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Original Research Paper

Histopathology

STUDY OF HISTOPATHOLOGICAL SPECTRUM OF OVARIAN TUMORS

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KEYWORDS :

INTRODUCTION:

Ovaries are the paired organs of the female reproductive system, lying on either side of the uterus in the pelvis and are a common site for occurrence of neoplasms in women.[1]

Ovary is a complex organ consisting of variety of cells like totipotent sex cells and multipotent mesenchymal cells, which can give rise to wide morphological spectrum of neoplasms, involving tumors arising from epithelial tissue, connective tissue, germ cells and embryonal cells.[2]

Ovarian cancer is the 8th most commonly occurring cancer in womenworldwide.[3]In India, ovarian cancer is the third most common cancer among women next to cervical and breast cancer.[4]According to The World Ovarian Cancer Coalition Atlas 2018, the world's second highest incidence of ovarian cancer was seen in India.[5]

The risk factors for ovarian tumors are not much clear but the incidence is high in postmenopausal women, unmarried women or in married women with low parity, family history and heritable mutations.[6]

Depending on their morphology, various types of ovarian tumors are categorized into benign, borderline and malignant. Benign ovarian tumors are common in the reproductive age group, and in post-menopausal women about 30% of ovarian neoplasms are malignant.[7]

According to WHO classification (2020), ovarian tumors are classified into five main categories depending on the type of the ovarian tissue where the neoplasm develops, and this divides the tumors into: Epithelial tumors, Germ cell tumors, sex cord-stromal tumors, metastatic tumors and miscellaneous tumors.[8]

Ovarian tumors are often difficult to detect until they are advanced in stage or size. This is due to their location deep in the pelvic cavity, lack of early screening modalities, lack of specific signs and symptoms.[9]Due to its late detection ovarian cancer is associated with high mortality rate, thus earning itself the term 'silent killer'.[10]

Diagnosing ovarian tumors on the basis of clinical signs, symptoms and radiological findings may be confusing, but provides important clues to arrive at a differential diagnosis.[11] However, the definitive diagnosis of ovarian tumor is done by histopathological study.[12]

Identifying the histological pattern of ovarian tumors is necessary for staging of tumor which helps to decide further management and to achieve better prognosis.[13]

Thus present study was undertaken to study the distinctive histopathological features of ovarian tumors in all the age groups, to analyze the frequency of various histological subtypes and the pattern of age distribution.

AIMS AND OBJECTIVES:

1. To study the distinctive histopathological features of ovarian tumors.
2. To study the pattern of age distribution in ovarian tumors.

MATERIALS AND METHODS:

Retrospective study was carried out at Khaja Banda Nawaz University, Faculty of Medical Sciences, Gulbarga, Karnataka, India over a period of 2 years i.e. from January 2020 to December 2021 in the Department of Pathology.

A total of 107 ovarian mass were studied. Relevant data like age, clinical signs, symptoms and radiological findings were noted from the requisition forms. Slides, blocks and histopathology reports of all the cases were retrieved from the department and studied in detail.

The specimens were fixed in 10% formalin, gross features were noted. Multiple sections were given from the representative areas and tissue were processed. Paraffin embedded blocks were made. Tissue sections of 5mm were cut on microtome and slides were stained with routine Hematoxylin and Eosin (H&E). Special stains (like PAS, Alcian blue) and IHC were done whenever necessary. Histopathological features were studied in detail and tumors were categorized according to the WHO classification 2020.

Inclusion Criteria:

All neoplastic lesions of ovary received during the study period were included.

Exclusion Criteria:

Non-neoplastic lesions and tumor-like conditions of ovary received during the study period were excluded.

RESULTS:

A total of 107 cases of ovarian tumors were studied at the Department of Pathology, Khaja Banda Nawaz University, Faculty of Medical Sciences, Gulbarga from January 2020 to December 2021.

Age Distribution:

Majority of the ovarian tumors were seen in the age group of 21-40 years, followed by 41-60 years age group. The youngest patient was 14 years old female with benign serous cystadenoma, and the oldest patient was 75 years old female with Adult Granulosa cell tumor.

Benign and borderline lesions were more common in the age group of 21-40 years, whereas malignant lesions were commonly found in the age group of 41-60 years. ***(Table - 1)***

Clinical Presentation:

The most common presenting symptom was abdominal pain in 55cases (51.4%), followed by mass in lower abdomen in 24cases (22.4%) and menorrhagia in 20cases (18.7%). These symptoms were seen presenting singly and also in combination.

Remaining 8 cases were found to be asymptomatic which were detected during ultrasonography done for other purposes.

