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Study of histomorphological spectrum of ovarian tumours

Dr. Neha Garg, Dr. AS Anand, Dr. Chaya Annigeri
Department of Pathology, Navodaya Medical College, Raichur, Karnataka, India

Abstract
Background: Ovarian tumours are a heterogeneous neoplasms with a varied clinical, morphological and histological features.
Objectives: To study the frequency, age distribution and the diverse histomorphological spectrum of ovarian tumours.
Materials and Methods: This retrospective and prospective study of 3 years comprised of 85 ovarian tumours diagnosed in the Department of Pathology, Navodaya Medical College, Raichur. After thorough gross examination, representative bits were routinely processed and stained with H & E. Tumours were classified as per WHO classification. Special stains were done wherever required.
Results: Out of 85 cases studied, majority were benign tumours (81.2%), followed by malignant (17.6%) and borderline tumour (1.2%). Age ranged from 11-70 years. Epithelial tumours were most common (70.6%), followed by germ cell tumours (18.8%), sex cord stromal tumours (8.2%) and metastatic ovarian tumours (2.4%). Serous cystadenoma was the commonest benign tumour and serous cyst adenocarcinoma was the commonest malignant ovarian tumour.
Conclusion: The prognosis and varying therapeutic strategies of ovarian tumours necessitate an accurate pathological evaluation. Although newer techniques like IHC and molecular analysis have made the diagnosis easier and more precise, in the institutes with provision of limited resources, histopathological study is still the gold standard in diagnosing most of these tumours.

Keywords: ovarian tumour, epithelial tumour, germ cell tumour

1. Introduction

Ovarian tumours include complex, wide spectrum of neoplasms involving a variety of histological patterns ranging from epithelial tissues, connective tissues, specialized hormone secreting germinal and embryonal cells [1]. The earliest report of the ovarian neoplasms have been reported by shushruta in his book 'Shushruta and Ayurveda' [2].

Ovarian tumour accounts for 3% of total cancer in females and is the 5th most common form of cancer related death in females. The poor survival is due to the fact that they do not clinically manifest early and approximately 60-70% of the neoplasms present as either stage III or stage IV [1, 3, 4]. Benign ovarian cysts are the commonest constituting about 80% of ovarian tumours and mostly occur in young women between the ages of 20-40 years. Borderline tumours occur at slightly older ages whereas the malignant tumours are common in older women between the ages of 40-65 years.[1, 4]Metastatic tumours subsequently involve the ovaries and mimic primary ovarian neoplasia. Approximately 7% of lesions presenting clinically as primary ovarian tumours are of metastatic origin [5, 6].

Natural history and response to treatment vary considerably from one group of tumours to others. As there are no screening tests for ovarian tumours and these tumours cannot be confidently distinguished from one another on the basis of their clinical, radiological or gross characteristics, it is important to determine the histological pattern of ovarian tumour to achieve the optimum treatment response as prognosis depends on the degree of differentiation [3, 7].

Thus present study was undertaken to analyse the frequency of various histological subtypes, age distribution pattern and the diverse histomorphological spectrum of ovarian tumours.

2. Material and Methods

This retrospective and prospective study was conducted for a period of 3 years (September 2013- August 2016) at the Navodaya Medical College, Raichur. The prospective study included all ovarian specimens that were received in the department of pathology, Navodaya Medical College, Raichur. For the retrospective study, the cases reported during September 2013-August 2014 were taken from the records of the department and blocks were retrieved and relevant clinical history was noted from the requisition form.

2.1 Methods

Specimens sent in 10% formalin were routinely processed with paraffin embedding after adequate fixation. Paraffin sections and slides from fresh blocks and the retrieved blocks were stained with H & E. Special stains like PAS and Reticulin were done using standard procedures whenever required. The slides were then reviewed microscopically in detail and tumours were classified according to the WHO classification of ovarian tumours.

Inclusion criteria

All histologically proven both primary and secondary ovarian tumours.

Exclusion criteria

Non- neoplastic ovarian lesions of prospective and

retrospective study period.

