Original Article

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Histomorphological Spectrum of Ovarian Tumors in A Tertiary Care Hospital

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ABSTRACT

Background: To study or analyse the histomorphological spectrum and distribution of benign and malignant ovarian neoplasms in women of different age groups

Methods: 633 cases of ovarian tumors were studied over a period of 6 years(from July 2011 to July 2017) at the Department of Pathology, SDMH. All the cases were subjected to histopathological examination and IHC as & when required.

Results: In total,633 ovarian tumor specimens were examined. Out of which ,468 cases (73.9%)were benign, 23 (3.6%)were boderline and 142(22.4%)were malignant. Most of the benign tumors occurred between 31 & 40 years of age while malignant lesions presented commonly between 41 & 50 years of age. Most common histological types were serous cystadenoma (24.18%) followed by mature cystic teratoma (22.90%).The commonest benign tumor was serous cystadenoma & the commonest malignant tumor was serous cystadenocarcinoma. Serous tumors showed bilateral involvement more commonly than bilateral mucinous tumors.

Conclusion: We noted that serous cystadenoma tumors are the commonest variety of ovarian tumors. Also the age of presentation of these malignant tumors was an earlier age as compared to others.

Keywords: *Ovarian Tumors, Histology, Surface Epithelial Tumors, Benign, Borderline, Malignant*

Introduction

Ovarian cancer accounts for about 3% of all cancers in women. [1]Ovarian malignancy is the second most common cancer of the female reproductive system and the leading cause of death from gynecologic malignancy.[2,3] The age adjusted incidence rates of ovarian cancer vary between 5.4 and 8 per 100,000 populations in different parts of the country.[4,5] Diversity in histological patterns of ovarian tumours is important in diagnosis, treatment as well as prognosis.[5] Indian Cancer Registry data project ovary as an important site of cancer in women, comprising up to 8.7% of cancers in different parts of the country.[3,6] Thus , in this study we highlight the histomorphological spectrum and clinical presentation of patients with ovarian tumors in a tertiary care hospital.

Materials and methods

This retrospective study included 633 cases of ovarian tumors studied over a period of 6 years. Detailed clinical information were recorded which included age and sex of the patients, signs & symptoms, FNAC finding of available cases, CBC, USG/CT findings and biochemical investigations like tumor markers CA125, AFP and Beta hCG.

Oophorectomy specimen, ovarian cystectomies, wedge sections as well as hysterectomy with unilateral or bilateral salphing oophorectomy specimens were included in this study. Formalin-fixed, paraffin-embedded tissue sections were stained with Hematoxylin and Eosin and other special stains as and when required. A protocol for SEE-FIM (Sectioning and Extensively examining the Fimbriated end of fallopian tube was followed to detect "early carcinoma". It entails amputation and longitudinal sectioning of the infundibulum and fimbrial segment (distal 2 cms). The isthmus and ampulla are cut transversely at 2- and 3 mm intervals. IHC stains were performed for further sub-typing whenever required (p53, AFP, PLAP, CK7, CK 20, Inhibin, EMA)

The patients were divided into groups based on WHO classification of ovarian tumors and we studied correlation of histopathological patterns with age, bilaterality, morphology and grading of the tumour

Results

Total 633 cases of ovarian tumours were studied during a 6-year period of 2011 to 2017.Out of which,468 cases (73.9%)were benign, 23 (3.6%) were borderline and 142(22.4%) were malignant as in Table1. The mean age was 32 years with the youngest patient as a case of mature cystic teratoma and oldest as a case of Mucinous cystadenoma.

