International Journal of Pharmaceutical Science Invention
ISSN (Online): 2319 – 6718, ISSN (Print): 2319 – 670X
www.ijpsi.org Volume 3 Issue 10 ǁ October 2014 ǁ PP.14-24

Histopathological Patterns of Germ Cell Tumours of Ovary in a Tertiary Level Hospital

Dr Ivy Sharma[1], Dr Tirtha Chaliha[2]
[1] *Assistant Professor, Department Of Pathology, Gauhati Medical college And Hospital,Guwahati,, India /Srimanta Sankaradeva University Of Health* Sciences,Guwahati, Assam.
[2] *Professor And Hod , Department Of Pathology,Gauhati Medical College And Hospital,Guwahati,India/ Srimanta Sankaradeva University Of Health Sciences,Guwahati, Assam.*

ABSTRACT : *The aim of the study was to evaluate the frequency and patterns of histopathologically diagnosed germ cell ovarian tumours of cases attending a tertiary level medical facility based hospital in Guwahati,Assam,India. Total of 102 cases of ovarian tumours were studied out of which 31 cases were germ cell tumors. Abdominal mass was the most predominant clinical presentation. The cases were investigated and surgically treated. The formalin fixed specimens (simple oophorectomy or hysterectomy with unilateral /bilateral salpingo-oophorectomy) were examined grossly ,processed routinely and the sections were stained with H& E stain . In germ cell tumours, benign cystic teratomas constituted highest numbers (26.47%), followed by dysgerminoma(1.96%),Immature teratoma(0.98%) and Yolk sac tumor(0.98%).*

KEYWORDS : *Alfa feto protein, Benign cystic teratoma , Dysgerminoma , Choriocarcinoma Immature teratoma , Polyembryoma, Yolk sac tumour*

I. INTRODUCTION

Germ cell tumours: [1,2,3]

Ovarian neoplasm of germ cell origin represent 15 to 20 percent of ovarian tumours (Scully, 1970). The neoplasm in this groups are derived from germ cells, either directly (dysgerminoma, embryonal carcinoma) or indirectly through embryonic (Teratoma) or extraembryonic (Choriocarcinoma, yolk sac tumour) differentiation (Serov et al 1973). They are relatively more frequent in children, as approximately 60 percent of ovarian tumours in patients less than 20 years of age are derived from germ cells and the younger the patient, the higher the likelihood that the tumour is malignant (Abell MR et al 1965, Norris HJ et al 1972). About 95 percent of germ cell tumours are benign cystic teratomas. The 5 percent of germ cell tumours that are malignant may pose problem in diagnosis, largely because of their varied and complex patterns (Kurman and Norris 1978). Since many malignant germ cell tumours produce and express on their cell surface tumour products (HCG,Alpha fetoprotein, placental alkaline phosphatase and lactate dehydrogenase), it has become possible to apply the technique of radioimmunolocalisation (RIL) to detect residual tumour masses (Newland and Bagashawe 1987).

Alpha feto protein [30,31]has been found to be constantly associated with all germ cell tumours of the ovary that contain yolk sac elements (Hyderman 1983). HCG as an indicator of trophoblastic differentiation (Taylor and warner 1983; Shousha and Miller 1984) has deepened the interest in this area. Clinical significance of these tumour markers in management of these patients (Romera and Schwartx 1981, Szymedera et al 1983) has now prompted all to look for them by using immunohistochemical techniques, which have thus become an important adjunct of routine histologic studies. Origin: There are two main theories of the origin of germ cell tumours. In the gonad, there has been no evidence in recent years to support the old theory that germ cell tumours arise from a somatic cell or a misplaced blastomere, a view still active for extragonadal germ cell tumours (Ashely 1973). It is universally acknowledge that gonadal species, the germ cells done not arise from the surface of the ovary. Germ cells arise in the yolk sac (Witschi 1984) and migrate to the ovary via transcoelomic amoeboid action and possibly via lymphatic vessels as well. Evidence based on studies of nuclear sex chromatin, electrophoretic enzyme patterns within teratomas (Linder et al 1975), the comparative pathology of germ cell tumours (Dehner et al 1970 and experiments involving transplantation of gonadal ridge (Stevens et al1967) have been helpful in clarifying the nature of germ cell tumours.

Teratomas of the ovary are sex chromatin positive 46XX. Linder and co-worker (1975) using chromosome banding and electrophoretic techniques, demonstrated that homologous chromosomes in cells of benign cystic teratomas of ovary of woman have identical centromeric markers and are homozygous at some, but not all, genetic loci for which the host cells are heterozygous. For this to occur the teratoma has to arise from a single germ cell after the first meiotic division, which occurs after crossing over and exchange of genetic material between homologous chromosomes. Human teratomas develop from pluripotential descendants of activated germ cells and these stem cells may differentiate into either somatic or extraembryonic tissues (Damjanov 1983)

Dysgerminoma: [4,5,] It accounts for one percent to two percent of all malignant ovarian tumours (Burkars et 1987, Gordon et al 1984, De Palo G et al 1988). Mayer (1931) introduced the term dysgerminoma. It represent 13.5% percent of the total germ cell tumours of the ovary (Kurman & Norris 1978). It usually occurs in the second and third decades. It is usally unilateral. The right ovary is more commonly involved (Garshenoson and Wharton 1985). Teilum (1959-65) postulated that the tumour arises from undifferentiated germ cell which has been accepted by FIGO (International federation of obstetrics & gynaecology and WHO.(World Health Organisation.) About 5% of dysgerminoma arise in abnormal gonads, pure/mixed gonadal dysgenesis (from a gonadoblastoma) or androgen insensitivity syndrome. The size of dygerminoma[5] varies from a few centimeters to large ones nearly filling the abdomen. Characteristically, the capsule is smooth, although the contour may be nodular. The consistency of the tumour is doughy or rubbery. There is little tendency towards formation of cysts unless the tumour is associated with teratoid elements, and in the latter the associated teratoma is generally solid (Novak and Woodruff 1979). If they are small with multiple foci of calcification associated gonadoblastoma may be present (Bajaj, 2000). Histologically, it is composed of large round or polygonal cells with vesicular nuclei containing one or more nucleoli, clearly or highly granular cytoplasm, abundant glycogen and a prominent cell membrane. Syncytiotrophoblastic giant cells, the source of increased levels of gonadotrophin detected in some patients are present in about 5 percent of dysgerminoma (Zaloudek et al 1981). A lymphocytic infiltrate located chiefly within the fibrous septae, is an almost constant finding and an important diagnostic characteristic of dygerminoma (Claude Gompel and Silverberg 1985). No prognostic significance is noticed in dysgerminoma with varying degree of lymphoplasmacytic infiltrate as previously thought. Anaplastic variety comprises 5% of dysgerminoma and their prognosis is a controversial debate (Bajaj, 2000).