3. Results

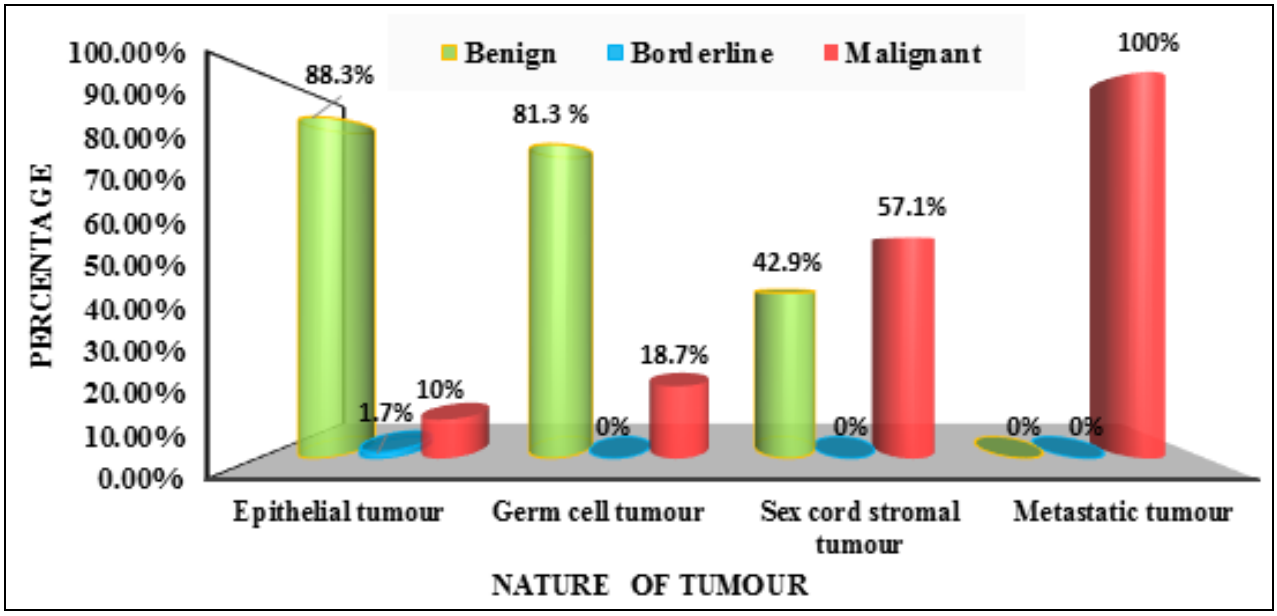
A total number of 85 cases were studied.

Distribution based on nature and cell of origin

Among these majority were primary ovarian tumours (83; 97.6%), while two were metastatic ovarian tumours (2; 2.4%). Of them 69 cases were benign (81.2%), 15 cases were malignant (17.6%) and rest 1 case (1.2%) was borderline. Epithelial tumours (ET) were the most common histological type (60; 70.6%), followed by Germ cell tumours (GCT) (16; 18.8%) and Sex cord stromal tumours (SST) (7; 8.2%) (Table 1).

Table 1: frequency of histological types of ovarian tumours based on cell of origin.

Histological Types	Frequency	Percentage (%)
Epithelial Tumours	60	70.6
Germ Cell Tumours	16	18.8
Sex Cord Stromal Tumours	7	8.2
Metastatic Tumours	2	2.4
Total	85	100.0



Graph 1: Distribution of benign, borderline and malignant tumours among the histological types

Age Distribution

Majority of the tumours occurred in the reproductive age group (35; 41.2%) followed by 41-50 years of age group (19; 22.3%).Youngest patient was 11 years of age and older patient was about 70 years. Epithelial tumours and Sex cord stromal tumours had its peak between 31 to 40 years, whereas Germ cell tumours showed a peak in 21 to 30 years. Metastatic tumours showed an equal age distribution between 41-50 years and 51-60 years of age group.