Maximum number of cases were seen in the age group of 31-40 years, 185 cases (29.2%). The malignant neoplasms were seen more commonly in the age group of 41-60 years, 33 cases (23.2% of malignant neoplasms) (Table 3). The youngest patient was a 9 month year old girl and the oldest was 72 years old. In the present study, the tumours had an average size of 12.15 cm.(table 2) The largest tumor encountered in the study was mucinous cystadenoma measuring 29 × 22 × 14 cm

Of 633 tumours, 338 (53.3%) were cystic, 255 (40.2%) were mixed and 40 (6.3%) were solid. 312 Cystic tumours (49.2%) were benign. 144 of the 255 cases with mixed consistency were benign and 106 were malignant, whereas out of 40 solid tumours, 12 were benign and 26 malignant as in Table4. Unilateral occurrence was more common than bilateral.Most of the unilateral cases were of mature cystic teratoma. Among the bilateral tumors, serous tumors were the most common tumors.(Table2)

Histologically serous cystadenoma was the most common tumor accounting for 24.18% followed by mature cystic teratoma (22.9%), serous cystadenofibroma (17.71%) and mucinous cystadenoma(7.59%)

Table1: Frequency of different classes of ovarian tumors.

Histological type	Number	Percentage of total tumor	U/L	B/L
Surface epithelial tumours				
Benign				
Serous cystadenoma	153	24.18%	110	43
Serous cystadeno-fibroma	112	17.71%	71	41
Mucinous cystadenoma	48	7.59%	43	5
Benign brenner tumour	5	0.78%	5	-
Borderline				
Borderline serous cystadenoma	3	0.47%	1	2
Borderline mucinous cystadenoma	5	0.79%	3	2
Malignant				
Serous cystadenocarcinoma	45	7.10%	10	35
Mucinous cystadenocarcinoma	28	4.43%	11	17
Endometroid cystadenofibroma	1	0.15%	1	-
Transitional cell carcinoma	-	-	-	-
Clear cell adenocarcinoma	1	0.15%	1	-
Germ cell tumours				
Benign				
Mature cystic teratoma	145	22.90%	128	17
Monodermal teratoma	2	0.32%	2	-
Malignant				
Immature teratoma	20	3.15%	19	1
Yolk sac tumor	8	1.26%	8	-
Mixed germ cell tumor	25	3.96%	15	-
Dysgerminoma	6	0.95%	5	1
Sex cord stromal tumour				
Benign				
Fibroma	1	0.15%	1	-
fibrothecoma	2	0.32%	2	-
Borderline				
Granulosa cell tumour	15	2.37%	16	9
Sertoli cell tumour	-	-	-	-
Malignant				
Steroid cell tumors	-	-	-	-
Metastatic tumours (Adenocarcinoma and signet ring cell carcinoma)	3	0.47%	3	-
Undifferentiated or poorly differentiated tumors	5	0.80%	4	1
Total	**633**	**100%**	**429**	**204**

Table2. Distribution of ovarian tumors as per WHO Classification and laterality

Class of tumor	No.	% of all tumors	Benign	Borderline	Malignant
Germ cell tumor	196	30.96	147	-	59
Surface epithelial tumor	401	63.34	318	8	75
Sex cord-stromal tumor	28	4.43	3	15	-
Secondary (metastatic) tumor	3	0.47	-	-	3
Undifferentiated/Poorly differentiated tumors	5	0.78	-	-	5
Total	**633**	**100%**	**468**	**23**	**142**

