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Morphological Study of Ovarian Tumors with Special Reference to Germ Cell Tumors

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Abstract:
Introduction: *The study includes the morphological and histological aspects of the common tumors and also rare and uncommon ovarian tumors, with clinical manifestation, morphological and histopathological appearances.*
Material and Methods: *Statistical incidence of ovarian tumors from 2001 to 2004 was taken. Specimens were processed routinely and sections, from representative sites, stained with hematoxylin and eosin were studied. Special stains like PAS, Vangieson, Reticulin and Alcian blue were done in special cases.*
Results: *A total number of 150 ovarian tumors received from 2001 to 2004 have been studied. Of them 88 are benign tumors, 3 are borderline tumors & 59 are malignant tumors. Out of 150 ovarian tumors 122 were surface epithelial tumors, 9 were sex cord stromal tumors, 16 were germ cell tumors and 3 were metastatic tumors.* ***Discussion:*** *Ovary is the third most common site of primary malignancy in female genital tract and accounts for 6% of all cancers in females. About 2/3 of ovarian tumors are seen in the reproductive age group and the commonest age group is between the ages of 20 and 65 years.*
Conclusion: *Of all the benign tumors of the ovary mucinous cystadenoma was the commonest tumor accounting for 50% of all benign ovarian neoplasms. The commonest malignant tumor was serous cystadenocarcinoma accounting for 58% of all malignant ovarian tumors. Germ cell tumors comprised 16 (10.7%) of all ovarian tumors; out of them 9 (6%) were benign and 7 (4.7%) were malignant.*
Keywords: *ovarian tumors, germ cell tumors, metastatic tumors in ovary*

I. Introduction

The most challenging, fascinating intriguing and perplexing disease of the mankind is cancer. The increase in incidence of malignant ovarian tumors during the last few decades parallels to the increasing incidence of human cancer. The present study will have a miniature representation of the overall increased rate of incidence of the ovarian cancers at large in the world.

The occurrence of embryonal malignant tumors from the ovary proves the presence of pleuri-potent cells. The structural and developmental diversity of the ovary makes it a seat for the development of a variety of tumors of epithelial, connective tissue and germ cell origin.

Urbanization and usage of several therapeutic agents, both hormonal and non-hormonal, influence the incidence of ovarian tumors, both benign and malignant.

In our present study, attempts are made for a more reasonable and workable classification of ovarian tumors mainly based on the histogenesis. Our present study includes the morphological and histological aspects of the commonly occurring tumors like surface epithelial etc. and also the study of rare and uncommon ovarian tumors, with clinical manifestation, morphological and histopathological appearances.

Biochemical analysis of various hormonal and polypeptide compounds expressed by the functionally active tumors may also give an insight into the prognosis and the genesis of the tumor, eg: virilizing tumors of the ovary.

In recent times, the introduction of immunohistochemistry and cytogenetic study for definite identification of cell of origin of tumor and also its prognostic evolution have revolutionized the concept of ovarian tumors and their behavior. The immunohistochemical analysis of tumors will help in initiating a correct line of treatment in the best interest of the patient.

The risk for developing ovarian cancer increases after 40 years of age with peak incidence between the ages of 50 and 55 years. The age specific incidence ranges from 2/100,000 between 20 and 29 of age to 55/100,000 at 70 years.

When compared to Japan the incidence of ovarian neoplasms is 3 to 7 times higher in the western countries. Blacks in the United States have a lower incidence than whites. The above observations suggest the role of genetic and environmental factors in the causation of ovarian cancer.

Germ cell tumors are more frequent in Japan, India and Uganda. Malignant teratomas and dysgerminomas are more common in blacks than in whites. The dysgerminoma has a high incidence in Peru but not in other South American countries.

Pregnancy, oral contraceptives have been reported to have a protective effect against ovarian cancer. The death rate is higher in nulliparous than parous women. Experimentally induced tumors implicate factors such as destruction of ova and granulosa cell and elevation of pituitary gonadotropins in the pathogenesis of these tumours.

II. Material And Methods

Ovarian tumors that were resected and sent to the Department of Pathology, Guntur Medical College, Guntur during the period between August 2001 and August 2004 were taken into study. The specimens were processed routinely using 10 % formalin as fixative. Bits were taken from representative sites and sections, stained with hematoxylin and eosin, were studied. Special stains like PAS, Vangieson, Reticulin and Alcian blue were done in cases of doubt. Statistical analysis of data based on age of incidence, bilaterality, cell of origin and histopathology were done.

