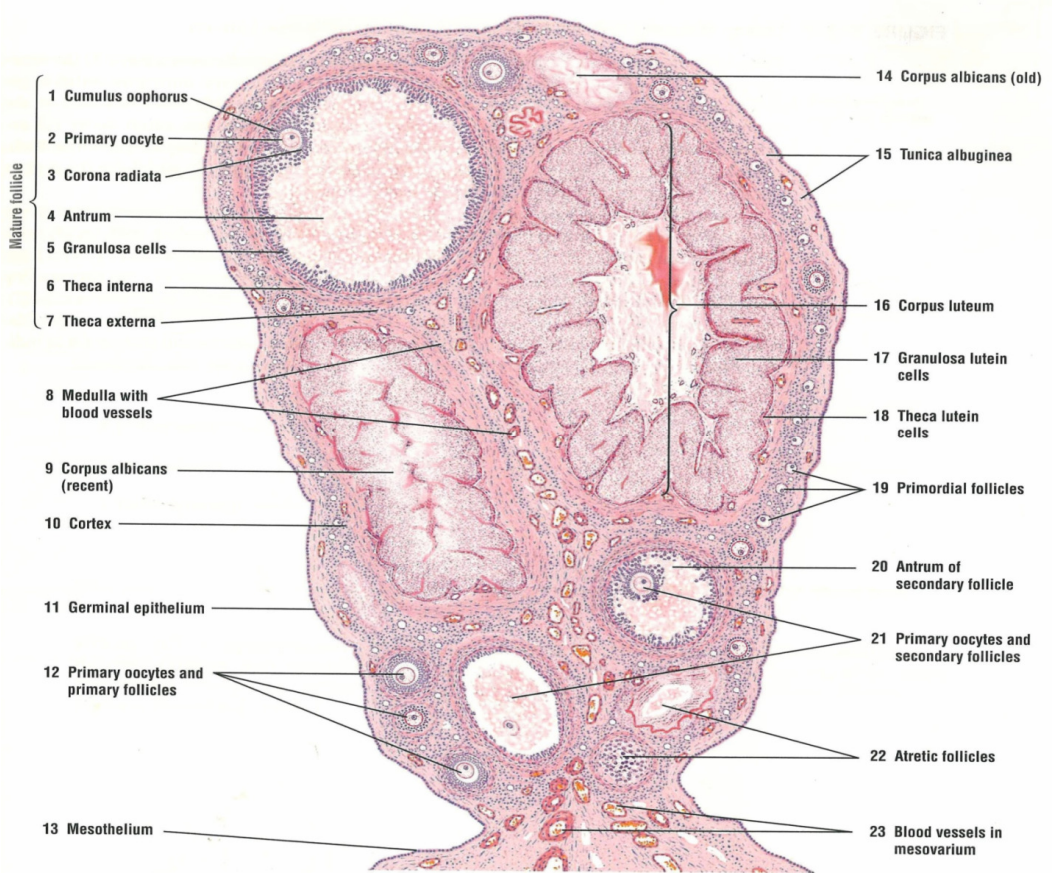


Fig 2

Follicles with antral cavities are called secondary follicles which exhibit a granulosa cell layer, a theca interna and an outer theca externa.[23]The largest ovarian follicle is the mature graffian follicle which ultimately ruptures and the ovum is shed from the ovary(ovulation). After ovulation the remaining part of the follicle undergoes changes that convert it into Corpus Luteum[23.] If the ovum is not fertilized, the corpus luteum,degenerates into corpus albicans,and if fertilized it persists and secretes progesterone .

The series of changes that begin with the formation of an ovarian follicle and end with the degeneration of the Corpus Luteum constitutes the ovarian cycle.

The main function of the ovary is to produce ova to implant after fertilization in the endometrium, and as an endocrine gland in the development of secondary sexual characters . Thus the ovary is always in dynamic state[85.]Ovaries serve as the main organ for maintaining the female fertility and at the same time, site of origin of the most complex as well as lethal neoplasms.

OVARIAN CANCER

Most primary ovarian neoplasms are derived from one of these components

1.Coelomic surface epithelium covering ovary.

2. The ovarian stroma , sex cord or both.

3. The germ cell.

CLINICAL FEATURES

Signs and symptoms of ovarian cancer are frequently absent early on and when they exist they may be subtle[32].Symptoms such as abdominal pain, mass, ascites, urinary urgency, constipation, ,abnormal vaginal bleeding, weight loss can occur[4]. Functionally active ovarian tumors in young girls(Juvenile granulosa cell tumors) may produce precocious puberty. Occasionally they produce androgens, masculinizing the patient.

DIAGNOSIS OF OVARIAN CANCER

Histopathology

Histopathology is the most common diagnostic method used for the diagnosis of ovarian tumors. Tissue samples from ovariotomy specimens are fixed in 10% buffered neutral formalin and then processed. Sections made with the help of microtomes are routinely stained with hematoxylin and eosin andthen studied microscopically in detail.. Ascitic fluid cytology is helpful in the diagnosis of metastasis in advanced stage of ovarian tumors.

SPECIAL STAINS:

The most commonly used stains are PAS and Reticulin stain. PAS stain is an extremely useful and aesthetically pleasing technique to differentiate mucinous carcinoma from krukenberg tumor. Mucinous carcinoma of ovary shows PAS positive mucin pools, and krukenberg tumor show intracellular PAS positivity .Reticulin stain is useful to differentiate granulosa cell tumor from fibrothecoma. It shows fibrils surrounding the nests and large aggregates of granulosa cell tumor whereas in Fibrothecoma, it highlights an investment of individual cells by fibrils.

IMMUNOHISTOCHEMISTRY:

Diagnostic IHC markers for epithelial ovarian tumors are Epithelial membrane antigen(EMA) and Cytokeratins, for sex cord stromal tumors are Inhibin, vimentin,calretinin,CD 99, Melan A,WT 1 and for Germ Cell Tumors the markers are Placental Alkaline Phosphatase (PLAP), Alpha Feto Protein (AFP), Human Chorionic Gonadotrophin (HCG).

Role of anticytokeratin in distinguishing primary and secondary ovarian adenocarcinoma

Keratins are intermediate filament proteins that contribute to the cytoplasm of epithelial cells. Human cytokeratin have been classified according to their molecular weight and isoelectric pH.20 epithelial cytokeratin polypeptides have been identified. Some of these have specific tissue distribution that can be exploited for the differential diagnosis of tumor.

CK7(+) / CK20 (-) :In all primary epithelial ovarian neoplasms,[18]

CK 7(-) / CK20(+) : Secondary (metastatic) tumors except in intestinal type of mucinous carcinoma of ovary.[18]

PROLIFERATIVE MARKERS:

The number of mitotic figures correlated with cancer stage and gradeas well as with their progression. Immunohistochemical proliferative markers like Ki 67 , proliferative cell nuclear antigen (PCNA) , AgNOR count are used to assess mitotic activity.[17] The number of mitotic figures increase progressively from benign to malignant tumors .

Ki 67 protein is a cellular marker for nuclear proliferation which is present in all phases of cell cycle (G1S,G2M) and is absent in resting phase (G0). Ki 67 is an excellent marker to determine the growth fraction of a given cell population. The determination of growth fraction using Ki 67 index is a simple method and has long been shown to have a prognostic value in a variety of malignancies like CNS tumors, Lymphoproliferative diseases, connective tissue tumors & breast tumors[69]. The fraction of Ki 67 positive tumor cells (Ki 67 labelling index) is often correlated with clinical course of cancer.

Tumor markers in ovarian cancer

Tumor markers are biochemical indicators of presence of tumor. The term usually refers to a molecule that can be detected in plasma or other body fluids [56]

None of the tumor markers for ovarian carcinoma is 100% specific or 100% sensitive.

a) Tumor markers for epithelial ovarian cancer

Approximately 90% of ovarian cancers are coelomic epithelial carcinomas and contain a coelomic epithelium related glycoprotein, designated Cancer Antigen 125. This can be recognized in most serous, endometrial, and clear cell ovarian carcinomas.

The other serological tumor markers for epithelial ovarian cancer include carcinoembryonic antigen (CEA), CA 15-3, CA 19-9, LASA (lipid associated safe acid) and tissue peptide antigen.

b)Tumor markers in non-epithelial ovarian cancer:

Alphafetoprotein and human beta HCG are the best known tumor markers in clinical practice and aid in treatment, follow-up of ovarian germ cell tumors[42].Serum placental alkaline phosphatase and lactate dehydrogenase are also sometimes useful as markers of dysgerminoma.

FLOW CYTOMETRY

The application of flow cytometry to ovarian tumor pathology may be considered principally in term of measuring the ploidy status of tumor. Most borderline tumors are diploid & if aneuploid it indicates progression.well

differentiated tumors are diploid whereas poorly differentiated tumors are aneuploid and having worse prognosis.

CYTOGENETICS:

It has been shown that p53 gene is mutated in 30-80% of ovarian carcinomas. p53 overexpression is associated with increased probability of relapse and decreased survival. BRCA 1, and BRCA 2 are expressed in hereditary tumors. Teratomas show chromosomal aberrations.

REVIEW OF INDIVIDUAL OVARIAN TUMORS

I) SURFACE EPITHELIAL TUMORS

In 1870, Heinrich waldeyer wrote a paper on epithelial ovarian tumors.He was among the first to suggest a histogenesis similar to that which is now widely accepted for the most common form of ovarian tumor**.** These tumors are derived from the epithelium that normally lines the outer aspect of ovary, referred to as surface coelomic or germinal epithelium and the adjacent ovarian stroma [85]

These tumors comprise 58% of all ovarian neoplasms and more than 90% of malignant tumors. They are classified into benign, borderline and malignant. Epithelial neoplasm may occur in young women and are rare before menarche. This incidence increase especially after the age of 55 years.

A)SEROUS TUMORS:

Constitute 30% of all ovarian tumors, making them the single most common group. About 50-70% are benign, 10-15% are borderline, while 25-35% are frankly malignant. About 30-50% are bilateral[16]

Benign Serous Tumors:

Commonest tumor making up about ¼ th of all ovarian tumors, occurs between 10-60years of age, average being 45 years. Majority of them are unilateral and cystic. These include serous cystadenomas, serous cystadenofibroma, serous adenofibroma and serous surface papillomas.

Gross:

Cystic, usually have a smooth pale yellow (or) gray white exterior with a prominent vascular pattern. It can be either unilocular or multilocular. They contain clear, thin serous fluid.

Microscopy:

Cyst wall and papillae lined by single layer of a mixture of tall ciliated and non-ciliated columnar cells with elongated oval nuclei interspersed with a variable number of peg shaped cells and clear cells resembling the normal tubal epithelium. Psammoma bodies are calcific spherules , seen in 15% of cases[82]

***Borderline Serous Tumors*:**

Howard C Taylor expanded on the concept of tumors intermediate between benign & malignant. He wrote a paper on borderline ovarian tumors.

These tumors are large usually multilocular , bilateral in 35-40% of cases. Coarse papillary excrescences arise from the cyst lining [17] . Most common in fourth and fifth decades with average age of 46 years.

Microscopy:

The characteristic microscopic features of borderline serous tumors are Hierarchial branching papillary pattern of growth with variable cytologic atypia, Cellular stratification greater than 3 cells. Frank stromal invasion is absent,Stromal microinvasion (<3mm) is occasionally identified in a borderline serous tumor.[17]

***Malignant serous tumors*:**

Occurs in mean age 56 years, bilateral–in 2/3 of cases [82]

Gross:

These are large, often bilateral neoplasm in which there is a mixture of cystic, papillary and solid growth patterns. The solid areas are tan or white and contain foci of haemorrhage & necrosis [17]

Microscopy:

These tumors diffusely infiltrate a fibrotic stroma. Papillary growth is usually present atleast focally. Tumor cells are arranged in solid nests and sheets. The papillae lined by stratified low columnar cells, show marked nuclear atypia and frequent mitotic figures in high grade tumors. The stroma may be scanty or desmoplastic with foci of necrosis.

B)MUCINOUS TUMORS:

Mucinous tumors account for 12-15% of all ovarian tumors of which 75% to 85% are benign, 10-15% borderline and remaining are frankly malignant. They attain largest size among ovarian neoplasms.

Benign mucinous tumors:

Gross: Mucinous cynadenomas are cystic & generally unilateral. The average diameter is about 10cm. Cut surface reveals unilocular or multilocular mucin filled cysts of varying sizes [17]

Microscopy:

Characterized by a lining of tall columnar epithelial cells with apical mucin and the absence of cilia akin to benign cervical or intestinal epithelia.

Borderline mucinous tumors:

Gross:

These are large, with an average diameter of about 15cm. Most are multilocular, filled with mucin.

Microscopy:

Two types:

1.INTESTINAL TYPE : Most common type.

Crowding of complex glands, papillae supported by thin cores of fibrovascular connective tissue. Goblet cells are conspicuous, focal stratification of the cells into two or three layers. The tumor cells have round to oval vesicular nuclei with mild to moderate atypia, nucleoli may be prominent & occasional mitotic figures seen.[17]

2.ENDOCERVICAL LIKE :

These tumors omprise 5-15% of borderline mucinous tumors. Branching papillary growth pattern lined by columnar mucinous endocervical like cells and a variable number of cells with eosinophilic cytoplasm. Goblet cells are absent, mitotic figures infrequent, minimal nuclear atypia present[83]

***Malignant mucinous tumors*:**

Mucinous carcinoma are less frequent than their serous counterparts.They differ from borderline tumors having evidence of ovarian stromal invasion.

Gross:

Large, multilocular cystic tumor averaging 15-20cm in diameter.Firm, fleshy, white or tan solid areas,often with foci of haemorrhage or necrosis . <10% bilateral[11]

Microscopy:

The glands and cysts are crossed and complex with irregular infoldings and protrusions into the surrounding stroma. Intestinal type cells predominate. The cells are columnar, have eosinophilic cytoplasm, and stratify into two or more layers. The nuclei are enlarged and vesicular with prominent nucleoli.Many typical and atypical mitotic figures, goblet cells and argyrophilic cells may be present.

Pseudomyxoma peritonei :

Occurs in tumors of intestinal type. It is seen in borderline or malignant mucinous tumors, but can occur with large benign tumors also. The cells produce mucin which fills the abdominal cavity.

C)ENDOMETRIOID TUMORS –

These tumors comprise 2-4% of all ovarian tumors. These tumors have an epithelial component that resembles proliferative hyperplastic or malignant endometrium.Occur most commonly in fifth and sixth decades[47] Benign & borderline tumors are rare.Endometroid Carcinomaaccount for about 20% of all ovarian cancers.15-20% coexist with endometriosis.15-30% are accompanied by carcinoma of endometrium.

Gross:

Cystic and solid or completely solid tumor measuring 10-20cm diameter. Firm or soft , gray or tan with haemorrhage and necrosis . Only 10-20% are bilateral.

Microscopy:

The growth pattern is glandular, papillary or mixture of two. The glands are small and relatively uniform in size and shape. The degree of atypia, nuclear stratification and the extent to which the glands coalesce into foci of solid growth increase as grade increases.[11]

D) Clear Cell Tumors:

These tumors comprise 5% of all ovarian cancers, common in age group 40 - 70 years. Accompanied by both ovarian and pelvic endometriosis. More aggressive and more malignant than serous adenocarcinoma of ovary [70]

Gross :

These are unilateral and solid. They typically measure 10-15 cm in diameter. The cut surface is white gray or tan and contain small to medium sized cysts[11]

Microscopy:

Tubules and cysts are lined by cuboidal or hobnail cells with clear or eosniophilic cytoplasm. These cells are irregularly distributed in a fibrous stroma.

The epithelium is stratified or tufted or grows as small circumscribed nests. The presence of mild to moderate nuclear atypia and scattered mitotic figures (usually <1 per HPF) differentiates borderline clear cell tumors from a benign one. The absence of stromal invasion differentiates them from clear cell carcinoma.

E) TRANSITIONAL CELL TUMORS:

Ovarian tumors composed of epithelial elements histologically resembling urothelium and its neoplasms[58]. Comprise 1– 2% of all ovarian neoplasms. It comprises Brenner and Non Brenner type.

1)Brenner Tumor

In 1907C Fritz Brenner was first to describe the cases of Brenner tumor which now bears his name.

Approximately 95% of Brenner tumors are diagnosed in women between ages of 30& 70 yrs. It usually coexists with mucinous cystadenoma.[82]. Most Brenner tumors are benign,but borderline and malignant Brenner have been reported.

Gross:

Benign tumors are circumscribed, firm, pale yellow or gray white, solid fibrous or cystic tumors. Usually unilateral, average size 1-2 cm[86]

Microscopy:

The fibrous stroma is marked by sharply demarcated nests of epithelial cells resembling the transitional epithelial cells of urinary tract often with mucinous glands in the centre. The nuclei are round or oval and have small nucleoli.A longitudinal nuclear groove is characteristic.

2) Transitional cell carcinoma (Non-Brenner type)

Gross :

Transitional cell carcinoma is a partly cystic tumor that averages 10 to 15cm in diameter [11]

Microscopy:

It is similar in appearance to malignant Brenner tumor except that Benign proliferating Brenner tumor is not identified and transitional cell carcinoma pattern must predominate (75%)[11]

II)SEX – CORD – STROMAL TUMORS

Neoplasms derived from the sex cords or ovarian mesenchyme comprise 5-12% of all ovarian neoplasms.

A)GRANULOSA CELL TUMORS:

The tumor shows differentiation towards follicular granulosa cells[101] and comprise 1-2% of all ovarian tumors.These tumors secrete oestrogen which stimulates the endometrium to proliferate. The presentation may be post menopausal bleeding, menorrhagia, metrorrhagia precocious puberty[27]. It is associated with endometrial hyperplasia & endometrial carcinoma, cystic disease of breast.It has small(5-25%) but distinct hazard of malignancy(recurrence,extension)

Two types:

Adult type occurs mainly in menopausal women and Juvenile type that occurs mainly in children[101]

a)Adult Granulosa Cell tumor:

In 1914,Von Werdt proposed the term " Granulosa cell tumor".

Gross:

These range from few millimeter to 30 cm in diameter. Entirely solid but most are partly cystic. The solid portions are pink, tan, brown, light yellow and vary from soft to firm in consistency[2].

Microscopy

The tumor cell resemble normal granulosa cells. Longitudinal folds or grooves are present in many nuclei giving a characteristic coffee bean appearance.

Several histologic patterns like follicular, trabecular, insular, watered silk pattern have been described. Of these the microfollicular pattern is the most characteristic and are termed Call-exner bodies.[1]

b)Juvenile Granulosa Cell tumor:

The incidence of Juvenile Granulosa Cell tumor in children is <5%. Average age is 15 years. But it can occur at any age from infancy to old age but most arise in children[17]

The tumor consists of both cystic & solid areas. Macrofollicular, solid and cystic growth patterns are characteristic.Focal or extensive luteinization is a typical finding. The tumor cell nuclei lack grooves and contain conspicuous nucleoli.

B)FIBROMA – THECOMA GROUP[101]

1)Thecoma

They account for 7% of sex cord stromal neoplasms. The average age is between 50 and 55 years[27] .5% bilateral .

Thecoma is a benign, firm tumor that varies in size from 1 - 20cm in diameter. The cut surface is gray or tan, with extensive yellow areas. [17.]The tumor is composed of fascicles or sheets of spindle or ovoid cells.

2) Fibroma

It is the most common sex-cord stromal tumor accounting for 1-5% of ovarian tumor.Average age is 50 years or more. Meig's syndrome, in which ovarian fibroma is accompanied by ascites and hydrothorax.

Firm tumor with a smooth, lobulated surface. Size 1 - 10cm ,solid white or tan cut surface. Fibromas are composed of thin spindle cells growing in whorled and anastamosing bundles[101]. Mitotic figures are rare.

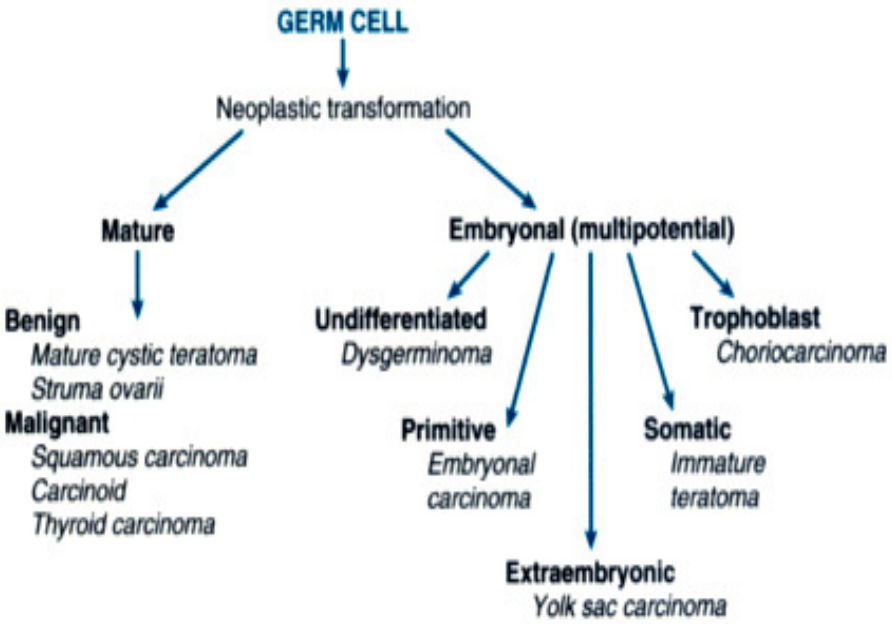
c)SERTOLI LEYDIG CELL TUMOR(ANDROBLASTOMA)

These tumors are seen in women of reproductive age, occurring unilaterally causing masculinization.Cut surface gray to golden yellow.

Microscopically well differentiated tumors show tubules composed of sertoli or leydig cells interspersed with stroma. The intermediate forms show only outlines of immature tubules & large eosinophilic leydig cells. Poorly differentiated tumors have a sarcomatous pattern with a disorderly disposition of epithelial cell cords.Leydig cells may be absent.

III)GERM CELL TUMORS

Germ cell tumors represent 15-20% of all ovarian tumors [33]. They are composed of cells derived from oocyte[46]. Most of these tumors are seen in children and young adults. Younger the patient, the more likely the germ cell tumor to be malignant.[57]



A)**Dysgerminoma:**

Mayer first applied the name Dysgerminoma in 1931 to a solid carcinomatous ovarian tumor histologically resembling testicular seminoma. It is the most common(50%) of all malignant germ cell tumors of the ovary[15].

Dysgerminoma is a large solid tumor usually more than 10cm in diameter, with convoluted outer surface. Usually unilateral, cut surface shows haemorrhage and necrosis in 50% of cases. [85].

The tumor is composed of large round to polygonal uniform cells with vesicular nuclei and prominent nucleoli, abundant clear to finely granular cytoplasm that contains glycogen and separated by thin fibrous septa which shows lymphocytic infiltration[85].

B)Yolk sac tumor(Endodermal sinus tumor):

Yolk sac tumor is rare but it is the second most common malignant tumor of germ cell origin [85]. Occurs in 2^{nd} and 3^{rd} decade.Prognosis is very poor.

Gross:

These are large, encapsulated, solid tumor with smooth and glistening external surface. The tumor has variegated cut surface.

Microscopy:

Yolk sac tumor shows variable microscopic appearance [31]. The festoon pattern containing pseudopapillary processes with central vessel (ie) Schiller Duval bodies described by Schiller. Other patterns are microcystic (reticular) , solid , polyvesicular vitelline pattern.

C) Embryonal carcinoma :

Embryonal carcinoma is seen more commonly in mixed germ cell tumors of ovary. Pure form is extremely rare. 5% of malignant germ cell tumors are of this category. Occurs in 2nd and 3rd decade of life.

Gross:

These tumors are large with smooth & glistening external surface and having variegated cut surface with extensive areas of haemorrhage and necrosis.

Microscopy:

These tumors are composed of solid sheets and nests of large primitive cells, syncytiotrophoblast like tumor cell and tumor giant cells are seen frequently. These are HCG positive immunohistochemically[85]. Prognosis is very poor.

D) Choriocarcinoma:

These tumors are more commonly of placental origin. Primary ovarian choriocarcinoma is exceedingly rare. It is divided into gestational type from placental origin and nongestational type from germ cell origin [30].Ovarian gestational choriocarcinoma can be primary or metastatic from uterine or tubal pregnancy. As the tumor is associated with high HCG levels, its diagnosis especially in young women is most often confused with an ectopic pregnancy [60,95]

Gross:

The tumor has smooth or nodular external surface. The cut surface shows variegated appearance, gray white with areas of haemorrhage and necrosis.

Microscopy:

The tumor shows admixture of cytotrophoblast and syncytiotrophoblast, the latter form villous like structures around the cytotrophoblast in a necrotic or haemorrhagic background [85].

Prognosis is poor. Gestational Choriocarcinoma has better prognosis & respond to chemotherapy in contrast to non – gestational counterpart.

E) Teratoma:

Willis (1960) had given a vivid description the genesis of teratomas. According to him teratomas are the tumors arising from foci of pluripotent,

embryonic tissue that escapes from the influence of the primary organizer during embryonic development.

Teratomas form the commonest group of germ cell tumors in the ovarian neoplasm. They constitute 25.86% of all ovarian tumors. Depending upon the nature of the tissue component [41],they are classified into mature and immature teratoma.

1.Mature cystic teratoma(Benign) :

These are the most common variety of germ cell tumors accounting for more than 95% of ovarian teratomas and 15-20% of neoplasm in general [94]

These are usually found in young women during the active reproductive years [103].

Gross:

They are unilateral in 88% of cases. Characteristically they are unilocular cysts containing greasy material composed of keratin, sebum and tuft of hair [85]. Within the wall, tooth structures and areas of calcification may be seen.

Microscopy:

Black well et al (1946) [9] found ectodermal derivatives in 100% of tumors, mesodermal derivatives in 93% and endodermal structure in 71% of cases. The tumor shows cyst lined by squamous epithelium in nearly all the cases with skin appendages and other elements like fat, cartilage, smooth

muscle and bone. Endodermal structures like bronchial & gastrointestinal epithelium are seen. Neural & thyroid tissue are also seen.

2.Immature teratoma:

These are rare tumors that differ from benign teratomas with component resembling embryonal and immature fetal tissue.Mean age of presentation is 18 yrs.Unilateral, large bulky with smooth external surface. Cut surface mostly solid with haemorrhage & necrosis. Microscopically varying amounts of immature epithelium, hair, cartilage, bone , calcification may be seen.Histological grading is done by assessing the amount of immature tissue and neuroepithelium.

3.Monodermal or specialized teratomas:

These specialized teratomas comprise a rare group ,of which struma ovarii and carcinoid are the most common. They are always unilateral. Struma ovarii is composed entirely of mature thyroid tissue. The ovarian carcinoid presumably arises from the intestinal epithelium in a teratoma.

Secondary malignancies in benign cystic teratoma are rare.Cutaneous adnexal neoplasms,benign salivary gland type tumors, meningioma, glomus tumor.Invasive squamous cell carcinoma is common and comprises 85%.Other tumors are basal cell carcinoma,melanoma,adenocarcinoma, sarcoma etc.

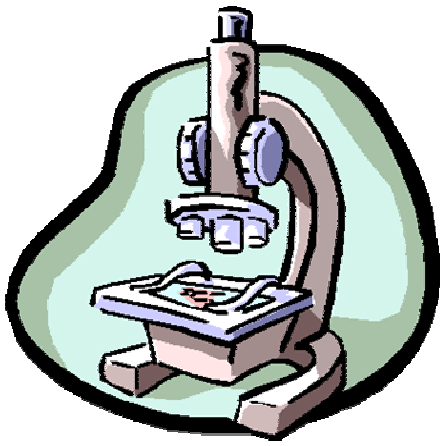
METASTATIC TUMORS

The most common metastatic tumors of the ovary are derived from tumors of mullerian origin:uterus, fallopian tube, contralateral ovary or pelvic peritoneum. The most common extra mullerian tumors metastatic to ovary are carcinoma of breast and gastrointestinal tract including colon, stomach, biliary tract and pancreas. Comprises 10% of all ovarian cancers[81].

The characteristic features of metastatic disease are bilateral presentation with smaller size than primary ovarian tumors, nodular growth pattern, surface involvement, infiltrative growth.

KRUKENBERG TUMOR:

A classical example of metastatic gastrointestinal neoplasia to the ovaries, characterized by bilateral metastases composed of mucin producing signet ring cells, most often of gastric origin.



Materials and Methods

MATERIAL AND METHODS

This prospective study is undertaken in the Department of Pathology, Madurai medical college, Madurai during the period 2009-2011.This study was conducted on 200 ovarian neoplasms (Ann.VI) out of 239 ovarian lesions received after exclusion of non-neoplastic lesions. This study was approved by the institutional ethical committee (Ann IV).

The tissue samples included in this study were 91 ovariotomy specimens and 109 hysterectomy with ovariotomy specimens received in buffered 10% neutral formalin from Government Rajaji Hospital, Madurai. A detailed history regarding clinical symptoms and signs were recorded and thorough gross examination in particular attention to laterality, size, consistency of the specimens were also done.(Ann I).

After adequate fixation, representative bits were taken. In cystic ovarian neoplasms, 4-5 bits were taken. In solid tumors, if <5cm, 3-4 bits were taken. If more than 5cm, 1 block per 1 cm of the tumors were taken across its greatest dimension, particularly if the appearance is variegated.

Tissue bits fixed in 10% buffered neutral formalin were processed in automated tissue processor. Sections were made manually with microtome of thickness 3-5 micrometer and routinely stained with hematoxylin and eosin stains. Special stains like Periodic Acid Schiff (PAS), Reticulin were done using standard procedures to study their different pattern of

expression in different tumors. Reticulin stain was done for all the Granulosa cell tumors (10 cases) and all Fibrothecomas (3 cases). PAS stain was done in all mucinous cystadenocarcinomas (8 cases) and all Krukenberg tumors (3cases).

(Ann II). These tumors were then tumors were classified according to WHO classification of ovarian tumors (Ann III).