Table 3.Distribution of ovarian neoplasms by age and type

Histopathological types 1 to 10		**Age in years**								**Total**
		11 to 20	**21 to 30**	**31 to 40**	**41 to 50**	**51 to 60**	**61 to 70**	**71 to 80**		
Benign Tumors	Serous cystadenoma	10	13	42	38	22	25	3	-	153
	Mucinous Cystadenoma	3	3	10	20	10	-	2	-	48
	Serous Cystadenofibroma	3	11	29	32	24	8	3	2	112
	Benign Brenner tumor	-	-	-	1	2	2	-	-	5
	Mature cystic teratoma	4	12	48	56	22	3	-	-	145
	Monodermal teratoma	-	-	1	1	-	-	-	-	2
	Fibroma	-	-	-	1	-	-	-	-	1
	Fibrothecoma	-	-	-	2	-	-	-	-	2
Broderline malignant	Mucinous cystadenoma	-	-	1	3	1	-	-	-	5
	Serous cystadenoma	-	-	1	2	-	-	-	-	3
	Granulosa cell tumor	1	2	1	3	4	2	1	1	15
	Sertoli cell tumor	-	-	-	-	-	-	-	-	-
Malignant Tumor	Serous cystadenocarcinoma	-	-	3	7	20	3	12	-	45
	Mucinous cystadenocarcinoma	-	3	2	9	6	5	3	-	28
	Endometrioid cystadenofibroma	-	-	-	1	-	-	-	-	1
	Clear cell adenocarcinoma	-	-	-	-	1	-	-	-	1
	Transitional cell carcinoma	-	-	-	-	-	-	-	-	-
	Immature teratoma	1	2	12	4	1	-	-	-	20
	Dysgerminoma	-	2	4	-	-	-	-	-	6
	Yolk sac tumor	3	4	1	-	-	-	-	-	8
	Mixed germ cell tumor	3	7	10	3	2	-	-	-	25
	Metastasis (Secondary)	-	-	-	2	1	-	-	-	3
	Undifferentiated or poorly differentiatied tumors	-	-	-	-	3	2	-	-	5
Total		**28**	**59**	**165**	**185**	**119**	**50**	**24**	**3**	**633**

Table 4: Consistency of ovarian tumors.

Leison	Solid + Cystic	Cystic	Solid	Total
Benign	144	312	12	468
Borderline	5	16	2	23
Malignant	116	-	26	142
Total	**265**	**328**	**40**	**633**

Table 5: Relationship between size of tumor and histological type.

Histopathological types		Mean Size (cm) ± SD <4	Size of tumor (cms)				Total
			5-9	10-19	>20		
Benign Tumors (8.93 ± 3.92 cm)	Serous cystadenoma	12.5 ± 3.9	12	84	46	11	**153**
	Mucinous Cystadenoma	15.9 ± 7.0	3	15	25	5	**48**
	Serous Cystadenofibroma	10.5 ± 4.2	9	43	59	1	**112**
	Benign Brenner tumor	3.5 ± 1.1	4	1	-	-	**5**
	Mature cystic teratoma	10.8 ± 3.8	19	103	22	1	**145**
	Monodermal teratoma	5.2 ± 1.4	-	2	-	-	**2**
	Fibroma	7.5	-	1	-	-	**1**
	Fibrothecoma	5.5 ± 1.2	-	2	-	-	**2**
Borderline Malignant (16.13 ± 5.53 cm)	Mucinous cystadenoma	18.2± 4.8	-	1	2	2	**5**
	Serous cystadenoma	14.0 ± 6.2	-	-	2	1	**3**
	Granulosa cell tumor	16.2 ± 5.6	1	5	9	-	**15**
	Sertoli cell tumor	-	-	-	-	-	**-**
Malignant Tumor (11.41 ± 4 cm)	Serous cystadenocarcinoma	16.0 ± 5.2	1	19	23	2	**45**
	Mucinous cystadenocarcinoma	19.5 ± 4.6	-	5	19	4	**28**
	Endometrioid Cystadenofibroma	9.5	-	1	-	-	**1**
	Clear cell adenocarcinoma	8.5	-	1	-	-	**1**
	Transitional cell carcinoma	-	-	-	-	-	**-**
	Immature teratoma	14.8 ± 3.2	1	4	13	2	**20**
	Dysgerminoma	13.0 ± 5.0	1	3	2	-	**6**
	Yolk sac tumor	13.4 ± 5.2	-	3	5	-	**8**
	Mixed germ cell tumor	10.2 ± 4.8	1	14	10	-	**25**
	Metastasis (Secondary)	5.5 ± 1.2	-	3	-	-	**3**
	Undifferentiated or poorly differentiated tumors	15.2 ± 2.8	1	1	3	-	**5**
Total		**12.15 ± 4.48**	**53**	**311**	**240**	**29**	**633**