Endodermal Sinus Tumour (Yolk sac tumour)[6] : It is a highly malignant tumour with a short life span. It constitute 0.8 percent of all ovarian tumour and 2.8 percent of all malignant ovarian tumour (Saxena et al 1989). It represent 22 percent of all malignant germ cell tumour (Moghe et al 1985). Children in 1939, described this tumour as mesonephroma ovarii hypothesizing its origin form mesonephric ridge. In 1946, Teilum suggested a germ cell origin of it. Pierce et al (1970) provided experimental support for the concept of Teilum. After that, Deily and Todd (1974), Kurman and Norris (1978), Jimerson et al (1977) confirmed the histogenesis of this tumour from extraembryonic tissues.

The age range is 14 months to 45 years, the median age is 19 years (Kurman, Norris 1976). Grossly, the tumour is predominantly solid, with multiple small cysts, haemorrhage and areas of necrosis. It is rarely bilateral (Claude Gompel and Silverberg 1985). Microscopically this tumour displays four basic patterns (Kurman, Norris 1976). The most common is the reticular pattern characterized by a loose meshwork of spaces and channels lined by flattened or vacuolated cells. In festoon pattern, papillary structures project into tubules forming structures referred to as Schiller Duval bodies. The polyvesicular vitelline pattern is characterized by microcysts lined by mucinous or clear columnar or flattened cells amidst a dense fibroblastic stroma. In solid pattern, a relatively dense proliferation of undifferentiated cells are found. Periodic acid Schiff (PAS) positive, nonglycogen droplets are present in nearly all endodermal sinus tumours and represents a variety of proteins including AFP and Alpha-I antitrypsin (Kurman & Norris 1976, Palmer et al 1976).Serum AFP seen in pure yolk sac tumour is always more than 1000ng/ml. AFT in yolk sac tumour can be demonstrated in serum, tumour and ascitic fluid. AFP levels are directly proportional to the bulk of yolk sac tumour. In the follow up, serum AFP levels start increasing 8-29 weeks prior to clinical recurrence (Bajaj, 2000).

Embryonal Carcinoma: It represents 5 percent of the malignant germ cell tumours of the ovary (Kurman and Norris 1978). Embryonal carcinoma is considered to be composed of totipotential cells capable of differentiation into embryonic or extra embryonic tissues. In the large and widely reported Armed Forces Institute of Pathology (AFIP) series, Kurman and Norris (1976) found only 15 embryonal carcinoma. In the University of Texas. M.D. Anderson Hospital (UTMADH) series (Gershenson et al 1984) embryonal carcinoma occurred in 24 percent of 42 mixed germ cells tumours. Grossly, these are large, unilateral solid neoplasms. Cut surface is fleshy and tan or grey, Microscopically it is composed of atypical cells having large, vesicular nuclei with one or two prominent nucleoli. The cytoplasm is relatively abundant and isclear or amphophilic. The tumour cells are

arranged predominantly in sheets, but primitive or well formed glands are frequently present, as is a papillary growth pattern. Other common features are the presence of multinucleated giant cells, hyaline bodies and isolated clusters of syncytiotrophoblastic cells. Necrosis and haemorrhage are common.

Polyembryoma: It is exceedingly rare tumour composed of numerous embryoid bodies morphologically resembling embryos. Wills (1958), Bech et al (1969) considered 'embryoid body' formation; a transient bizarre differentiation in teratoma possibly in response to local response of organizer in the malignant teratoma. Grossly, these tumours are usually unilateral, solid and contain haemorrhage and necrosis. Microscopically they contain numberous embryoid bodies of varying differentiation and size. Trophoblastic differentiation may occasionally be observed Takeda et al (1982) have reported AFP production with immunuoperoxidase staining confirmation in a 9 years old girl with polyembryoma.

Choriocarcinoma:[7,8,9] **:** Pick (1904) first described the presence of choriocarcinoma in an ovarian teratoma. Robert Meyer (1930) and Teilum (1964) included this tumour into the category of germ cell series. Most primary choriocarcinoma in the ovary is combined with other malignant germ cell elements and is best placed in the category of mixed germ cell tumours (Kurman JR, Norris HJ 1976). Among 8 cases of non gestational ovarian choricarcinoma in the Armed Forces Institute of Pathology (AFIP) files, at least 6 were mixed tumours (Noris and Adams 1981).

Most chrocarcinomas involving the ovary represent metastasis from uterine tumours. Primary ovarian choriocarcinoma can develop form an ovarian pregnancy or as a germ cell neoplasm. Nongestational choriocarcinoma can be pure or a component of mixed germ cell tumour and are always malignant. (Gerlive et al 1973). exposing friable dark coloured haemorrhagic masses Microscopically, the tumour is composed of solid cords and sheets or syncytiotrophoblast and cytotrophoblast. The cytotrophoblast is composed or medium sized polygonal, round or oval cells with clear cytoplasm and sharp unclear border. The syncytiotrophoblast is composed of large basophilic vacuolated cell with irregular outlines. They contain multiple hyperchromatic nuclei varying in size and shape. These form plexiform patterns with central nests or cytotrphoblast enclosed by rims or syncytiotrophoblast. Haemorrhage and necrosis may be prominent (Gershenson and Ruttedge 1987).