Ki 67 protein is a cellular marker for nuclear proliferation which is present in all phases of cell cycle (G1S,G2M) and is absent in resting phase (G0).It is an excellent marker to determine the growth fraction of a given cell population. The fraction of Ki 67 positive tumor cells (Ki 67 labelling index) is often correlated with the clinical course of cancer.

Ki 67 immunohistochemical proliferative marker study using peroxidase-antiperoxidase technique (Ann II) was done in 24 selected cases which comprised benign ,borderline and malignant ovarian tumor.

Positive Ki 67 staining was observed as brown granular nuclear staining. For Ki 67 scoring the most positive area of the tumor was selected avoiding foci of inflammation. The number of positive nuclei is counted in 500 tumor cells in a high power field(x 400 magnification). The average of 3 counts over the same slide was taken and expressed as the percentage of Ki 67 positive cells in the tumor.

The expression of immunohistochemical markers like vimentin, inhibin, EMA , cytokeratin and chromogranin was studied in 10 ovarian tumors which were histopathologically diagnosed as Granulosa cell tumors.

Observation & results

OBSERVATION AND RESULTS

In the present study, a total of 7964 gynaecological specimens were received in the Department of Pathology, Madurai medical college, Madurai. Among them 882 cases were gynaecological malignancies including 239 ovarian lesions and in that after exclusion of non –neoplastic lesions , 200 were ovarian neoplasms constituting 2.5 %.

THE DISTRIBUTION OF INDIVIDUAL OVARIAN TUMORS:

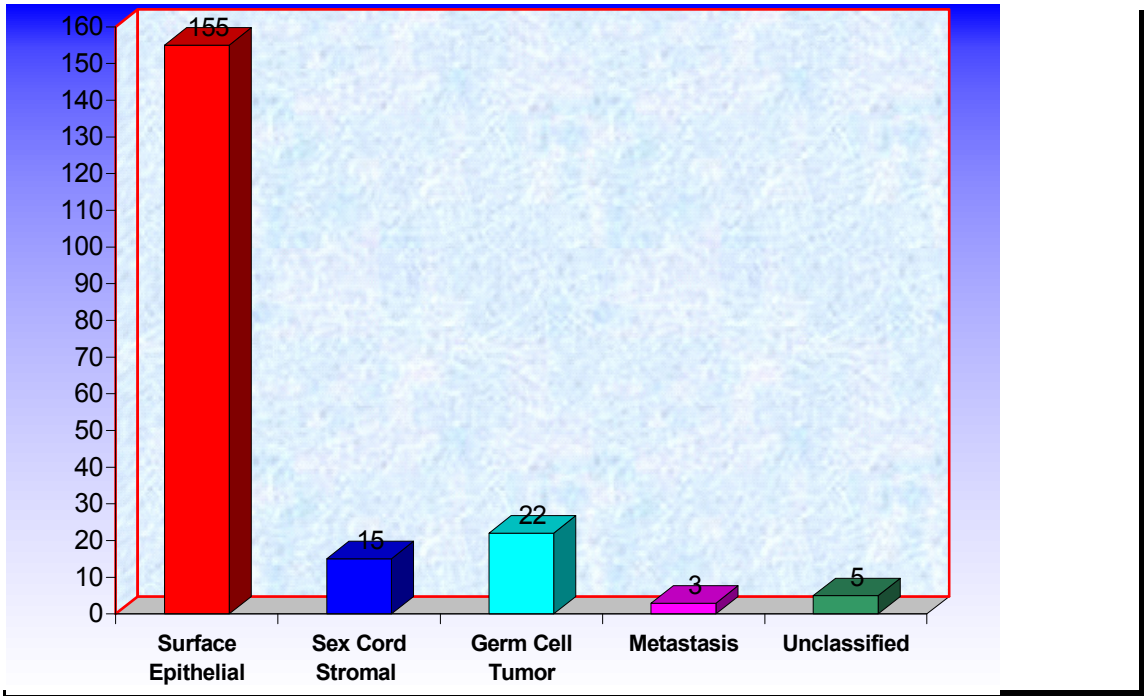
Among 200 cases of ovarian tumors studied 155 cases were surface epithelial tumors (77.5 %),22 cases were germ cell tumors(11%),15 cases were sex cord stromal tumors(7.5%), 5 cases were unclassified (2.5%), 3 were krukenberg tumors(1.5%) .

Out of 200 cases,124 were benign(62%) ,11 were borderline(5.5%) , 65 were malignant tumors(32.5%).Three patients had both benign and malignant tumors. They were included under malignant tumors.

The distribution of cases has been illustrated in table 1.

Table 1 : Diagnosis and type of tumor

Diagnosis	No. of cases	Type of tumor					
		Benign		Borderline		Malignant	
		No	%	No	%	No	%
I.Surface epithelial	155	98	63.2	11	7.1	46	29.7
II. Sex cord stromal	15	15	100	-	-	-	-
III. Germ cell tumor	22	13	59.1	-	-	9	40.9
IV. Metastasis	3	-	-	-	-	3	100
V. Unclassified	5	-	-	-	-	5	100
Total	**200**	**124**		**11**		**65**	



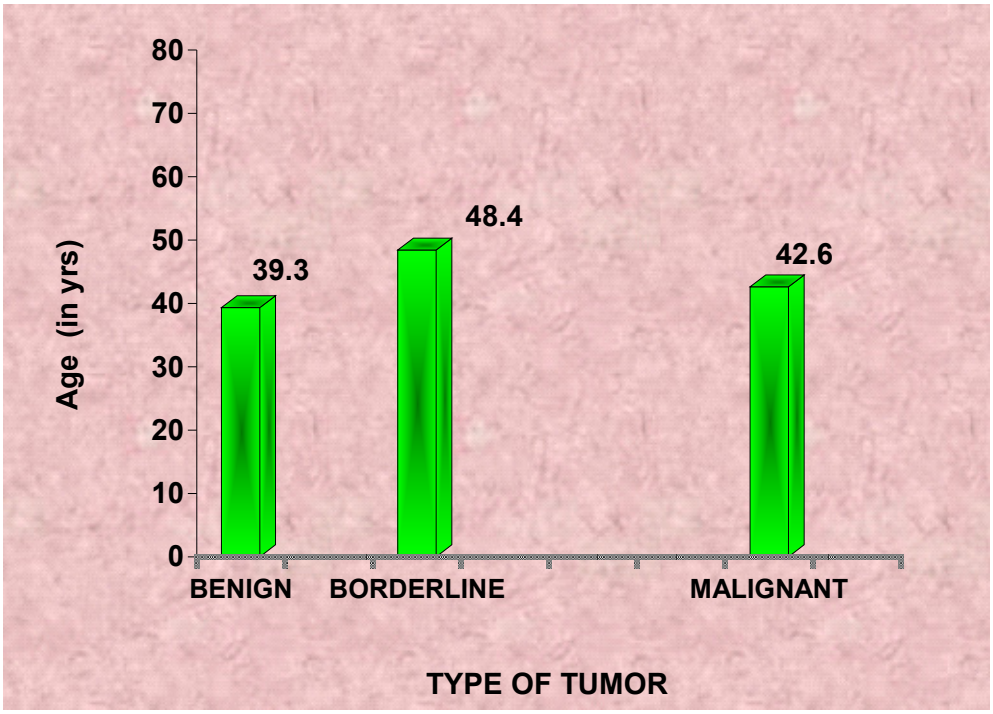
AGE INCIDENCE OF OVARIAN TUMORS:

According to this study , ovarian neoplasms occur in the age group between 2 to 76 years. There was a high incidence of ovarian neoplasms in the age group of 41-50 years. The youngest patient in this study was 2 years old who presented with precocious puberty and was diagnosed as Juvenile granulosa cell tumor.The oldest patient was 76 years old ,presented with mass abdomen (15x13x6) and was diagnosed as Fibrothecoma.

Benign tumors were more common in age group 21-30 years, Borderline in more than 60 years, malignant in age group 41-50 years.Benign tumor cases had lower mean age and borderline tumor cases had higher mean age. But the difference was not statistically significant.

Table - 2 : Age and type of tumor

Age group	**No. of cases**	**Type of tumor**					
		Benign		**Borderline**		**Malignant**	
		No	**%**	**No**	**%**	**No**	**%**
Upto 20 years	15	10	66	-	-	5	33.3
21- 30 years	39	31	79.5	1	2.6	7	17.9
31- 40 years	46	27	58.7	3	6.5	16	34.8
41- 50 years	56	31	55.4	3	5.4	22	39.3
51- 60 years	29	18	62.1	1	3.4	10	34.5
> 60 years	15	7	46.7	3	20	5	33.3
Total	200	124	62	11	5.5	65	32.5
Mean SD		39.3 years 14.3 years		48.4 years 14.8 years		42.6 years 13.2 years	



graph 2 : Age and type of tumor

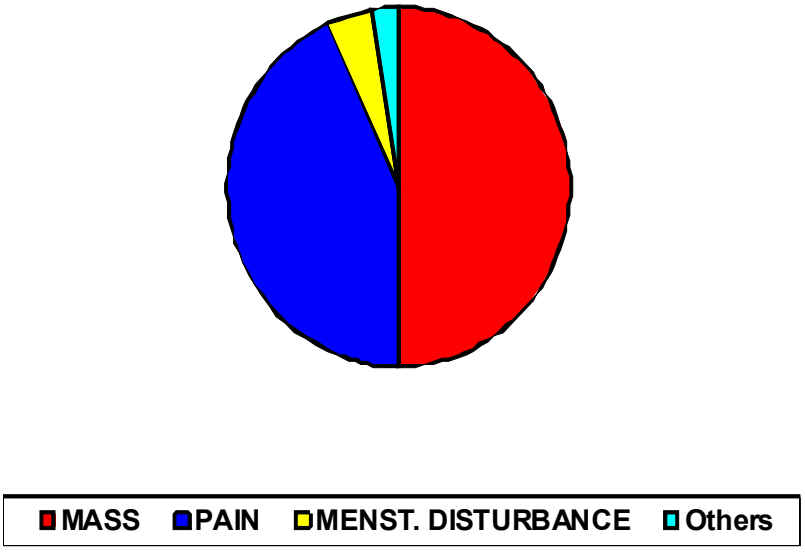
CLINICAL FEATURES

All the cases were evaluated clinically at the time of admission as in the following table. Abdominal mass was the most common clinical presentation (117 cases, 58.5%) followed by pain (101 cases, 50.5%). Other symptoms like menstrual disturbances, precocious puberty, weight loss, abdominal distention urinary frequency, constipation were present in 6 cases(3%). Many cases had more than one clinical features

Table – 3: Clinical Features

Clinical features	Cases	
	No	%
Mass	117	58.5
Abdominal Pain	101	50.5
Menstrual disturbance	10	5
Other symptoms	6	3

Graph 3 **Clinical Features**

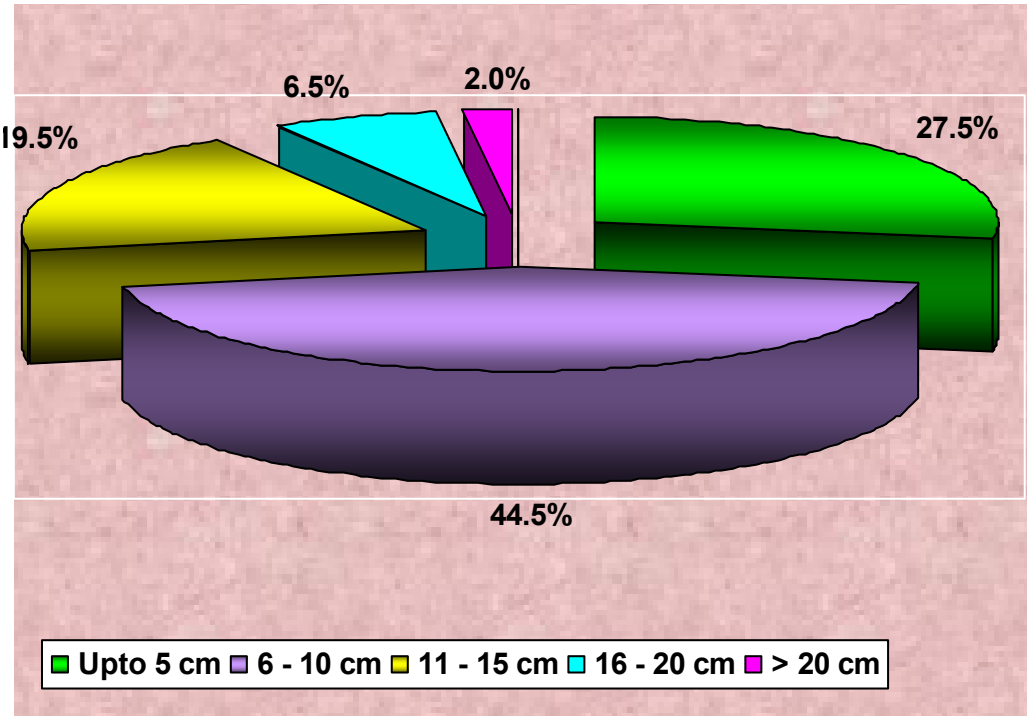


SIZE OF THE OVARIAN TUMORS:

The largest ovarian tumor in this study was Benign mucinous cystadenoma measuring 30x25x10 cm and smallest tumor was a Benign serous cystadenoma measuring 2x2x0.5 cm. The size of the ovarian tumor in this study ranged from 2.5cm to 30cm. The average size was 9 cm.

Graph 4

Size



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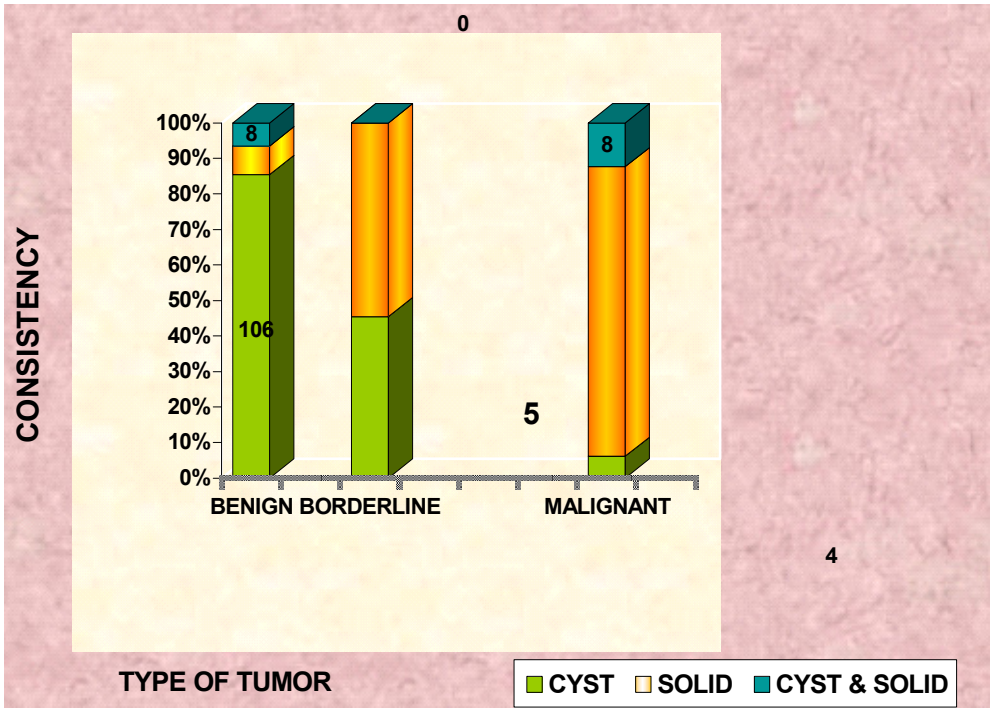
CONSISTENCY OF OVARIAN TUMORS:

The consistency of ovarian tumors was cystic in 115 tumors(57.5%), solid in 69 tumors(34.5%) and partly cystic and solid in 16 tumors(8%).

Consistency was cystic in majority (85.5%) of benign tumor cases.. It was solid in 81.5% of malignant cases. Papillary lesions were seen in 31 ovarian tumors.

Graph 5

Type of tumor and consistency



LATERALITY OF OVARIAN TUMORS

In the present study ,out of 200 cases 163(81.5%) were unilateral and 37 were bilateral (18.5%)In that 90.3% of benign ovarian tumors were unilateral and 64.6% of malignant ovarian tumors were unilateral, whereas 9.7% of benign ovarian tumors were bilateral and 35.4% of malignant ovarian tumors were bilateral. .

Bilaterality is more common in serous than mucinous tumors. Unilaterality is more common in sex cord stromal tumors (93.3%), bilaterality more common in metastatic tumors(66.7%). The more common surface epithelial tumors show unilaterality in 81.3 % of cases and bilaterality in 18.7% cases.

Table 4

Diagnosis and Laterality

Diagnosis	**No. of cases**	**Laterality**			
		Unilateral		**Bilateral**	
		No	**%**	**No**	**%**
I.Surface epithelial tumors	155	126	81.3	29	18.7
II. Sex cord stromal	15	14	93.3	1	6.7
III. Germ cell tumor	22	19	86.4	3	13.6
IV. Metastasis	3	1	33.3	2	66.7
V. Unclassified	5	3	60	2	40
Total	**200**	**163**	**81.5**	**37**	**18.5**

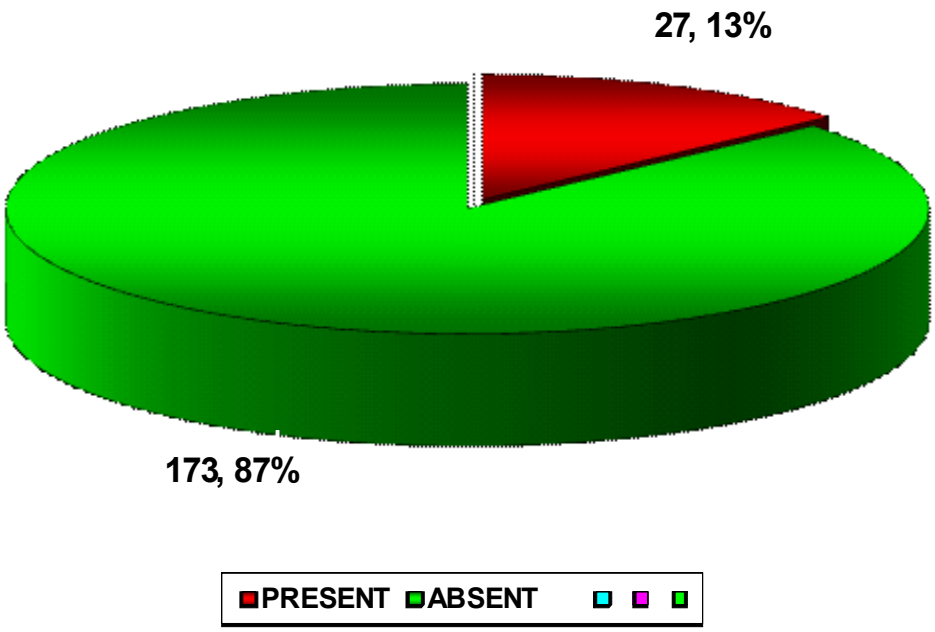
As severity of tumor increases, laterality becomes more bilateral.

METASTASIS OF OVARIAN TUMORS

Metastasis to omentum, ascites were present in 41.5% of malignant tumors.

Graph 6

Metastasis



HISTOLOGICAL TYPES OF OVARIAN TUMORS

SURFACE EPITHELIAL STROMAL TUMORS

This was the commonest group encountered in the present study ,155 cases out of 200 were Surface Epithelial tumors.(77.5%). 31 cases showed papillary pattern.(fig 15) .The distribution of Surface Epithelial tumors encountered in this study has been illustrated in the table 5.

Table 5

Diagnosis	Cases	
	No	%
I. Surface epithelial tumours		
a) Cyst		
i) Benign serous cyst	8	4
ii) Benign mucinous cyst	1	0.5
Total	10	5
b) Cyst adenoma		
i) Benign serous cystadenoma	50	25
ii) Benign mucous cystadenoma	38	19
Total	88	44
c) Borderline		
i) Borderline serous cystadenoma	1	0.5
ii) Borderline mucous cystadenoma	9	4.5
Total	10	5.
d) Malignant		
i)Serous adeno carcinoma	35	17.5
ii) Mucinous adrnocarcinoma	8	4
Total	43	21.5
e) undifferentiated tumors	5	2.5
TOTAL	155	

SEX-CORD STROMAL TUMORS

15 sex cord stromal tumors which were encountered in the present study have been depicted in table 6.

Table 6

TUMOR TYPE	No. OF CASES	%
a) Granulosa cell tumor	10	5
b) Fibrothecoma	3	1.5
c) Fibroma	2	1
Total	15	7.5

Among 15 cases, 10 were histopathologically diagnosed as Adult Granulosa cell tumor. These tumors showed microfollicular, insular and watered silk pattern with Call-Exner bodies (Fig21). A case of juvenile granulose cell tumor was reported (fig22).Two cases of fibroma and three cases of fibrothecoma were recorded in this series (1%) .

In this study, we applied reticulin stain for all the Granulosa cell tumors(10 cases) and all the cases of fibrothecomas(3 cases). The stain shows fibrils surrounding the nests and large aggregates of granulosa cells in Granulosa cell tumors (fig 24). In Fibrothecoma, reticulin stain highlights an investment of individual cells by fibrils.

GERM CELL TUMORS

22 germ cell tumors which were encountered in the present study have been depicted in table 7.

Table 7

TUMOR TYPE	No. OF CASES	%
a) Teratoma	15	7.5
b) Dysgerminoma	3	1.5
c) Yolk sac tumor	4	2
d) Embryonal carcinoma	-	-
Total	22	11

In the present study out of 22 germ cell tumors, 15 cases were diagnosed as benign cystic teratoma (7.5%).Tumors showed presence of squamous epithelium and dermal appendages, fat, cartilage, respiratory and gastrointestinal epithelium (fig.29).One case of immature teratoma with neuroectodermal elements was encountered (fig.30).

Three cases of dysgerminoma were encountered. The tumor was grey white nodular external surface (cerebriform) with intact capsule(fig11).Four cases of yolk sac tumor encountered. Tumor arranged in

reticular patter and endodermal sinus pattern with Schiller–Duval bodies (fig 28). Intracellular and extracellular hyaline globules were seen.

METASTATIC TUMORS / KRUKENBERG TUMORS

In the present study, 3 cases of krukenberg tumors were noted. Tumor was solid in consistency(fig 13). Histologically composed of signet ring cells admixed with benign appearing mucinous areas(fig 32).

Primary carcinoma were in stomach in 2 cases. In our study mucinous carcinoma of ovary shows extra cellular PAS positive mucin pools (fig 34) where as in Krukenberg tumor show intracellular PAS positivity in signet ring cells (fig 33).

PROLIFERATIVE MARKER STUDY

RESULTS OF Ki 67 LABELLING INDEX

Ki 67 labelling index was studied in 24 selected cases which comprised of 4 benign cystadenoma (2 serous,2 mucinous), 4 borderline cystadenomas(2 serous,2 mucinous), 4 carcinoma (2 serous, 2 mucinous adenocarcinoma), 2 germ cell tumors , all the 10 Granulosa cell tumors.

One way analysis of variance test was used to assess the statistical difference between Benign,borderline & malignant epithelial ovarian tumors.

The comparative analysis of Ki 67 labelling index has been shown in table 8.

COMPARATIVE ANALYSIS OF Ki 67 LABELLING INDEX

Table 8

s.no	TYPE OF CASES	NO.OF CASES	Ki67 INDEX
1	BENIGN SEROUS CYSTADENOMA	2	2.8
2	BENIGN MUCINOUS CYSTADENOMA	2	3.0
3	BORDERLINE SEROUS CYSTADENOMA	2	8.3
4	BORDERLINE MUCINOUS CYSTADENOMA	2	6.1
5	SEROUS CYSTADENOCARCINOMA	2	29.1
6	MUCINOUS CYSTADENOCARCINOMA	2	32.4
7	DYSGERMINOMA	1	25.3
8	YOLK SAC TUMOR	1	31.3

The results were

a) Both cases of benign serous cystadenomas had a mean Ki 67 index of 2.8 % and both cases of benign mucinous cystadenomas had a mean Ki 67 index of 3 % (fig 36)

b) Two cases of borderline serous cystadenomas had a mean Ki 67 index of 8.3 % and both cases of borderline mucinous cystadenomas had a mean Ki 67 index of 6.1% (fig 38).

c) Both cases of malignant serous cystadenocarcinomas had a mean Ki 67 index of 29.1 % and both cases of mucinous cystadenocarcinomas had a mean Ki 67 index of 32.4 % (fig 40).

d) Both the cases of germ cell tumors showed an average Ki 67 index of 28.3% (fig42).

Benign tumors had a mean Ki 67index of 2.9% , borderline tumors had a mean Ki 67 index of 7.2% ,while the malignant tumors had a mean Ki 67 index of 29.9% .

The difference in the mean value between benign, borderline, and malignant epithelial tumors were statistically significant ($p =<0.001$).

IMMUNOHISTOCHEMICAL MARKER STUDY IN GRANULOSA CELLTUMORS (GCT):

We received a total of 10 cases of Granulosa cell tumors in our study.

Out of the ten cases which were histopathologically diagnosed as Granulosa cell tumor, two cases turned out to be primary ovarian carcinoid and poorly differentiated carcinoma respectively after immunohistochemical study.

The results of expression of various immunomarker in all these tumors are shown in table 9.

Table 9

S.N	case	vimentin	Inhibin	chromogranin	EMA	Ki 67 index	STAGE
1	G2955/09	+	+	-	-	5.4	I(a)
2	G4613/09	+	+	-	-	4.8	I(a)
3	G1879/10	+	+	-	-	4.4	I(a)
4	G1888/10	+	+	-	-	7.9	I(c)
5	G2652/10	+	+	-	-	2.8	I(a)
6	G3169/10	+	+	-	-	3.4	I(a)
7	G3928/10	+	+	-	-	4.2	I(a)
8	G762/11	+	+	-	-	8.4	I(c)
9	G232/10	-	-	+	-	3.0	
10	G1857/10	-	-	-	+	25.1	

DIAGNOSTIC SIGNIFICANCE OF IMMUNOHISTOCHEMICAL STUDY IN GRANULOSA CELL TUMORS:

1. ***GCT TURNED OUT TO BE PRIMARY OVARIAN CARCINOID AFTER IHC:***

We received a clinically suspected specimen of ovarian tumor in a 55 year old postmenopausal woman.Grossly , it was a large yellowish tumor of size 12x11x11 cm with predominant solid areas. Initially histopathological diagnosis of Granulosa cell tumor/Carcinoid tumor were considered. With immunohistochemical study, tumor cells showed strong expression of

chromogranin and synaptophysin and was negative for vimentin.. Final diagnosis of Ovarian Carcinoid was made.

(fig 25,26)

On retrospective analysis, no other tumor mass was detected elsewhere by abdominal ultrasonography and CT scan. Isolated Tricuspid regurgitation was incidentally found in pre-operative echocardiography.

In correlation with the above findings, we came to conclusion of Primary Ovarian Carcinoid tumor with Tricuspid regurgitation.

2.GCT TURNED OUT TO BE A POORLY DIFFERENTIATED CARCINOMA AFTER IHC :

In another case of ovarian tumor received, provisional diagnosis of Granulosa cell tumor was made based on histopathological features. On further evaluation with immunohistochemical markers Vimentin and Inhibin were negative and EMA was positive and so the final diagnosis of poorly differentiated carcinoma was made .

The remaining 8 cases showed vimentin positivity and EMA negative.These tumors were diagnosed as Granulosa cell tumors .

Ki 67 LABELLING INDEX IN GCT:

Mean Ki 67 index for 8 cases of histologically and immunohistochemically proven case of granulosa cell tumor was 5.1%.

In the present study , Ki 67 index was higher in 2 cases of. Granulosa cell tumors (7.9% and 8.4%) which correlated clinically with higher stage (FIGO stage I(c) disease).

Ki 67 index in the rest of the Granulosa cell tumors was low which correlated clinically with FIGO stage I(a) disease.

Thus in the present study, Ki 67 index reflected more closely the clinical behavior and clinical stage of Granulosa cell tumors tumors (fig 44).

RETICULIN STAIN IN GRANULOSA CELL TUMOR:

In this study, we applied reticulin stain for all granulosa cell tumors and fibrothecomas (3 cases). The stain shows fibrils surrounding nests and large aggregates of granulosa cells(fig 24). In Fibrothecoma, reticulin stain highlights an investment of individual cells by fibril.

INTERESTING TUMORS:

In this study we came across 7 interesting cases .They are as follows

1. MIXED TUMORS:

2 cases of mixed epithelial tumors were observed. Combinations of mucinous cystadenoma of ovary with benign Brenner tumor in the same ovary in both cases.(fig18)

2.BILATERAL MALIGNANT BRENNER:

One case of bilateral malignant Brenner tumor was observed in a 65 year old female who presented with abdominal mass. Grossly the tumor measured 10x8x5 cm and 4x3x2 cm on each side. The tumor was arranged in sheets with stromal invasion.(fig 20)

3. JUVENILE GRANULOSA CELL TUMOR :

One case of Juvenile granulosa cell tumor in a 2 year old girl who presented with precocious puberty(breast enlargement, vaginal bleeding). Grossly the tumor measured 8x6x5 cm. Both solid and cystic areas were seen(fig 10)

Microscopically the tumor showed predominantly macrofollicular pattern.(fig 22)

4. IMMATURE TERATOMA:

One case of immature teratoma with neuroectodermal elements was encountered (fig.30).

5.GCT WITH ASSOCATED ENDOMETRIAL CARCINOMA:

One case of unilateral granulosa cell tumor in a 65 year old female was associated with well differentiated endometrial adenocarcinoma with omental metastatic deposits.

6.CYSTIC TERATOMA WITH MALIGNANT EPITHELIAL COMPONENT:

Secondary malignancies in benign cystic teratoma are rare. Invasive squamous cell carcinoma is common and comprises 85%.But we encountered a relatively rare association of adenocarcinoma occuring as a secondary malignancy in benign cystic teratoma in a 45 year female.