III. Results

A total number of 150 ovarian tumors received from 2001 to 2004 have been studied.
Of them 88 are benign tumors, 3 are borderline tumors and 59 are malignant tumors (Table 1).

Out of 150 ovarian tumors 122 were surface epithelial tumors, 9 were sex cord stromal tumors, 16 were germ cell tumors and 3 were metastatic tumors (Table 2).

Age incidence of various tumors varied between 11 to 80 years. The most common age group for surface epithelial tumors and sex cord stromal tumors was found to be 31-50 years. Germ cell tumors showed a peak incidence in 20-30 age groups with a gradual decline in 31-40 years age group and they were found to be uncommon after the age of 50 years. Metastatic tumors were reported in ages between 31 and 50 years(Table 3).

Out of 122 surface epithelial tumors 75 (61.5%) were benign 3 (2.5%) borderline and 44 (36%) were malignant. Out of 44 malignant surface epithelial tumors 9 cases show secondary deposit in omentum, and all are from serous carcinoma of the ovary.

Mucinous cystadenomas comprised 29.3% of all ovarian tumors (Figure1a). Endometrioid carcinoma and clear cell carcinoma were less frequent.

We reported a total of 9 sex cord stromal tumors of which Granulosa cell tumor accounted for the maximum number of cases (Figure 1b).

Of the total 16 germ cell tumors reported 9 were benign and 7 were malignant. Teratomas comprised of 6% of all ovarian tumors. Mixed malignant germ cell tumors comprised 1.3% of all ovarian tumors. One case of dermoid cyst with malignant transformation (Squamous cell carcinoma) was seen (Figure 2b). In another case both ovaries show benign cystic teratoma and in which one ovary in addition showing serous cystadeno fibroma. One case of strumal carcinoid was reported in a patient aged 50 years and was unilateral (Figure 2c).

Two cases showed malignant mixed germ cell tumors. One malignant mixed germ cell show combination of dysgerminoma and yolk sac tumor(Figure 2a) and the other tumor showed a combination of embryonal carcinoma and yolk sac tumor. We also reported 3 cases of Dysgerminoma (Figure 2d).

A peak incidence was seen in younger age group of 21-30 years which were uncommon after the age of 50 years.

The incidence of metastatic ovarian tumors was 5% of all malignant ovarian tumors (Figure 1c). Most of them were in the age group 30-45 years, and most of them were adenocarcinomatous deposits. An incidence of 5-10% was reported by various authors.

Bilateral ovarian tumors were reported in 26 cases constituting 17.3% of all cases. Serous tumors and endometrioid tumors showed a higher percentage of bilaterality (Table 4). The clinical data and bilaterally of ovarian tumors were not well documented. Available data shows that serous tumors are mostly bilateral and this is consistent with the present study.

The incidence of primary ovarian carcinoma against age has been shown in table 3. It is observed that there was a gradual rise of occurrence of tumors from 11-20 years with a peak in between 31-50 years age group; returning to low levels in later age groups.

In most of the ovarian tumors studied, the clinical data was not available to correlate and study the hormonally active tumors. Special stains like PAS, Alcian blue, and Vangeison were done for correlation.