Gross Features

Most of the cases in this study were unilateral (81; 95.3%) and few were bilateral (4; 4.7%). Out of the total 60 Epithelial tumours, 50 were cystic in nature (83.3%), followed by those with cystic to solid in consistency (9; 15%) and solid (1; 1.7%), whereas most of Germ cell tumours were cystic in nature (12; 75%), followed by solid in consistency (3; 18.8%). Majority of Sex cord stromal tumours (4; 57.1%) and all of the metastatic tumours were partly solid to cystic in consistency.

Microscopy

The most common benign tumour was Serous cystadenoma (32; 37.64%), followed by Mucinous cystadenoma (13; 15.29%) and Mature cystic teratoma (12; 14.12%). Serous cyst adenocarcinoma was the most common malignant tumour (5; 5.88%), followed by Adult granulosa cell tumour (4; 4.7%). Borderline mucinous tumour was the only borderline tumour. There were 2 cases of metastatic ovarian tumours where, one was Krukenberg tumour and another was Extra Ovarian Primary Peritoneal carcinoma (Table 2).

Table 2: Histomorphological spectrum of ovarian tumours as per who classification.

WHO Classification (2014)	No. of Cases	Percentage
I) Epithelial Tumours		
A. Serous tumours		
1) Serous cystadenoma	32	37.64%
2) Serous cyst adenofibroma	4	4.71%
3) Serous cyst adenocarcinoma	5	5.88%

B. Mucinous tumours		
1) Mucinous cystadenoma	13	15.29%
2) Borderline mucinous tumour	1	1.17%
C. Endometrioid tumours		
Endometrioid carcinoma	1	1.17%
D. Seromucinous tumours		
Seromucinous cystadenoma	4	4.71%
Ii) Sex Cord Stromal Tumours		
1) Adult Granulosa cell tumour	4	4.71%
2) Fibroma	2	2.35%
3) Steroid cell tumour	1	1.17%
Iii) Germ Cell Tumours		
1) Benign cystic teratoma	12	14.12%
2) Struma ovarii	1	1.17%
3) Dysgerminoma	2	2.35%
4) Embryonal carcinoma	1	1.17%
V)Secondary / Metastatic Tumours		
1) Krukenberg tumour	1	1.17%
2) Extra ovarian primary peritoneal carcinoma	1	1.17%
Total	85	100%

4. Discussion

Ovarian tumours are one of the major health problems and their diagnosis can be difficult due to variety of pathologic conditions affecting the ovaries. Thus knowledge of morphology and age-specific characteristics can help refine the diagnosis [8, 9].

In the present study of 85 ovarian tumours, Primary ovarian neoplasms (97.6%) were the most common tumours of all ovarian tumours. Similar observations were made by Bhagyalakshmi A *Et al.* [10] (98.5%) and Tejeswini *Et al.* [3] (98.9%). Most of the tumours belonged to ET category (70.6%) which was comparable to the results seen by Swati *Et al.* [11] (69.17%), Krishna M & Maurya G [12] (77.7%) and Badge S *Et al.* [13] (77%). GCT and SST accounted for 18.8% and 8.2% respectively in our study compared to 42.2% and 3.1% reported in the literature [14]. (Table 3)

Table 3: Comparative analysis of frequency of ovarian neoplasms based on cell of origin.

Study	Epithelial Tumours (ET) (%)	Germ Cell Tumours (GCT) (%)	Sex Cord Stromal Tumours (SST) (%)	Metastatic Tumours (%)
Jha R & Karki S(2008) [14]	52.2	42.2	3.1	2.4
Badge S *Et al.*(2013) [13]	77	16	6	1
Krishna M & Maurya G (2015) [12]	77.7	15.5	6.1	2
Swati *Et al.*(2016) [11]	69.17	25.83	4.17	0.83
Present study	70.6	18.8	8.2	2.4

In the present study, majority of the tumours were benign (81.2%) followed by malignant tumours (17.6%) and rest was borderline (1.2%). Findings of the present study correlated well with the studies of various authors as shown in table 4.

However, in our study the frequency of malignant tumours (17.6%) was little less than the study of Gupta *Et al.* [15] (40%). This is probably because the study was undertaken in an institutional hospital and malignant tumours when diagnosed before surgery get referred to speciality oncology centres.