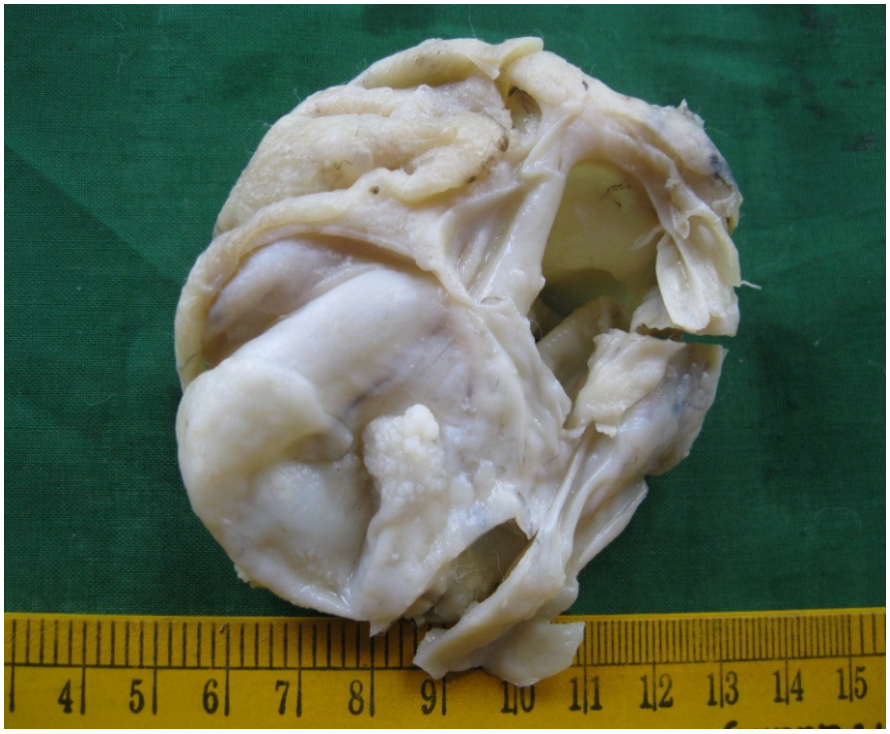
7.OVARIAN NEOPLASM WITH ASSOCIATED ENDOMETRIAL CANCER:

Out of 200 ovarian tumors, 5 were associated with endometrial carcinoma (2.5%). Among those 5cases,3 showed the same histologic pattern in both ovary and endometrium. One case was ovarian Granulosa cell tumor with endometrial adenocarcinoma and the other was bilateral mucinous cystadenoma with endometrioid type of endometrial adenocarcinoma.

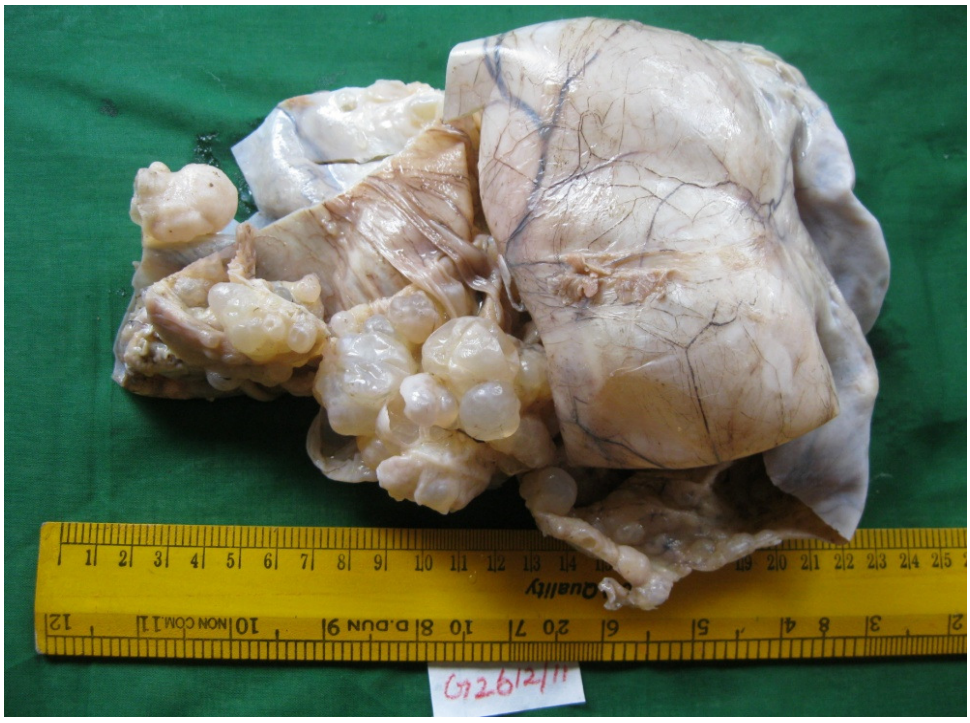
TABLE 10

S.No	BIOPSY NO	OVARIAN TUMOR TYPE	ENDOMETRIAL CARCINOMA TYPE	OTHER FEATURES
1	G2575/09	b/l endometrioid carcinoma	endometrioid carcinoma	
2	G2125/09	b/l mucinous cystadenocarcinoma	well differentiated mucin secreting adenocarcinoma	
3	G4613/09	papillary cystadenocarcinoma	papillary adenocarcinoma	fallopian tubes tumor +
4	G762//11	u/l granulosa cell tumor	well differentated adenocarcinoma	omentum tumor +
5	G695/11	b/l mucinous cystadenoma	endometrioid type of adenocarcinoma	

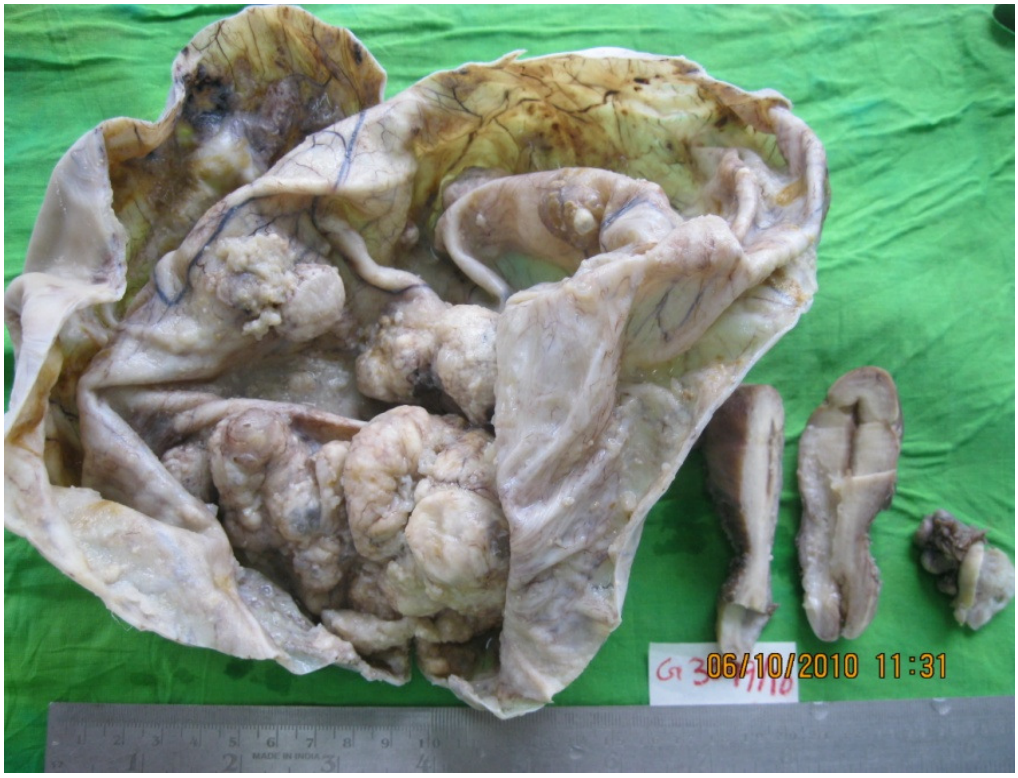
Photographs



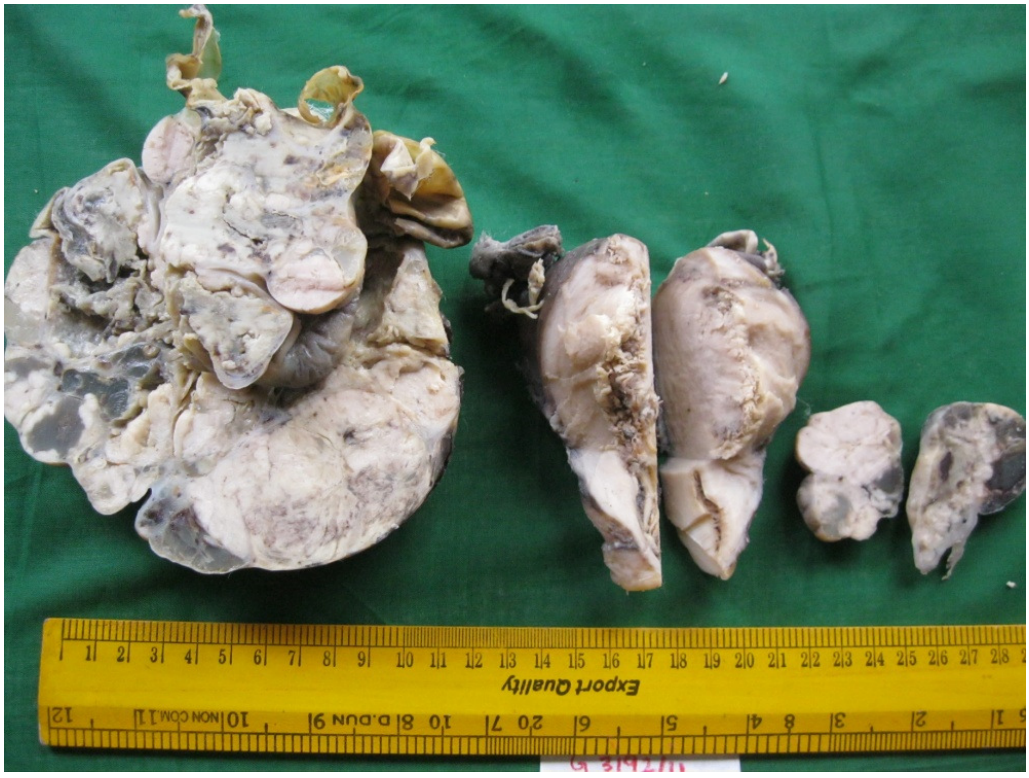
BENIGN PAPILLARY SEROUS CYSTADENOMA
Fig.3 G4026/09 Glistening cyst wall with papillary excrescences



BENIGN MUCINOUS CYSTADENOMA
Fig.4 G3577/10 Cystic mass filled with mucinous material



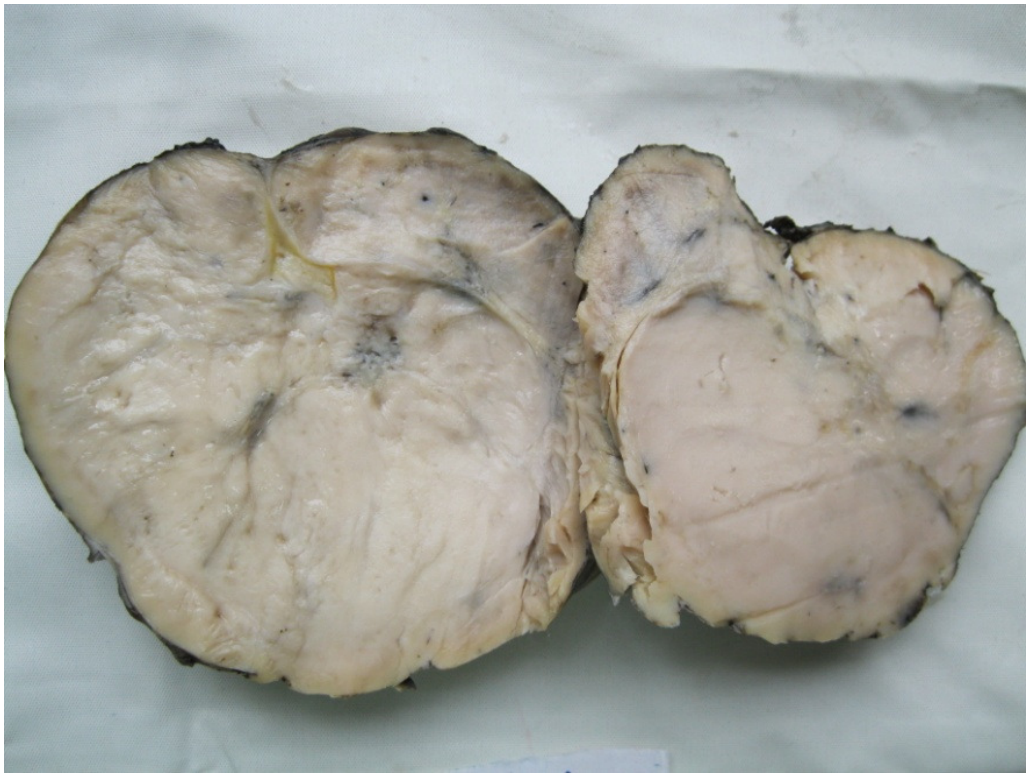
PAPILLARY SEROUS CYSTADENOCARCINOMA
Fig.5 G60/11 C/S solid and cystic with papillae



B/L ENDOMETRIOID CARCINOMA
Fig.6 G2575/09 C/S showing greyish-white solid areas

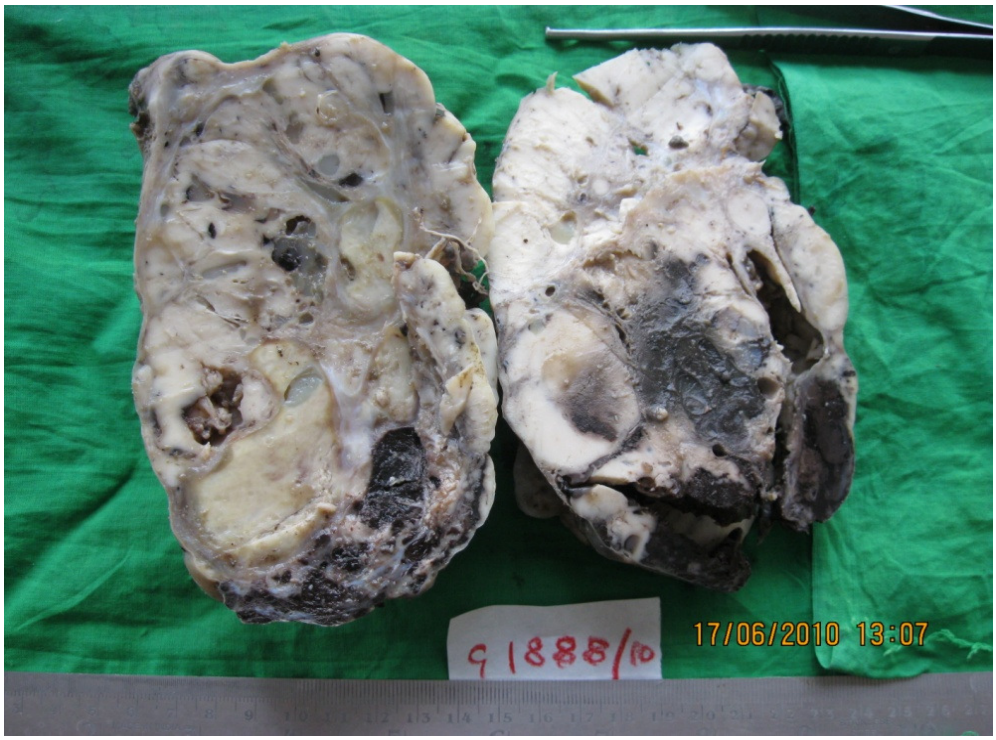
B/L MALIGNANT BRENNER TUMOR

Fig.7 G 476/11 C/S solid and yellowish white areas



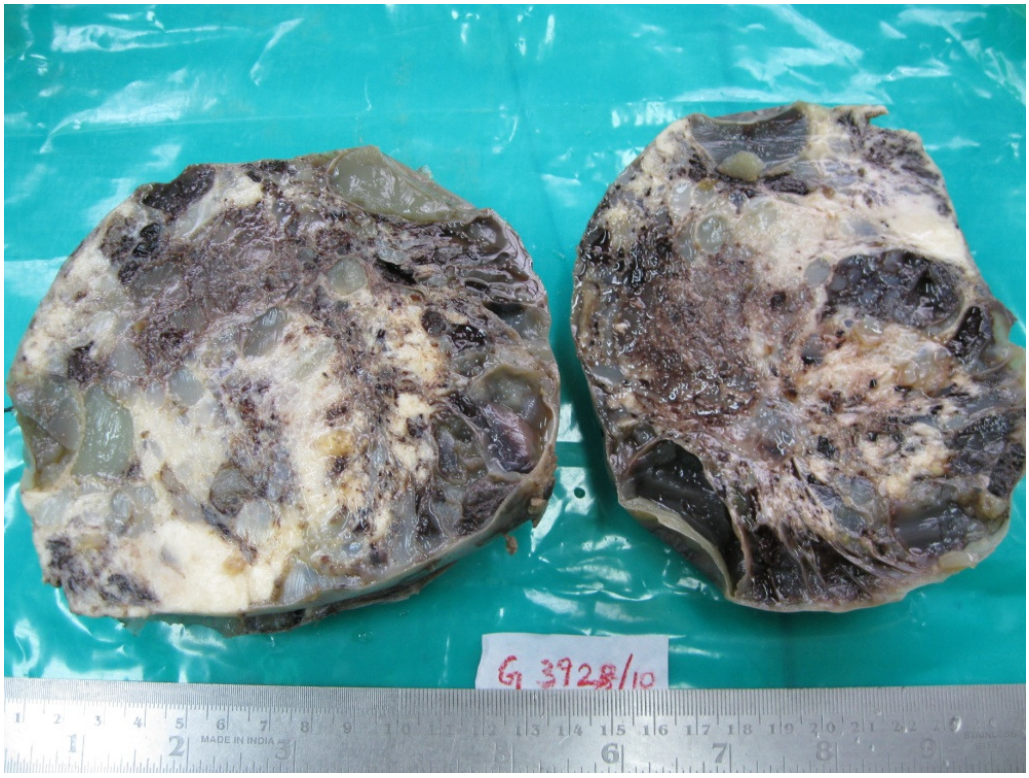
FIBROMA

Fig.8 G1137/11 Cut surface showing uniformly whitish solid areas



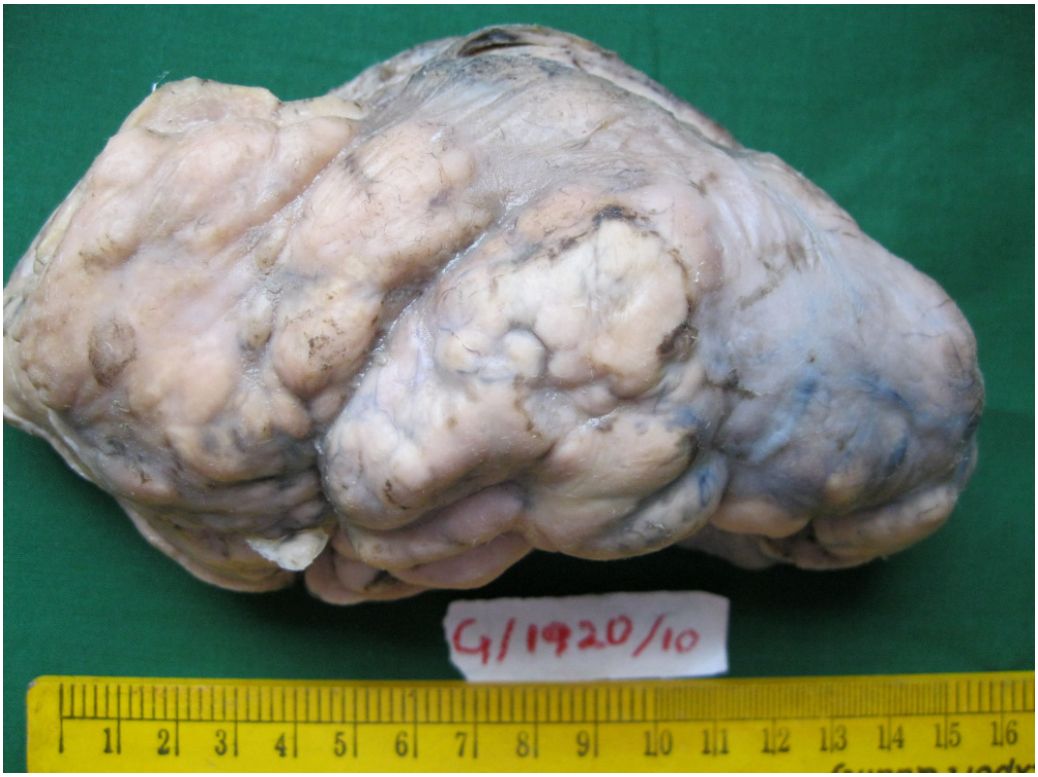
ADULT GRANULOSA CELL TUMOR

Fig.9 G1888/10 C/S solid yellowish areas with cystic degeneration

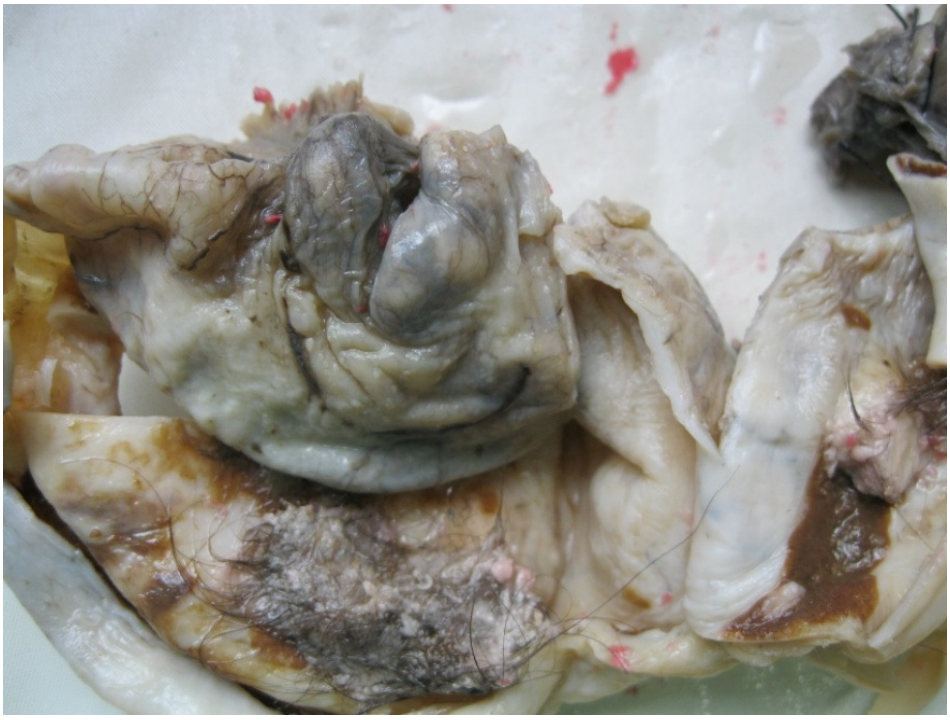


JUVENILE GRANULOSA CELL TUMOR

Fig.10 G3928/10 Cut surface solid and cystic with areas of hemorrhage



DYSGERMINOMA
Fig.11 G1920/10 Typical lobulated outer surface



BENIGN CYSTIC TERATOMA
Fig.12 G 2081/10 Admixture of sebum and hair within the cystic cavity

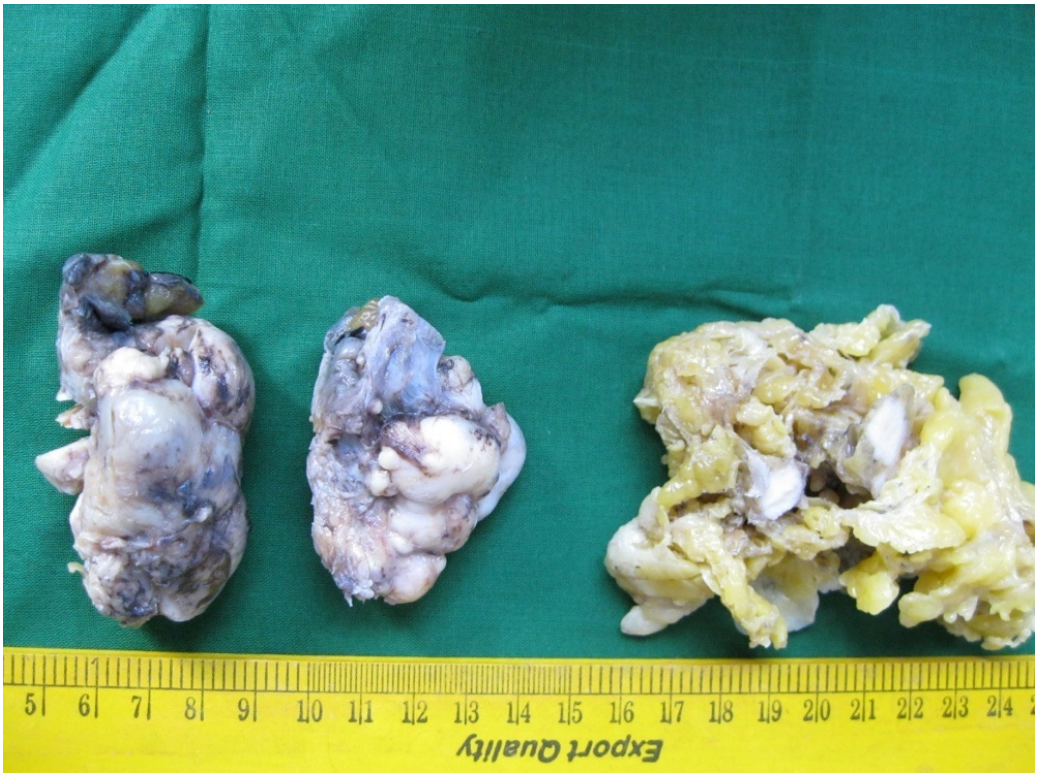
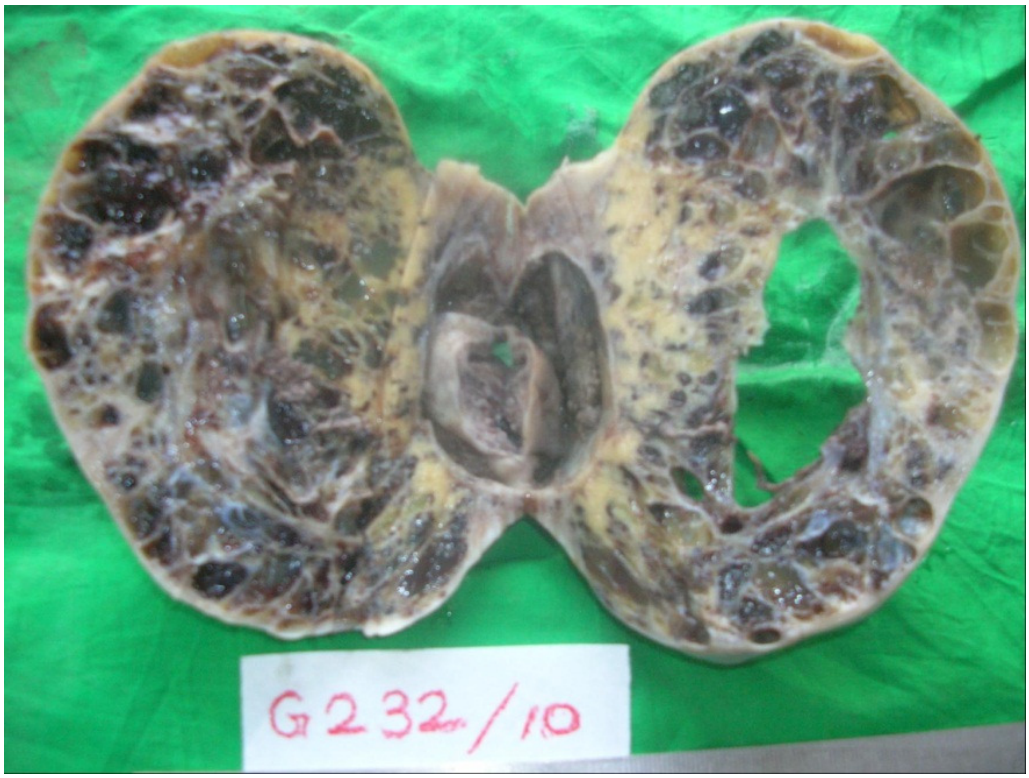