Teratomas: [8,9] : Teratomas are characterized by tissue derived form more than one germ cell layer which resemble those found in the embryo (immature) or those in the adult (mature). Histologically these tissues can include squamous epithelium, cartiliage, bone, smooth muscle, intestinal epithelium and neuroectodermal tissue. The degree of histological differentiation of the teratoma is important in determining the prognosis (Norris and Adams 1981).

Teratomas develop from pluripotential descendants of activated germ cells and that these stem cells may differentiate into either somatic or extraembryonic tissues (Damjanov 1983). In 1940, Ewing proposed the sex cell theory according to which teratoma is a spontaneous growth of a parthenogenetic ova. Willis (1953) considered teratomas arising from foci of pluripotential cells which escapes from the influence of primary organizers. If the tumour differentiates and matures as fast a benign picture of benign cystic teratoma is produced (Dermoid cysts). If the saturation is slow the picture is more embryonic and malignant in behaviour.

Ashely (1973) had proposed 4 possible genesis namely-

a. incomplete twinning
b. Neoplastic proliferation sequestered totipotent blastomeres or primordial germ cells.
c. Depression of totipotent genetic information in the nuclei of somatic cells
d. Parthenogenetic development of germ cells- the last explains most satisfactory the high frequency of these tumours in the ovary.

The mature ovarian teratomas usually have 46XX chromosomal constitution (Corfman and Richart 1964). Linder et al (1975) analysed a small number of ovarian teratomas, noted structural homozygosity for centromere markers and some heterozygosity for loci distant form the centromere. They concluded that mature ovarian teratomas arose from cells that had completed the first meiotic division but had failed to progress further along the meiotic pathway. The most likely interpretation of the study of Parrington et al (1984) is that the development of mature teratoma is associated with an attempt to complete the whole of meiosis, and to continue into the development of zygote within the ovary and without the stimulus of fertilization.

Immature (Malignant) teratoma: [10-13]

These tumours constitute about 1.3% of all ovarian tumours (Naka Shima et al 1965-1988). They are composed of a mixture of embryonal and adult tissues derived from all three germ layers. The main component is

neurogenic but mesodermal elements are also common. (Nagales et al 1976.) Some tumours are predominantly composed of endodermal derivatives, including oesophagus, liver and intestinal structures (Nogales et al 1993.

The tumour is common in children and young adolescent. Grossly, it may be solid or solid with multiple cysts or predominantly cystic.

The prognosis depends on the nature and amount of embryonal component (Beilly et al 1975). It is best when the latter is predominantly made up of neural tissue. Two types of histological grading systems are described in literature (Bajaj, 2000).

Grade 0- All tissues mature

Grade I- Some immaturity present,

With neuroepithelium not more

than one focus per slide. Tumour contains < 10% neuroepithelium

Grade II- Higher immaturity than grade I. Neuropeithelium does not exceed 3LPF/ slide

One third of tumour consists of Neuropeithelium

Grade III- Immaturity and neuroectoderm Prominent occupying 4 or

Neuroepithelium

>4LPF/ slide

Half of tumour consists of Neuroepithelium (Pramila Bajaj 2000)

NEOPLASMS WITH AN EXCLUSIVE OR ALMOST EXCLUSIVE MALIGNANT NEUROECTODERMAL COMPOSITION ARE DESIGNATED MALIGNANT NEUROECTODERMAL TUMOUR AND ARE REGARDED AS A FORM OF MODODERMAL TERATOMA (AQUIRE AND SCULLY 1982, KLEIMAN ET AL 1993). IF THE NEUROECTODERMAL COMPONENT IS MADE UP OF ENTIRELY EPENDYMAL STRUCTURES THAN TUMOUR IS TERMED AS OVARIAN EPENDYMOMA (KLEIMAN ET AL 1984, 1993).

Mature solid teratoma [13] : It is composed entirely of adult tissue derived from all three germ layers (Peterson et al 1956, Thurlbeck & Scully 1960). The tumour has a predominantly solid gross appearance, but multiple small cystic areas are also present. Some authors refer to mature solid teratoma as grade O immature teratoma. It usually occurs in young women in the second decade. Prognosis is excellent even if peritoneal implants are present (Benirsche et al 1960).

Mature Cystic Teratoma.[14,15,16] : They make up almost 20 percent of all ovarian neoplasms. They constitute the most ovarian tumour in childhood (Ein et al 1970). Grossly, they are usually multiloculated. The cystic contents are greasy, largely composed of keratin, sebum and hairs. They are unilateral in 88 percent of the cases. Teratomas often contain teeth and sometimes even an imperfectly formed human body like structure- fetiform teratoma (Miyake et al 1986). Microscopically, ectodermal derivatives are found in 100% of tumours, mesodermal structures in 93% and endodermal derivatives in 71% (Blackwell et al 1996). The cystic cavities are lined by mature epidermis and skin appendages and neural tissue are very common. Other tissues include cartilage, respiratory tissue, gastrointestinal tract tissue, thyroid, anterior pituitary tissue etc. Rashad et al in 1966 showed that 46xx pattern is present in all cases. Linder et al in 1975 showed that these tumours are of parthenogenetic origin and probably arise from a single germ cell after first meiotic division. Malignant change in cystic teratoma maybe squamous cell carcinoma (90-97%), carcinoid tumour, adenocarcinoma, malignant melanoma, paget's disease. Peritoneal implants of mature glial tissue may be found in all teratomas- condition being called gliomatosis peritonei (Robby & Scully 1970, Wheeler 1978). [17,18,19]

Monodermal Teratoma [20,21] : The most common monodermal teratoma is struma ovarii. This is composed totally or in overwhelming proportion of thyroid tissue. According to Dockerty 1945, Novak and Woodruff 1976 and others the single tissue overgrow and blotted out other elements of the teratomas.