Table 4: Comparative analysis of cases based on nature of tumours.

Study	Benign (%)	Borderline (%)	Malignant (%)
Couto F *Et al.* (1993) [15]	80.76	2.33	16.91
Gupta *Et al.* (1986) [27]	59.4	0.6	40.0
Kuladeepa A VK *Et al.* (2011) [17]	82.35	3.68	13.97
Swati *Et al.* (2016)[11]	80.83	1.67	17.5
Present study	81.2	1.2	17.6

In the present study, the patient's age ranged from 11 years to 70 years and this was supported by the study done by GG Swamy *Et al.* [16] where the youngest patient was 12 years old and the oldest was 70 years old. The majority of ovarian tumours (58.8%) were seen in the age group of 21-40 years, which was consistent with the study done by Kuladeepa A VK *Et al.* [17] (58.9%) and Pilli GS *Et al.* [18] (58.3%) (Table 5).

Table 5: Comparative analysis of age distribution of ovarian tumours.

Age in years	Pilli G S *Et al.* (2002) [18] (%)	Jha R & Karki S (2008) (%) [14]	Kuladeepa A VK *Et al.* (2011) [17] (%)	Present study %
Upto-20	7.43	6.8	3.57	7.1
21-30	30.11	20.5	22.32	17.6
31-40	28.25	26.7	36.61	41.2
41-50	15.98	21.1	25	22.3
51-60	13.38	14.3	10.71	10.6
61-70	4.8	10.6	1.79	1.2

In our study, majority of the tumours were unilateral (95.3%) and least were bilateral (4.7%) which were consistent with the findings of Tejeswini V *Et al.* [3], Umesh J [8] and Prabhakar and Maingi [19]. In the present study, majority of the tumours were cystic (73%), followed by partly cystic & solid (18.8%) and few were solid (8.2%). These findings were comparable with the findings of Misra RK *Et al.* [20] where most of the tumours were cystic (78.2%) and few were solid (4.1%), whereas Couto F *Et al.* [15] have found 10.2% solid tumours which was close to our findings.

Benign ET were the commonest type (88.3%), followed by malignant ET (10%) and the rest was borderline ET (1.7%). These findings were almost similar as observed in the study conducted by Kuladeepa A VK *Et al.* [17], Sharma I *Et al.* [21] In this study, maximum number of ET (72%) were noted in 31-50 years age group. All malignant tumours were seen in the cases above 40 years of age. The results corroborated with the various studies done by Kar T *Et al.* (2005) [22], Jha R & Karki S [14] and Jindal U [8]. Among the histomorphological types of ET, Serous tumours (68.3%) were the most common, followed by Mucinous tumours (23.3%), Seromucinous tumours (6.7%) and least common were Endometrioid tumours (1.6%). Similar results were seen by Krishna M & Maurya G [12] and Ranu Sarkar [23]. Serous cystadenoma was the commonest ET (53.3%) followed by Mucinous cystadenoma (21.7%) and Serous cyst adenocarcinoma (8.4%). Similar results were reported by various authors in their studies as shown below in the table 6:

Table 6: Comparative analysis of histomorphological sub-types of epithelial tumours.

Epithelial tumours	Sharma I (2014) [21]	Krishna M & Maurya G (2015) [12]	Present study
1) Serous cystadenoma	59.6%	51.3%	53.3%
2) Serous Cystadenofibroma	-	1.7%	6.7%
3) Serous cyst adenocarcinoma	4.8%	10.4%	8.4%
4) Mucinous cystadenoma	19.3%	16.5%	21.7%
5) Borderline mucinous tumour	1.6%	2.6%	1.6%
6)Endometrioid adenocarcinoma	3.2%	1.7%	1.6%
7)Seromucinous cystadenoma	-	4.3%	6.7%