Fig.13 G 1891/10 B/L KRUKENBERG TUMOR
WITH OMENTAL DEPOSITS



OVARIAN CARCINOID TUMOR
Fig.14 G232/10

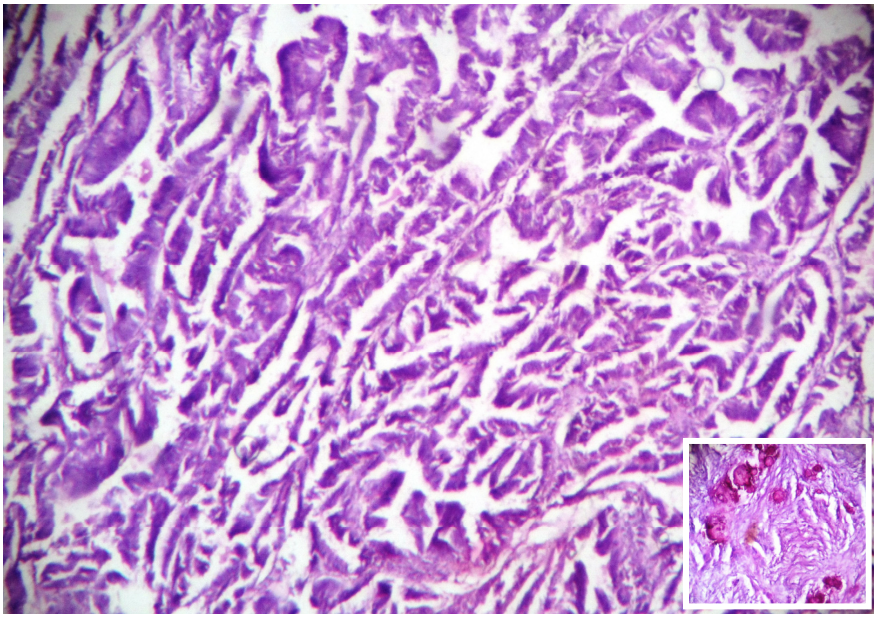
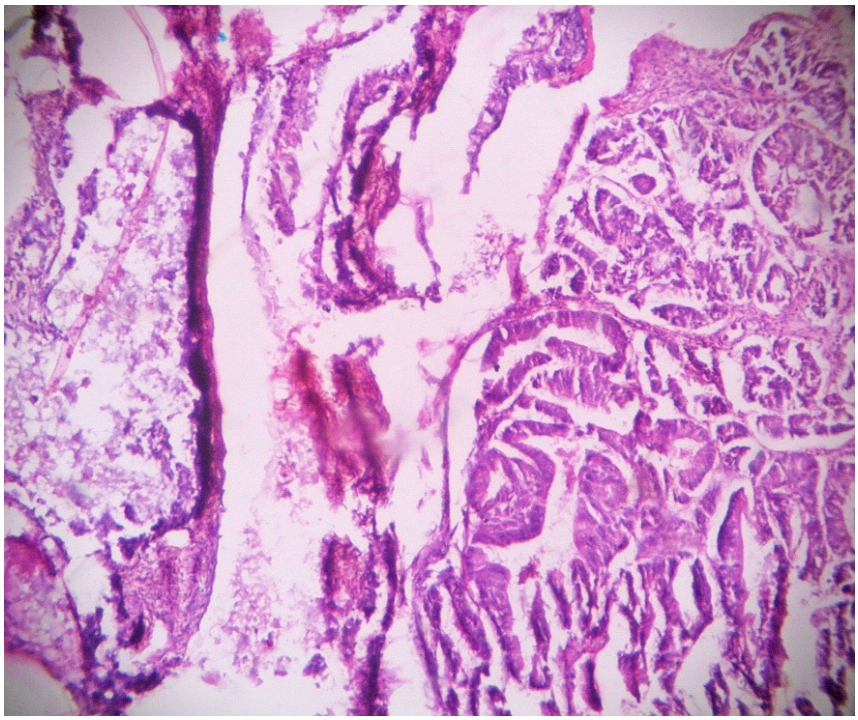
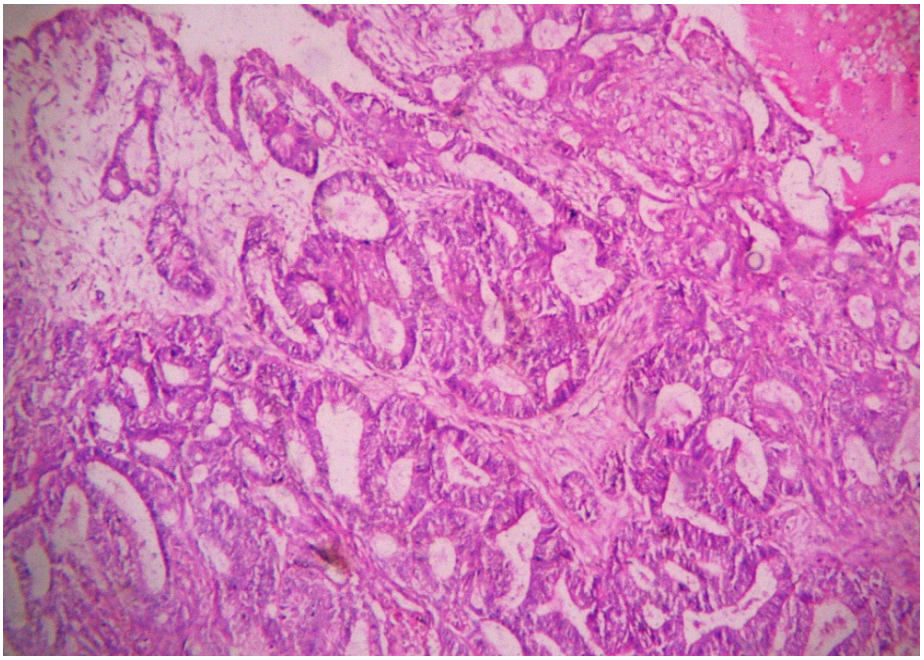


Fig. 15: G1673/10 PAPILLARY SEROUS CARCINOMA
Tumor cells arranged in papillary pattern with fibrovascular core with insert showing psammoma bodies (H&E x 100x)

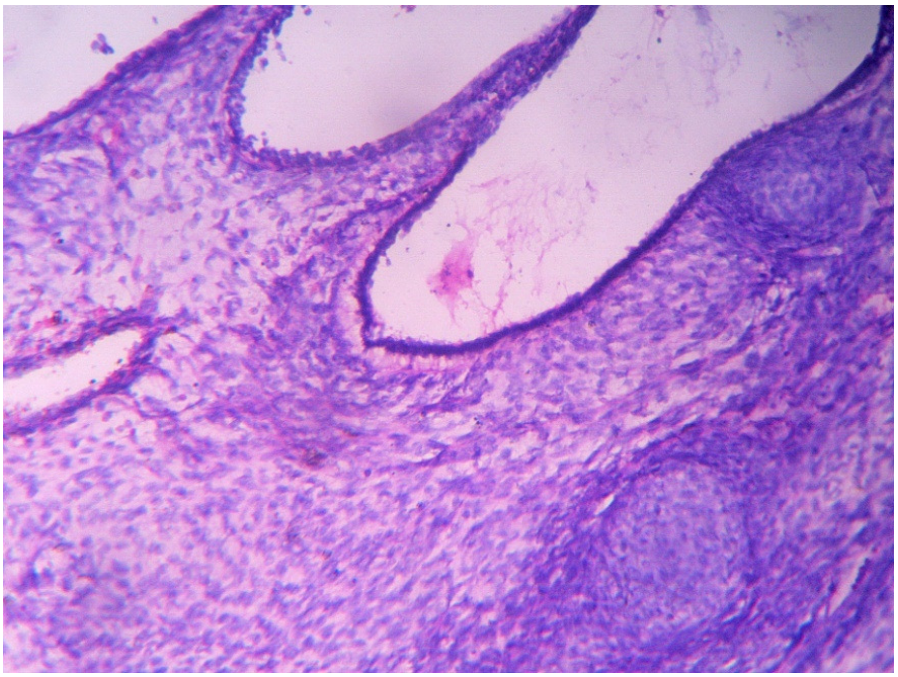


MUCINOUS CYSTADENOCARCINOMA
Fig.16 .G 934/11 Confluent pattern of growth with back-to-back glands with mucinlakes(H&E x 100X)



ENDOMETRIOID CARCINOMA

Fig.17 G2575/09 Back-to-back glands lined by columnar cells with stratified hyperchromaticnuclei(H&E x 100X)



MIXED EPITHELIAL TUMOR-BRENNER TUMOR WITH MUCINOUS CYSTADENOMA

Fig.18 G 884/10(H&E x 100X)

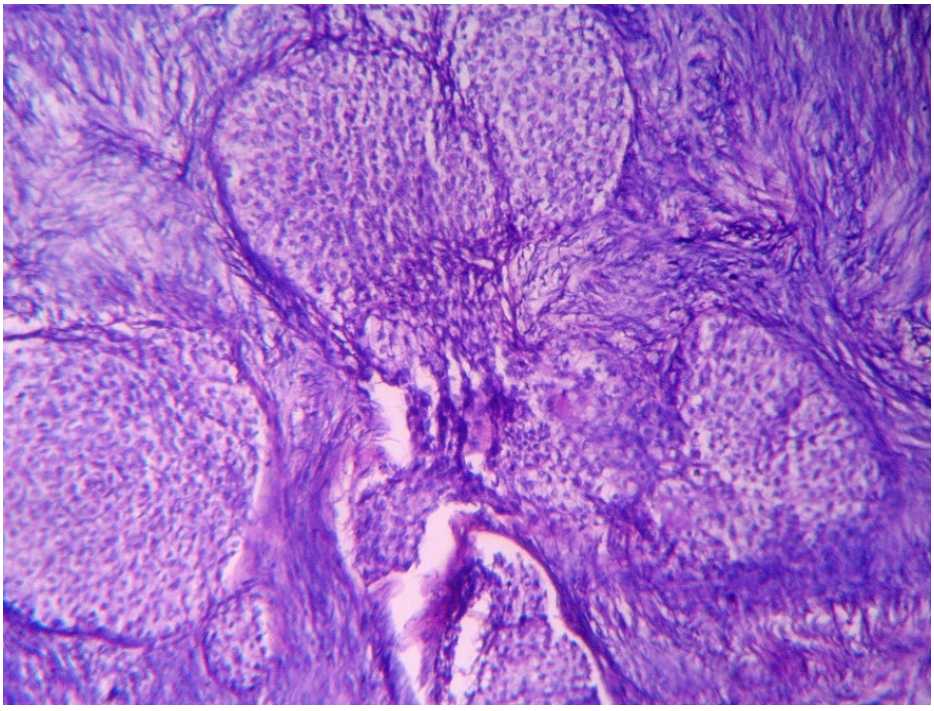
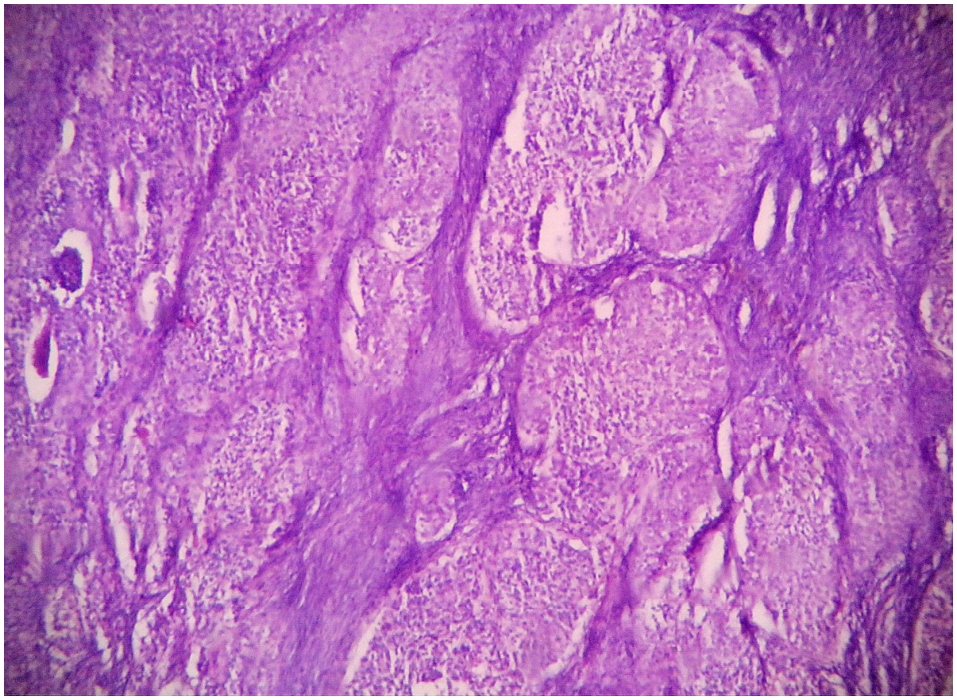
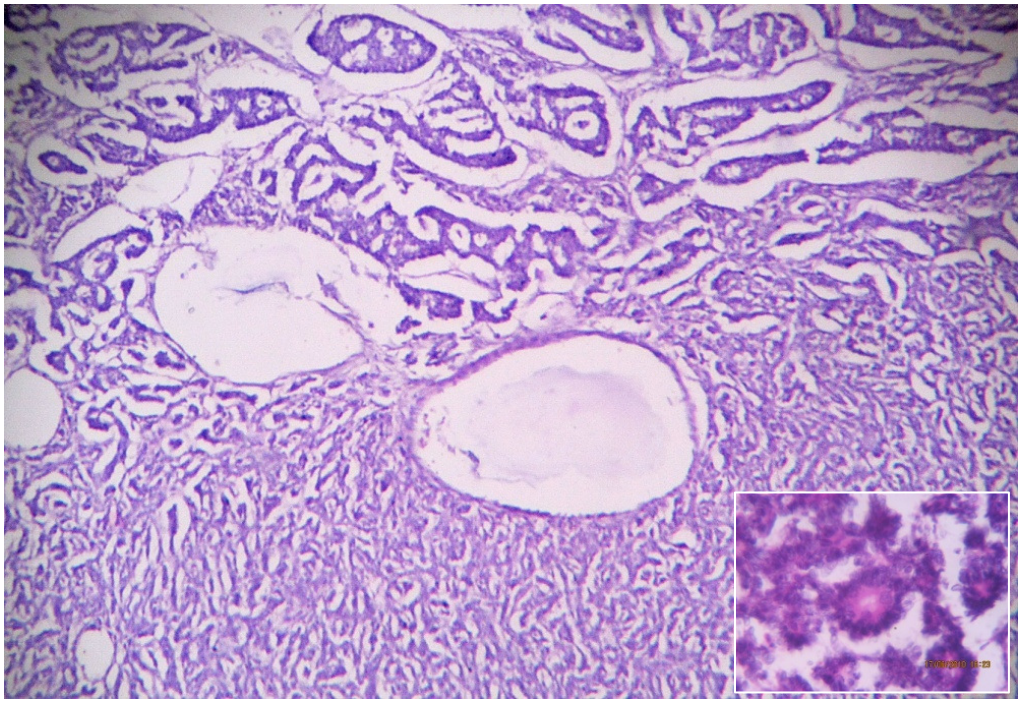


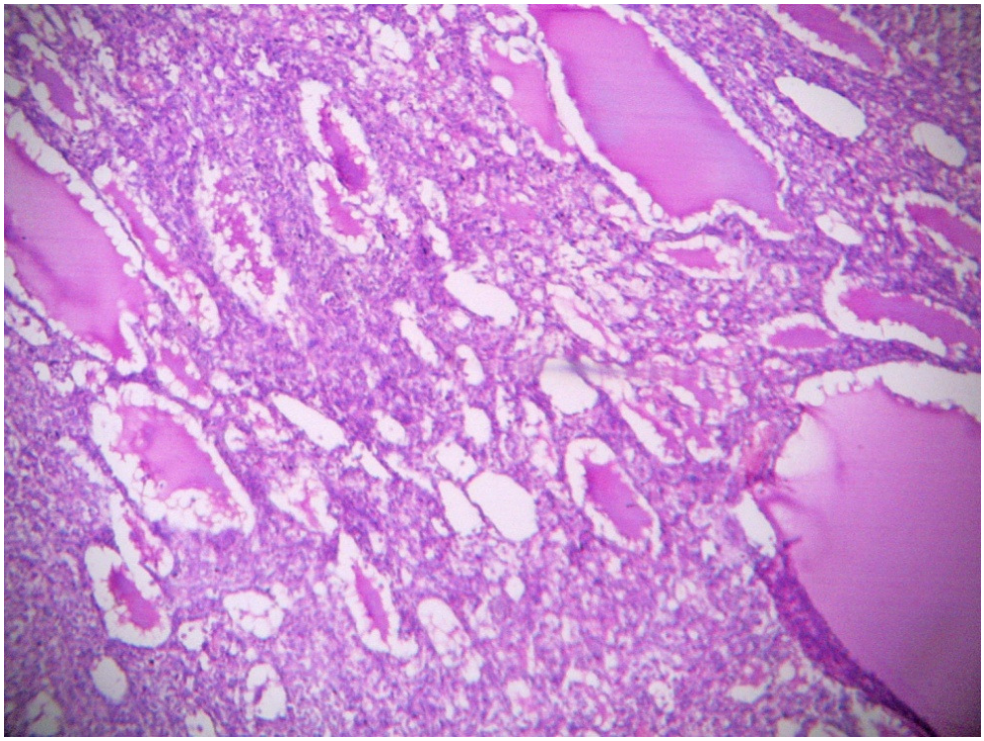
Fig.19 **BRENNER TUMOR SHOWING EPITHELIAL NESTS EMBEDDED WITHIN FIBROUS STROMA G 4175/11(H&E x 100X)**



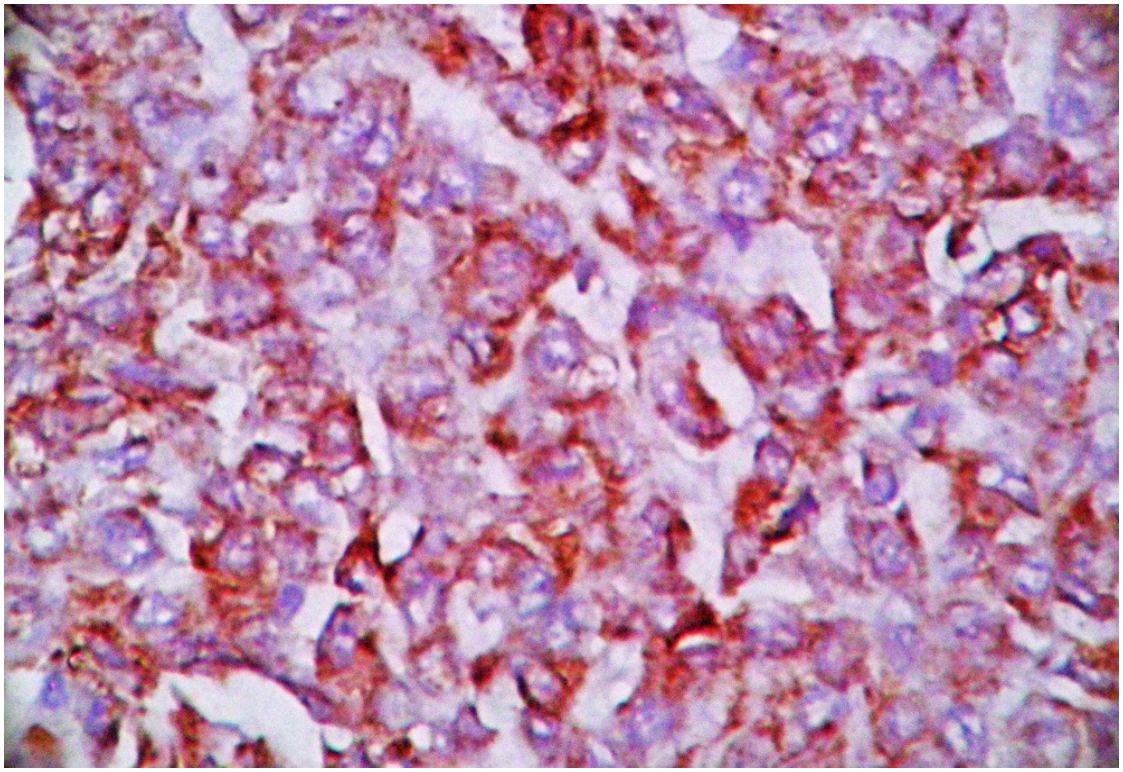
BILATERAL MALIGNANT BRENNER
Nests and islands of tumor cells
infiltrating the stroma. Fig.20 G 476/11 (H&E x 100X)



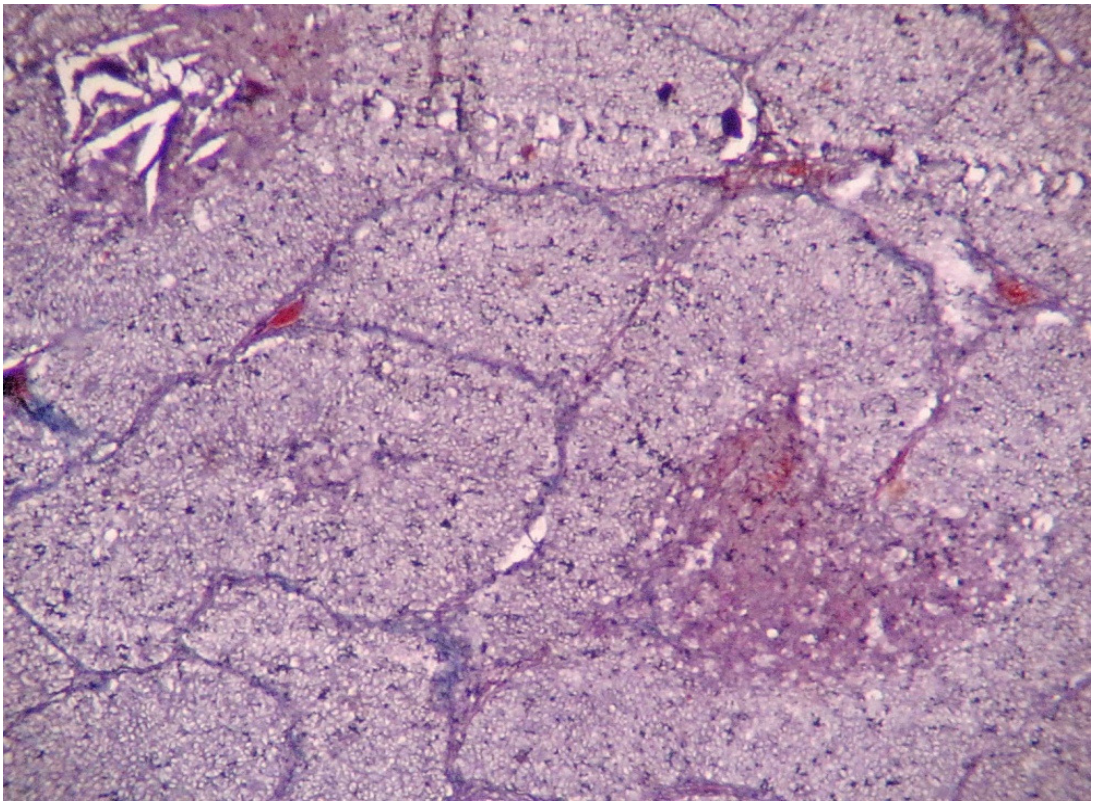
ADULT GRANULOSA CELL TUMOR
Fig.21 G3713/11 Watered silk pattern with insert showing Call Exnerbodies(H&E x 100X)



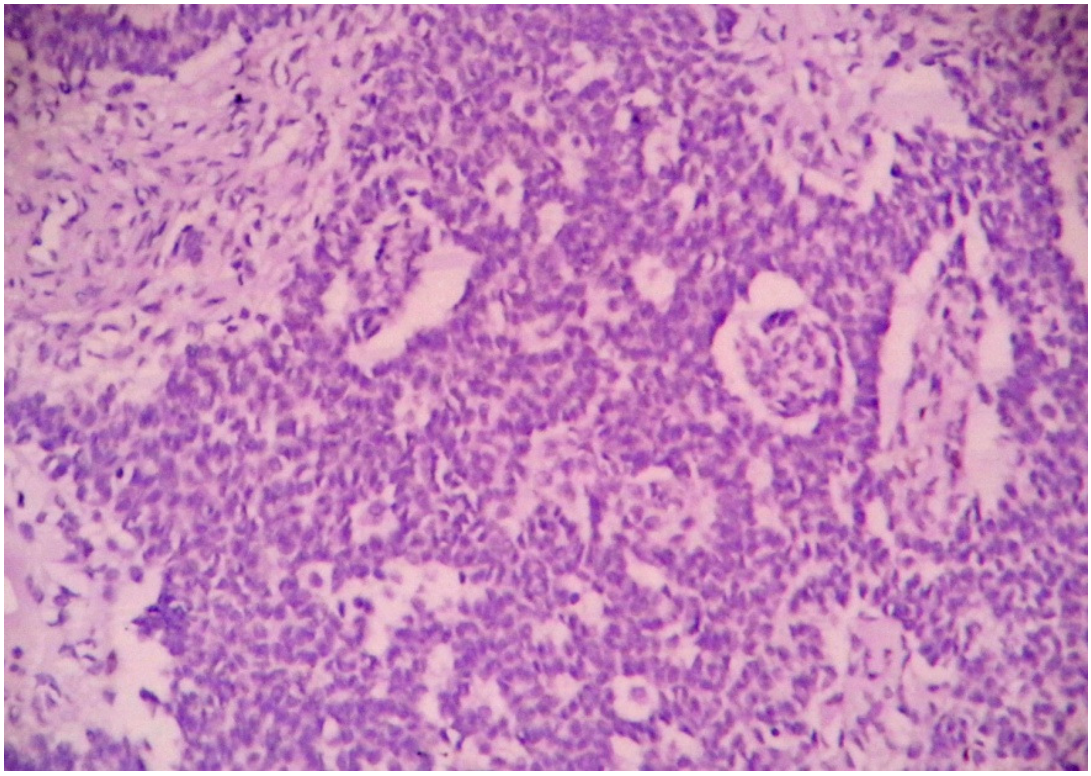
JUVENILE GRANULOSA CELL TUMOR
Fig.22 G3928/10 Irregular macrofollicles filled with eosinophilic secretions and surrounded by neoplastic granulosacells(H&E x 100X)



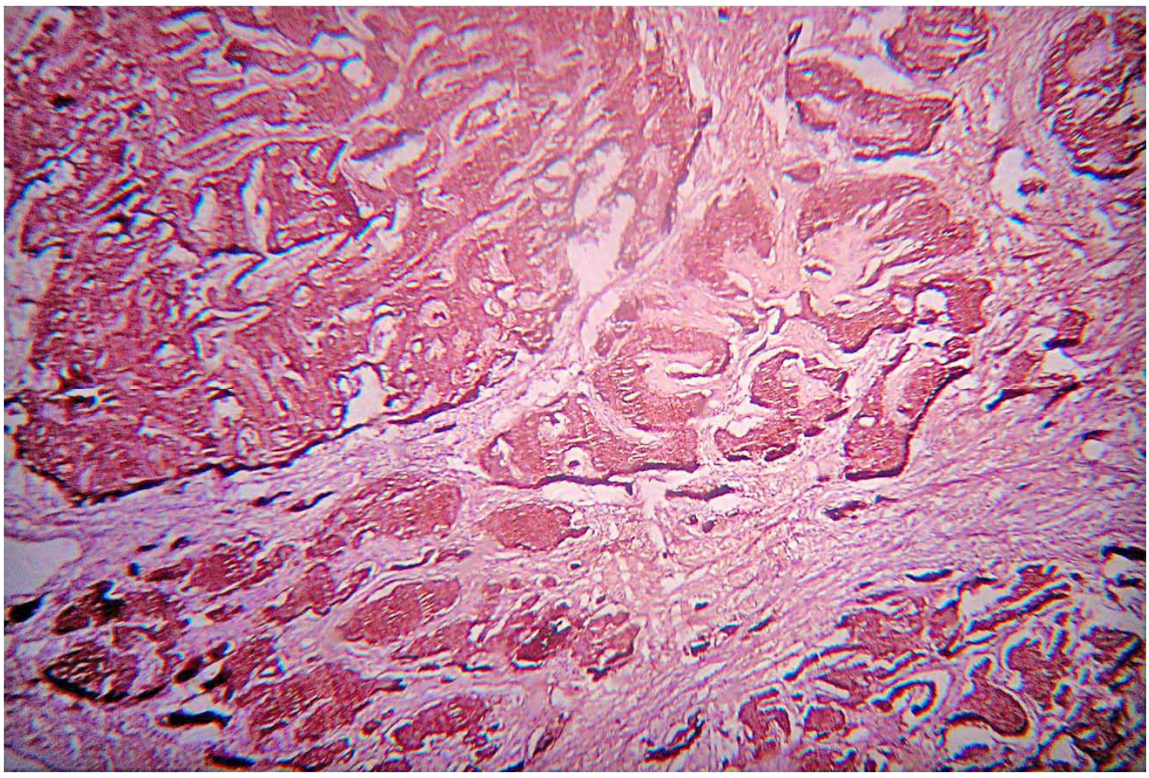
ADULT GRANULOSA CELL TUMOR
Fig.23 G 3713/11Vimentinpositivity(H&E x 400X)



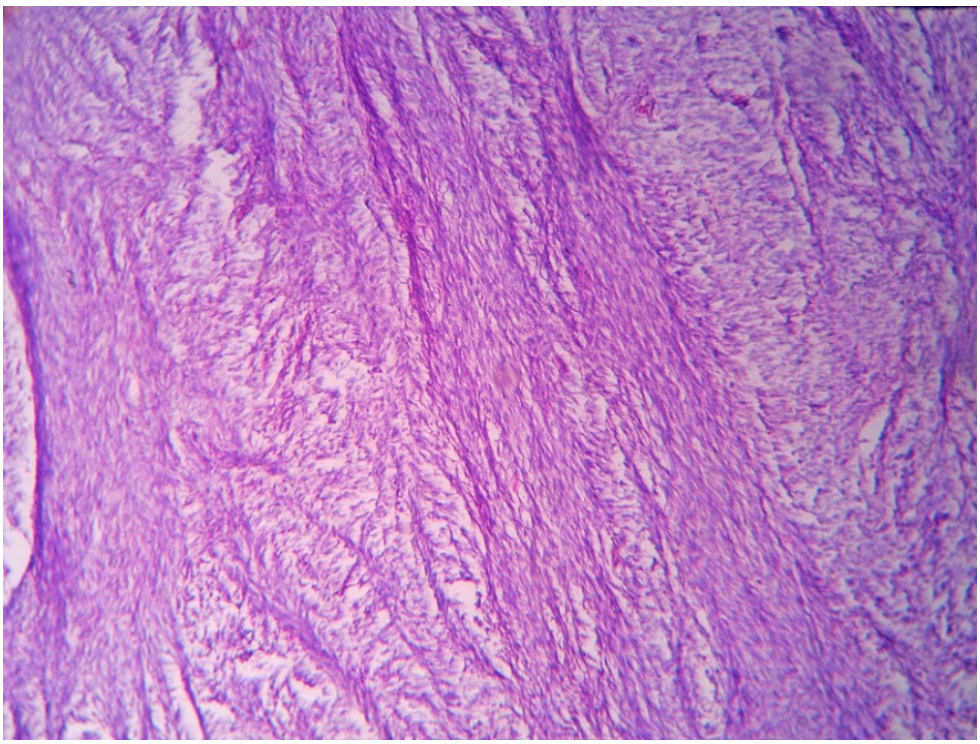
ADULT GRANULOSA CELL TUMOR
Fig.24 G 1888/10 Exhibitingreticulin wrapping around nests (H&E x 100X)