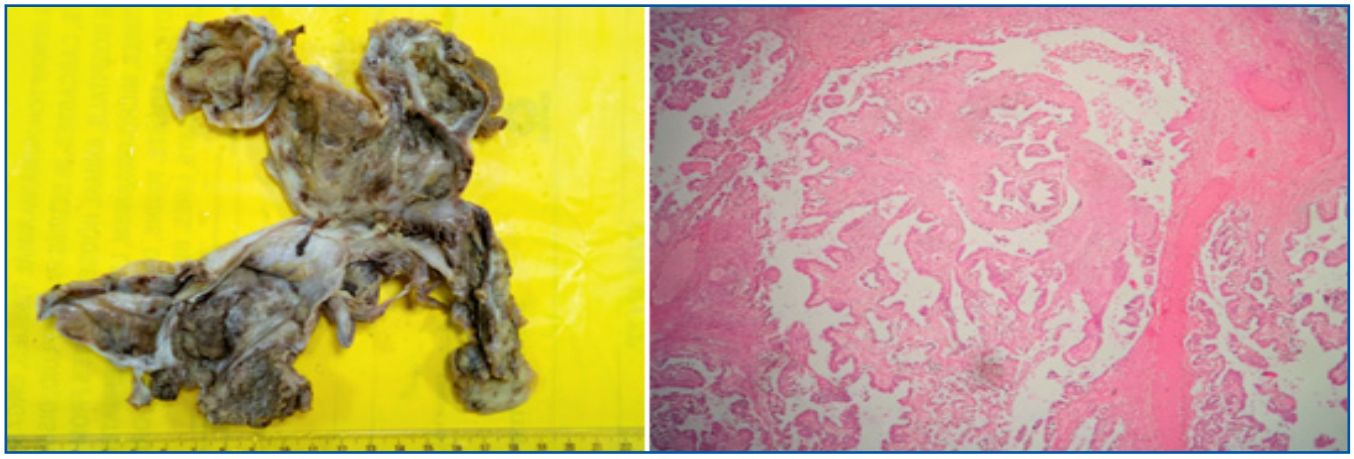

Fig. 1: Serous papillary cystadenocarcinoma-a) Grossly, cut surface shows a cystic tumor with few solid areas. Papillary excrescenses also seen. b) On histology, moderately differentiated tumor composed of crowed papillae lined by pleomorphic cells.

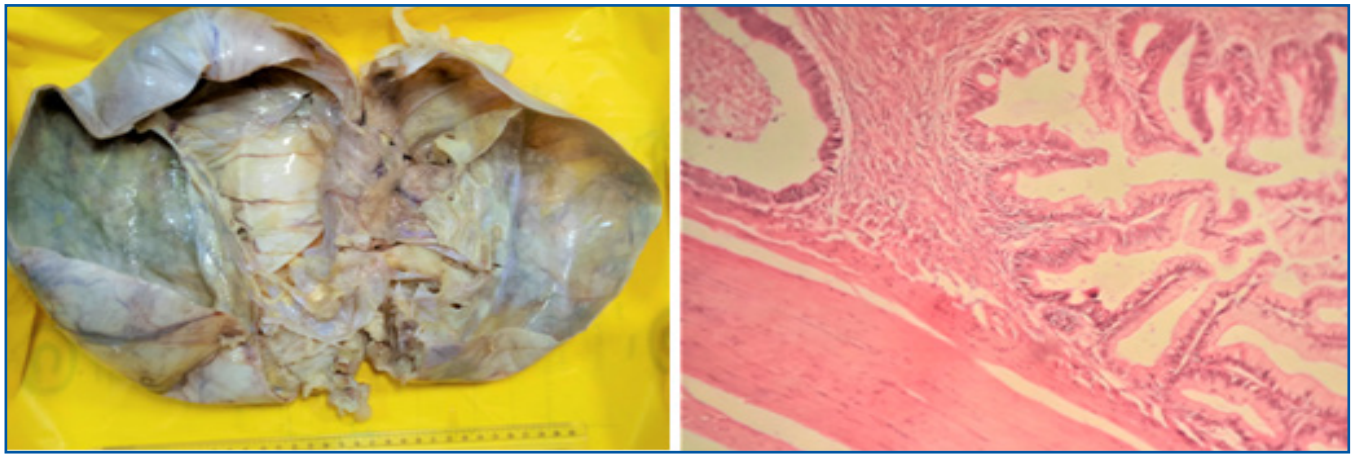

Fig. 2: Borderline mucinous tumor-a)Grossly, cut surface shows a multiloculated tumor with focal solid areas. b) Histologically, the photomicrograph shows a well encapsulated ovarian tumor. Stratified mucinous epithelium with nuclear enlargement and hyperchromasia is seen.