Table 1: Age distribution

Age range	Benign lesions	Borderline lesions	Malignant lesions
≤ 20	6 (5.6%)	0	2 (1.86%)
21-40	57 (53.3%)	3 (2.8%)	2 (1.86%)
41-60	19 (17.8%)	1 (0.93%)	9 (8.42%)
≥61	6 (5.6%)	0	2 (1.86%)
Total	88 (82.3%)	4 (3.7%)	15 (14%)

Gross Features:

Most of the cases in this study were unilateral i.e. 96cases (89.7%) and 11cases (10.3%) were bilateral.

Majority of the tumors were cystic in nature i.e. 73cases (68.2%), followed by those with solid to cystic consistency 22cases (20.5%) and 12cases (11.3%) were solid in consistency.

Most of the benign tumors were cystic i.e. 69cases (78.4%), 13 cases (14.8%) were of solid to cystic consistency and 6cases (6.8%) had solid consistency. All the 4 borderline tumors were cystic in consistency, among which 2 showed papillary excrescences on the cut section.

Majority of the malignant tumors were of solid to cystic consistency i.e. 9cases (60%) and 6cases (40%) were solid in consistency. ***(Table - 2)***

Table 2: Consistency Of Tumors On Gross Examination

Consistency	Benign	Borderline	Malignant	Total
Cystic	69	4	0	73
Solid	6	0	6	12
Solid to cystic	13	0	9	22

Microscopy:

Distribution Of Ovarian Tumors:

Out of 107 cases, 88(82.3%) were benign, 4(3.7%) were borderline and 15(14%) were malignant. ***(Table 1)***

Distribution Based On Origin Of Tumor:

Surface epithelial tumors constituted majority of the ovarian tumors with 77cases(71.97%), followed by Germ cell tumors which constituted of 19cases(17.76%), Sex cord-stromal tumors 9cases(8.41%), miscellaneous tumor 1case(0.93%) and Metastatic tumor 1case(0.93%).***(Chart 1)***

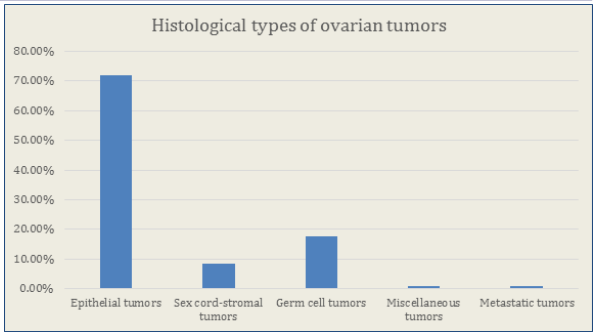

Chart 1: Histological types of ovarian tumors

Out of 77 cases of surface epithelial tumors, serous tumors were the most common comprising of 44 cases (57.2%), mucinous tumors were 27(35%), seromucinous tumors were 3(3.9%), endometrioid tumor 1 (1.3%), transitional cell tumor 1(1.3%) and mixed epithelial tumor 1 (1.3%).

Out of 9 Sex cord-stromal tumors, 5cases (55.6%) were benign and 4cases (44.4%) were malignant. We also reported one rare case of Fibrosarcoma.

Out of 19 Germ cell tumors, 16cases (84.2%) were benign and 3cases (15.8%) were malignant. Mature teratoma was the most common benign germ cell tumor and Dysgerminoma was the common malignant germ cell tumor.

We also reported one rare case of Small cell carcinoma and one metastatic tumor from Colorectal Adenocarcinoma.

The most common benign tumor was Serous cystadenoma comprising of 40cases (37.4%), followed by Mucinous cystadenoma 21cases (19.6%) and Mature cystic Teratoma 15cases (14%). Mucinous cystadenocarcinoma was the most common malignant tumor comprising of 4cases (3.73%), followed by Granulosa cell tumor 3cases (2.8%) (***Table - 3***)

DISCUSSION:

Ovarian tumors are one of the major health problems and their diagnosis is a challenge to the gynecologists, as symptoms are vague and non-specific in the early disease. By the time they are diagnosed, most of the tumors will be in advanced stage of the disease.[14]

The observations and analysis of this study provides the knowledge about the various histopathological patterns of ovarian tumors and their age-specific characteristics, which can help in early treatment and better prognosis.

The current study presents data on 107 cases of ovarian tumors, out of which maximum numbers of patients were from age group of 21 to 40 years (53.3%). Similar findings were seen in studies done by Neha Garg *Et al*[15], Jha and Karki[16] and Muni Bhavani Et al[17]. Benign tumors were more commonly reported in the age group of 21-40 years and malignant tumors in more than 40 years of age group. These findings were similar to the findings of studies done by Jha and Karki[16] and Pachori G Et al[18], but were in contrast with study done by Ramachandran *et al*[19], where maximum number of malignant tumors were seen in the age group of 31-40 years.