CARCINOID TUMOR
Fig.25 G232/10Insular pattern(H&E x 100X)

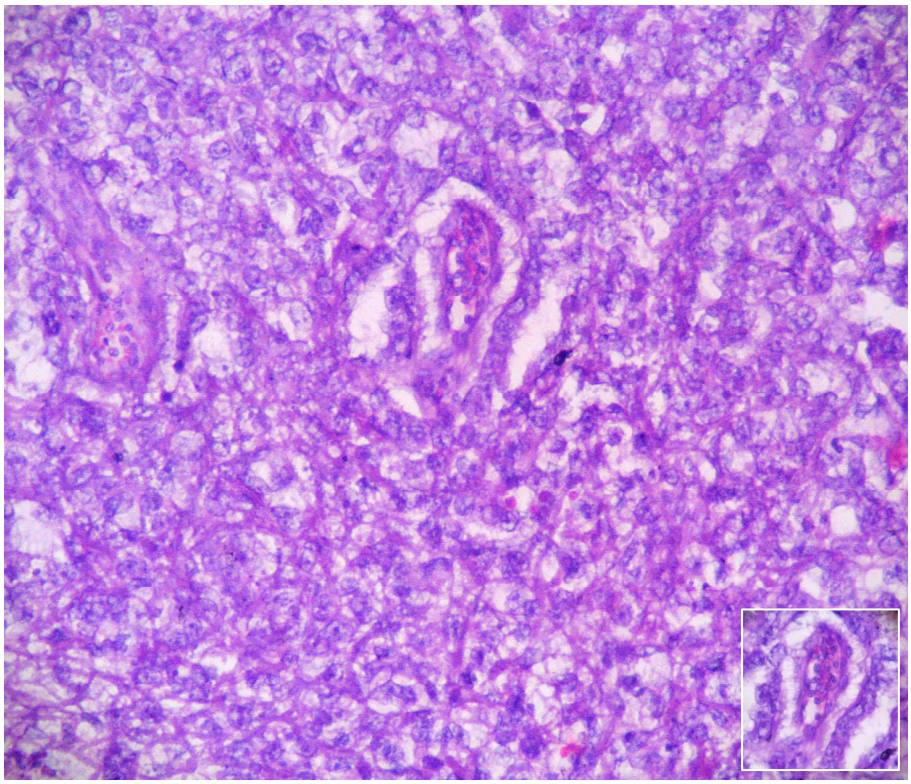


CARCINOID TUMOR
Fig.26 G232/10 Chromogranin positivity(H&E x 100X)



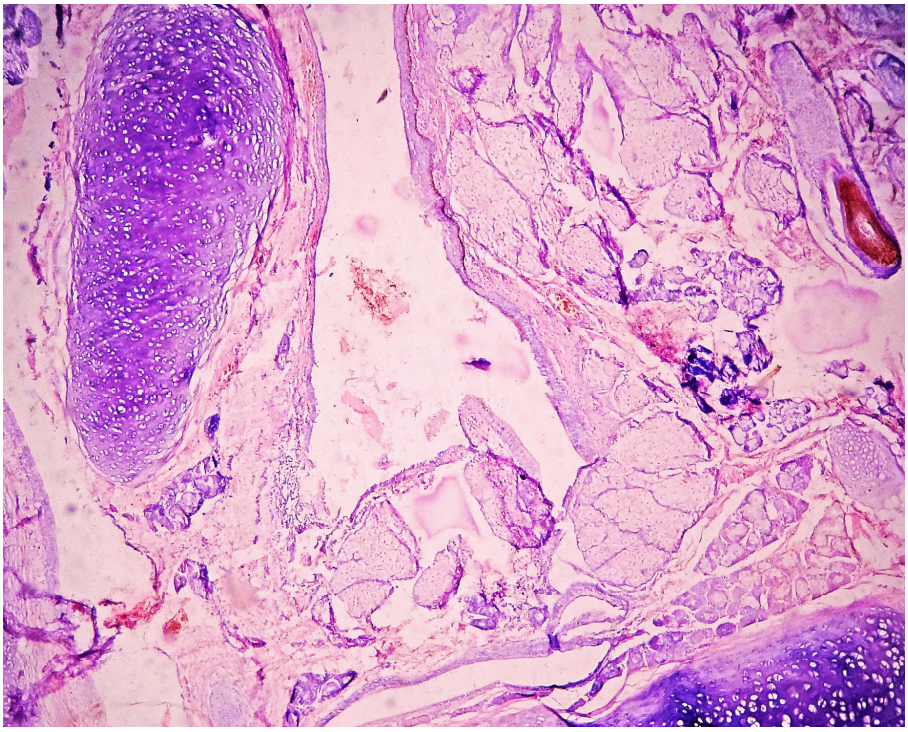
FIBROTHECOMA

Fig.27 G4444/09Pale lipid containing theca cells merge with spindle cell areas characteristic of fibroma(H&E x 100X)

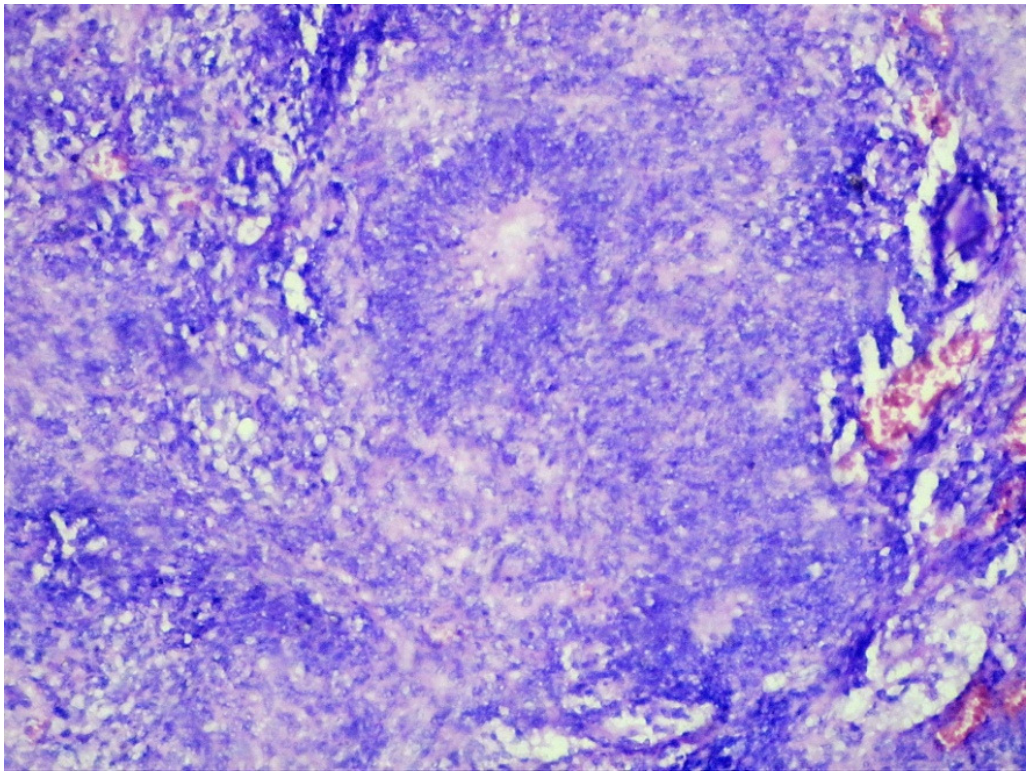


YOLK SAC TUMOR WITH INSERT SHOWING SCHILLER- DUVAL BODIES

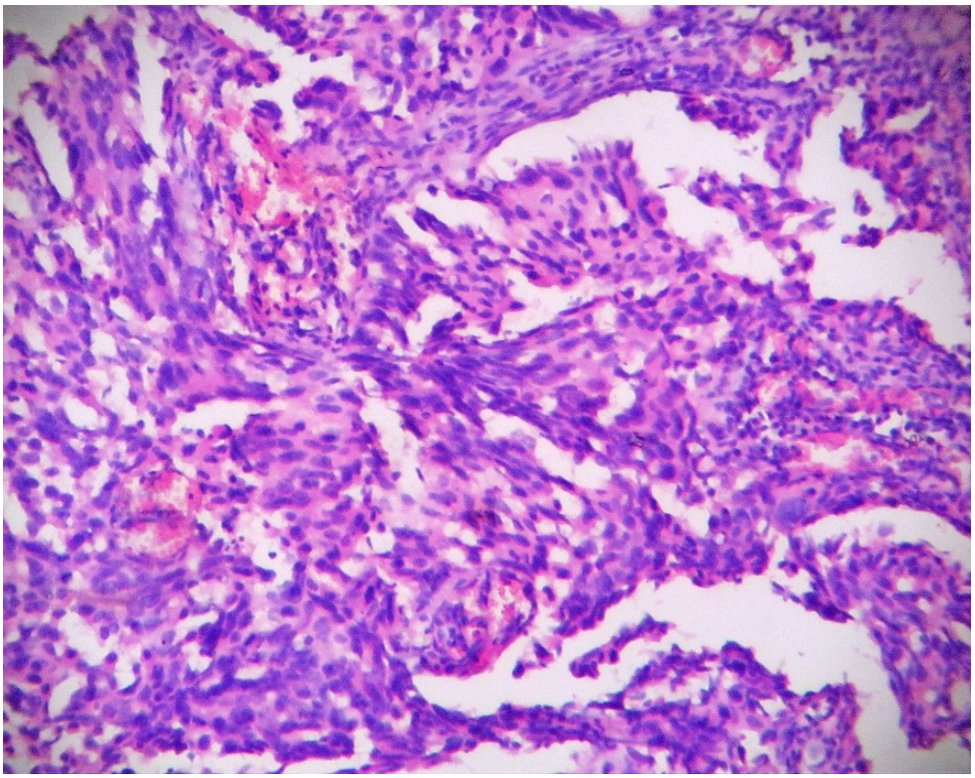
Fig.28 G3173/10(H&E x 100X)



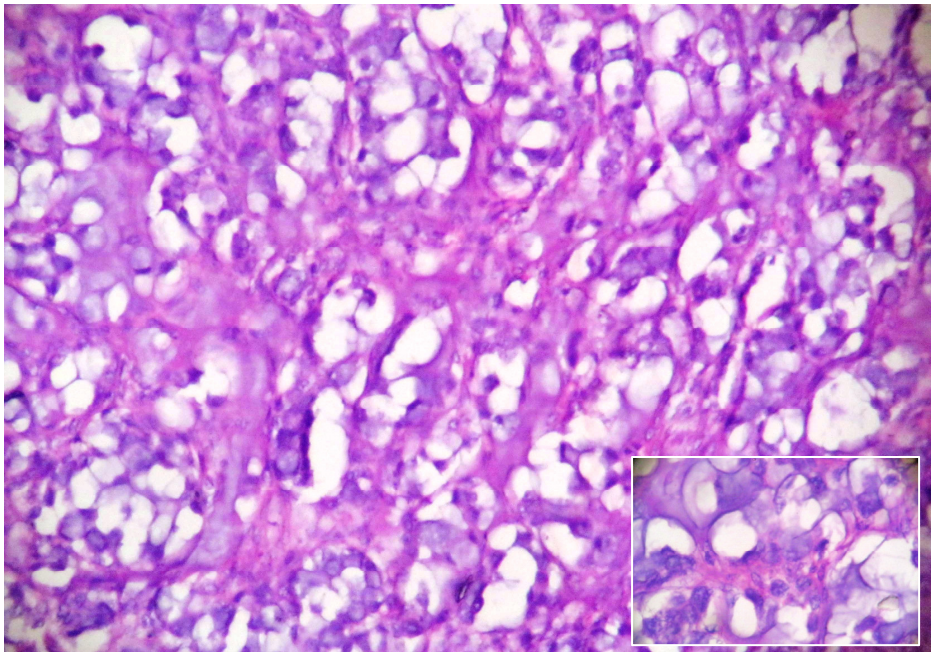
BENIGN CYSTIC TERATOMA
Fig. 29 G 2081/10 showing areas of cartilage, hair, squamous epithelial lining (H&E x 100x)



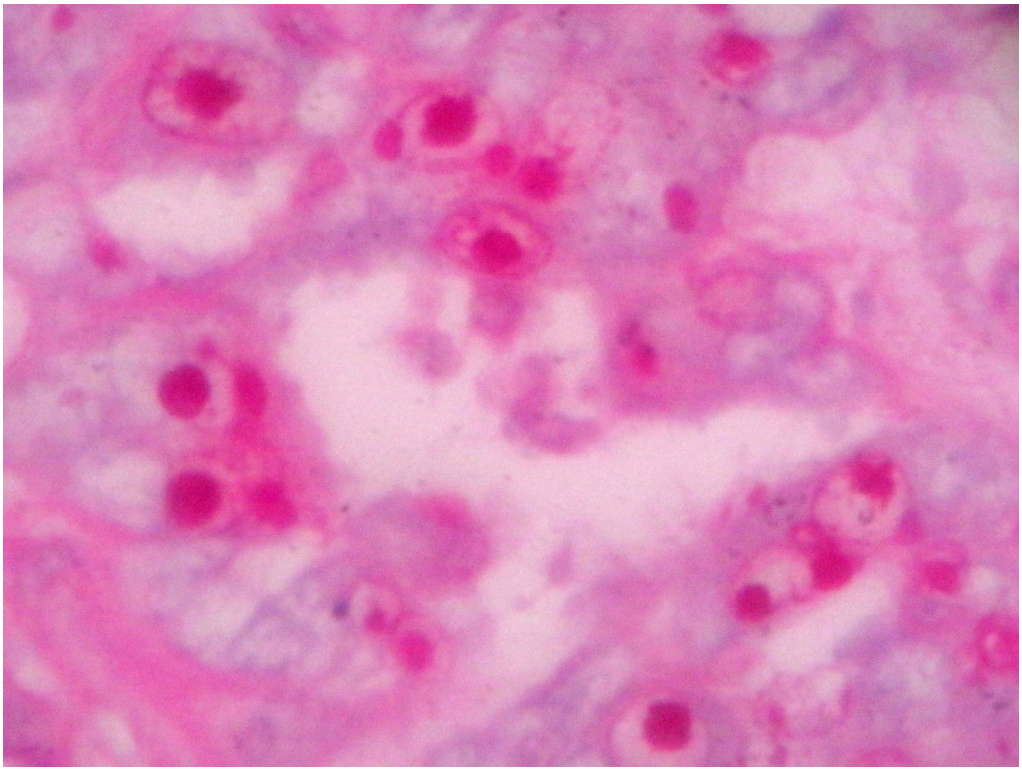
OVARIAN IMMATURE TERATOMA
With Primitive neuroepithelial elements
Fig.30 G2016/10(H&E x 100X)



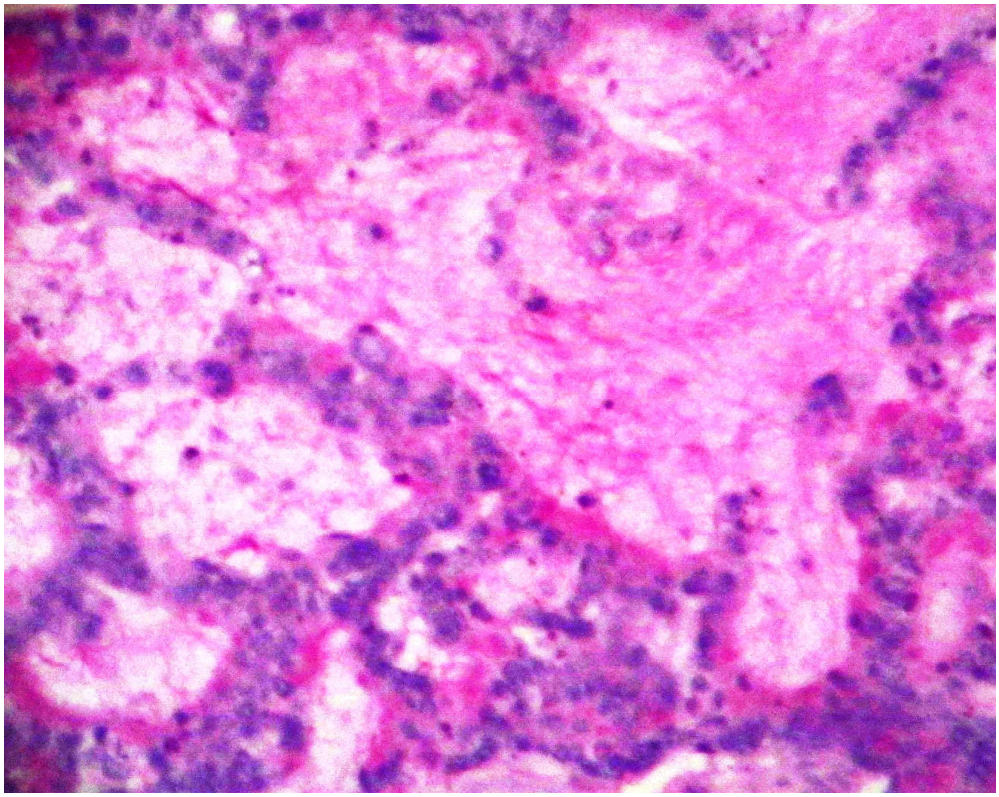
UNDIFFERENTIATED CARCINOMA
Fig.31 Sheets of pleomorphic epithelial cells with marked nuclear atypia G 1644/10 (H&E x 100X)



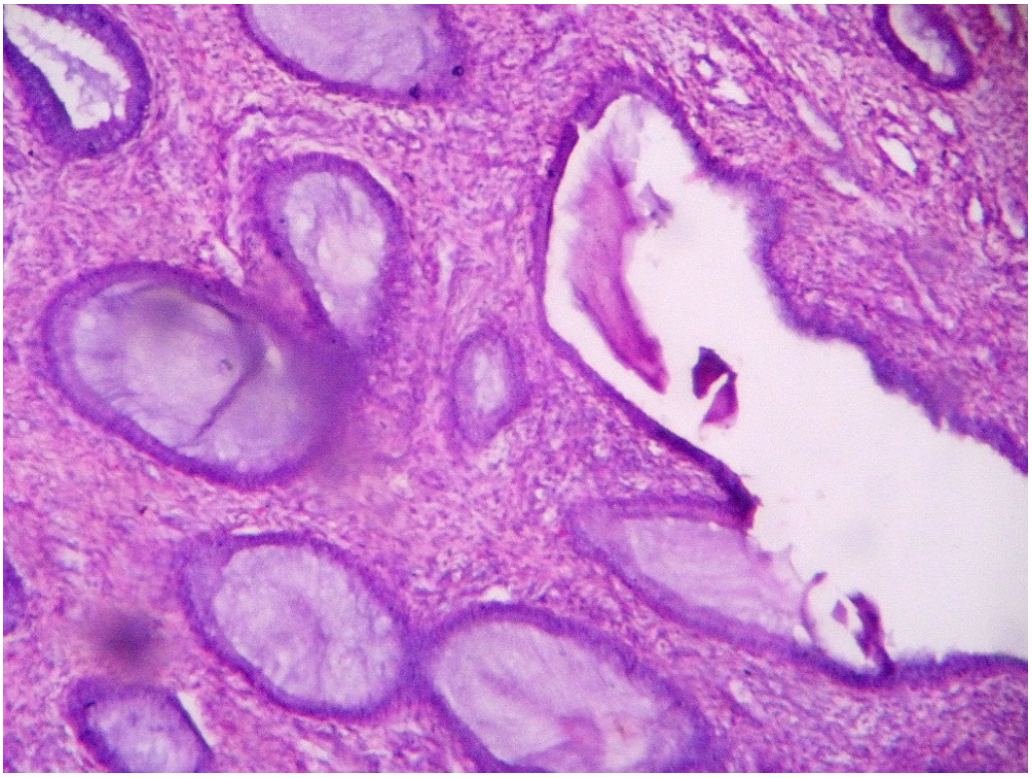
KRUKENBERG TUMOR
Fig.32 G1891/10 Insert showing signet ring cells. (H&E x 100X)



KRUKENBERG TUMOR
Fig.33 G1891/10 Signet ring cells showing PAS positivity (H&E x 400X)

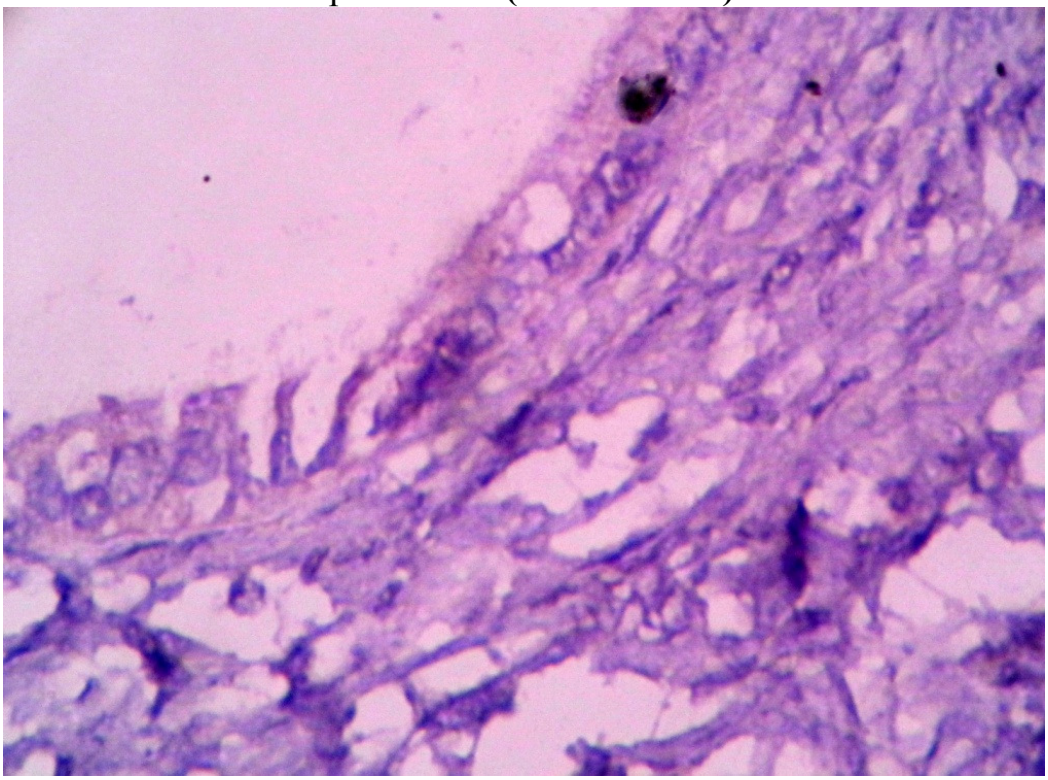


MUCINOUS CYSTADENOCARCINOMA
Fig. 34 G934/11 Tumor Cells with extracellular mucin pools showing PAS positivity **(H&E x 400X)**



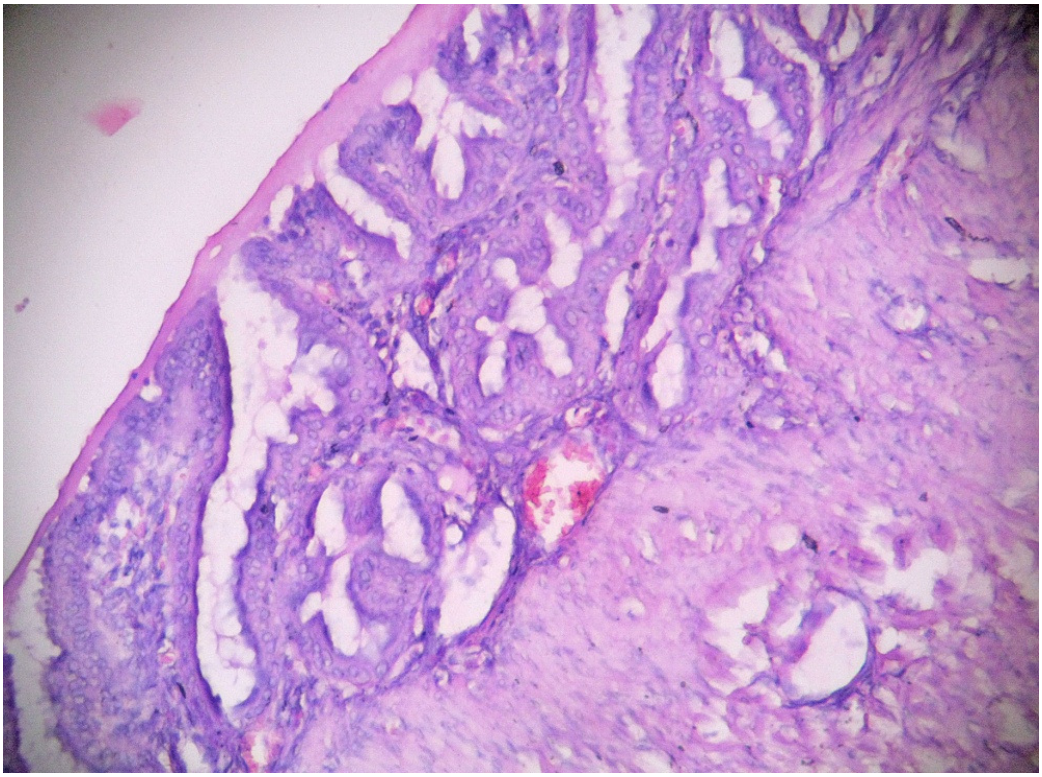
BENIGN MUCINOUS CYSTADENOMA

Fig.35 G 3577/10 Cyst lined by columnar cells with bland basal nuclei and apical mucin**(H&E x 100X)**

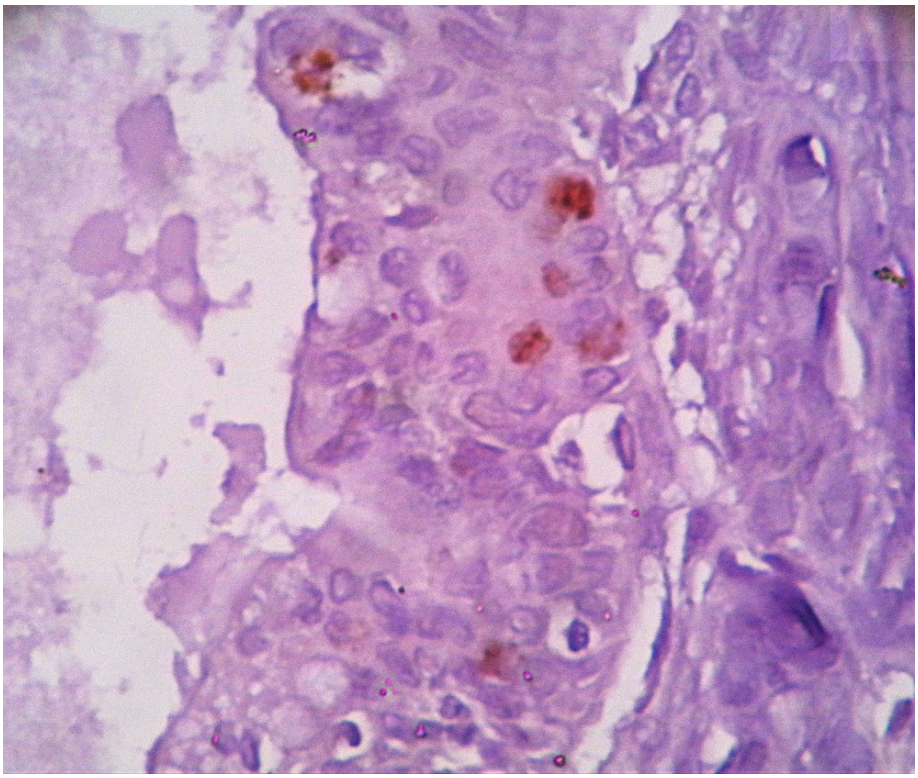


BENIGN MUCINOUS CYSTADENOMA

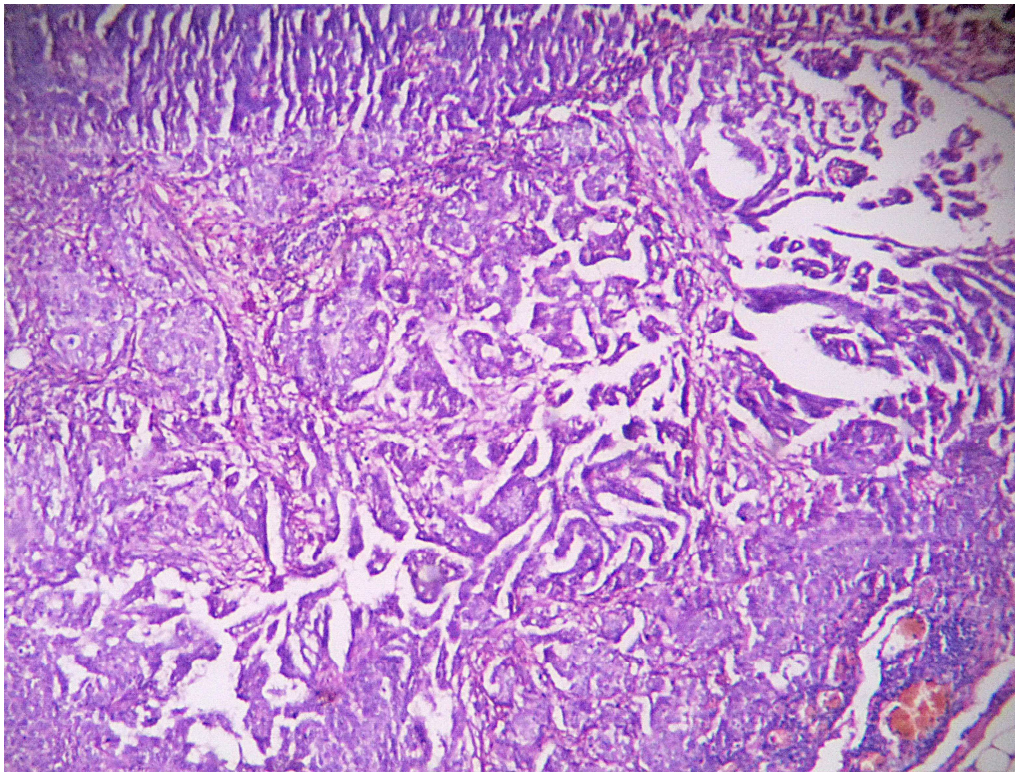
Fig.36 G 3577/10 Ki-67 index 3.1%(H& E x 400X)