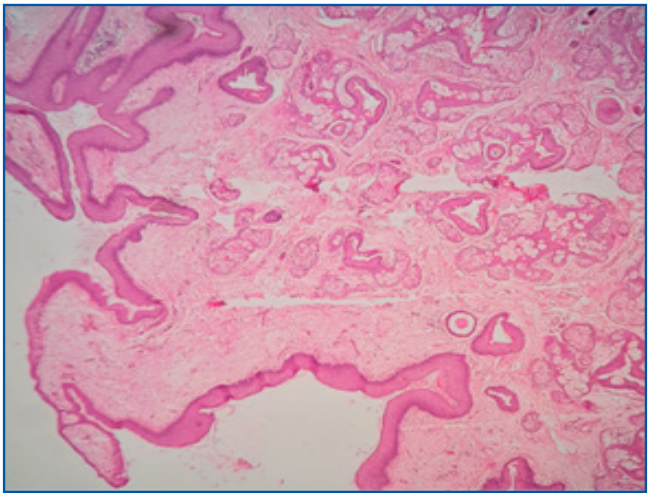

Fig. 3: Mature cystic teratoma-Histologically, a cyst lined by keratinized squamous epithelium with underlying cutaneous structures.

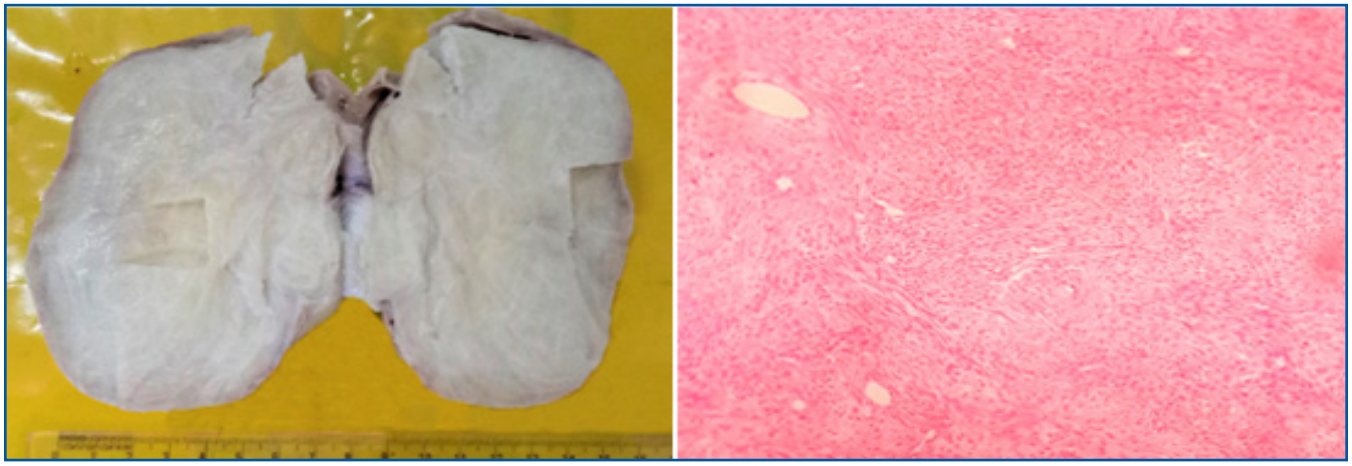

Fig. 4: Thecoma-a)Cut surface shows a well circumscribed tan yellow solid tumor mass replacing the ovary. b)Microscopically, the tumor is composed predominantly of plump spindle cells with pale cytoplasm.