In the present study, majority of the GCT were benign (81.3%) and include Mature cystic teratoma and Struma ovarii. These results were closer to the findings of Agrawal P *Et al.* [24] and Verma & Bhatia [25] with 77.7% and 83.5% respectively. Malignant tumours include Dysgerminoma and Embryonal carcinoma. GCT showed maximum cases below 30 years of age, with a gradual decline in 31-40 years age group and they were found to be uncommon after the age of 60 years. These findings were consistent with the studies of Jha R & Karki S [14] and Agrawal P *Et al.* [24]

In this study, majority of the SST were malignant (57.1%) and the results were similar to the findings of Rao KN *Et al.* [26] (55.6%) and were lower when compared to the findings of Jindal U [8] (75%). On the contrary study of Badge S *Et al.* [13] (66.7%) showed mostly benign SST against malignant SST. The age range of SST tumours in our study was 31-70 years whereas Bhagyalakshmi A *Et al.* [10] recorded age range of 21-70 years in their study. Adult granulosa cell tumour which is potentially malignant tumour occurred in 4.7% of all ovarian tumours. The frequency was consistent with the findings of Gupta *Et al.* [27] and Pilli GS *Et al.* [18] who recorded it as 4.4% and 3.54% respectively.

Our study showed 2 cases of secondary tumours and constituted 2.4% of all ovarian tumours. This was lower when compared to the findings of Santosh *Et al.* [9] (10.9%) but was almost similar to the studies of Gupta N *Et al.* [28] (2%), Jha R & Karki S [14] (2.4%) and Bhagyalakshmi A *Et al.* [10] (1.5%). One case was Krukenberg tumour (1.2%) and other was Extra Ovarian Primary Peritoneal Carcinoma (EOPPC) (1.2%). The former when compared with the studies of Misra RK *Et al.*[20] (1.07%), Prabhakar and Maingi [19] (1.57%) and Couto F *Et al.* [15] (1.46%) showed a good correlation. EOPPC occurred in a 45 years old woman and when compared with studies of Heda K *Et al.* [29], Punashetty KB *Et al.* [30] and Alvarez JV *Et al.* [31], it almost correlated, where the age of the case was 55 years, 45 years and 73 years respectively.

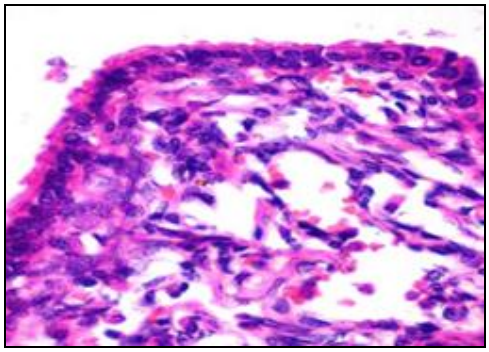


Fig 1: Microscopy of Serous cystadenoma: cyst wall lined by single layer of ciliated cuboidal epithelium resting on a fibro collagenous stroma (H and E, 400 X).

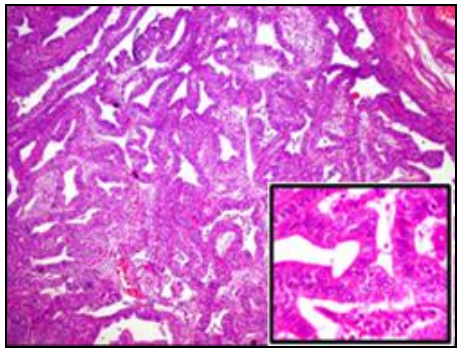


Fig 2: Microscopy of Endometrioid carcinoma: Villoglandular pattern lined by multilayered atypical columnar cells (H & E, 100X). Inset shows nuclear atypia and mitosis. (H& E, 400X).

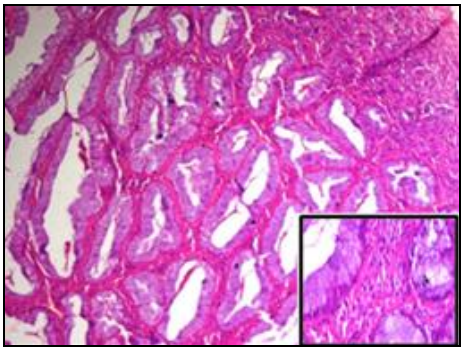


Fig 3: Microscopy of Borderline mucinous tumour: cluster of complex branched mucinous glands showing focal stratification with no stromal invasion (H&E, 100 X).