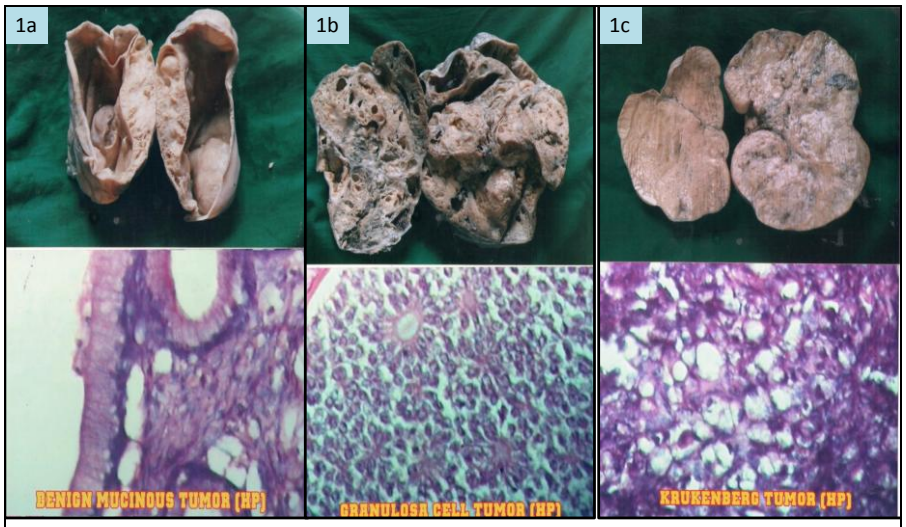

Figure 1 a: Benign mucinous tumor
1b: Granulosa cell tumor
1c: Krukenberg Tumor

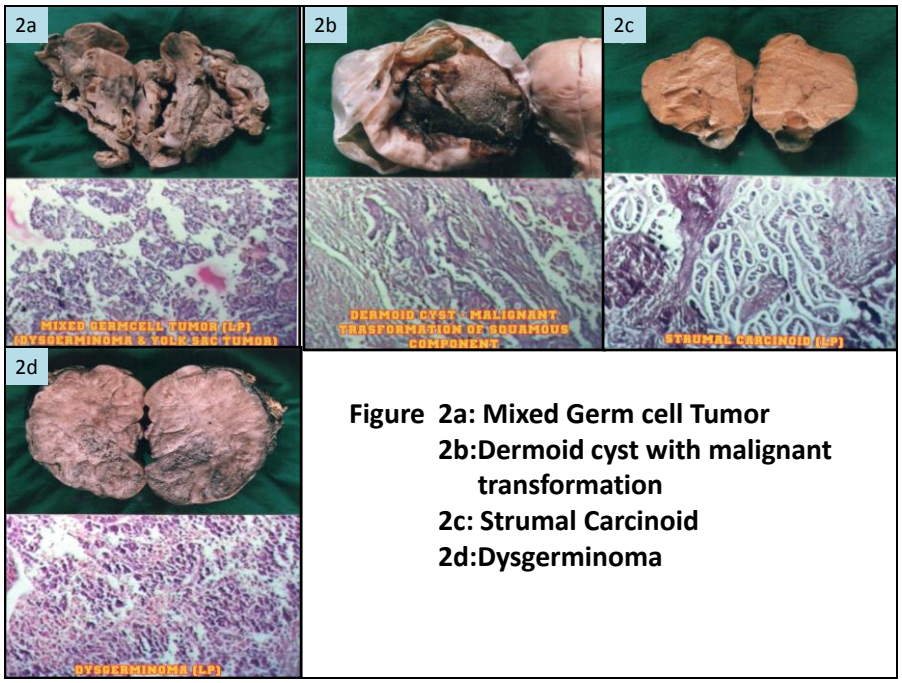

Figure 2a: Mixed Germ cell Tumor
2b:Dermoid cyst with malignant transformation
2c: Strumal Carcinoid
2d:Dysgerminoma

IV. Discussion

Ovary is the third most common site of primary malignancy in female genital tract and accounts for 6% of all cancers in females.

Though cervical cancer is 3 times more common than ovarian malignancy, more deaths are reported from ovarian than cervical carcinoma due to delay in diagnosis. Early diagnosis of ovarian cancer is thus very important.

Combination of cytodiagnosis, radiodiagnosis, biological and biochemical tests, tumor markers, histopathology examination and immunohistochemistry play an important role in diagnosis.

About 2/3 of ovarian tumors are seen in the reproductive age group and the commonest age group is between the ages of 20 and 65 years. Less than 2% are found in children. 80-85% of them are benign. The malignant tumors are more common in older women between 40 and 60 years.

Carcinoma of ovary may present as a solid or a cystic tumor, the latter being more common. The most common clinical presentation of ovarian tumors is abdominal mass, pain and abnormal vaginal bleeding if the

tumor is hormonally active with or without ascitis. One fourth of ovarian tumors which are of them benign are asymptomatic and detected only on pelvic examination or at operation.

Risk factors for ovarian carcinoma are identified as nulliparity and family history. Higher risk is noticed in unmarried women and married women with low parity. Gonadal dysgenesis in children is associated with a higher risk of ovarian cancer (germ cell tumors).