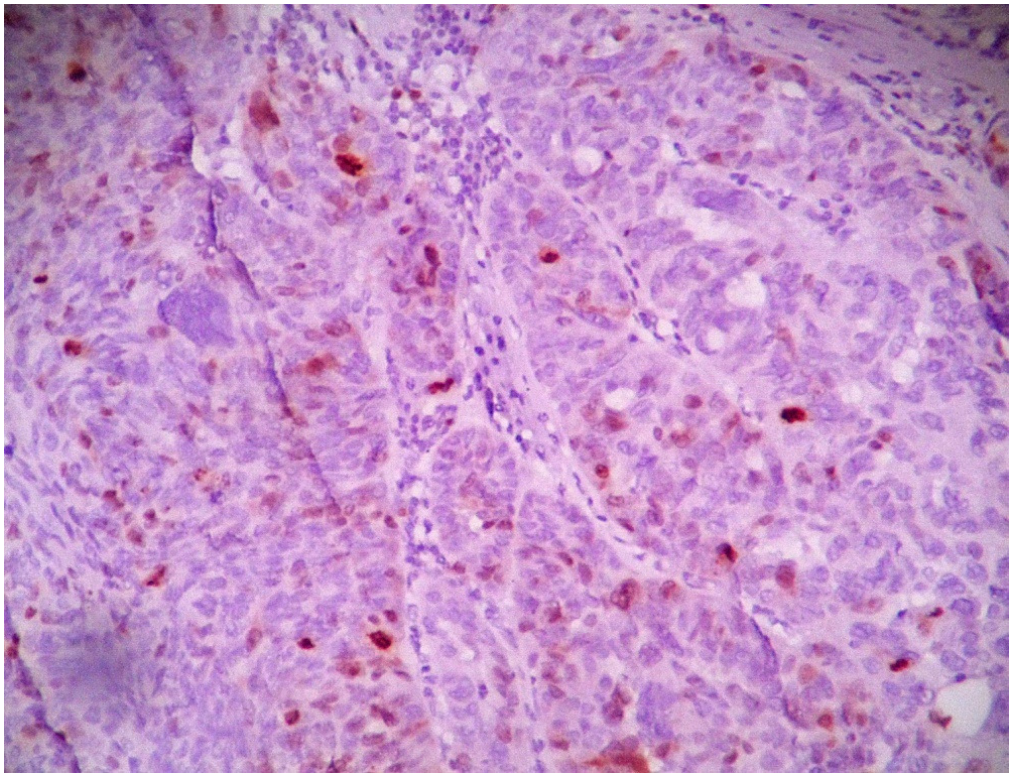
BORDERLINE MUCINOUS CYSTADENOMA
Fig.37 G4079/10(H&E x 100X)



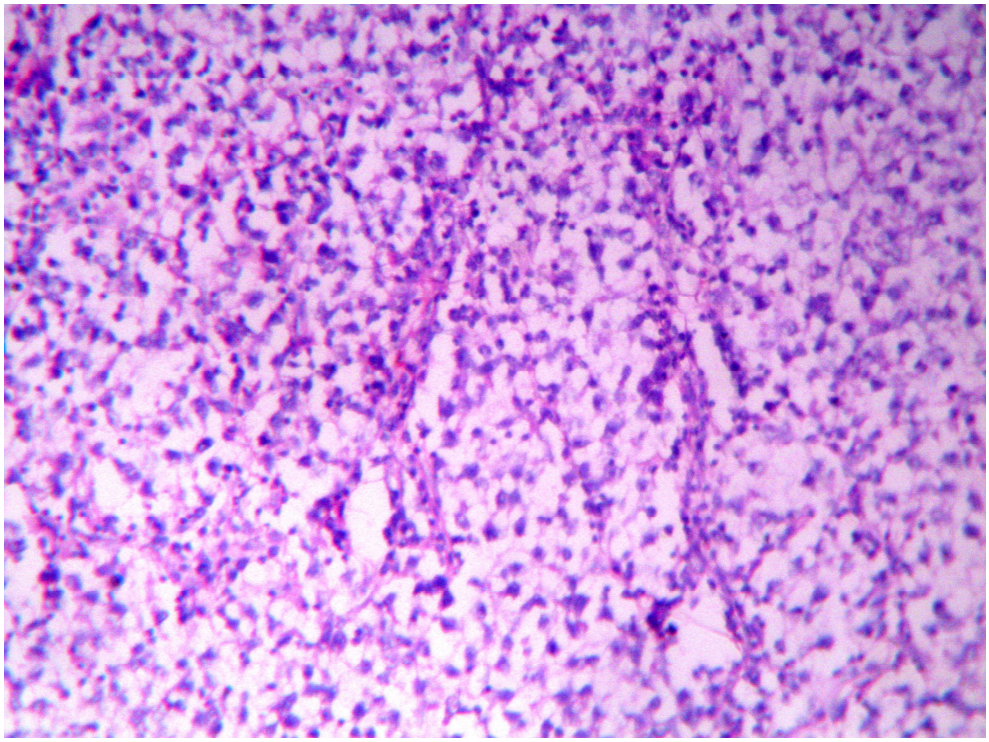
BORDERLINE MUCINOUS CYSTADENOMA
Fig.38 G4079/10(H&E x 100X) Ki-67 index 6%(H& E x 400X)



PAPILLARY SEROUS CYSTADENOCARCINOMA
Fig.39 G 104/10 Tumor cells arranged in solid nests and papillary pattern (H& E x 100X)

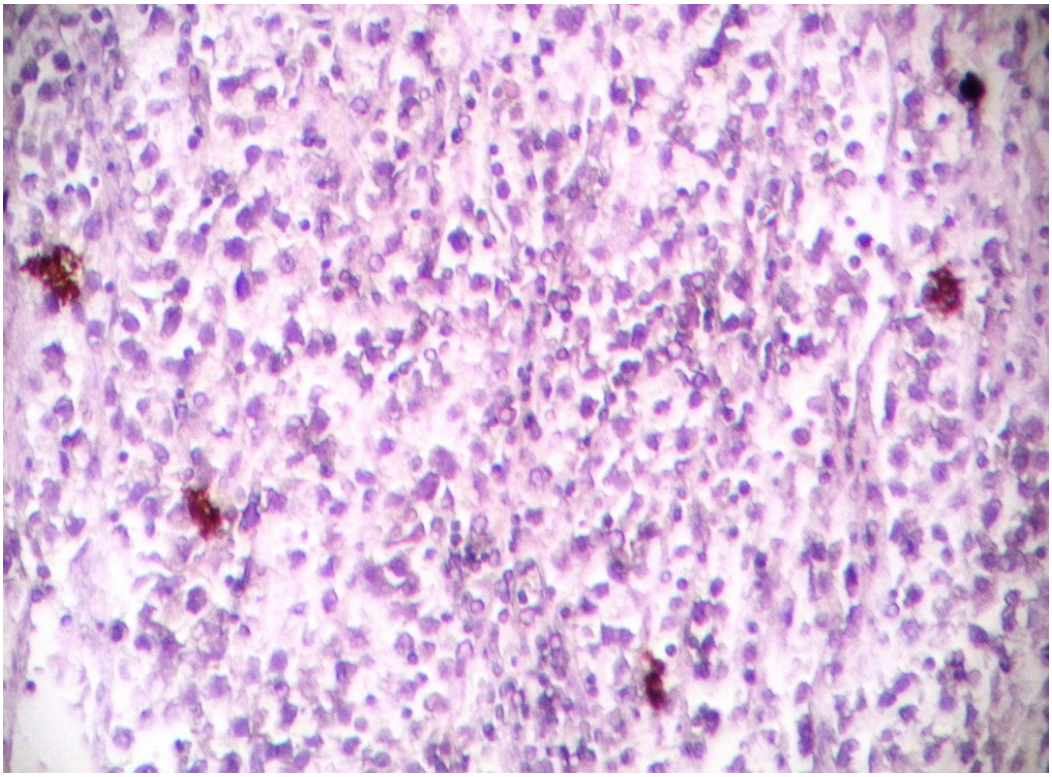


PAPILLARY SEROUS CYSTADENOCARCINOMA
Fig.40 G 104/10(H& E x 400X) Ki-67 index 29%



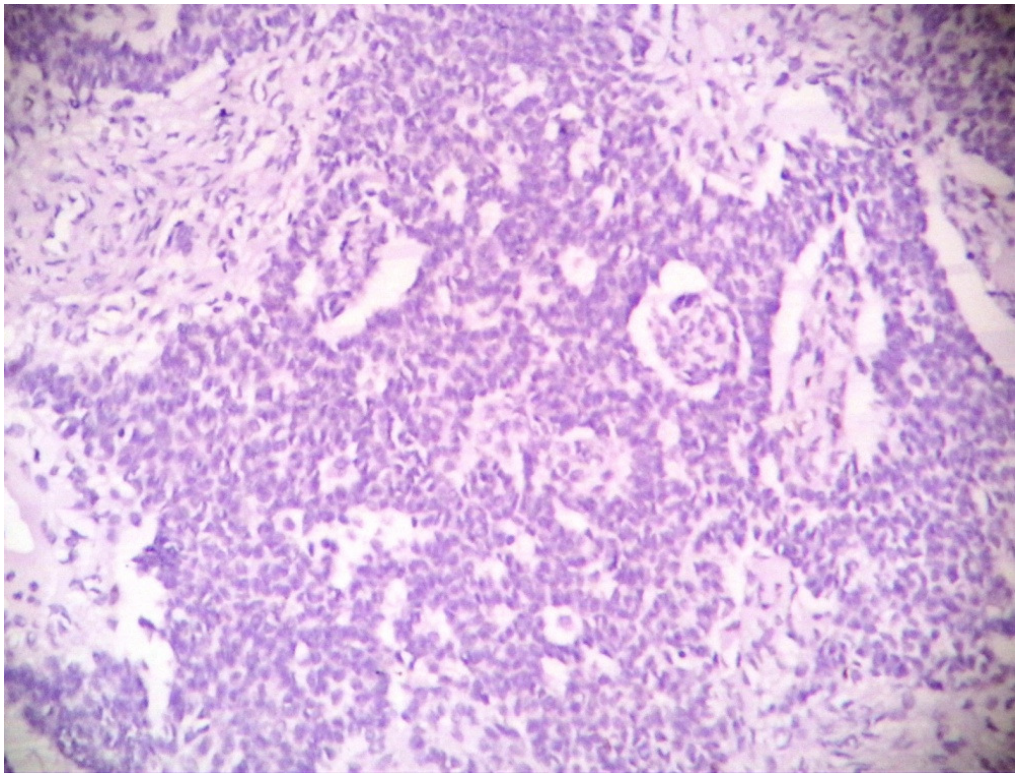
DYSGERMINOMA

Fig.41 G1920/10 Well defined nest of tumor cells separated by fibrous strands infiltrated by lymphocytes(H& E x 100X)

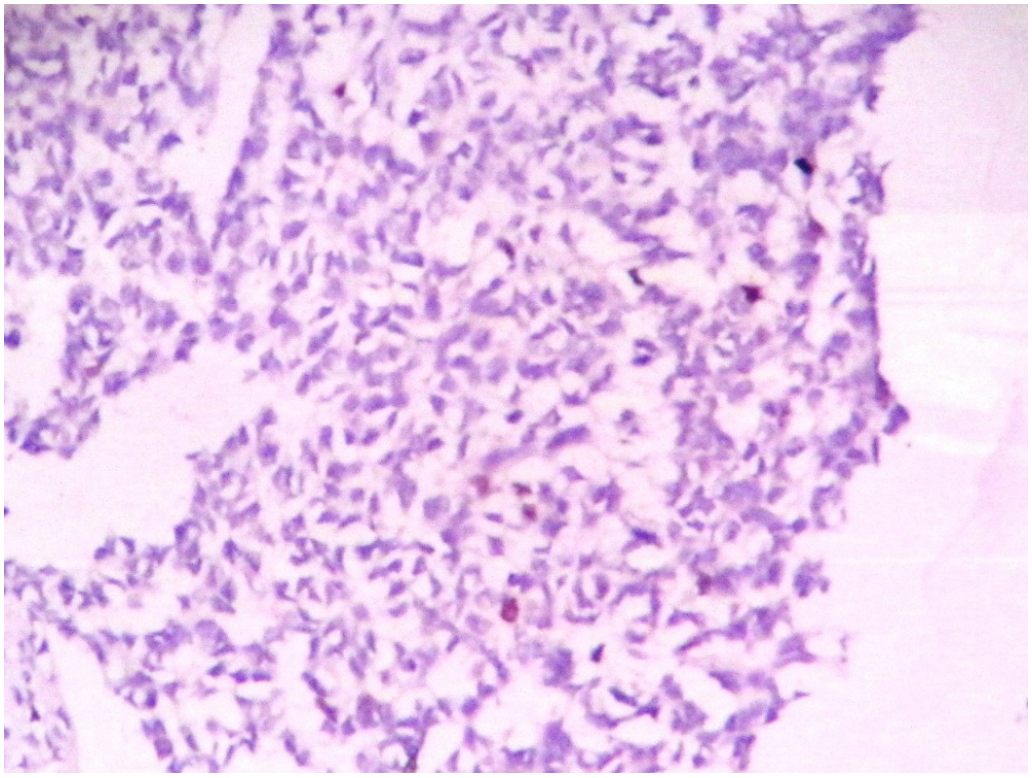


DYSGERMINOMA

Fig.42 G1920/10 Ki-67 index 25.3%



ADULT GRANULOSA CELL TUMOR
Fig.43 G2652/10 (H&E x 100X)



ADULT GRANULOSA CELL TUMOR
Fig.44 G2652/10 Ki-67 2.8%(H&E x 400X)

Discussion

DISCUSSION

The tumors of the ovary pose a major problem to the gynaecologist due to their higher complication rate and they are the biggest diagnostic challenge in the field of gynaecological oncology. The absolute number of the new cancer patients in India is increasing rapidly due to an increase in the size of the population as well as an increase in the proportion of elderly persons due to improved life expectancy[59]. The increased incidence of cases is partly due to more widespread screening programmes, improved certification and registration procedures in certain countries.

Though many authors have worked extensively in the field of ovarian tumor pathology, the wide variation in facts and figures from these studies causes the confusion in the area of tumor nomenclature and different morphological subtypes of tumor. In this study, an attempt has been made to study the histomorphology of ovarian tumors,and usefulness of immunohistochemical markers for accurate diagnosis and to assess the prognosis using Ki 67 immunoproliferative marker. These results are correlated with other studies.

INCIDENCE OF OVARIAN TUMORS:

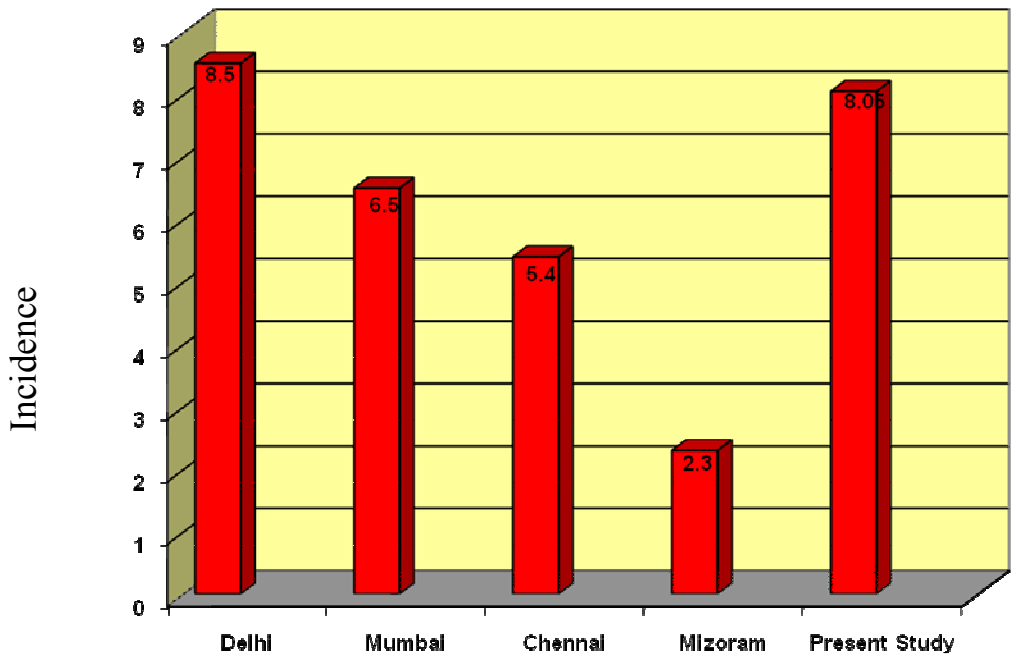
The comparison of incidence rates of ovarian tumors in Indian registries are illustrated in table 11 and graph 7.

COMPARISON OF INCIDENCE RATES IN INDIAN REGISTRIES

Table 11

Place of Study	Incidence
Delhi	8.5%
Mumbai	6.5%
Chennai	5.4%
Mizoram	2.3%
Present study	8.05%

Graph 7



The incidence of ovarian malignant neoplasms among other gynaecological malignancies in this study period was 8.05%.This ranks next to Delhi, where the incidence was 8.5%. Mizoram has the lowest incidence 2.3% [12]

These observations suggest that the possible environmental and life style factors have an influence on the incidence rate. Hence in urban areas like Mumbai, changes in life style factors such as increase in age of marriage, delay in age at first birth, reduction in parity and improved socioeconomic conditions might have contributed to the increase in incidence in contrast with the rural area like Mizoram with the lower incidence.

As per the present study, ovarian carcinoma is the second most common gynaecologic malignancy in females (8.05%) next to cancer cervix (67%)(table 12)

Table 12

S.No.	**Site**	**No. of malignancies**	**%**
1.	Cervix	593	67.23
2.	Ovary	71	8.05
3.	Endometrium	41	4.64
4.	Vulva	8	0.91
5.	Vagina	1	0.11
6.	Fallopian tube	0	0.11

AGE INCIDENCE OF OVARIAN TUMORS:

No age group was exempted from the occurrence of ovarian tumors including childhood. In the present study the majority of benign tumors occurred in the age group of 21-30 years (79.5%). This is in accordance with the studies conducted by Ramachandran et al (1972)[93] and Jagadeeshwari N et al (1971)[43]. Majority of the malignant neoplasms occurred in the age group of 41-50 years in our study, which goes in hand with studies conducted by Jegadeeshwari N et al (1971)[43] and Jha R and Karki S[49], but in contrast with the study conducted by Ramachandran et al (1972)[99] wherein, the maximum malignant tumors occurred in age group between 31-40 years.

Table 13 Comparison of age in other studies

S.No.	Authors	Age (group) in years					
		< 20yrs	21-30yrs	31-40yrs	41-50yrs	51-60yrs	>60
1.	Tyagi SP [70]	7.5	40.09	28.34	20.00	3.33	0.83
2.	Ramachandran et al [5]	11.57	26.24	21.37	22.70	12.29	4.53
3.	Saxena et al [3]	10.67	31.17	27.52	20.25	6.75	3.65
4.	Present study	7.5	19.5	23	28	14.5	7.5

Benign tumor cases had lower mean age and borderline tumor cases had higher mean age. But the difference was not statistically significant.

As per the literature and studies conducted by various authors, borderline forms are detected after the age of 40 years and 30-40% of them after the age of 68 years [82]. In contrast, in our study borderline tumors stand in peak at the 3rd decade.

CLINICAL FEATURES OF OVARIAN TUMORS:

The following table shows the occurrence of clinical features in the different studies in comparison with the present study.

Table 14

Sl. No.	Clinical Features	Gupta et al[33]	Couta F et al [21]	Present Study
1.	Pain in lower abdomen	46.2%	39.25%	50.2%
2.	Mass per abdomen	60.5%	90.20%	58.5%
3.	Menstrual disturbances	40.2%	31.70%	5%
4.	Others (Pressure symptoms)	34.5%	39.08%	3%

According to the studies of Gupta et al, the most common clinical feature was mass per abdomen which goes in accordance with our present study.

As per literature, menstrual irregularities were seen in 40.2% of cases (Gupta et al) whereas in our study only 5% of cases had similar symptoms.

CONSISTENCY OF OVARIAN TUMORS:

Table 15 comparison of Consistency of benign tumors with other studies

Study	Cystic	Solid	Mixed
Jagadeeswari N et al[79]	97.4	2.4	-
Gupta et al [33]	76.2	2.4	21.5
Kapas MM pal NC [51]	82.0	-	18
Chhanda met al [72]	30.8	-	69.2
Present Study	6.2%	81.5%	12.3%

Table16 comparison of Consistency of malignant tumors with other studies

Study	Cystic	Solid	Mixed
Jagadeeswari N [91] et al	111	2.4	-
Gupta et al [73]		2.4	21.5
Kapas MM pal NC[196]		-	18
Chhanda met al [72]		-	69.2
Present Study		81.5%	12.3%

. Various studies have shown that benign tumors are most often cystic in consistency while malignant tumors tend to be mixed (solid & cystic) or solid in consistency. This scenario has also been found in the present study

LATERALITY OF OVARIAN TUMORS:

Table 17 Comparison of laterality of benign ovarian tumors

Study	Unilateral (%)	Bilateral (%)
Pilli et al [74]	92.2%	7.8%
Jha R & Karki S [49]	93.3%	6.67%
Present Study	90.3%	9.7%

Table 18 Comparison of laterality of malignant ovarian tumors

Study	Unilateral (%)	Bilateral (%)
Prabhakar & Maingi [76]	78.10%	21.9%
Misra RK et al (1991) [67]	82.98%	17.2%
Couto et al (1993) [13]	72.4%	27.6%
Present Study	64.6%	35.4%

In our present study 90.3% of benign ovarian tumors were unilateral and 64.6% of malignant ovarian tumors were unilateral, whereas 9.7% of benign ovarian tumors were bilateral and 35.4% of malignant ovarian tumors were bilateral. These findings imply that bilaterality is more common in malignant tumors. This is in accordance with the findings of other studies.

According to the literature, bilaterality is more common in serous than mucinous tumors, which goes in accordance with the present study.

HISTOLOGICAL TYPES OF OVARIAN TUMORS:

SURFACE EPITHELIAL TUMORS

In our study , Surface epithelial tumor stands as the most common ovarian neoplasm (155/200 cases – 77.5%) followed by germ cell tumors (22/200 cases – 11%) , sex cord stromal tumors (15/200 cases – 7.5%) and metastatic tumors (3/200 cases – 1.5%).

Of the surface epithelial tumors, serous epithelial tumors contribute 61.2% and mucinous epithelial tumors contribute 36.20%.

These findings are in accordance with the literature. In the study by katsube et al, koonings et al [80] and Petterson et al, mucinous borderline tumors are less common than serous borderline tumors but in our study mucinous borderline tumors out number the serous borderline tumors in close correlation with the studies by Isarangkul in Thailand.

Brenner tumors are often associated with other tumors such as mucinous cystadenoma, mature cystic teratoma and transitional cell carcinoma of bladder [28],[62] .In our study 2 such associations with benign mucinous cystadenoma has been observed(fig18). Association may be due to overgrowth of metaplastic mucinous epithelium.

Other associations with mucinous cystadenoma commonly seen were with teratoma (4-5%)and carcinoid tumor.

One case of bilateral malignant Brenner tumor was observed in a 65 year old female who presented with abdominal mass. Grossly the tumor measured 10x8x5 cm and 4x3x2 cm on each side(fig7). The tumor was arranged in sheets with stromal invasion.(fig 20)

GERM CELL TUMORS

Dysgerminoma :

Three cases were diagnosed as dysgerminoma which accounted for 1.5% of all the tumors in the present study (fig41). This was the third most common malignant germ cell tumor in our study in contrast to studies conducted by Kurman RJ et al, Bjorkholm et al and Mankad MH et al [55] wherein, dysgerminoma was the most common.

Yolksac tumor:

Yolk sac tumor was seen in 4 patients accounting for 2% of all ovarian tumors. Krigman et al highlighted the fact that this was the second commonest type of malignant germ cell tumor of the ovary with a median age of 19 years[54]. Which is in accordance with our study.

Microscopically tumor cells were arranged in microcystic reticulated pattern. PAS positive, diastase resistant intra and extra cellular hyaline globules and Schiller – duval bodies were seen (fig 28). Kurman et al[55] observed that though reticular pattern is the common type, festoon pattern with Schiller – duval bodies was the easiest to identify.

3) Teratoma

This was the commonest germ cell tumor found in the present study constituting 7.5% of all the tumors. All were benign cystic teratomas (fig 29) except one immature teratoma. These findings were similar to those observed by Sahn L et al, Gupta SC et al and Couto F et al.[13]

One case of unilateral immature teratoma grade II tumor was observed in a 12 year girl who presented with mass per abdomen, tumor measuring 13x10x5 cm, cut surface was solid & cystic. Microscopically showed tissues derived from all germ cell layers and immature neuroectodermal elements (Fig 30).

We encountered a relatively rare association of adenocarcinoma occuring as a secondary malignancy in Benign cystic teratoma in a 45 year female.

Two cases of mixed epithelial tumors were observed. Combinations of mucinous cystadenoma of ovary with benign Brenner tumor was observed in the same ovary in both cases (fig.18).

SEX – CORD STROMAL TUMORS

Granulosa cell tumor is the commonest sex cord stromal tumor. Further it is also the commonest functional ovarian tumor with hormone (oestrogen) production. In the present study 8 cases (4%) were reported as granulosa cell tumor.

Tyagi SP, Tyagi GK and logani KP found an incidence of 3.3% in a pathological study of 120 cases [60]. Jagadeswari N, Reddy RS and Rao[78] found an incidence of 3.7% while Ramachandran G et al [77] found an incidence of 2.7% as shown in table.

Table 19 Incidence of Granulosa Cell Tumors In Different Studies

S.No.	Authors	Incidence (%)
1.	Tyagi SP et al 104	3.30
2.	Jagadeswari et al 107	3.70
3.	Ramachandran G et al 106	2.70
4.	Gupta SC et al	4.40
5.	Present Study	4.0

The commonest presenting symptom in the granulosa cell tumor was menorrhagia, similar symptom was encountered by Stenwit JT et al[93], while this was the second commonest symptom in the study by Pancratz E et al [26].

Microscopy:

Microscopically a mixture of microfollicular, trabecular and diffuse patterns were seen along with typical Call-Exner bodies(Fig 21). Though Stenwing et al[39] observed that these characteristic bodies were found only in 60% of the cases. Well differentiated tumor has a longitudinal nuclear groove. Presence of 3 or more mitosis / 10HPF and degree of cellular atypia correlated with a worst prognosis in the study by Stenwing was JT et al[83]. In this study, we applied reticulin stain for granulosa cell tumors and fibrothecoma. The stain shows fibrils surrounding the nests and large

aggregates of granulosa cells(fig.24). In thecoma reticulin stain highlights an investment of individual cells by fibrils.

2) Fibroma:

2.35% of all tumors were fibromas in the studies by Gupta SC et al[73]. These percentage was higher than 1% in the present study.

3) Fibrothecoma:

According to the Evan AT et al, the peak age of occurrence was 51–60 yrs. This goes in accordance with the present study wherein the mean age incidence was 50.2 years. Cut section of the tumor was solid grey – yellow, this feature according to Evans AT et al. helps to distinguish grossly, thecoma from fibroma which have greyish white appearance [26].

METASTATIC TUMORS

Three cases of Krukenberg tumor were found among the 200 cases of ovarian tumors(fig 32). This was lower than study reports by Holt ZF and Hart WR (1982) (3-5%). [39]

PAS stain is an extremely useful and aesthetically pleasing technique. In our study mucinous carcinoma of ovary shows PAS positive mucin pools (fig 34), and Krukenberg tumor show intracellular PAS positivity(fig 33). In a study by Powari M et al[75], out of 19 metastatic tumors, 31.5% (6 cases) were Krukenberg tumors. The incidence is much higher compared to the present study.

IMPORTANCE OF IMMUNOHISTOCHEMICAL CONFIRMATION IN GRANULOSA CELL TUMORS:

During the study period ,out of 200 cases 10 were histopathologically diagnosed as granulosa cell tumor. We did immunohistochemical marker study in all these cases for confirmation. Surprisingly,in one case tumor cells showed strong expression of chromogranin and synaptophysin and negative for vimentin.. Final diagnosis of ovarian Carcinoid was made.

On retrospective analysis, no other tumor mass was detected elsewhere by abdominal ultrasonography and CT scan, Isolated Tricuspid regurgitation was incidentally found in preoperative echocardiography.

In correlation with the above findings , we came to conclusion of Primary ovarian Carcinoid tumor with isolated Tricuspid regurgitation.

And in another case Vimentin and Inhibin were negative and EMA was positive. And so the final diagnosis of poorly differentiated carcinoma was made. The significance of differentiating Granulosa cell tumor and poorly differentiated carcinoma lies in the fact that the treatment modalities of both these tumors vary markedly. Granulosa cell tumor is a benign in which case total abdominal hysterectomy with bilateral salphingo oopherectomy (TAH-BSO) alone would suffice whereas in a case of poorly

differentiated tumors of ovary along with TAH-BSO, chemotherapy is mandatory.

The remaining 8 cases showed vimentin positivity and were negative for EMA. These tumors were diagnosed as Granulosa cell tumors .

Thus Immunohistochemical confirmation is always necessary in Granulosa cell tumors to rule out other differential diagnosis which simulate them histopathologically. This is very important because treatment protocol varies for each.