Smith (1946) observed that only in 4 percent of cases, the tumour is bilateral. Smith has put the average age in his series as 42 years. Grossly, the strumas are encapsulated neoplasm grayish brown in colour and spongy in consistency. On sectioning, it is partly solid and partly cystic. Sometimes, large cystic areas may be present either as a part of the struma or as an associated teratoid structure or a mucinous cyst (Novak and Woodruff 1979). The tumour is generally benign, although any of the histologic types of thyroid carcinoma may develop in a struma (Fasleton et al 1978). Most of these have been classified as carcinomas on histologic grounds alone but cases with metastasis have been reported. (Bardo-mindan et al, 1983). [32-37]

The second most common monodermal teratoma of the ovary is the carcinoid which is occasionally apparently pure, but is associated more often with grossly or microscopically demonstrable teratoma elements of other types (Scully 1987). The primary ovarian carcinoid is usually of the insular or midgut type (Robboy et al 1975), but may be trabecular, with a ribbon like pattern or growth (Robboy et al 1977). The insular carcinoid is accompanied by the carcinoid syndrome in approximately one third of the cases. Macroscopically, carcinoids are firm, solid tan or yellow tumours. They are unilateral and frequently develop in the wall of dermoid cyst. Microscopically, carcinoids are composed of regular round or cuboidal cells with moderate amount of clear or eosinophilic cytoplasm. The nuclei are round and have coarse chromatin. Fine dark granules can be demonstrated by argentaffin stains (Claude Gompel and Silverberg 1985). Strumal carcinoids are tumours that combine the features of carcinoid tumour and struma ovaii (Greco et al 1979, Robboy et al 1975). Archelger and Scully in 1974 suggested that the carcinoid like component represents a medullary carcinoma arising out of thyroid C-cells. But Synder in 1986 and Stagus et al 1987 showed that the morphologic and immunohistochemical profile of the tumours are more akin to those of trabecular carcinoid of hindgut derivation. Very rare forms of mondermal teratomas include malignant neuorectodermal tumours that resemble primitive malignant tumours of the central nervous system (Aquire and Scully 1982), ependymomas (Kleiman et al 1984), retinal analouge tumours and sebaceous gland neoplasms.

Mixed Germ cell tumour : Germ cell tumours, that contain more than one malignant germ cell pattern are referred to as mixed germ cell tumours (Kurman and Norris 1978). These represent around 8 percent of malignant germ cell tumours of the ovary. (Jain et al 1989). In AFIP files, they represent 8 percent of the malignant germ cell tumour and age ranges from 5 to 33 years. External surface is smooth but the cut surface is varied, solid fleshy tan areas in dysgerminiomas, mucoid cystic areas in teratoma, hemorrhage and necrosis in case of endodermal sinus tumour and choriocarcinoma (Dhamne et al 1985).

Gonadoblastoma: [22-28] : It is also know as dysgenetic gonadoma and included among the gonocytomas in Teter's classification (Teter 1963). It almost always occurs in sexually abnormal individuals, most commonly affected by gonadal dysgenesis and carrying the Y chromosome (Bjersing et al 1977). Tumour is chracterised by the presence of germ cells, cells derived form the sex cords and mesenchymal cells (Govan et al 1977, Hart et al 1979, Woodcock et al 1979). Hyalinization and calcification are common. It is a benign tumour, unless overgrown by a dysgerminoma or less frequently some other type of malignant germ cell tumour (Hart et al 1979).

II. METHODOLOGY

The present research is based on a study of 102 specimens of ovarian tumours received in the Department of Pathology, Gauhati Medical College from the gynecology OT during the period from 1st June 2011 to 31st May 2012. The study was cleared by Institutional ethical committee of GMCH prior to the start of the research. Written Consent of patient was taken. Most of the patients presented with mass abdomen followed by pain abdomen , irregular menstruation ,amenorrhoea ,Constipation and urinary complaints . Investigations were done according to patients' requirement and managed surgically. Specimens were fixed in 10% formalin solution.

The nature of specimen was either in the form of simple oopherectomy or hysterectomy with unilateral /bilateral salpingo-oopherectomy. For gross examination, we followed the guideline described by Rosai J Ackerman,s Surgical pathology[29]. Omentum was looked for any nodularity. Lymph nodes were also dissected out and all were processed for HPE. On the basis of the gross finding, the sections were taken, processed routinely and stained with Haematoxylin & Eosin stain . The microscopic slides were viewed under low power field and high power field. The findings were noted and interpreted according to WHO classification.

III. RESULTS AND OBSERVATION

The most common clinical presentation was abdominal swelling for both benign and malignant variety (95.09%). In analyzing the age distribution, we have found that ovarian tumours are commonest in the age group of 31-40 year (36.27%). Out of the 102 ovarian tumours, 46 cases (45.09%) were cystic, 42 cases

(41.17%) were solid/cystic and 14 cases (13.74%) were predominantly solid tumours[Table1]. Bilaterality was detected in 8.86% of the total cases.Most of the benign ovarian tumour presented as cystic mass.
. In germ cell tumour category, benign cystic teratomas constituted highest numbers (26.47%), followed bydysgerminoma(1.96%).). Germ cell tumour was found in age group

-1 year-40 years.

GERM CELLS TUMOURS (31)
The commonest tumour of the group was teratoma (28) followed by dysgerminoma (2).

A.Teratoma (28)
Benign cystic teratoma (27)
These were the commonest tumours of the germ cell series and constituted 87.09% of germ cell tumours.

The youngest patient in our series was a 9 year old girl most of the othere tumours occurred in 2nd and 3rd decade. Clinically, all the patients had lump abdomen and 27% patients had associated pain abdomen. Only one case was bilateral.

Grossly, the tumours were usually smooth externally and cystic internally containing characteristic sebaceous material, hair and cartilage. The smallest tumour was 3cm diameter weighing approx. 150gm and the largest one was 14cm (weighing 1500gm). All tumours were partly cystic and partly solid.