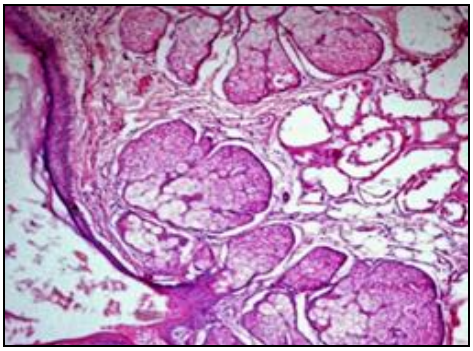


Fig 4: Microscopy of Mature cystic teratoma: squamous epithelium with underlying adnexal structures, respiratory epithelium and adipose tissue (H& E, 100X).

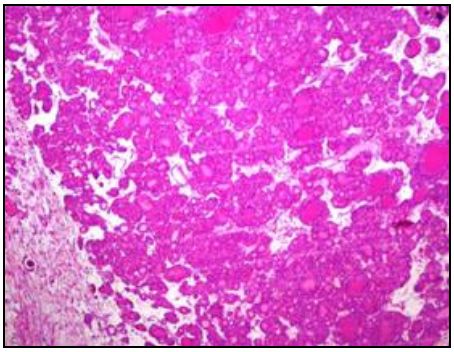


Fig 5: Microscopy of Struma ovarii: thickened cyst wall with scanty ovarian and underlying variable sized colloid filled thyroid follicles (H& E, 40X).

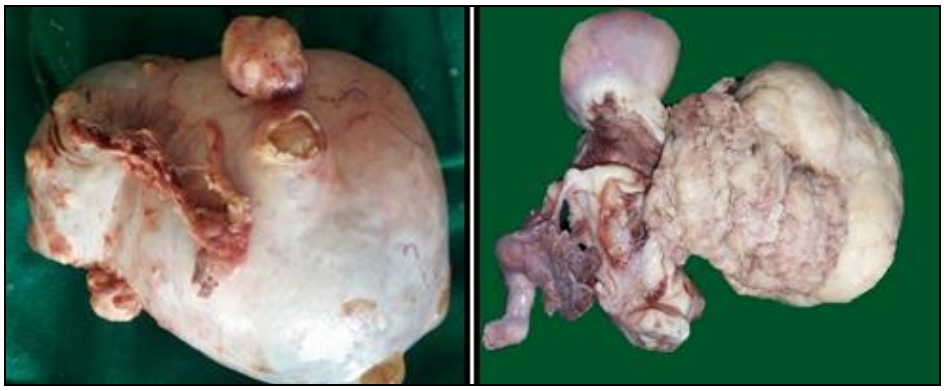


Fig 6: Case of Bilateral Serous cyst adenocarcinoma: 6a: one ovary showing nodular external surface with breached capsule; 6b: showing uterus with attached other ovarian mass.

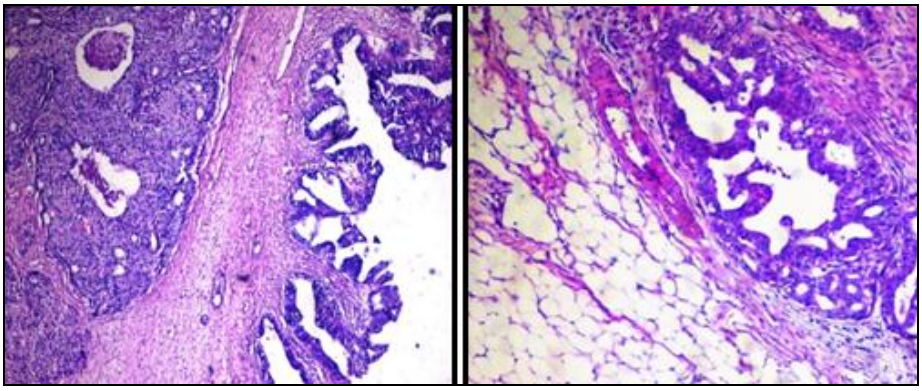


Fig 7: Microscopy of Serous cyst adenocarcinoma: 7a: Tumour cells showing papillary architecture with solid nests infiltrating the stroma (H& E, 40X); 7b: Infiltration of tumour cells in the omental fat (H& E, 100X).