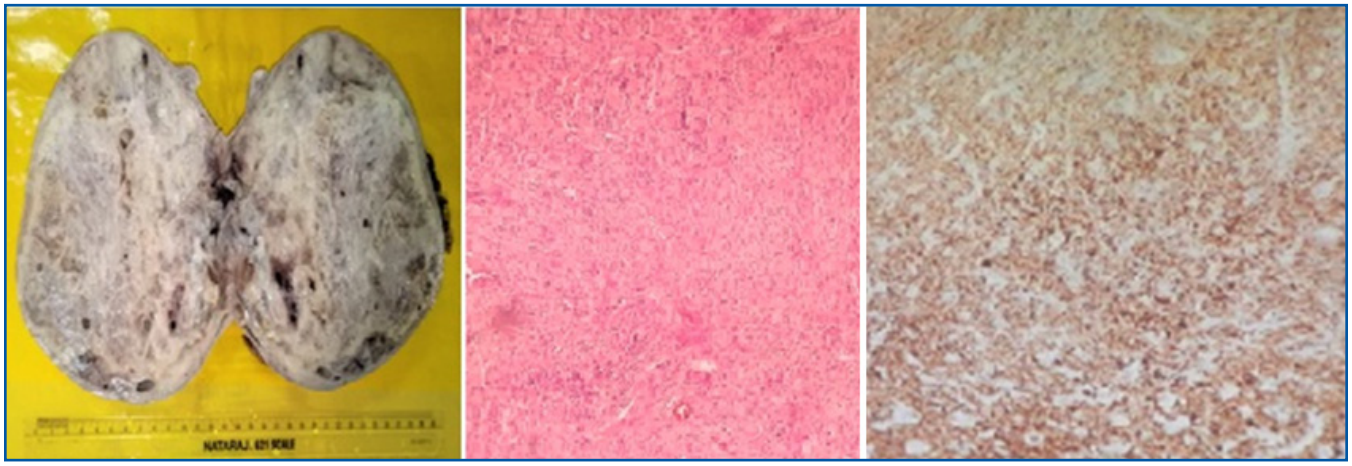

Fig. 5: Granulosa cell tumor- a) Grossly, cut surface shows variegated tan appearance. b) Microscopically, the tumor is composed of diffuse sheets of tumor cells with round to oval nuclei, nuclear grooves and inconspicuous nuclei. c) Tumor cells are positive for inhibin.