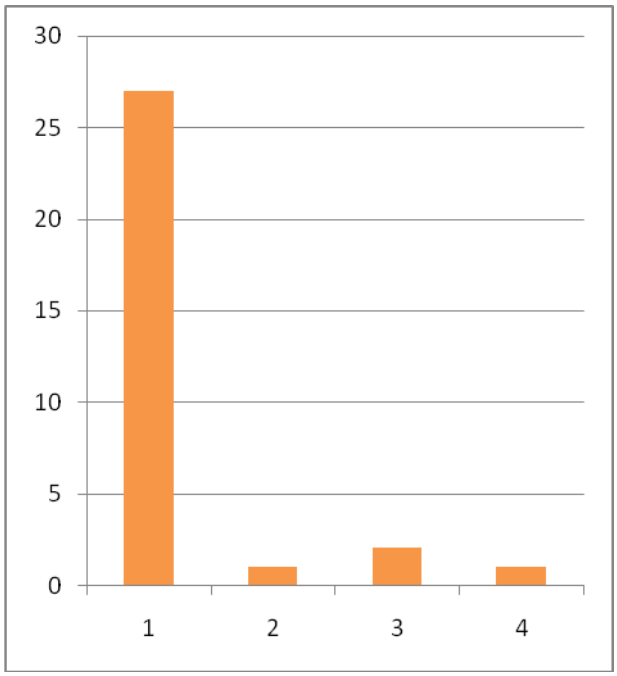
Microscopically, skin and its appendages were seen in the inner lining of the cysts in all cases. The lining of the cyst wall consisted of stratified squamous epithelium with sebaceous glands and hair follicles. Mesodermal elements were also present with endodermal derivatives like glands with columnar lining cells.

A. Dysgerminoma (2)
Dysgerminoma represented 6.45% of germ cell series. The youngest patient was a 10 years old girl. Clinically, all patients presented with lump abdomen, all except one had associated pain abdomen and one patient presented with retention of urine. Grossly, tumours were mostly solid with convoluted surface and grayish white in colour. The size of the tumours were variable.

B. Yolk sac Tumour (1)
Histologically, the tumour cells were large round or polygonal with vesicular nuclei containing one or more nucleoli, clear pale or translucent cytoplasm and a distinct cell membrane. The cells were separated by delicate connective tissue stroma or broad trabeculase of fibrocollagenous tissue infiltrated by variable number of lymphocytes. Large areas of haemorrhage and necrosis were also seen. One case of yolk sac tumour was diagnosed in a 1 ½ year old girl who presented with lump abdomen and pain abdomen of 3 months duration. Grossly, a large friable tumour mass, brownish in colour was received. The parietal peritoneum was adherent to the tumour mass. On cut section, multiple cystic spaces along with largely solid areas were seen with extensive areas of haemorrhage and necrosis. Microscopically, multiple sections taken from different parts of the tumour showed a variable picture. Most of the sections showed sheets of undifferentiated cells alongwith tubular structures, some of these showed typical differentiation of Schiller Duval bodies.

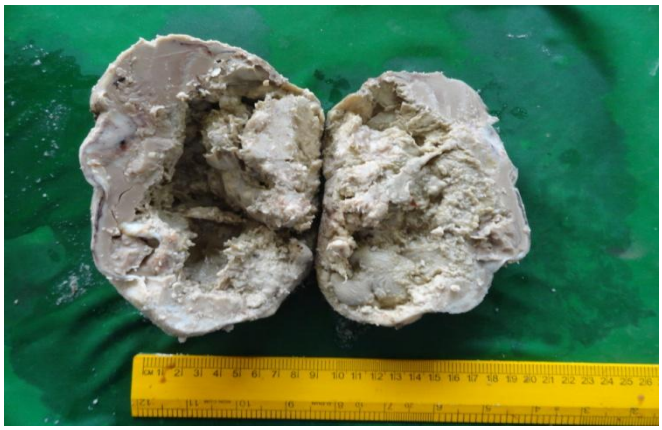
Table1 of Germ Cells Tumours (31 out of 102 tumours)

NEOPLASM	NUMBER	PRRCENTAGE	BILATERAL
A.TERATOMA	**28**	**27.45**	**_**
i)Benign cystic teratoma	**27**	**26.47**	**1**
ii)Immature teratoma	**1**	**0.98**	**_**
B.Dysgerminoma	**2**	**1.96**	**1**
C.Yolk sac tumor	**1**	**0.98**	**_**

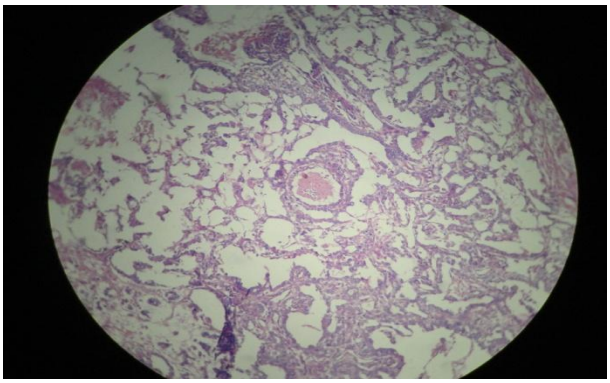


[1] Benign cystic teratoma
[2] Immature teratoma
[3] Dysgerminoma
[4] Yolk sac tumour

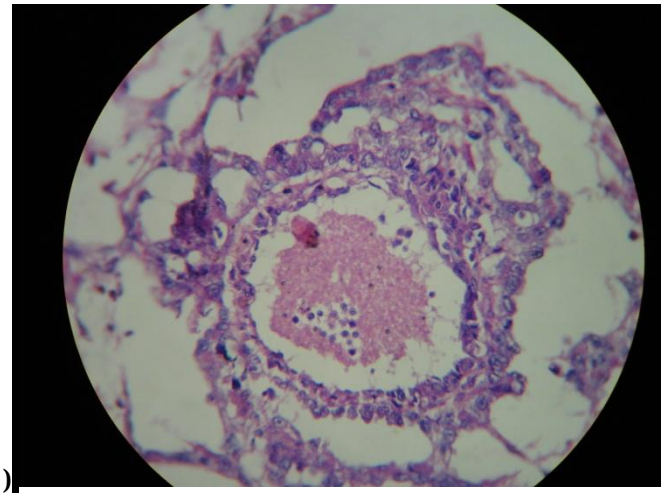
Fig. Showing breakup of Germ Cell Tumours