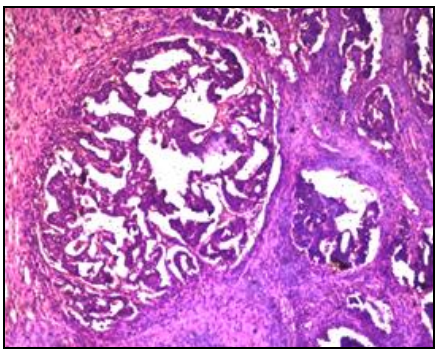


Fig 8: Microscopy of Embryonal carcinoma: Tumour cells in nests and occasional clefts showing anaplasia (H & E, 100X).

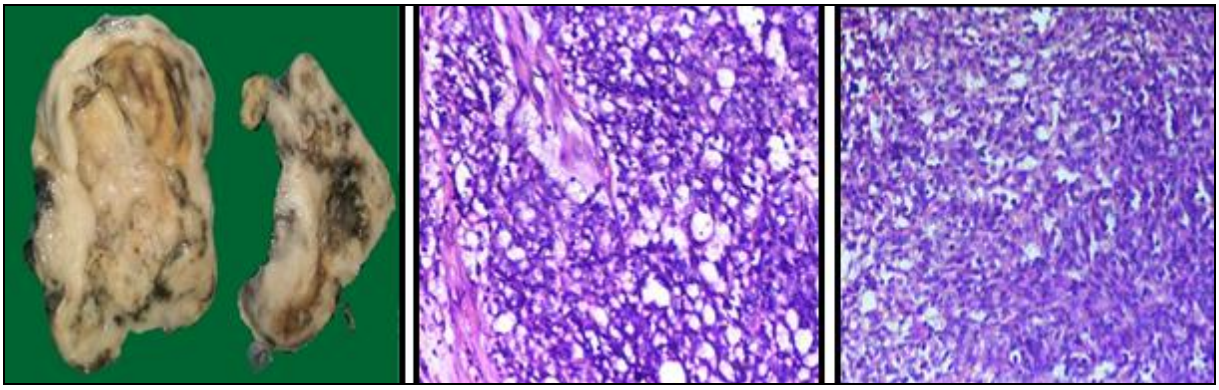


Fig 9: Steroid cell tumour: 9a: cut section with tan yellow variegated appearance; 9b: Microscopy: polygonal cells with abundant clear vacuolated cytoplasm; 9c: cells with pale eosinophilic cytoplasm and small round nuclei. (H& E, 400X).

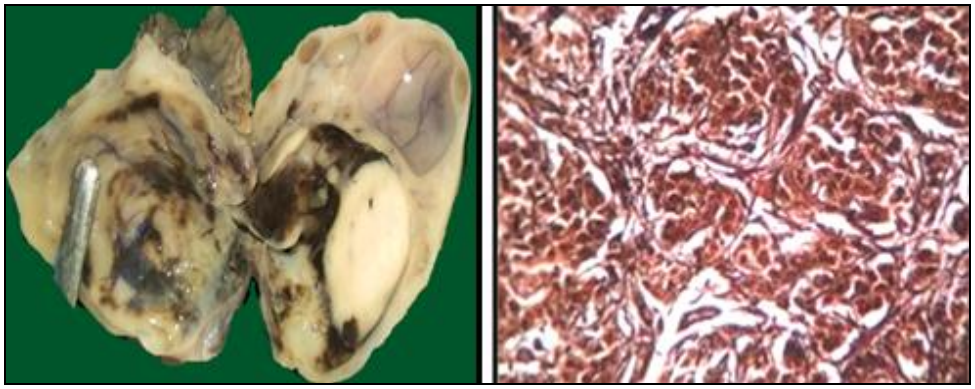


Fig 10: Adult granulosa cell tumour: 10a: cut section showing solid and cystic areas; 10b: Microscopy: reticulin stain showing reticulin fibres surrounding group of tumour cells (H& E, 100X).