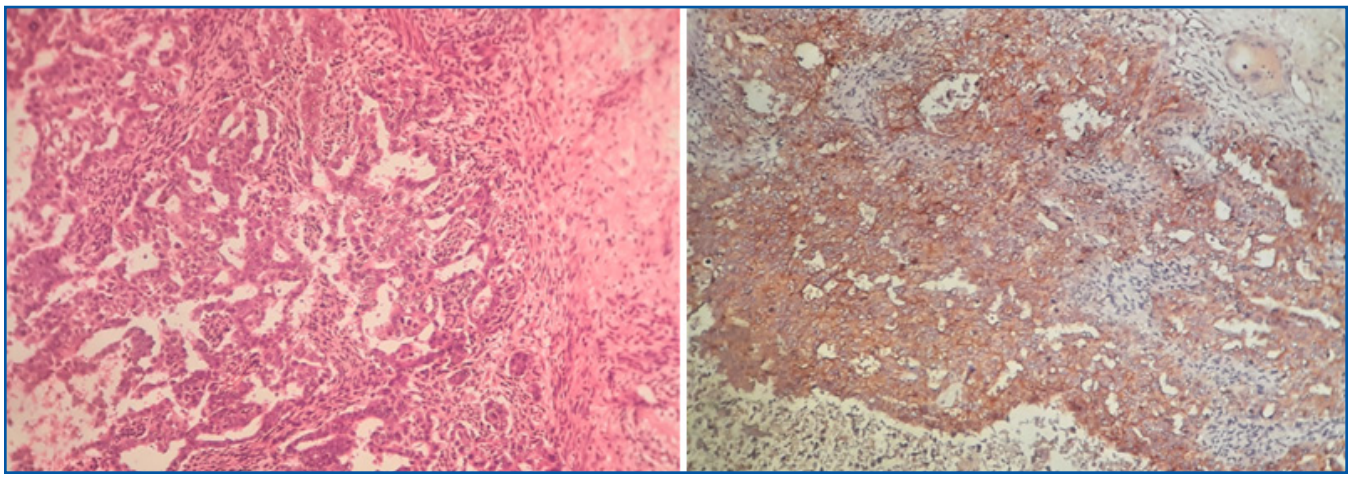

Fig. 6: Embryonal cell carcinoma. a) Histologically sheet like growth pattern of anaplastic malignant germ cells is seen. b) tumor cells are immunopositive for CD30.

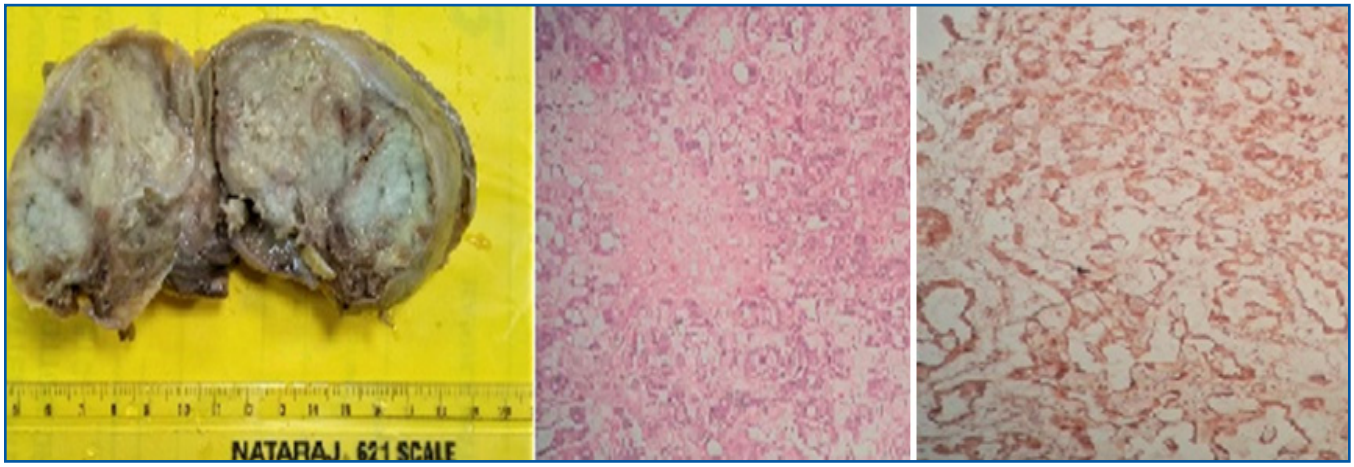

Fig. 6: Embryonal cell carcinoma. a) Histologically sheet like growth pattern of anaplastic malignant germ cells is seen. b) tumor cells are immunopositive for CD30.

Discussion

Ovarian tumors are regarded as one of the most complex tumour of women in terms of histiogenesis, clinical behaviour and malignant potentiality . It represents the sixth most common female cancer and the fourth leading cause of death due to cancers in women.[7,8] Histomorphological classification of ovarian tumours forms an integral part of the evaluation of the neoplasms.[8,9]

In the present study , a total 633 ovarian tumor specimens were examined. Out of which ,468 cases (73.9%)were benign, 23 (3.6%)were boderline and 142(22.4%)were malignant. Similar results were observed by Gupta N et al and Maheshwari V et al where benign tumours constituted 71.9% in each study, borderline tumours constituted 4.4% and 4.1%, and malignant tumours constituted 23.7% and 22.9% of tumors respectively.[8,10,11,12]