GROSS PICTURE OF YOLK SAC TUMOR

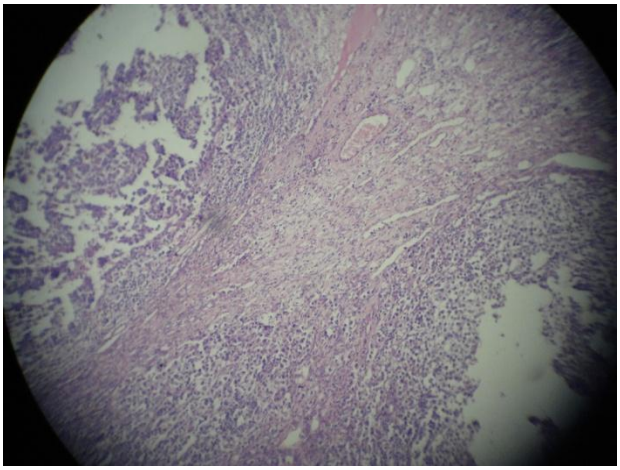


MICROPHOTOGRAPH OF YOLK SAC TUMOR(LOW POWER VIEW)



)

MICROPHOTOGRAPH OF YOLK SAC TUMOUR SHOWING SCHILLAR DUVAL BODY (HIGH POWER VIEW)



MICROPHOTOGRAPH OF DYSGERMINOMA

IV. DISCUSSION:

Thirty one of a total of one hundred and two ovarian tumours in this series belonged to germ cell tumours comprising 30.39% of all ovarian tumours, Tyagi[43] et al (1967) reported an incidence of 23.08%, Francisco[7] et al (1993) reported an incidence of 20.39%, Sarkar[44] (1996) reported an incidence of 27.09%,
Robbins and Cotran (2010) reported an incidence of 15-20%. The most common germ cell tumour in the present series was benign cystic teratomas (27 cases) comprising 26.4%. According to Scully (1970), benign cystic teratomas account for 14 to 19% of all ovarian neoplasms. Francisco[7] et al (1993) reported 15.45%, Rajan[46] (1994) reported 17.74% incidence and Sarkar[44] (1996) reported 16.9%. Out of a total of 870 cases of ovarian tumours studied by Dhanne et al (1985) benign cystic teratomas accounted for 12.76%. The parthenogenesis of teratomas was a point of controversy for many years. Marchand and Bannet (1911) considered that teratoma originate form blastomere. According to Ewing (1940), teratoma is a spontaneous growth of parthenogenetic ova. Novak[38] (1953) regarded both the theories as highly speculative .Willies (1953) considered teratomas arising from foci of plastic pleuripotential cells which escape form the influence of primary organizers. If the tumour differentiates and matures fast, a benign cystic teratoma is produced (dermoid cyst). if the maturation is slow, the picture is more embryonic and malignant in behaviour. According to Teilum[47](1971) teratoma follows embryonic differentiated pathway and so a variable picture may be present in different individuals. All 187 ovarian teratomas studied by Rashad et al (1966) and almost in all literature, have had a female sex (positive)[4] chromatin pattern, and all cases with chromosome analysis have been 46 XX. These findings as well as studies of teratomas from women heterozygous for 6 phosphogluconate and glucose 6 phosphate dehydrogenase and experimental studies in which many benign teratomatous elements can be derived form single embryonal

carcinoma cell (Pierce 1974) have strengthened the concept of origin of gonadal teratomas by parthenogenesis form single haploid germ cell of post meiotic origin (Asley 1973, Linder et al 1975).

Caruso et al (1971) reported that 10% of benign cystic teratomas are bilateral. Scully (1979) reported an incidence of 15-20%. Dhanne et al (1985) reported 9.8%. In our series, one case of bilateral cystic teratoma was seen which corresponds to 0.98%. The tumours of germ cell series varied greatly in size. The smallest tumour in the present series was 4cm (250gm wt) and the largest one was more than 10cm (1500gm). Peterson (1956) reported that 75% of the mature teratoma were 10cm or less while less than 4% were more than 20 cm in diameter. The gross appearance of benign cystic teratomas with smooth external surface and cystic interior containing sebaceous material usually mixed with hair, cartilage and sometimes bone are characteristic. The lesion often contains a solid prominence called Rokitansky protruberance located usually at a point of contact with the residual ovarian tissue. It is here that such structure as teeth and bone are commonly found and this is also the area from which sections should be made, since here the greatest variation in the cellular elements will be recognized (Novak and Woodruff 1979).[38] Microscopically, skin and its appendages were seen in the inner lining of the cysts in almost all the cases. The dermal tissues were usually stratified squamous epithelium with typical sebaceous glands and hair follicles. Mesodermal elements were also present with endodermal derivatives occurring less commonly. No malignant change was seen in benign cystic teratomas in our series. Francisco[7] et al (1993) reported an incidence of 0.58%, Bajaj (2000)[39] reported an incidence of 0.8-5% (Avg 1.4%)

No benign solid teratoma was found in the present series.

Only one case of immature teratoma was found in the present series representing 0.98% of the total ovarian tumours. Prabhakar and Maingi (1989) reported an incidence of 0.94%, Francsco et al (1993) reported an incidence of 1.17% and Sarkar[34] (1996) reported an incidence of 1.6%. The patient in the present study was 26 years old. The 58 patients in the Armed Forces Institute of Pathology (AFIP) series (Norris et al 1976) ranged in age from 14 months to 40 years. The tumour was unilateral in the present study. In the AFIP series, all the tumours were unilateral except for one that had metastasized to the contralateral ovary. Microscopically wide range of tissues having various degree of maturity were present. Two cases of dysgerminoma were found in the present study representing 1.96% of all ovarian tumours and 6.46% of all germ cell tumours. Jagadeshwari et al (1971) and Gupta et al (1986) reported 3.4% and 3.53% Francisco et al (1993) reported an incidence of 2.9%. Sarkar (1996) reported 5.3% incidence of dysgerminoma. Dysgerminomas usually occur in the younger group of women. According to Novak and Woodruff [38](1979), 40-45% dysgerminoma occurs before the age of 20 years and 80-85% occurs before the age of 30 years. The youngest patient in the present study was 11 years old. One case was bilateral at presentation which corresponds to a percentage of 0.98%. Kurman and Norris (1967), Asadourian[4] (1969) held the view that about 10% are bilateral at operation .Francisco[7] et al (1993) in his 10 year study of 343 ovarian tumours found no bilateral involvement in dysgerminoma. Microscopically, the tumour was composed of aggregates of large round or polygonal cells with vesicular nuclei containing one/more nucleoli, clear pale cytoplasm and a prominent cell memberane. The cells were separated by fibrous septae containing lymphocytes. One case (0.98%) of endodermal sinus tumour was seen out of a total of 102 ovarian tumours Prabhakar and Maingi (1989) reported 0.3%., Francisco et al (1993) reported 0.29% and Sarkar (1996) reported an incidence of 2.1%. Patient was a 1 ½ year old girl with lump abdomen. Microscopically, a variable picture was seen with typical glomeruloid bodies and Schiller Duval bodies with extensive areas of haemorrhage and necrosis.