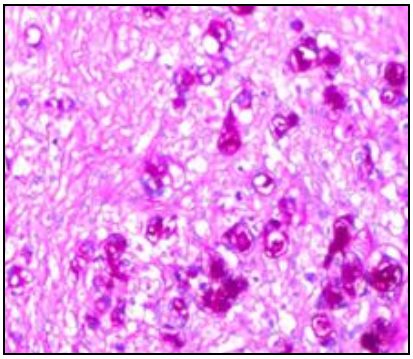


Fig 11: Microscopy of Krukenberg tumour: Signet ring cells with intracytoplasmic mucin and peripherally placed nucleus strongly positive with PAS stain (400X**).**

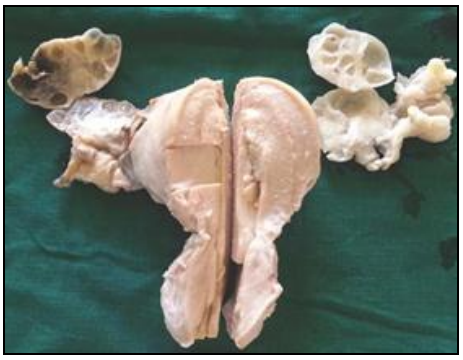


Fig 12: EOPPC: cut section showing both ovaries with follicular cysts and appear unremarkable

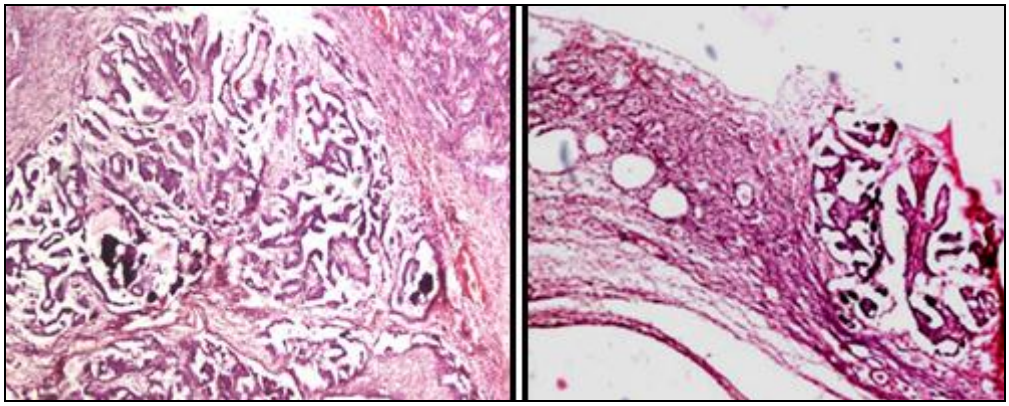


Fig 13: Microscopy of EOPPC; 13a: metastatic deposits in the cortex of left ovary; 13b: metastatic deposits just beneath the surface epithelium of right ovary (H & E, 100X).

5. Conclusion

Ovarian tumour is a silent menace that presents as a tremendous clinical challenge to gynaecologist, medical oncologist and radiotherapists. Emergence of borderline tumours with prognostic difference from the benign and malignant counterparts, has added a wing to research in the field of ovarian tumours. Accurate diagnosis of ovarian tumours can be rendered in almost all of cases by correlating the clinical presentation, radiographic appearance and histomorphological features, which remains the gold standard. Even then, in the modern era by the application of specialised methods like special stains, IHC markers, ultrastructural studies and cytogenetics, there is a vast scope for reaching specific & reliable diagnosis of difficult dilemmatic cases of ovarian tumours, by which the therapeutic and prognostic implications could be modified.

6. References

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