Ki-67 LABELLING INDEX :

The rate at which a tumor proliferates has long been considered to bear a relationship with its clinical course. The determination of growth fraction using Ki- 67 index is a simple method and has long been shown to have a prognostic value in a variety of malignancies like CNS tumors, Lymphoproliferative diseases, connective tissue tumors and breast tumors [69]. Ki67 expression in different ovarian tumors has long been studied by various authors across the world. However , there is a paucity of such a study in the Indian literature. Few literature clearly document the importance of Ki 67 proliferative marker in assessing the prognosis of ovarian cancers.

We evaluated Ki 67 expression in 24 selected cases which included 4 benign cystadenoma(2 serous,2 mucinous), ,4 borderline cystadenomas (2

serous,2 mucinous),4 carcinoma (2 serous, 2 mucinous adenocarcinoma), 2 Germ cell tumors, 8 granulosa cell tumors.

1) Ki 67 INDEX IN BENIGN , BORDERLINE AND MALIGNANT OVARIAN TUMORS:

The Ki 67 index gradually increase from benign to malignant tumors [69]. We observed the same in our study with ki-67marker.

Benign tumors had a mean Ki 67index of 2.9% , borderline tumors had a mean Ki 67 index of 7.2% ,while the malignant tumors had a mean Ki 67 index of 29.9% .

A statistically significant difference ($p =<0.001$) was obtained between the mean Ki 67 indices of benign, borderline & malignant tumors. These findings are in close agreement with Garzetti et al [29] and with Monisha chowdhury et al.[69]

Ki 67 index is especially useful in borderline epithelial ovarian tumors of low malignant potential. These are seen in younger premenopausal women between 30-50 years of age. They remain confined to ovary for a longer time. Overall about 15-25 % of borderline tumors behave in a malignant fashion, invading locally and even metastasizing. It is thus important to identify those borderline neoplasms which are likely to behave in a malignant fashion, for it is possible that histological grading of the

degree of severity of the epithelial proliferation and atypia may prove to have some prognostic benefits.[7]

b) Ki 67 INDEX IN GRANULOSA CELL TUMORS:

Granulosa cell tumors behave unpredictably. Histopathologic evaluation of Granulosa cell tumors offers only few clues. It is difficult to predict their prognosis by pathologic means. Tumors larger than 15 cm, bilateral tumors, spread beyond ovary(FIGO stage >1A) or ruptured have less favourable prognosis. The 'stage' is the single most powerful prognostic indicator [17] .

Ki 67 index provide insight into nuclear proliferation and to predict the clinical behavior of Granulosa cell tumors[19].

In this study Ki 67immunohistochemistry was assessed in all the Granulosa cell tumors (8 cases) and the results were correlated with tumor stage at presentation. Mean Ki 67 index for 8 cases of histologically and immunohistochemically proven case of granulosa cell tumor was 5.1%.(fig 44).

In the present study , Ki 67 index was higher in 2 cases of. Granulosa cell tumors (7.9% and 8.4%) which correlated clinically with higher stage (FIGO stage I(c) disease).This is in correlation with the study conducted by Costa MJ,Walls J et al [19]

who also proved that higher Ki 67 index in GCT was associated with worst prognosis.

Ki 67 index in the rest of the Granulosa cell tumors was low which correlated clinically with FIGO stage I(a) disease. This goes in hand with study conducted by Costa MJ,Walls J et al [19] who also proved that lower Ki 67 index in GCT was associated with better prognosis.

Thus in the present study, ki 67 index was higher in advanced stage tumors, and thereby pointing toward the aggressive clinical behavior and poorer clinical outcomes.

Even though Granulosa cell tumor usually has good prognosis, it is a tumor of unquestionable malignant potential and has a tendency for late relapse. Case series and reports suggest that post operative chemotherapy is of most benefit in advanced diseases and long term follow-up is recommended.[100-102]

OVARIAN CANCER WITH ASSOCIATED ENDOMETRIAL CANCER:

The simultaneous development of multiple primary cancers in the upper female genital tract is a well known phenomenon. Of these the commonest is the endometrioid carcinoma of the ovary and the uterus. Diagnosis of this type of tumor either as a separate independent primary or as a metastatic tumor is difficult. A careful consideration of a number of gross, histological and immunohistochemical features may be helpful in the

distinction between metastatic and synchronous primary tumors which have different therapeutic and prognostic implications [45,104,68]

Out of 200 ovarian tumors, 5 were associated with endometrial carcinoma (2.5%).Among those 5cases, 3 showed the same histologic pattern in both ovary and endometrium. One was bilateral mucinous cystadenoma with endometrioid type of endometrial adenocarcinoma. Other case was ovarian Granulosa cell tumor with endometrial adenocarcinoma.It is due to estradiol overproduction which continuously stimulates endometrium. Endometrial cancer occurs in association with Granulosa cell tumor in atleast 5% of cancer and 25% to 50 % are associated with endometrial hyperplasia.[7]

Summary

SUMMARY

In the present prospective study of 200 ovarian neoplasms evaluated with clinical, histopathological, histochemistry and immunohistochemistry, the following conclusions are made.

1. The incidence of ovarian neoplasms was 8.05% and ranked second among the malignancies of female genital tract.
2. The incidence of ovarian neoplasms wass highest during the 5th decade. The peak age incidence of benign tumors was 3rd decade and that for borderline and malignant tumors was 4th and 5th decade respectively.
3. The most common symptom was mass per abdomen (58%), followed by pain (51%) and menstrual disturbances(5%).
4. 81.5% of ovarian tumors were unilateral and 18.5%were bilateral.
5. 85.5% of benign tumors were predominantly cystic and 81.5% of malignant tumors were predominantly solid and cystic or purely solid.
6. The size of the ovarian tumors varied from 2 to 30 cm .
7. 77.5% were Surface Epithelial tumors, 7.5% were Sex Cord Stromal tumors, 11% were Germ Cell tumors, 1.5% were metastatic tumors and 2.5% were undifferentiated tumors.
8. .In Surface epithelial tumors, benign serous cystadenoma was the most common (25%).

9. In Sexcord stomal tumors, Granulosa cell tumor was the most common(5%).
10. In Germ cell tumors, benign cystic Teratoma was the most common(7.5).
11. 62% of ovarian tumors were benign, 5.5% were borderline and 32.5% were malignant.
12. Reticulin stain plays a vital role in distinguishing between Fibrothecoma and Granulosa cell tumor. PAS stain is used to differentiate between krukenberg tumor and mucinous cystadeno carcinoma.
13. In this study, 2 cases which were histolopathologically diagnosed as ovarian granulosa cell tumor was finally diagnosed as Primary ovarian Carcinoid tumor and Poorly differentiated carcinoma respectively after immunohistochemical study.
14. Benign ovarian tumors had a mean Ki 67 index of 2.9%, borderline tumors had a mean Ki- 67 index of 7.2%, while the malignant tumors had a mean Ki 67 index of 29.9%.

The difference in the mean value between benign, borderline, and malignant epithelial tumors were statistically significant ($p =<0.001$).

15. In Granulosa cell tumors, the mean Ki 67 index was 5.1%. (fig 44) and it was higher in two cases with higher clinical stage.

16. Several interesting cases which we encountered were

A. Two cases of mixed epithelial tumors composed of mucinouscystadenoma of ovary and benign Brenner tumor (fig 18)

B. One case of bilateral malignant Brenner tumor in a 65 yearold female (fig 20

C. One case of juvenile granulosa cell tumor in a 2 year old girl with precocious puberty (fig 22)

D. A case of unilateral granulosa cell tumor associated with well differentiated endometrial adenocarcinoma and omental metastatic deposits.

E. A rare association of adenocarcinoma occuring as a secondary malignancy in Benign cystic teratoma .

F. One case of immature teratoma with neuroectodermal elements .

G. 2.5% (5 cases) ovarian tumors were associated with endometrial carcinoma.

Conclusion

CONCLUSION

Accurate diagnosis of ovarian tumors can be rendered in most of the cases by correlating the clinical presentation, gross and microscopic features. Histochemistry and immunohistochemistry are essential in certain ovarian tumors with doubtful diagnosis. In our study , immunohistochemical markers were very useful in accurate diagnosis of Granulosa cell tumors.

Ki 67 immunostaining is a simple method which provides robust prognostic information for patients with ovarian cancers. This biomarker is very much useful to identify borderline tumors which are likely to behave in a malignant fashion,to assess the prognosis in Granulosa cell tumors and may define subgroups of patients who would be more likely to benefit from cell- cycle dependent chemotherapy regimens, and may guide the development of future therapeutic strategies.

Annexures

Annexure – I

PROFORMA

Name :
Age :
IP.No / Unit :
Biopsy No. :
Clinical Features : Pain / Mass Abdomen / Acute Abdomen / Menstrual Irregularity
Clinical Diagnosis :
Gross :
Laterality : Unilateral / Bilateral
Size :
Consistency Cystic : Solid / Solid & Cystic
Microscopy :
1. Tumor differentiation : Benign / Borderline / Malignant
2. Histological Types : Surface Epithelial / sexcord stromal I Germ Cell
3. Subtypes :
Metastasis :
IHC / Special Stain/ Ki67 index :
Clinical & Histological Correlation :

Annexure – II

PROCEDURES

HEMATOXYLIN AND EOSIN

1. Bring the sections to water.
2. Stain in Harris Hematoxylin for 5 minutes
3. Wash well in tap water
4. Differentiate in 1% acid alcohol
5. Wash in running tap water for 10-15 minutes
6. Stain in 1% eosin for 1 to 2 minutes
7. Wash in tap water for 1 to 5 minutes

Dehydrate with alcohol, clear in Xylene and mount in DPX.

SPECIAL STAINS

PERIODIC ACID SCHIFF STAIN: modified McMannus 1946

Periodic acid solution

Periodic acid : 1 gm
Distilled water : 100 ml

PREPARATION OF SCHIFF REAGENT

Dissolve 1gm of basic fuchsin and 1.9gm of sodium metabisulfite in 100ml of 0.15N Hydrochloric acid. Shake the solution at intervals, until it is clear and yellow to light brown in colour. Add 500mg of activated charcoal and shake for 1 to 2 mins. Filter the solution through a No.1 Whatman filter. The filtered solution should be clear and colourless. Store at 4 degree centigrade.

Method:

1. Bring the sections to water
2. Treat with periodic acid for 5 minutes
3. Wash well with several changes of distilled water
4. Cover with schiff's reagent for 15 minutes
5. Wash in running tap water 5-10 minutes

6. Stain nuclei with Harris Hematoxylin. Differentiate in acid alcohol and blueing in tapwater for 5 minutes.
7. Wash in water
8. Rinse in absolute alcohol
9. Clear in Xylene and mount with DPX

RESULTS

Glycogen : Magenta

Nuclei : Blue

RETICULIN STAIN (GOMORI'S METHOD)
Preparation of silver solution:

To 10ml of 10% potassium hydroxide solution add 40ml of 10% silver nitrate solution. Allow the precipitate to settle and decant the supernatant. Wash the precipitate several times with distilled water. Add ammonia drop by drop until the precipitate has just dissolved. Add further 10% silver nitrate solution until a little precipitate remains. Dilute to 100 ml and filter. Store in a dark bottle.

Method:

1. Deparaffinize sections and bring to water.
2. Treat with 1% potassium permanganate solution, 2 minutes.
3. Rinse in tap water.
4. Bleach in 2% potassium metabisulfate solution.
5. Rinse in tap water.
6. Treat with 2% iron alum, 2 minutes.

7. Wash in several changes of distilled water.
8. Place in Coplin jar of silver solution, 1 minute.
9. Wash in several changes of distilled water.
10. Reduce in 4% aqueous formalin solution, 3 minutes.
11. Rinse in tap water.
12. Tone in 0.2% gold chloride solution, 10 minutes.
13. Rinse in tap water.
14. Treat with 2% potassium metabisulfite solution, 1 minute.
15. Rinse in tap water.
16. Treat with 2% sodium thiosulfate solution, 1 minute.
17. Rinse in tap water.
18. Counterstain as desired (Van Gieson or eosin is suitable.)
19. Dehydrate
20. Clear in xylene and mount in permanent mounting medium.

Results:

Reticular fibers	black
Nuclei	Gray
Other tissues	according to counterstain

IMMUNOHISTOCHEMISTRY:

An assay that shows specific antigens in tissues by the use of markers that are either fluorescent dyes or enzymes (such as horseradish peroxidase)

Visualising an antibody-antigen interaction can be accomplished in a number of ways.

Immunoperoxidase staining an antibody is conjugated to an enzyme, such as peroxidase, that can catalyse a colour-producing reaction.

Immunofluorescence staining: the antibody can also be tagged to a fluorophore, such as FITC, rhodamine, Texas Red, Alexa Fluor, or DyLight .

Sample preparation

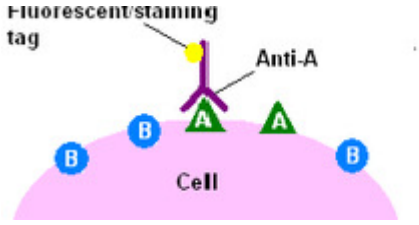
In the procedure, either thin (about 4-40 μm) slices are taken of the tissue of interest, or if the tissue is not very thick and is penetrable it is used whole.

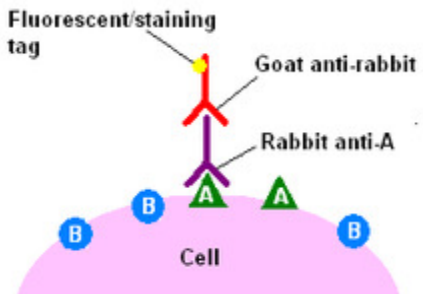
Direct and indirect IHC

DIRECT METHOD : One labelled antibody, which binds directly to the antigen being stained for

INDIRECT METHOD : One antibody against the antigen being probed for, and a second, labelled, antibody against the first

In a common procedure, a biotinylated secondary antibody is coupled with streptavidin-horseradish peroxidase. This is reacted with 3,3'-Diaminobenzidine (DAB) to produce a brown staining wherever primary and secondary antibodies are attached in a process known as DAB staining. The reaction can be enhanced using nickel, producing a deep purple/gray staining.





. DIRECT METHOD ***INDIRECT METHOD***

Annexure – III

WHO CLASSIFICATION OF OVARIAN TUMORS

Surface epithelial-stromal tumors

Serous tumors
- Malignant
  - Adenocarcinoma
  - Surface papillary Adenocarcinoma
  - Adencarcinofibroma(malignant adenofibroma)
- Borderline tumor
  - Papillary cystic tumor
  - Surface papillary tumor
  - Adenofibroma,cystadenofibroma
- Benign
  - Cystadenoma
  - Papillary cystadenoma
  - Surface papilloma
  - Adenofibroma and cystadenofibroma

Mucinous tumors
- Malignant
  - Adenocarcinoma
  - Adenocarcinofibroma (malignant adenofibroma)

Borderline tumor
- Intestinal type
- Endocervical – like

Benign
- Cystadenoma
- Adenofibroma and cystadenofibroma
- Mucinous cystic tumor with mural nodules
- Mucinous cystic tumor with pseudomyxoma peritonei

Endometrioid tumors including variants with squamous differentiation

- Malignant
  - Adenocarcinoma not otherwise specified
  - Adenocarcinofibroma (malignant adenofibroma)
  - Malignant mullerian mixed tumor (carcinosarcoma)
  - Adenosarcoma
  - Endometrioid stromal sarcoma (low grade)
  - Undifferentiated ovarian sarcoma

- Borderline tumor

- Cystic tumor
- Adenofibroma and cystadenofibroma

Benign
- Cystadenoma
- Adenofibroma and cystadenofibroma

Clear cell tumors

Malignant
- Adenocarcinoma
- Adenocarcinofibroma (malignant adenofibroma)

Borderlinetumor
- Cystic tumor
- Adenofibroma and cystedenofibroma

Benign
- Cystadenoma
- Adenofibroma and cystadenofibroma

Transitional cell tumors

Malignant
- Transitional cell carcinoma (non-Brenner type)
- Malignant Brenner tumor

Borderline
- Borderline Brenner tumor
- Proliferating variant

Benign
- Brenner tumor

Metaplastic variant

Squamous cell tumors
- Squamous cell carcinoma
- Epidermoid cyst

Mixed epithelial tumors (specify components)
- Malignant
- Borderline
- Benign

Undifferentiated and unclassified tumors
- Undifferentiated carcinoma
- Adenocercinoma,not otherwise specified

Sex cord-stromal tumors

Granulosa -stromal cell tumors

Granulosa-stromal cell tumor group
- Adult granulosa cell tumor
- Juvenile granulosa cell tumor

Thecoma-fibroma group

Thecoma,not otherwise specified
Typical
Luteinized
Fibroma
Cellular fibroma
Fibrosarcoma
Stromal tumor with minor sex cord elements
Sclerosing stromal tumor
Signet-ring stromal tumor
Unclassified (fibrothecoma)
Sertoli-stromal cell tumors
Sertoli – Leydig cell tumor group (androblastomas)
Well differentiated
Of intermediate differentiation
Variant with heterologous elements(specify type)
Poorly differentiated (sarcomatoid)
Variant with heterologous elements (specify type)
Retiform
Variant with heterologous elements (specify type)
Sertoli cell tumor
Stromal-Leydig cell tumor
Sex cord-stromal tumors of mixed or unclassified cell type
Sex cord tumor with annular tubules
Gynandroblastoma (specify components)
Sex cord-stromal tumor,unclassified

Steroid cell tumors
Stromal luteoma
Leydig cell tumor group
Hilus cell tumor
Leydig cell tumor,non-bilar type
Leydig cell tumor,not otherwise specified
Steroid cell tumor,not otherwise specified
Well differentiated
Malignant

Germ cell tumors
Primitive germ cell tumors
Dysgerminoma
Yolk sac tumor
Polyvesicular vitelline tumor

- Glandular variant
- Hepatoid variant

Embryonal carcinoma
- Polyembryoma
- Non-gestational choriocarcinoma
- Mixed germ cell tumor (specify components)

Biphasic or triphasic teratoma
- Immature teratoma
- Mature teratoma
  - Solid
  - Cystic
    - Dermoid cyst
  - Fetiform teratoma (homunculus)

Monodermal teratoma and somatic-type tumors associated
With dermoid cysts
- Thyroid tumor group
  - Struma ovarii
    - Benign
    - Malignant (specify type)

- Carcinoid group
  - Insular
  - Trabecular
  - Mucinous
  - Strumal carcinoid
  - Mixed
- Neuroectodermal tumor group
  - Ependymoma
  - Primitive neuroectodermal tumor
  - Medulloepithelioma
  - Glioblastoma multiforme
  - Others
- Melanocytic group
  - Malignant melanoma
  - Melanocytic naevus
- Sarcoma group (specify type)
- Sebaceous tumor group
  - Sebaceous adenoma
  - Sebaceous carcinoma
- Pituitary –type tumor group
- Retinal anlage tumor group
- Others

Germ cell sex cord-stromal tumors
- Gonadoblastoma
  - Variant with malignant germ cell tumor
- Mixed germ cell-sex cord-stromal tumor
  - Variant with malignant germ cell tumor

Tumors of the rete ovarii
- Adenocarcinoma
- Adenoma
- Cystadenoma
- Cystedenofibroma

Miscellaneous tumors
- Small cell carcinoma,hypercalcemic type
- Small cell carcinoma,pulmonary type
- Large cell neuroendocrine carcinoma
- Hepatoid carcinoma
- Primary ovarian mesothelioma
- Wilms tumor
- Gestational choriocarcinoma
- Hydatidiform mole
- Adenoid cystic carcinoma
- Basal cell tumor
- Ovarian wolffian tumor
- Paraganglioma
- Myxoma
- Soft tissue tumors not specific to the ovary
- Others

Tumor-like conditions
- Luteoma of pregnancy
- Stromal hyperthecosis
- Stromal hyperplasia
- Fibromatosis
- Massive ovarian oedema
- Others

Lymphoid and haematopoetic tumors
- Malignant lymphoma (specify type)
- Leukaemia (specify type)
- Plasmacytoma

Secondary tumors

Annexure – IV

K.Dis.No.4933/E4/1/10

Govt.Rajaji Hospital,Madurai.20.
dated. 3.11.2010.

Sub: Establishment-Govt.Rajaji Hospital,Madurai-20-
Minutes of the Ethical committee-meeting held on
19.8.2010-regarding.

Minutes of theEthical Committee meeting held at 12.00 Noon. on 19.8.2010 at the MedicalSuperintendent"s Chamber, Govt. Rajaji Hospital, Madurai.The following members of the committee where present and the following points were decided in the meeting.

1.Dr.S.M.Sivakumar,MS., Govt.Rajaji Hospital,Madurai.	MedicalSuperintendent.	Convenor
2.Dr.N.Vijayasankaran,M.ch(Uro.)	Sr.Consultant Urologist Madurai Kidney Centre, Sivagangai Road,Madurai	Chairman
3.Dr.T. Meena, M.D,	Prof. of Physiology Madurai Medical College	Member
4.Dr.Moses K.Daniel,MD.,	Professor of Medicine Madurai Medical College	Member
5.Dr.M.Gobinath,MS(Gen.Surgery)	Professor of Surgery Madurai Medical College	Member
6.Dr.S.S. Dilsath ,MD(O&G)	Professor of Ob&Gyn Madurai Medical College	Member
7.Dr.B.K.C.MohanPrasad,M.ch, (Surg.Oncology)	Professor of Surg.Oncology Madurai Medical College	Member -Secy.
8.Shri.M.Sridher,B.sc.B.L.	Advocate, 623-B.II.Floor,East II Cross, K.K.Nagar,Madurai.20.	Member
9.Shri.O.B.D.Bharat,B.sc.,	Businessman Plot No.588, K.K.Nagar,Madurai.20.	Member
10. Shri S. Sivakumar, M.A. (Social), M.Phil ., Sociologist	Plot. No. 51, F.F. K.K. Nagar, Madurai-20.	Member.

a)The Committee has considered the revised study-specific informed Consent Document version of 30 Apr,2010, pertaining to the previously approved clinical trial "H3E-MC-S103:A Randomized phase 2 study comparing Erlotininib-Pemetrexed, Pemetrexed alone, and Erlotinib alone, as second-line treatment for Non-smoker patients with locally advanced or Metastatic Nonsquamous Non-Small celll lung cancer", and finds it satisfactory. The same is approved.

b)The Committee has considered the revised Tamil Translation of study-specific informed Consent document version of 20 May 2010, pertaining to the previously approved clinical trial "HeE-MC-S103:A Randomized phase 2 study comparing Erlotininib-Pemetrexed, Pemetrexed alone, and Erlotinib alone, as second-line Treatment for Non-Smoker Patients with locally Advanced or Metastatic Nonsquamous Non-small Cell Lung Cancer", and finds it satisfactory. The same is approved.

c)The committee reviewed the clinical trial proposal submitted by Dr.J.Jebasingh, Principal Investigator, Dept of Medical Oncology,Govt.Rajaji Hospital,Madurai. "Phase II study of Coagulation Factor VIIa Inhibitor PCI-27483 in Pancreatic Cancer patients Receiving Treatment with Gemcitabine"-Protocol #PCYC-1001"(Considered by the Committee in its meeting of 04 Mar 2010) alongwith the letter of Undertaking received from the sponsors confirming that the study patien's samples will not be used for purposes other than that specified in the clinical trial protocol. The clinical trial proposal is found to be satisfactory, and is approved.

S.No	Name of the applicant	Course	Name of the Project	Remarks
1.	B.Sc. (N) IV Year Students	College of Nursing Madurai Medical College Madurai.	Statistical date from MRD and various departments in GRH Madurai.	Approved
2.	Dr.K.PreethaRani,	PG.Student in MS, MMC,Madurai.	Role of Laparoscopic Surgery Versus open surgery for colorectal cancers,	"
3.	Dr.N.Mohanraj,	PG.Student in MS/ MMC,Madurai.	Role of Diagnostic Laparoscopy Preoperatively in Assessing the Operability in Various Intra-Abdominal Malignancies.	"
4.	M.Sc.Nursing 1st Year.Student.	College of Nursing, MMC,Madurai.	Statistical data from MRD and Various departments.	"
5.	Dr.C.Baskar.	PG. in MS.Ortho. MMC,Madurai.	A study on Functional outcome of Intraarticular Distal Radius Fractures fixed with locking compression plate.	"
6.	Dr.S.Suresh.	PG.Student,MS.Ortho., MMC,Madurai.	A study on Functional outcome of Proximal Humerus Fractures Fixed with Proximal Humerus locking compression plate.	"

7.	Dr.V.Anandkumar,	PG.Student in MS.Ortho.MMC,Madurai.	A Study of Functional outcome of Translaminar Facetal Screw fixation for Grade.1 Lumbar spondylolisthesis.	approved
8.	Dr.K.Subathra,	PG.in Pathology, MMC,Madurai.	Histopathological study of prostate lesions, Assessment of Premalignant and Malignant Conditions a Statistical Evaluation.	"
9.	Dr.R.Lavanya.	-do-	A Clinico Pathological study of Ovarian Tumors.	"
10.	Dr.S..Dilshath,MD,DGO.	Prof.of OG.GRH,Madurai	Evaluation of progesterone vaginal ring(PVR)as a new contraceptive option in India study.	"
11.	Dr.P.Sangaia Raja	PG.in MS.MMC,Madurai	Limb Salvage Procedures in Diabetic Foot Ulcers.	"
12.	Dr.R.Ashok kumar	PG.Student,MS.Ortho, MMC,Madurai.	Natural History of Obstetric Brachial plexus palsy-A Prospective study of 25 cases.	"
13.	Dr.S.Prathiba.	PG.in MD,DVL., MMC,Madurai.	A Clinicopathological study of Perforating Dermatoses.	"
14.	Dr.Jayanthi,OR.	-do-	Study and Analysis of Cutaneous small Vessel Vasculitis.	"
15.	G.Jeyanthi.	M.Sc.Nursing,II.Year. Appollo college of Nursing,Chennai.	An Experimental study to Assess the Effectveness if /changing positions upon serum bilirubin level among newborn under phototherapy at GRH,Madurai.	"

16.	Dr.P.Jayakumar,	Lead Investigator, TorchProject, Wd.121, GRH, Madurai.	Peadiatric HIV Status Disclosure-Impact on Immunological status, Psychiatric status, and treatment adherence A Prospective approach.	"
17.	Dr.Aneesh,B.Rahiman	PG in MD, MMC, Madurai.	TIMI Risk Score-A Convenient, Bedside, Clinical Score for Risk Assessment in ST Elevation Myocardial infarction.	"
18.	Dr.A.Tamilvanan.	PG in GM, III Unit, MMC, Madurai.	Study of Etiological Profile of Late(Adult)Onset Seizures.	"
19.	Dr.P.Sivasubramania-Barathi,	PG in MD(GM) MMC, Madurai.	Anemia in Type 2 Diabetes Mellitus Risk Factor for the presence and the severity of Micro Vascular Complication(Diabetic Retinopathy.	"
20.	Dr.Prasanth.S	PG in MD(GM) MMC, Madurai.	Pulmonary manifestations in Rheumatoid Arthritis Patients.	"
21.	Dr.Magesh.B	PG in GM, MMC, Madurai.	An Epidemiological study of Poisonous Snake bite in and Around Madurai from December 2009 to December.2010	"

22.	Dr.A.JeyaJancy Selvi Ratnam,MD.,	Asst.Professor, Institute Physiology, MMC,Madurai	Cord Blood Prolactin Birth Weight Respiratory compliance in Newborns.	"
23.	Dr.P.Balamanikandan,	PG in GM,MMC, Madurai.	A study of Cardiac Function in Non Diabetic Non-Smoker Chronic Kidney Disease patients from July 2010 to December 2010	"
24.	Dr.Suraj.P.Haridas.	-do-	A study of Glucose tolerance In non-diabetic Chronic kidney disease patients from July 2010 to Decmber 2010.	"
25.	Dr.Irshad Ali.KM.	-do-	Cardiovascular Autonomic Neuropathy in type 2 Diabetes Mellitus.	"
26.	Dr.A.Sivakumar	-do-	A study of Asymptomatic bacteriuria in women with type 2 Diabetes Mellitus.	"
27.	Dr.Shajudeen.K.	-do-	Cardiovascular Autonomic Nervous Dysfunction in Rheumatoid Arthertis.	"
28.	Dr. Durgadevi,	P.G in MD (O.G) M.M.C., Madurai.	Infraumbilical injection of 20 Units of Oxytgocin diluted in 20 ml of normal saline by pipingas technique and its effect on III rd stage of labour	"
29.	Dr. R. Priyadharshini	-do-	Intracutaneous Injection of sterile water over Sacrum for Labour Analgesia	"
30.	Dr.K.Kalpana	-do-	Evaluationg the accuracy and usefulness of predicting birth weight by measuring fetal thigh circumference by ultrasound	"
31.	Dr.R.Sasikala	-do-	Critical analusis of casues and course of cerebral venous thrombosis in pregnancy and puerperium	"

Please note that the investigator should adhere the following:

1) She/He should get a detailed informed consent from the patients/participants and maintain Confidentially.

2) She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution to Government.

3) She/He should inform the institution Ethical Committee in case of any change of study procedure site and investigation or guide.

4) She/He should not deviate for the area of the work for which applied for Ethical clearance.

5) She/He should inform the IEC immediately, in case of any adverse events pr Serious adverse reactions

6) She/he should abide to the rules and regulations of the institution.

7) She/He should complete the work within the specific period and apply for if any Extension of time is required She should apply for permission again and do the work.

8) She/He should submit the summary of the work to the Ethical Committee on Completion of the work.

9) She/He should not claim any funds from the institution while doing the work or on completion.

10) She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

MEDICAL SUPERINTENDENT.

Annexure – V

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ABSTRACT

BACKGROUND AND OBJECTIVES

The ovarian tumors manifest a wide spectrum of clinical, morphological and histological features. Their complex nature, unpredictable behaviour, prognosis and varying therapeutic strategies, necessitates an accurate diagnosis.

Hence this study was undertaken to correlate the clinical and pathological parameters and to analyse the role of Ki 67, a nuclear protein expressed by mitotic cells, as a prognostic marker in ovarian tumors and also to evaluate the usefulness of immunohistochemical markers for confirmatory diagnosis of Granulosa cell tumors.