Ovarian tumors may be bewildering because of their remarkable diversity. It is necessary to recognize a spectrum of aggressiveness that is divided into benign, borderline and malignant. Benign tumors are lined by single layer of columnar epithelial cells, papillary projections supported by fibro-vascular core. Malignant tumors show anaplastic changes in the epithelial cells with loss of polarity of nuclei and epithelium of several layers thick. Border line tumors are identified by the absence of invasion in a highly proliferative neoplasm. Though their behavior is unpredictable, they have better prognosis than the malignant counterpart.

The incidence of surface epithelial tumors, sex cord stromal tumors and germ cell tumors in the present study is on parallel lines with the statistics reported in the world literature with a few exceptions. However, in our study we did not report any case of embryonal carcinoma. Incidence of endometrioid carcinoma in our study was much lower than those reported in other studies of world literature (Table 5).

Table 1: Incidence Of Benign, Borderline And Malignant Tumors

		No. of Cases	% among respective broad classification	% among all ovarian tumors
1.	Benign surface epithelial tumors	75	61.5%	50%
2.	Borderline surface epithelial tumors	3	2.5%	2%
3.	Malignant surface epithelial tumors	44	36%	29.3%
4.	Sex cord-stromal benign tumors	4	44.4%	2.7%
5.	Sexcord-stromal malignant tumors	5	55.6%	3.3%
6.	Benign germ cell tumors	9	56.25%	6%
7.	Malignant germ cell tumors	7	43.75%	4.7%
8.	Metastatic tumors	3		2%
	Total	150		100%

Table 2: Incidence And Percentage Of Ovarian Tumours Of All Types

I. Surface Epithelial tumors	**No. of Cases**	**Percentage**
a. Benign serous cystadenomas	26	17.3%
b. Serous cystadeno fibromas	4	2.7%
c. Serous borderline tumors	2	1.3%
d. Serous Carcinomas	36	24%
e. Mucinous cystadenomas	44	29.3%
f. Mucinous borderline tumors	1	0.7%
g. Mucinous adeno Carcinomas	2	1.3%
h. Endometrioid carcinomas	3	2%
i. Clear cell carcinomas	1	0.7%
j. Brenner tumors – benign	1	0.7%
k. Brenner tumors – malignant	1	0.7%
l. Undifferentiated carcinomas	1	0.7%
Total	**122**	**81.3%**
II. Sexcord-stromal tumors	**No. of Cases**	**Percentage**
a. Granulosa cell tumors	5	3.3%
b. Thecoma	2	1.3%
c. Fibroma	1	0.7%
d. Sertoli-leydig cell tumors of intermediate differentiation	1	0.7%
Total	**9**	**6%**
III. Germcell Tumors	**No. of Cases**	**Percentage**
a. Dysgerminomas	3	2%
b. Yolk Sac tumors	1	0.7%
c. Dermoid cyst-mature	8	5.3%
d. Dermoid cyst with malignant transformation	1	0.7%
e. Strumal carcinoid	1	0.7%
f. Mixed germcell tumors	2	1.3%
Total	**16**	**10.7%**
IV. Metastatic tumors	**No. of Cases**	**Percentage**
	3	2%
Total No. of all types of tumors	**150**	

Table 3: Age Incidence Of Benign And Malignant Ovarian Tumours

Type of Tumour	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Total
Surface Epithelial Benign Tumors	6	27	17	13	9	2	1	75
Surface epithelial borderline tumors	1	1	1	-	-	-	-	3
Surface epithelial malignant tumors		1	19	15	7	2	-	44
Sex cord stromal benign tumors	2	1	-	-	-	1	-	4
Sex cord malignant tumors		1	3	-	-	1	-	5
Germ cell Benign tumors	1	2	2	2	2	-	-	9
Germ Cell Malignant tumors	5	1	-	-	-	1	-	7
Secondary deposits	-	-	1	2	-	-	-	3
Total	**15**	**34**	**43**	**32**	**18**	**7**	**1**	**150**

Table 4: Bilaterality Of Ovarian Tumors And Their Incidence

Histologic Type	Benign	Malignant	Total	% of Respective tumors
1. Serous tumors	4	12	16	23.5% of all serous tumors.
2. Mucinous tumors	3	2	5	10.7% of all mucinous tumors.
3. Endometrioid tumors	-	1	1	33.3% of all endometrioid tumors.
4. Teratomas	1	-	1	10% of all teratomas
5. Secondary deposit	-	3	3	5.08% of all malignant tumors.
Total	**8**	**18**	**26**	