WHO classification of ovarian tumours is based on the tissue of origin of the tumours which have been found to arise from one of three ovarian components: (1) surface epithelium (2) the germ cells and (3) the stroma of the ovary. [8]Among histopathological patterns the commonest category of the ovarian tumours encountered in our series as surface epithelial tumours followed by germ cell tumours. This observation is consistent with other studies conducted by Ahmad Z et al , Pilli et al and Malik et al [5,13,14,15]

The most common benign tumour were serous cystadenoma (24.18%) followed by mature cystic teratoma (22.90%) , similar results reported by Yasmin et al[16] and Pachori et al .[17] Mucinous tumors were seen in 12% cases of all ovarian tumors, which is similar to the studies conducted by Pachori et al where mucinous tumors constituted 14.87%. [17] The commonest malignant tumor was serous cystadenocarcinoma. Similiarly , Sheikh S also observed that most of the malignant tumours, about 90% were also of the epithelial origin.[8]

When the tumor is confined to the ovaries, such as in borderline tumor, intraepithelial carcinoma and microinvasive carcinoma (with stromal invasive foci <10mm ^{2}),the prognosis is good as compared to carcinoma with invasive implant or carcinoma with peritoneal lesions like pseudomyxoma peritonei. [18]

Common problems encountered while diagnosing tumors of Epithelial origin especially serous and mucinous ovarian tumors is that tumor may include benign and borderline components in one area and malignant counterpart in other area. Therefore, extensive sampling including including upto 1 histological section per 1-2 cms of tumor diameter as well as sampling of suspicious lesions (solid area or mural nodule) is essential. Also, at times, it is difficult to differentiate primary tumor from metastatic carcinoma from appendix, large intestine, stomach, pancreas or cervix. The tumor morphology of these tumors resemble primary mucinous ovarian carcinoma.IHC staining such as CK7 and CK20 ,along with clinical information evaluation , is necessary to determine the origin of the cancer. [18,19]

One case (0.15%) of endometrioid carcinoma in this study, which was lower than the percentage of Ahmad Z et al [13] , Zaman et al [20] and pachori et al[17] studies 12.03% , 3.87% and 0.41% respectively. In this study, 2.37% of granulosa cell tumors were seen, which was comparable to the study conducted by Zaman et al [20] and pachori et al .[17] Fibroma were encountered in 0.15% of cases in this study as observed in the study which were similar to the results found by pachori et al.[1]

Most of the benign tumors occurred between 31 & 40 years of age while malignant lesions presented commonly between 41 & 50 years of age. Similiarly sheikh S [8] observed that with maximum number of cases in 21-30 years, 43.5%,. However, a study by Murthy NS [21] et al, involving data across various cities in India, revealed that the incidence of ovarian cancer increases from 35 years of age reaching its peak between 55-64 years. Though similar age related trends were followed by malignant tumours in our study but a fair percentage (21.9%) of malignant neoplasms especially surface epithelial adenocarcinomas was also seen in younger age groups (<30 years). This can be attributed to the possible effects of environmental and life style changes adopted by younger population. [21]

The mean size of ovarian tumors were 12.15 cm. The largest tumor encountered in the present study was a mucinous cystadenoma measuring 29 × 22 × 14 cm in size. Similar observation was made by Pachori et al [17] who reported a mucinous cystadenoma with a maximum diameter of 35 cm. Serous tumors showed bilateral involvement more commonly than bilateral mucinous tumors. Benign tumors (49.2%) were more often cystic in consistency in this study, which was comparable to the results of Kanthikar et al and Pachori et al.[17,22]All the malignant tumors had solid consistency which was also comparable to the study of Kanthikar et al and pachori et al.[17,22] Thus, the present study gives the most comprehensive picture of the current state of ovarian tumor incidence and histopathological pattern.

Conclusion

To conclude, histomorphologically, majority of the ovarian tumors are benign. Among the malignant tumors, tumors originating from surface epithelium are the commonest. Awareness among public and doctors is essential for early detection and treatment of ovarian lesions.

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