In present study, the most common presenting symptom was pain in abdomen (51.4%), followed by mass in lower abdomen (22.4%) and menorrhagia (18.7%). These findings were similar to the findings of studies done by Manzoor A S*et al*[14] and Chandekar S A *et al*[20], where most common presenting symptom was pain in abdomen. These findings were in contrast to the findings of study done by Amod S *et al*[21], where menstrual complaints were most common clinical presentation.

In the present study majority of cases were unilateral (89.7%) and few were bilateral (10.3%), which correlates well with studies done by Muni B *et al* and Swarnalatha P *et al*[22].

Majority of the tumors were grossly cystic (68.2%), followed by those with solid to cystic consistency (20.5%) and few were solid in consistency (11.3%). These findings were concordant with the findings of Vaddadi M *et al*[23], Deepesh K A[8]. But findings of our study were not in accordance with the findings of the study done by Swarnalatha P *et al*[22] where majority of the ovarian tumors were solid & cystic (mixed) in consistency, followed by purely solid and purely cystic in consistency.

Most of the benign tumors were cystic (78.4%), followed by solid to cystic consistency (14.8%) and few had solid consistency (6.8%). All the borderline tumors in this study were cystic. Majority of the malignant tumors were of solid to cystic consistency (60%) and few were solid (40%). These findings were similar to the findings of Sivakumar*et al*.[24]

Majority of the tumors were benign (82.3%), followed by malignant tumors (14%) and rest were borderline (3.7%). These findings were concordant with the findings of most of the studies.[1,2,7,11,13,14] but were opposing the findings of study done by Swarnalatha P *et al*[22] where majority of the ovarian tumors were malignant, followed by benign and borderline.

All the Ovarian tumors were classified according to WHO classification. Among the different histopathological patterns, Surface epithelial tumors were the most common (71.97%), followed by Germ cell tumors (17.76%) and Sex cord stromal (8.41%) tumors. Similar observations were made by Amita S P *et al*[1], Deepesh K A *Et al*[8], Gupta N *et al*[13] and Amod S *et al*[21].

Epithelial Tumors:

Out of 77 epithelial tumors, in this study serous tumors were most common (57.2%), followed by mucinous tumors (35%), correlating well with the study done by Amita S Patel *et al*.[1]

Endometrioid tumor was diagnosed in a 71 years old female. Ovarian malignancy was suspected clinically and radiologically. Grossly, ovary was measuring 5x5x3cm, Cut section showed both solid and cystic areas. Microscopically, sections showed benign endometrial glands, fibrous tissue and a cyst lined by benign endometrioid epithelium. It was reported as Endometrioid Cystadenofibroma. ***(Fig 1)***

Germ Cell Tumors:

In the present study, out of 19 Germ Cell Tumors, majority were benign (84.21%) and include Mature cystic teratoma ***(Fig 2)*** and Struma ovarii. These results were closer to the findings of Verma& Bhatia [25] with 83.5% of benign germ cell tumors. Malignant tumours included Dysgerminoma (10.53%)and Yolk sac tumor (5.26%) ***(Fig 3).***

Sex Cord - Stromal Tumors:

Out of 9 sex cord stromal tumors, 5(55.6%) were benign and 4(44.4%) were malignant. Similar results were seen in the study done by Sonia M *et al*[2]. Among 4 malignant sex cord stromal tumors, 3 were granulosa cell tumor and 1 fibrosarcoma ***(Fig 4).***

Juvenile Granulosa cell tumor was reported in a 22 years female. Grossly, ovary was measuring 7x4x2cm, cut section showed solid and cystic areas, drained serous fluid. Microscopically, sections showed tumor cells arranged in solid sheets, papillary pattern and insular pattern, having intranuclear grooves, prominent nucleoli, few cells showed coffee-bean appearance, Call-Exner bodies were seen and mitotic figures were seen focally. ***(Fig 5)***

Miscellaneous Tumors:

One case of Small cell carcinoma was reported in a 18 year old female. Grossly, ovary was measuring 11x6x3cm, nodular on outer surface, cut section was solid with hemorrhage and necrosis. Microscopically, sections showed small, round tumor cells arranged in sheets, with small hyperchromatic nuclei, scant cytoplasm. Necrosis and few mitotic figures were also seen. ***(Fig 6)***

Metastatic Tumors:

One case of metastasis to Left ovary was reported in a 60 years old female. Ovary was solid and measured 5x4x3cm, cut section showed necrotic material. Microscopically, sections showed glands lined by pleomorphic cells having hyperchromatic, pleomorphic nuclei, normal ovarian tissue was also seen. It was diagnosed as Micropapillary Colorectal Adenocarcinoma with metastasis to para-aortic lymph nodes and left ovary.

CONCLUSION:

This study represented a wide histological spectrum and all the ovarian tumors were classified according to WHO classification. Surface epithelial tumors were found to be the commonest of all ovarian tumors followed by germ cell tumors.