Table 5: Incidence Of Ovarian Tumours – Comparision By Various Authors

Histologic Type	Blaustein %	Gompel %	AFIP %	Fletcher %	Present Study %
Serous Cystadenoma	20	20	25	22	20
Serous border line tumors	15	15	5-10	15	1.3
Serous carcinoma	40	35	25	50	24
Mucinous cystadenoma	20	20	15	14	29.3
Mucinous border line tumors	6	Not available	Not available	1	0.7
Mucinous Carcinoma	6-10	5-15	6-10	1	1.33
Endometrioid carcinoma	20	20-30	15-25	3	2
Clear cell carcinoma	5-11	5	5	5-10	0.7
Brenner tumors	1.7	2	2.3	2	1.3
Undifferentiated tumors				5	0.7
Granulosa cell tumors	1-2	1-3	2	1-2	3.3
Thecoma	Not available	2.5	1	1	0.7
Fibroma	4	1.5	4	1-5	0.7
Sertoli – Leydig cell tumor	0.5	Not available	0.2	< 1%	0.7
Gynandro blastoma	Rare	Rare	Rare	Rare	Nil
Dysgerminoma	1-2	1-2	1	1-2	2
Yolk Sac Tumor	Uncommon	1	1.2	1	0.7
Embryonal Carcinoma	Uncommon	Rare	Rare	Rare	Nil
Chorio-Carcinoma	Rare	Rare	Rare	Rare	Nil
Teratoma-benign	10-25	15-20	20	25%	5.3%
Teratoma with malignant transformation				1-3	0.7
Strumal Carcinoid				1-3	0.7
Mixed Malignant Germ Cell tumor	Not available	5-10	Not available	5-20	1.3
Metastatic tumors	Not available	10	Not available	5-10	5% of all malignant ovarian tumors.

V. Conclusion

A total of 150 ovarian tumors were studied during the period from 2001 to 2004 in the department of pathology. Guntur Medical College, Guntur.

The highest incidence of ovarian tumors that occurred were surface epithelial tumors which consist of 122 tumors (81.3%) of them 75 tumors (50%) were benign 3 borderline tumors (2%) and 44 tumors (29.3%) were malignant. Nearly 1/3 of the tumors were malignant. Serous tumors were the commonest tumors (45.3%).

The commonest age group affects in surface epithelial tumors were 31-50 years.

Of all the benign tumors of the ovary mucinous cystadenoma was the commonest tumor accounting for 50% of all benign ovarian neoplasms.

The commonest malignant tumor was serous cystadenocarcinoma accounting for 58% of all malignant ovarian tumors.

The incidence of most of the ovarian tumors in the present study was in close agreement to that of various authors. But endometrioid carcinoma which is said to be very common (20-30%) in other series, recorded a low incidence of 2% in the present study. Serous borderline tumors which were said to be 5-15% in other series, recorded a low incidence of 1.3% in the present study.

Mucinous cystadenoma which is said to be 15-20% in other series, recorded a high incidence of 29.3% in the present study.

Some of the surface epithelial tumors whose incidence is less than 2% of all ovarian tumors are Brenner tumor, Clear cell carcinoma, undifferentiated carcinoma, Serous borderline tumors, Mucinous borderline tumors and Mucinous carcinoma.

Sex cord-stromal tumors consists of 9 (6%) of all ovarian tumors, out of them 4 were benign and 5 malignant. The commonest tumor in this category was granulosa cell tumor.

Most common age group occurance of sex cord-stromal tumor was in between 40 to 60 years of age. Uncommon sex cord-stromal tumors are Sertoli-Leydig cell tumor, Fibroma and Thecoma.

Germ cell tumors comprised 16 (10.7%) of all ovarian tumors; out of them 9 (6%) were benign and 7 (4.7%) were malignant. Most common germ cell tumors was benign cystic teratoma and the rest were malignant.

Germ cell tumors in contrast to the other groups occurred in children and young adolescents below 20 years of age. Teratomas which were said to be 15-25% in other series, recorded a low incidence of 5.3% in the present study.

Uncommon tumors of germ cells encountered were Yolk sac tumor, Malignant mixed germ cell tumor, Teratoma with malignant transformation.

Metastatic tumors comprised 5% of all malignant ovarian tumors and all of the tumors reported were bilateral.

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