Other members of the germ cell tumours like embryonal carcinoma choriocarcinoma, polyembryoma and carcinoid tumours are the rarest of germ cell tumours (Gierbie et al 1975, Kurman and Norris[45](1976). In the present study, none of the above mentioned tumours were found. Although we do not have facilities to study tumour markers in ovarian neoplasms, it has become adjunct of routine histologic studies. Serum tumour markers are important in the diagnosis and management of patients with malignant ovarian germ cell tumours. Since the time alpha fetoprotein (AFP) was recognized to be an oncodevolopmental marker reflecting the immature phenotype of cancer cells (Rudder 1982), it has been found to be constantly associated with all germ cell tumours of the ovary that contain yolk sac elements (Hyderman 1983) with good relation between serum AFP level and the amount of yolk sac element in the tumour (Ishigura et al 1981). Reappearance of serum AFP level after excision of the tumour was found to be sure indication of its recurrence (Romera and Schwartz 1981). Serum AFP seen in the pure yolk sac tumour is always more than 1000mg/ml. AFT in yolk sac tumour can be demonstrated in serum, tumour andascitic fluid. In the follow up, serum AFP levels start increasing 8-29 weeks prior to clinical recurrence (Bajaj, 2000). [39]HCG as an indicator of trophoblastic differentiation (Taylor and Warner 1983),[40] Shouse and Miller 1984) has further deepened the interest of observers in this area. Twenty cases of germ cell tumours studied by Suman et al (1988), immunohistochemistry for the presence of AFP and HCG revealed AFP in all 3 endodermal sinus tumours, all 5 embryonal carcinoma, all 4 mixed germ cell tumours and 2 out of 4 immature teratoma making this to be the single most important tumour marker in these

tumours. All 5 embryonal carcinoma, one dysgerminoma (out of 4), one immature teratoma (our of 4) showed presence of HCG and they could easily distinguish embryonal carcinoma (AFP + HCG +) from endodermal sinus tumour (AFP +, HCG-ve) by this method. In the study of 40 cases of germ cell tumours by Grover et al (1989), the result of immunoperoxidase staining for AFP and morphological diagnosis on histopathological examination correlated will in all the cases. Immunohistochemistry has thus enabled us to probe deeper into the histogenetic and biological aspects of germ cell tumours of the ovary, asserting its importance as a diagnostic procedure. So, serum tumour markers are important in the diagnosis and management of patients with malignant ovarian germ cell tumours.[41,42.] Patients should have serial serum measurements of HCG, AFP< placental alkaline phosphatase (PLAP) and lactate dehydrogenase (LDH). Since many malignant ovarian germ cell tumours produce and express on their cell surface tumour products (HCG, AFT and PLAP) become possible to apply the technique of radioimmunolocalization (RIL) to detect residual tumour masses

V. CONCLUSION

The main strength of this study is that it gives the most comprehensive picture of the current state of germ cell ovarian tumour incidence and histopathologic pattern..The incidence of Germ cell ovarian tumours corresponded to the data available for the study. The germ cell tumours accounted for 31 cases (30.39%) of total ovarian tumours. Out of these, benign cystic teratomas constituted 27 cases (26.47%), Dysgerminoma 2 cases (1.96%), immature teratoma 1 case (0.98%) and yolk sac tumour 1 case (0.98%) . The benign cystic teratomas were commonest in this group. The youngest patient was a 9 year old girl and most of the patients belonged to second and third decade of life. Histologically, almost all tumours were composed of skin and its appendages and showed other tissues like respiratory epithelium, nervous tissue, gastrointestinal epithelium, cartilage etc.