Various parameters like age, clinical signs, symptoms, laterality, size and consistency were studied, and were found to be interrelated. The present study has shown occurrence of primary ovarian malignancies in both younger and older age groups, hence the possibility of ovarian malignancy in a young female should not be neglected. Thus, correlation of clinical, radiological and gross findings can give important clues for the diagnosis of ovarian tumors and can avoid the delay in the diagnosis of malignant ovarian tumors which are usually diagnosed at an advanced stage.

But for the confirmation of ovarian tumors and for the knowledge of their histological subtypes, which is important for further management and good prognosis of the disease, histopathological study is necessary. Therefore, histopathological examination is the gold standard method for the accurate diagnosis and proper management of ovarian tumors.

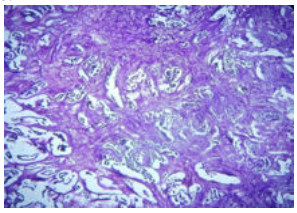

Fig 1: Microscopic image of endometrioid cystadenofibroma showing multiple cysts lined by benign endometrioid epithelium few forming glands with fibrous stroma. H&EX40

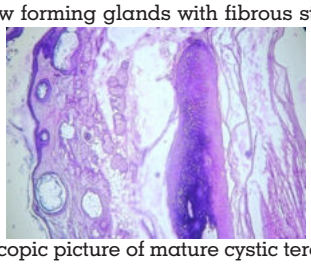

Fig 2: Microscopic picture of mature cystic teratoma showing skin with adnexal structures, cartilage, fat. H&EX10

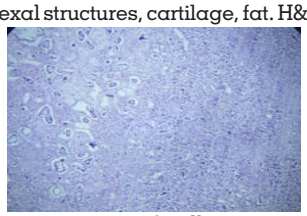

Fig 3: Microscopic image of yolk sac tumor showing cells

arranged in endodermal sinus pattern and microcystic pattern. H&EX10

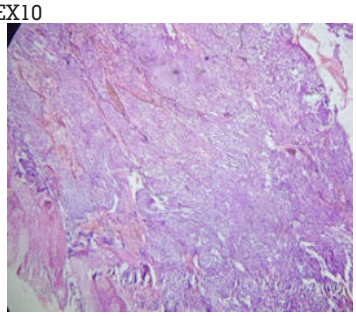

Fig 4: Microscopic image of fibrosarcoma showing spindle cells arranged in interlacing fascicles with nuclear atypia. H&EX10

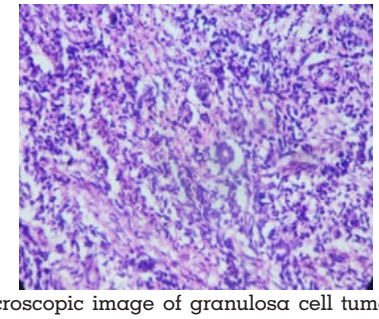

Fig 5: Microscopic image of granulosa cell tumor showing tumor cells in various patterns. Call-Exner bodies are seen. H&EX40

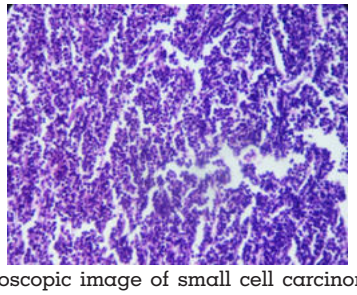

Fig 6: Microscopic image of small cell carcinoma showing tumor cells arranged in sheets. Cells are small, round, with hyperchromatic nuclei and scant cytoplasm. Mitotic figures are seen. H&EX40

Table 3: Distribution according to WHO classification 2020.

Who classification 2020	Nature of tumor	Types	No. of cases	%
Epithelial tumors	Serous	Benign	40	37.39
		Borderline	2	1.87
		Malignant	2	1.87
	Mucinous	Benign	21	19.6
		Borderline	2	1.87
		Malignant	4	3.74
	Endometrioid	Cystadeno - fibroma	1	0.94
	seromucinous	Benign	3	2.80
	Transitional cell tumor	Benign Brenner tumor	1	0.94
	Mixed epithelial tumor	Mucinous cystadenoma with Benign Brenner tumor	1	0.94
Sex cord - stromal tumors	Pure stromal tumors	Fibroma	3	2.80
		Thecoma-Fibroma	2	1.87
		Fibrosarcoma	1	0.94
	Pure Sex-cord tumors	Granulosa cell tumor	3	2.80
Germ cell tumors	Mature teratoma		15	14.0
	Monodermal teratoma-Struma ovarii, NOS		1	0.94
	Dysgerminoma		2	1.87
	Yolk sac tumor		1	0.94
Miscellaneous tumors	Small cell carcinoma of ovary1		1	0.94
Metastatic tumors	Colorectal Micropapillary Adenocarcinoma1		1	0.94
Total			107	100

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