METHODS

This study was done in the Department of Pathology, Madurai Medical College, Madurai, for a period of two years (2009-2011), on 200 ovarian neoplasms out of 239 ovarian lesions received after exclusion of non-neoplastic lesions. A detailed history regarding the clinical symptoms and signs were recorded. Representative bits were processed and stained with hematoxylin and eosin . Special stains like PAS, reticulin were done in selected cases.

Immunostaining was performed on 24 selected cases with proliferative marker Ki 67 using peroxidase-antiperoxidase technique and immunohistochemical marker study was done in all cases of Granulosa cell tumors with vimentin ,inhibin and for selected cases with chromogranin and EMA.

RESULTS

The incidence of ovarian neoplasms was 8.05% and ranked second among the female genital tract malignancies. The peak age incidence was fifth decade. Mass per abdomen was the most common clinical presentation (58%). 81.5% were unilateral and 18.5% were bilateral. Surface epithelial tumors were the commonest (77.5%), sex cord stromal tumors 7.5% and germ cell tumors 11%. Out of 200 cases, benign tumors constituted 62%, borderline tumors constituted 5.5% and malignant tumors 32.5%. There were 3 cases (1.5%) of Krukenberg's tumor. The difference in the mean Ki 67 index between benign (2.9%), borderline (7.2%) and malignant tumors (29.9%) was statistically significant. In Granulosa cell tumors the mean Ki 67 index was 5.1% and it was higher in two cases with higher clinical stage.

In this study, two cases which were histopathologically diagnosed as Granulosa cell tumors were finally diagnosed as Primary ovarian carcinoid tumor and Poorly differentiated carcinoma respectively after immunohistochemical study.

CONCLUSION

Accurate diagnosis of ovarian tumors can be rendered in most of the cases by correlating the clinical and pathological parameters. Immunohistochemistry is essential in Granulosa cell tumors with doubtful diagnosis. Ki 67 immunostaining provides robust prognostic information and is very much useful to identify borderline ovarian tumors which are likely to behave in a malignant fashion and also to assess the prognosis of Granulosa cell tumors.

Key words:

ovarian tumors, surface epithelial tumors, germ cell tumors, granulosa cell tumors, immunoproliferative marker Ki 67.

								GROSS									
S. No	Bio. No	I.P.No	Age	Clinical features	CONSISTENCY			Size	laterality		Tumor type			Metastasis	DIAGNOSIS	IHC	Ki 67%	FIGO stage
					CYSTIC	CYSTIC & SOLID	SOLID		U/L	B/L	benign	borderline	malignant					
1	G 2125/7/ 09	41357	26	A.MASS		P		3.5X2 X 0.5	P	P			P	ASCITES	MUCINOUS CYSTADENOCARCINOMA			
2	G 2151/7/09	57854	33	mass ABDOMEN	P			8 X 5X2	p		P				DERMOID CYST			
3	G 2258/7/09	53216	53	MASS		P		11X9X6	P				P		SEROUS PAPILLARY CYSTADENOCARCINOMA			
4	G2259/7/09	41144	50	MASS		P		9X5X4	P				p	ASCITES	PAPILLARY MUCINOUS CYSTADENOCARCINOMA			
5	G2355/7/09	406606	63	MASS	P			10X8X2	P		P				BENIGN SEROUS CYSTADENOMA			
6	G2358/7/09	40610	43	mass ABDOMEN	P			18X6X4	P		P				BENIGN MUCINOUS CYSTADENOMA			
7	G2369/7/09	57490	23	MASS		P		8X5X3	P				P	OMENTUM	YOLK SAC TUMOR			
8	G2402/7/09	57205	25	mass ABDOMEN	P			6X4X3	P		P				BENIGN SEROUS CYSTADENOMA			
9	G2403/7/09	57228	48	MASS	P			15 X5X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
10	G2437/7/09	40861	40	mass ABDOMEN	P			8X4X2	P		P				BENIGN SEROUS CYST			
11	G2526/7/09	40483	40	MASS, PAIN		P		7X6X2	P				P		PAPILLARY SEROUS CYSTADENOCARCINOMA			
12	G2527/7/09	40567	44	PAIN	P			8X5X3	P		P				BENIGN SEROUS CYSTADENOMA			
13	G2539/7/09	41036	45	MASS	P			7X5X2	P		P				BENIGN MUCINOUS CYSTADENOMA			
14	G2540/8/09	O61709	50	PAIN, MASS		P		6X4X2	P			p			MUCINOUS TUMOUR OF BORDERLINE MALIGNANCY			
15	G2575/8/09	40821	50	MENSTRUAL DISTURBANCES		P		8X6X2		P			P		ENDOMETRIOID CARCINOMA OVARY			
16	G2576/8/09	41063	40	MENSTRUAL DISTURBANCE	P			16X10X6	P		P				BENIGN MUCINOUS CYSTADENOMA			
17	G2578/8/09	58721	50	MASS	P			7X6X2	P		P				BENIGN MUCINOUS CYSTADENOMA			
18	G2624/8/09	57129	40	MASS	P			4X3X2	P		P				BENIGN SEROUS CYST			
19	G2627/8/09 411	41182	21	MASS			P	5x4x3	P				P		DYSGERMINOMA			
20	G2636/8/09	40737	50	mass ABDOMEN	P			5X3X2	P		P				BENIGN SEROUS CYSTADENOMA			
21	G2655/8/09	40862	32	massABDOMEN				4X3X2	P		P				BENIGN SEROUS CYST			
22	G2715/8/09	40829	60	MASS	P			18X16X7	P			P			MUCINOUS TUMOR OF BORDERLINE MALIGNANCY			
23	G2725/8/09	62641	42	MASS	P			10X6X4	P		P				BENIGN MUCINOUS CYSTADENOMA			
24	G2726/8/09	41269	27	mass ABDOMEN	P			6X5X3	P		P				BENIGN CYSTIC TERATOMA			
25	G2767/8/09	41012	41	MASS				5X3X2	P		P				BENIGN MUCINOUS CYSTADENOMA			
26	G2838/8/09	41227	29	PAIN	P			6X3X1	P		P				BENIGN SEROUS CYST			
27	G2840/8/09	41083	28	MASS PAIN	P			4X3X2	P		P				BENIGN SEROUS CYSTADENOMA			
28	G2878/8/09	64258	60	MASS PAIN		P		10X6X2	P				P		PAPILLARY SEROUS CYSTADENOCARCINOMA			
29	G2955/8/09	59862	60	MASS			p	5x4x1	P		p				GRANULOSA CELL TUMOR	VIM + ,INH +	5.40%	Ia
30	G3024/9/09	41380	42	MASS	P			14X10X6	P		P				BENIGN MUCINOUS CYSTADENOMA			
31	G3059/9/09	73709	22	PAIN	P			10X7X2	P		P				BENIGHN SEROUS CYSTADENOMA			
32	G3070/9/09	70836	45	PAIN	P			7X5X3	P		P				BENIGN CYSTIC TERATOMA			
33	G3072/9/09	70753	60	MASS		P		6X3X2	P		p				FIBROTHECOMA			
34	G3087/9/09	8809	32	MASS	P			8X8X4	P		P				BENIGN SEROUS CYSTADENOMA			
35	G3167/9/09	41490	27	MASS				6X4X2	P		P				BENIGN SEROUS CYSTADENOMA			
36	G3242/9/09	51917	58	MASS, PAIN, MENSTRUAL DISTUF		P		7X6X5		p			p		RIGHT- PAPILLARY CYSTADENOCARCINOMA, LEFT - PAPILLARY SEROUS CYSTADENOCARCINOMA			
37	G3359/9/09	77280	35	MASS		P		10X8X6	P				P	ASCITES+	MUCINOUS CYSTADENOCARCINOMA			
38	G3487/10/09	9656	47	MASS	P			15X10X 3	P		P				BENIGN SEROUS CYSTADENOMA			
39	G3429/10/09	41556	76	MASS		P		15X13X6	P		p				FIBROTHECOMA			
40	G3454/10/09	41712	60	mass ABDOMEN	P			5X4X2 (BOTH)		P	P				BENIGN MUCINOUS CYSTADENOMA			
41	G3489/10/09	76007	46	MASS, PAIN		P		12X8X2		P			p		PAPILLARY SEROUS CYSTADENOCARCINOMA			
42	G3517/10/09	42003	55	PAIN	P			18X10X3		P	P				BENIGN SEROUS CYSTADENOMA			
43	G3518/10/09	80421	25	MASS, PAIN	P			8X3X2	P		P				BENIGN SEROUS CYSTADENOMA			
44	G3520/10/09	75381	55	MASS		P		8X5X2	P				P		PAPILLARY SEROUS CYSTADENOCARCINOMA			
45	G3525/10/09	42088	67	MASS		P		14X9X5	P				P	EM, MYO, AS	SEROUS ADENOCARCINOMA			
46	G3524/10/09	79818	21	MASS, PAIN		P		25X15X3	P			p			MUCINOUS TUMOR OF BORDERLINE MALIGNANCY			

47	G3654/10/09	77726	1	MASS	P			10X8X2	P		P				BENIGN SEROUS CYSTADENOMA			
48	G3566/10/09	83217	50	MASS, PAIN		P		4X3X0.5	P				P		PAPILLARY SEROUS ADENOCARCINOMA			
49	G3616/10/09	O42021	38	MASS, MENSTRUAL DISTUR	P			8X5X2	P		P				BENIGN SEROUS CYSTADENOMA			
50	G3659/10/09	81972	45	PAIN	P			10X7X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
51	G3660/10/09	42294	35	PAIN	P			15X10X3	P		P				BENIGN SEROUS CYSTADENOMA			
52	G3708/10/09	42346	50	PROLAPSE	P			10X6X3	P		P				BENIGN CYSTIC TERATOMA			
53	G3710/10/09	81987	30	MASS	P			15X8X6	P		P				BENIGN MUCINOUS CYSTADENOMA			
54	G3754/10/09	42878	55	PAIN, MASS	P			15X6X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
55	G3785/10/09	42049	45	MASS		P		1-16X10X4,2-17X15X8		P		p			MUCINOUS TUMOR OF BORDERLINE MALIGNANCY			
56	G3839/11/09	87014	19	PAIN, MASS	P			10X5X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
57	G3858/11/09	89965	19	MASS	P			9X6X1	P		P				BENIGN MUCINOUS CYSTADENOMA			
58	G3861/11/09	18343	26	MASS	P			13X6X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
59	G3863/11/09	87362	32	PAIN	P			5X3X1	P		P				BENIGN SEROUS CYST			
60	G3864/11/09	42937	32	MASS, PAIN	P			6X5X2	P		P				BENIGN SEROUS CYSTADENOMA			
61	G4021/11/09	42588	60	MASS		P		8X6X3	P				P		SEROUS PAPILLARY CYSTADENOCARCINOMA			
62	G4026/11/09	42711	45	PAIN, MASS	P			5X4X2	P		P				BENIGN SEROUS PAPILLARY CYSTADENOMA			
63	G4071/11/09	42601	65	MASS	P			8X5X3		P	P				BENIGN PAPILLARY SEROUS CYSTADENOMA			
64	G4088/11/09	43135	28	MASS	P			10X5X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
65	G4117/11/09	42722	37	MASS, PAIN		P		11X7X2	P				P		PAPILLARY SEROUS CYSTADENOCARCINOMA			
66	G4190/111/09	90565	36	PAIN	P			7X5X4	P		P				BENIGN MUCINOUS CYSTADENOMA			
67	G4243/12/09	95878	60	PAIN	P			6X3X1	P		P				BENIGN PAPILLARY SEROUS CYSTADENOMA			
68	G4244/12/09	92151	23	MASS	P			10X4X1	P		P				BENIGN SEROUS CYSTADENOMA			
69	G4339/12/09	94915	17	MASS		P		20X15X5		P			P	OMENTUM +,	WELL DIFFERENTIATED SEROUS CYSTADENOCARCINOMA			
70	G4351/12/09	94661	35	PAIN		P		2.5X2X1		P			P	OMENTUM	PAPILLARY ADENOCARCINOMA			
71	G4352/12/09	91256	37	MASS, PAIN	P			15X6X4	P		P				BENIGN SEROUS CYSTADENOMA			
72	G4353/12/09	97007	27	PAIN	P			6X4X2	P		P				BENIGN SEROUS CYSTADENOMA			
73	G4374/12/09	42953	40	MENSTRUAL DISTURBANCES		P		7X3X2		P			P		PAPILLAYR SEROUS CYSTADENOCARCINOMA			
74	G4431/12/09	88198	48	MASS		P		18X10X4	P				P	CERVIX & END	POORLY DIFFERENTIATED CARCINOMA			
75	G4444/12/09	207017	47	PAIN			P	7X6X2	P		p				FIBROTHECOMA			
76	G4450/12/09	95607	50	MASS		P		8X6X3		P			P		PAPILLARY SEROUS CYSTADENOCARCINOMA			
77	G44409/12/09	99869	63	PAIN		P		3X2X1	P			p			MUCINOUS TUMOR OF BORDERLINE MALIGNANCY			
78	G4509/12/09	43681	36	PAIN	P			4X3X2	P		P				BENIGN PAPILLARY SEROUS CYSTADENOMA			
79	G4603/12/09	73548	42	MENSTRUAL DISTURBANCE	P			13X5X2	P		P				BENIGN SEROUS CYSTADENOMA			
80	G4613/12/09	97878	65	MASS,menstrual disturbances		P		22X15X6	P						GRANULOSA CELL TUMOR	VIM +, INH+	4.80%	Ia
81	G11/1/10	43778	60	PAIN	P			5X3X1	P		P				BENIGN SEROUS CYSTADENOMA			
82	G15/1/10	44024	35	MASS		P		10X4X3	P				P		MUCINOUS CYSTADENOCARCINOMA		32.20%	
83	G104/1/10	43933	42	ABDOMINAL DISTENSION		P		12X7X5	P				P	ASCITES+	PAPILLARY SEROUS CYSTADENOCARCINOMA		29%	
84	G105/1/10	43629	45	ABDOMINAL DISTENSION		P		8X6X4	P				P	ASCITES+	SEROUS CYSTADENOCARCINOMA		29.20%	
85	G142/2/10	107571	45	ABDOMINAL DISTENSION	P			5X4X2	P		P				BENIGN SEROUS CYSTADENOMA			
86	G169/2/10	98490	48	PAIN	P			10X8X3	P				P		PAPILLARY SEROUS CYSTADENOCARCINOMA			
87	G173/2/10	36221	19	PAIN, MASS	P			8X5X3	P		P				BENIGN SEROUS CYSTADENOMA			
88	G176/2/10	103285	53	PAIN	P			5X3X1	P		P				BENIGN SEROUS CYSTADENOMA			
89	G177/2/10	720	45	PAIN	P			15X6X5	P		P				BENIGN MUCINOUS CYSTADENOMA			
	G232/2/10	44144	52	PAIN		P		15X4X3	P		p				CARCINOID TUMOR	INH -,CHR +	3.00%	
91	G419/3/10	OOO490	46	PAIN	P			13X6X4	P		P				BENIGN MUCINOUS CYSTADENOMA			
92	G437/3/10	OO5O9	35	PAIN	P			14X9X5		P			P	ASCITES+	ENDOMETRIOID TYPE OF ADENOCARCINOMA			
93	G619/3/10	50569	35	PAIN	P			3X2X1	P		P				BENIGN SEROUS CYSTADENOMA			
94	G695/3/10	4534	49	MASS	P			30X25X10	P		P				BENIGN MUCINOUS CYSTADENOMA			
95	G698/3/10	10367	45	PAIN	P			6X4X2	P		P				BENIGN MUCINOUS CYSTADENOMA			
96	G727/3/10	1109	25	MASS, PAIN		P		15X6X3	P				P		YOLK SAC TUMOR			
97	G773/3/10	15119	40	ABDOMINAL DISTENSION		P		4X2.5X2		P			P	OMENTUM+,	ADEN OCARCINOMA			
98	G774/3/10	715	36	PAIN	P			4X3X2	P		P				ENDOMETRIOTIC CYST WITH BENIGN MUCINOUS CYSTADENOMA			
99	G828/3/10	136011	27	PAIN	P			7X4X2	P		P				BENIGN SEROUS CYST			
100	G833/3/10	1345	30	PAIN	P			6X4X2	P		P				BENIGN MUCINOUS CYSTADENOMA			
101	G840/3/10	1462	49	ABDOMINAL DISTENSION		p		12x3x2	p				p	ASCITES+	MALIGNANT SEROUS CYSTADENOCARCINOMA			
102	G884/3/10	1555	72	MASS		P		15X5X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
103	G912/4/10	15596	55	ABDOMINAL DISTENSION		P		4X3X2	P				P	OMENTUM+,	MALIGNANT PAPILLARY SEROUS CYSTADENOCARCINOMA			
104	G990/4/10	1858	35	MASS, MENSTRUAL DISTURBANC	P			5X4X2.5		P	P				B/L BENIGN MUCINOUS CYSTADENOMA			
105	G1040/4/10	1744	60	PAIN	P			7X3X2	P		P				BENIGN SEROUS CYSTADENOMA			
106	G1042/4/10	1942	20	MASS, PAIN	P			12X5X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
107	G829/4/10	1956	28	MASS	P			10X4X2	P		P				BENIGN MUCINOUS CYSTADENOMA			
108	G1060/4/10	207197	22	PAIN, MASS	P			10X6X3	P		P				BENIGN CYSTIC TERATOMA			
109	G1133/4/10	15594	42	MASS	P			14X6X3	P		P				BENIGN MUCINOUS CYSTADENOMA			
110	G1134/4/10	1656	32	PAIN, MASS			P	20X11X4	P				P	ascites+	SEROUS PAPILLARY ADENOCARCINOMA			
111	G1226/4/10	1740	39	MASS	P			11X4X2	P		P				BENIGN SEROUS CYSTADENOMA			
112	G1227/4/10	2156	30	PAIN	P			4X3X2	P		P				BENIGN SEROUS CYST			
113	G1229/4/10	2569	28	PAIN	P			12X5X3	P		P				BENIGN CYSTIC TERATOMA			

114	G1276/5/10	24718	16	PAIN	P			12X3X2	P		P				BENIGN CYSTIC TERATOMA			
115	G1286/5/10	2495	52	MASS	P			8.5X5X1.5	P		P				BENIGN MUCINOUS CYSTADENOMA			
116	G1365/5/10	28611	40	MASS, PAIN		P		4X2.5X2		P			P	ascites+	PAPILLARY SEROUS CYSTADENOCARCINOMA OVARY			
117	G1447/5/10	3684	30	MASS	P			3,5X2.5X2	P		P				BENIGN SEROUS CYSTADENOMA			
118	G1459/5/10	30514	55	PAIN		P		4X3X2	P				P		PAPILLARY ADENOCARCINOMA			
119	G1491/5/10	4149	50	MASS	P			30X25X8	P		P				BENIGN MUCINOUS CYSTADENOMA			
120	G1571/5/10	4610	25	PAIN	P			10X5X2	P		P				BENIGN SEROUS CYSTADENOMA			
121	G1644/5/10	3369	41	MASS, PAIN			P	8X5X3	P				P		ADENOCARCINOMA			
122	G1646/5/10	3158	37	MASS, PAIN	P			5X4X3	p		p				BENIGN SEROUS CYSTADENOMA			
123	G1673/6/10	3134	39	MASS, PAIN			P	5X3X2	P				P	ascites+	PAPILLARY SEROUS ADENOCARCINOMA			
124	G1730/6/10	36369	42	MASS		P		11X5X2	P			P			BORDERLINE SEROUS TUMOR			
125	G1731/6/10	3504	61	MASS		P		1-16X5X3,,2-8X5X3		P	P(both)		P(both)	ASCITES +	1. BENIGN MUCINOUS CYSTADENOMA, 2.MUCINOUS CYSTADENOCARCINOMA		32.60%	
126	G1856/6/10	3814	40	MASS, PAIN	P			5X3X2	P		P				BENIGN SEROUS CYSTADENOMA			
127	G1857/6/10	37644	19	MENSTRUAL DISTURBANCES			P	10X6X4	P		p				POORLY DIFFERENTIATED SEROUS CARCINOMA	INH -, EMA +	25.10%	
128	G1879/6/10	5445	40	MASS			P	11X9X4	P		p				ADULT GRANULOSA CELL TUMOR	VIM +, INH+	4.40%	Ia
129	G1888/6/10	3662	23	MASS			P	15X13X7	P		p				ADULT GRANULOSA CELL TUMOR	VIM +, INH+	7.90%	Ic
130	G1891/6/10	3673	50	mass ABDOMEN		P		4X2X1		P			P		KRUKENBERG TUMOR			
131	G1912/6/10	41477	59	MASS		P		8X5X3		P			P	OMENTUM +	SEROUS CYSTADENOCARCINOMA			
132	G1920/6/10	41791	32	PAIN			P	3X2X1	P				P		DYSGERMINOMA		25.30%	
133	G 1940/6/10	O4119	45	MASS	P			4x4x3			p							
134	G2016/7/10	41498	12	MASS		P		13X10X5	P				P		IMMATURE TERATOMA GARDE 11			
135	G2032/7/10	2925	27	PAIN	P			6X2X2	P		P				DERMOID CYST			
136	G2040/7/10	3835	51	MASS	P			5x3x2					P	OMENTUM+	METASTATIC DEPOSITS			
137	G2059/7/10	40560	35	MASS	P			14X5X5	P		P				BENIGN MUCINOUS CYSTADENOMA			
138	G2062/7/10	7403	30	PAIN	P			6X3X3	P		P				BENIGN SEROUS CYSTADENOMA		2.60%	
139	G2064/7/10	44158	30	PAIN	P			6X2X2	P		P				BENIGN SEROUS CYSTADENOMA			
140	G2O81/7/10	4081	27	MASS	P			14X6X6	P		P				BENIGN MATURE TERATOMA			
141	G2083/7/10	43121	30	PAIN	P			6X4X2	P		P				ENDOMETRIOTIC CYST			
142	G2085/7/10	42476	40	MASS		P		17X10X8	P						FIBROMA			
143	G2114/7/10	4571	26	PAIN	P			8X5X5	P		P				BENIGN PAPPILARY SEROUS CYSTADENOMA			
144	G2218/7/10	4752	40	PAIN	P			3X2X2		P	P				B/L BENIGN SEROUS CYSTADENOMA			
145	G2275/7/10	46094	60	PAIN	P			5x3x3		p	p				BENIGN SEROUS CYSTADENOMA			
146	G2299/7/10	42116	34	MASS, PAIN	P			9X6X4		P	P				BENIGN SEROUS CYSTADENOMA			
147	G2316/7/10	52171	23	PAIN	P			5X3X3	P		P				BENIGN CYSTIC TERATOMA			
148	G23338/7/10	51181	45	PAIN		P		8X5X5,		P	P(both)		p(both		CYSTIC TERATOMA WITH ADENOCARCINOMA			
149	G2394/8/10	40618	28	PAIN	P			5X3X3	P		P				BENIGN MUCINOUS CYST			
150	G2437/78/10	43214	48	MASS, PAIN		P		10X7X5	P				P	ASCITES+	PAPPILARY CYSTADENOCARCINOMA			
151	G2493/8/10	46144	40	PAIN	P			9X7X3.5	P		P				BENIGN SEROUS CYSTADENOMA			
152	G2499/8/10	30619	42	PAIN	P			2X2X1	P		P				BENIGN SEROUS CYSTADENOMA			
153	G2502/8/10	52116	35	PAIN	P			15X4X6		P	P				BENIGN SEROUS CYSTADENOMA			
154	G2556/8/10	54061	47	PAIN	P			3X2X1		P	P				SEROUS PAPPILARY CYSTADENOMA OF BORDERLINE MALIGNANCY		8.30%	
155	G2605/8/10	53216	65	MASS	P			10X6X2	P		P				SIMPLE SEROUS CYST			
156	G2652/8/10	55416	17	MENSTRUAL DISTURBANCES		P		9X5X5	P		p				GRANULOSA CELL TUMOR	VIM + ,INH +	2.80%	Ia
157	G2703/8/10	45326	50	PAIN		P		4X2X1,		P			P	ASCITES+	SEROUS ADENOCARCINOMA			
158	G2831/9/10	44613	60	MASS	P			7X3.5X1		P	P				BENIGN SEROUS CYSTADENOMA			
159	G2928/9/10	43216	55	PAIN	P			8X3.5X1	P		P				BENIGN SEROUS CYST			
160	G2930/9/10	52164	60	MASS		P		9X5X3	P				P	asites+	MUCINOUS CYSTADENOCARCINOMA			
161	G2936/9/10	43144	12	PAIN	P			3X2X2	P		P				BENIGN CYSTIC TERATOMA			
162	G2951/9/10	4861	50	MASS	P			9X5X3	P		P				BENIGN SEROUS CYSTADENOMA			
163	G3044/10/10	4321	45	MASS, PAIN	P			8X6X3	P		P				BENIGN SEROUS CYSTADENOMA			
164	G3045/8/10	5628	28	MASS		P		10X5X6		P			P	ASCITES+	PAPPILARY CYSTADENOCARCINOMA			
165	G3120/10/10	5698	48	PAIN		P		4X3X2	P				P		PAPPILARY MUCINOUS CYSTADENOCARCINOMA			
166	G3169/10/10	1123	28	MASS		P		7X5X2,		P	p				GRANULOSA CELL TUMOR	VIM +, INH+	3.40%	Ia
167	G3171/10/10	6754	45	PAIN		P		8X6X2	P				P	ascites+	PAPPILARY SEROUS CYSTADENOCARCINOMA			
168	G3173/10/10	5656	15	MASS, PAIN		P		16X7X4		P			p	ASCITES+	YOLK SAC TUMOR		31.30%	
169	G3228/10/10	8767	30	MASS	P			12X9X5	P		P				BENIGN SEROUS CYSTADENOMA			
170	G3253/10/10	9876	70	MASS	P			7X5X2	P		P				BBENIGN MUCINOUS CYSTADENOMA			
171	G3076/10/10	4567	58	PAIN	P			13X6X4	P		P				BENIGN MUCINOUS CYSTADENOMA			
172	G3277/10/10	4324	30	PAIN		P		7X4X3		P			P	ASCITES+,OM	PAPILLARY SEROUS ADENOCARCINOMA			
173	G3406/11/10	7656	38	PAIN	P			6X5X2	P		P				BENIGN MUCINOUS CYST			
174	G3407/11/10	5463	45	PAIN	P			4X3X2	P		P				BENIGN CYSTIC TERATOMA			
175	G3433/11/10	6545	42	MASS, PAIN	P			3X5X2	P		P				BENIGN SEROUS CYSTADENOMA		3%	
176	G3535/11/10	5643	20	MASS			P	13X10X9	P				P		DYSGERMINOMA			
177	G3577/11/10	5674	49	MASS	P			18X12X6	P		P				BENIGN MUCINOUS CYSTADENOMA		3.10%	
178	G3657/11/10	3421	35	MASS	P			4X3X2	P				p		KRUKENBERG TUMOR			
179	G3680/12/10	5645	39	PAIN	P			10X5X2	P			P			MUCINOUS TUMOR OF BORDERLINE MALIGNANCY		6.20%	
180	G3694/12/10	4567	40	PAIN	P			5X3X2	P			P			BENIGN MUCINOUS CYSTADENOMA			

181	G3695/12/10	4567	43	MASS		P		5X3X2	P				P		PAPILLARY MUCINOUS CYSTADENOCARCINOMA			
182	G3696/12/10	4545	16	MASS		P		10X5X4	P				P		YOLK SAC TUMOR			
183	G3792/12/10	3654	38	MASS, PAIN		P		16X6X4	P				P	ASCITES+, OM	PAPILLARY SEROUS CYSTADENO CARCINOMA			
184	G3793/12/10	3456	47	PAIN			P	4X3X2	P				P		PAPILLARY ADENOCARCINOMA OVARY			
185	G3861/12/10	3455	65	PAIN	P			4X2X1	P		P				BENIGN MUCINOUS CYSTADENOMA		3%	
186	G3880/12/10	4567	43	PAIN		P		3X2X1	P				P	OMENTUM=	adenocarcinoma			
187	G3928/12/10	6745	2	PAIN,mass, precocious puberty		p		4x3x2	p		p				juvenile granulosa cell tumor	VIM +, INH+	4.20%	Ia
188	G 4079/12/10	22567	65	MASS	P			17X7X4	P			P			BORDERLINE MUCINOUS CYSTADENOMA		6%	
189	G4158/1/11	4534	70	PAIN	P			8X4X2	P			P			MUCINOUS TUMOR OF BORDERLINE MALIGNANCY			
190	G4175/1/11	2234	53	MASS		P		8X5X2	P		P				BENIGN MUCINOUS CYSTADENOMA WITH BRENNER TUMOR			
191	G45/1/11	3324	45	PAIN		P		7X5X3	P				P		ENDOMETRIOID CARCINOMA OVARY			
192	G58/1/11	4534	40	PAIN		P		8X4X2	P				P	OMENTUM +	papillary adenocarcinoma			
193	G60/1/11	10110	43	MASS		P		14X12X5	P				P	OMENTUM +	PAPILLARY SEROUS ADENOCARCINOMA			
194	G269/2/11	3122	29	MASS, PAIN		P		8X5X2		P			P		B/L KRUKENBERG TUMOR			
195	G476/2/11	8234	65	PAIN			P	6X3X2, 2x1x0.5		P			P		B/L MALIGNANT BRENNER TUMOR			
196	G695/3/11	1525	62	PAIN		P		5X4X3		P	P(both)		P(both)		1.PAPILLARY ADENOCARCINOMA, 2. SEROUS CYSTADENOMA			
197	G762/12/11	1618	55	PAIN, MENSTRUAL DISTURBANCE		P		6X4X2	P		p				GRANULOSA CELL TUMOR	VIM +, INH+	8.40%	Ic
198	G934/3/11	2803	37	PAIN		P		3X2X2,		P		P			B/L PAPILLARY MUCINOUS CYSTADENOMA OF BORDERLINE MALIGNANCY		6.10%	
199	G1089/3/11	17758	36	MASS, PAIN	P			9X7X4	P		P				BENIGN CYSTIC TERATOMA			
200	G1137/3/11	ESI-11179009	56	PAIN	P			4X3X2	P		p				FIBROMA			