REFERENCES

[1] Koulos JP, Hoffman JS, Steinoff MM: Immature teratoma of ovary. Gynecol. Oncol. 34:46-49, 1989.
[2] Kawai M, Kano T, Furuhashi Y, Iwata M, Nakashima N, Lmai N, Kuzuya K; Immature teratoma of ovary. Gynecol. Oncol. 40:133-137, 1991.
[3] Ein SH, Darte JMM, Stephens CA: Cystic and solid ovarian tumours in children. A 44 year review J. Paediatr. Sing 5: 148-156, 1970.
[4] Asadourian LA, Tayler HBDysgerminoma: An analysis of 105 cases. Obstet. Gynecol. 33:370-379, 1969.
[5] Freel JH, Cassir JF, Pierce VK, Woodruff J, Lewis JL: Dysgerminoma of ovary. Cancer 43:798-805, 1979.
[6] Gerohenson DM, Del Junco G, Herson J, Ruttedge FN: Endodermal sinus tumour of the ovary. The MD Anderson experience. Obstet, Gynecol. 61:194-202, 1983.
[7] Francisco C, Nadkarni N, Rebello M: Ovarian tumours in Goa; A clinicopathologic study. Ind.l J. Obstet & Gynecol. 43:408-412, 1993
[8] Friedlander: Prognostic factors in Ovarian
[9] cancers 1st ed. Sharp F, Blachett T., Berck J, Blast R (Eds), ISIS Med Media, Std Oxford, 1998.
[10] Linder D, Mc Caw BK, Hecht F: Parthenogenic origin of benign ovarian teratomas. N Engl. J. Med 292:63-66, 1975.
[11] Hata K et al: A multivariant logistic regression analysis in predicting malignancy for patients with ovarian tumours, Gynaecologic Oncology 68:256-262, 1998.
[12] Hirakawa T, Tsuneyoshi M, Enjoji M: Squamous cell carcinoma arising in mature cystic teratoma of ovary. Am J. Sing. Pathol. 13:397-405, 1989.
[13] N, Rebello M, Francisco C, Nadkarni Ovarian teratomas. Ind. J Obstet & Gynecol. 44:773-776, 1994.
[14] Gershenson MD:Contemporary treatment of borderline ovarian tumours.Mini series/special article-Cancer investigation 17(3):206-210,1999.
[15] Barsky SH, Hunnah JB: Extra cellular hyaline bodies are basement memberane accumulations AM. J. Clin. Pathol. 87:455-460, 1987.
[16] Breen JL, Neubacker RD: Ovarian malignancy in children whith special reference to the germ cell tumours. Am NY. Acad. Sci. 142:658-674, 1967.
[17] Barowick KW, Li. Volsi VA: Malignant mixed mesodermal tumours of ovary. A clinicopathologic assessment of 12 cases. Am. J. Surg. Pathol. 4:37-42, 1980.
[18] Clement PB: Histology of the ovary. AM J.Surg. Pathol. 11:277-303, 1987.
[19] Colgan TJ, Norris HJ: Ovarian epithelial tumours of low malignant potential. A review. Int. J. Gynaecol. Pathol. 1:367-382,1983.
[20] CarterJ,FowlerJ,CarlsonJ,CarlsonTwiggsLB:Borderlineandinvasiveiepithelialovarian tumours in young women. Obstet, Gynecol. 82:752-756, 1993
[21] Chaitin BA, Gershenson DM, Evans HL:Mucinous tumours of ovary. A. clinicopathologic study of 70 cases. Cancer 55: 1958-1962, 1985
[22] Camistra SA: Cancer of ovary. N. Engl. J. Med. 329:1550-1559, 1993
[23] Yancik R: Ovarian cancer. Age contrasts in incidence, histology, disease stage at diagnosis and mortality. Cancer 71: 517-523,
[24] Yanai- Inbar, Scully RE: Relation of ovarian dermoid cysts and immature teratomas. An analysis of 350 cases of immature teratomas and 10 cases of dermoid cyst with microscopic features of immature tissue. Int. J. Gynecol. Pathol. 6:203-212, 1987.
[25] Young RH, Jacob AF, Celvin RB, Flotte TJ, Preffer F, Scully RE, Swyner CH, Bell DA: Yuvenile granulose cell tumours of ovary. Gynecol. Oncol, 46:97-103, 1992.
[26] Young RH, Scully RE: Metastic tumours in ovary. A problem oriented approach and a review of recent literature. Semin. Diagn. Pathol. 8:250-276,1991.
[27] .Zaloudek CJ, Norris HJ: Am J. Surg. Pathol. 6 Pg: 503-512, 1982.
[28] Woodruff JD, Perry H Genadery, Parmley T: Mucnous cystadenocarcinoma of ovary. Obstet. Gynecol. 51: 483-489, 1978.
[29] Reddy RS, Jagadeshwari N, Rao KS; J. Obstet & Gynecol. Ind 21:727, 1971.

[30] Rosai J: Ackerman's Surgical Pathology. Ninth edition.2009, Pg. 1649—1706.
[31] Blackwell WJ, Dockerty MB, Masson JC, Mussery RD: Dermoid cysts of ovary. Their clinical and pathologic significance. Am J. Obstet. Gynecol. 51:151-172, 1946.
[32] Berezowski K et al. Cytokeratins 7 and 20 and CEA in ovarian and colonic carcinoma. Mod Pathol. 9(4): 426-429, 1996.
[33] Carter J, Fowler J, Carlson J, Carlson L, Twiggs LB: Borderline and invasive epithelial ovarian tumours in young women. Obstet, Gynecol. 82:752-756, 1993.
[34] Abell MR: Malignant Brenner tumour of ovary. Cancer 10: 1263-1274, 1957.
[35] Bell DA: Mucinous adenofibroma of ovary. Am. J. Surg. Pathol. 15:227-232, 1991
[36] De Palo, G. Pilotti, Kenda R, Ratti E, Rossi G: Natural history of dysgerminoma. Am J. Obstet Gynecol. 143:799-807, 1982.
[37] Daya D Nazerali L, Frank GL-Metastatic ovarian tumours simulating primary ovarian tumour.Am J Clin. Pathol.97:799-807,1982.
[38] De Nictolis M, Monteroni R, Tommasoni S: Benign, borderline and well differentiated malignant intestinal mucinous tumours of ovary. Int. J. Gynecol. Pathol. 13:10-21, 1994.
[39] Novak ER, Woodruff JD: Gynaecologic and Obstet. Pathology. 8th Edition, P. 380,1979.
[40] Bajaj P: Ovarian tumours: Proceedings of fifth international CME and update in surgical pathology: 71-85, 2000
[41] Taylor HB, Norris HJ: Lipide cell tumours of ovary. Cancer 20:1953-1962, 1967.
[42] Zheng W et al; Alpha and beta subunits of inhibin/activin as sex coard stromal differentiantion markers, Int. J. Gynaecol Pathol. 16 (3): 263-271, 1997.
[43] Tulika S, Mohsin S.Khan A. Hakim S: Cytohistomorphological study of ovarian tumours. Ind. J. Obstet & Gynecol. 49:65-69, 1999/
[44] Tyagi SP, Madan A, Mohsin S, Hameed F, Saxena K: Ind. J. Pathol. Microbiol. 21, 281, 1978.
[45] Sarkar R: Ovarian neoplasms- A 14 years study. Obstet & Gynecol. J. India. 46:156-159, 1996.
[46] Kurman RJ, Norris HJ: Endoderm sinus tumours of ovary. A clinical & pathologic analysis of 71 cases. Cancer 38:2404-2419, 1976. **46** .Rajan R: Analysis of ovarian pathologies in the modern persopective. Ind. J. Obstet & Gynecol 44:764-770, 1994.
[47] Teilum G: Classification of ovarian tumours. Acts. Obstet. Gynecol. Scand. 31; 302-312, 1952