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Study of morphological patterns of ovarian neoplasms

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Abstract: ***Background****: The ovarian neoplasms are the cause of highest mortality in female genital tract. Histomorphological study is the gold standard to assess the treatment modalities and prognosis of various tumors.*
Aim*: This study is done to determine the age incidence, prevalence and morphological variants of ovarian neoplasms*
Materials and methods*: This is retrospective and prospective study done from January 2002 to October 2008. Thorough sampling from representative areas were given and stained with H & E. Special stains like reticulin, vangieson, PAS, mucicarmine were done if necessary.*
Results*: Out of 278 ovarian neoplasms analysed in this study, 275 were primary (98.92%) and 3 were metastatic tumors (1.08%). Among primary ovarian tumors, the surface epithelial tumors ranked first (85.25%), followed by germ cell tumors (9.71%) and sex cord stromal tumors (3.95%). Most of the benign tumors were observed in 4^{th} decade, while the malignant tumors in 5^{th} decade .*
Conclusions: *The study of macroscopic and microscopic features of different ovarian tumors will enable for categorization into exact morphological type which will help the gynecologist for proper management.*
Key words*: Histomorphological study, germ cell, sex cord stromal, surface epithelial.*

I. Introduction

The ovary is the second most common site for cancer in the female reproductive organs and is associated with the highest mortality rate. [1] The poor survival is due to the fact that they do not clinically manifest early and approximately 60-70% of the neoplasm present as either stage III or stage IV. [2] The emergence of tumors of low malignant potential has changed the prognosis of ovarian tumors and produce peritoneal nodules which may be mistaken for secondaries, should be differentiated by histopathology.

In spite of significant advances in imaging modalities, sometimes they are also misleading. Cytological interpretation of aspirates from ovary is most challenging and immunohistochemistry provides a functional correlation for the traditional morphological classification. Natural history and response to treatment vary considerably from one group of tumor to others, especially in the area of chemotherapy and radiotherapy.[3] Hence an accurate histology is often a critical factor in acheiving an optimum treatment response. As there are no screening tests or tumor markers, histopathology plays a key role in detection of ovarian cancer.

In view of the above facts we have made an attempt for a detailed study of the morphological patterns of ovarian tumors and tried to correlate with other clinical details, hoping to obtain some meaningful relationship between incidence and distribution of various types of ovarian cancers, the ultimate goal being better management.

Aim of the study

The prospective and retrospective study of the ovarian neoplasms was undertaken to determine the prevalence, the age incidence and the morphologic variants of ovarian neoplasms.

II. Materials And Methods

A detailed retrospective and prospective study of 278 ovarian neoplasms was done from January 2002 to October 2008, taking into account relevant clinical data. In the retrospective study, the available H & E stained slides and available paraffin blocks of the ovarian tumors, in the department were studied from January 2002 to June 2006 and relative information were recorded from the biopsy records and statistical books. In the prospective study, the material comprised of excised surgical specimens of ovarian tumors from June 2006 to October 2008. Thorough grossing was done and multiple representative sections given. The tissue was processed by routine histological techniques and subjected for Haematoxylin & Eosin staining. Special stains like Mucicarmine, Vangeison's, Periodic acid Schiff and Reticulin stain were done whenever necessary

Inclusion criteria:

Both the primary & secondary histologically proven ovarian tumors were included.

Exclusion criteria:

Tumor like conditions were excluded in order to avoid confusion

III. Results

From the present study comprising the analysis of 3956 female genital tract neoplasms recorded from 2002 to 2008, the ovarian tumors accounted for 278, giving the incidence of 7.02%. Out of these 278 tumors 217 (78.05%) were benign & 61 (21.95%) were malignant, 275 were primary ovarian tumors (98.92%) and remaining 3 were secondary ovarian tumors (1.08%). The commonest presenting symptom was mass per abdomen followed by pain abdomen and menstrual disturbances for both benign and malignant tumors

Primary Ovarian tumors were broadly divided into 3 categories based on WHO Classification as shown in TABLE 1.Out of 278 ovarian tumors 237 were surface epithelial tumors (85.25%), 11 were sex cord stromal tumors (3.95%), 27 were germ cell tumors (9.72%) and 3 were metastatic (1.08%).

Among surface epithelial tumors, serous type was highest (72.15%), followed by mucinous tumors (25.32%). In sex cord stromal tumors, granulosa cell is the most common malignant cell tumor and fibrothecoma (36.36%) constituted the predominant group among germ cell tumors. Out of 171 serous tumors, 141 were benign (82.46%), 3 were of low malignant potential (1.75%) and 27 were frankly malignant (15.79%). Out of 60 mucinous tumors, 47 were benign (78.33%), 2were tumors of low malignant potential (3.33%) and 11 were malignant (18.34%). Other epithelial tumors observed in the present study are clear cell carcinoma and Brenner tumor. It is well evident from the present study that sex cord stromal tumors are the least common among the primary ovarian tumors (3.95%). Granulosa cell tumor (36.36%) constituted the predominant tumor of this category. Out of 27 germ cell tumors, benign cystic teratoma were the commonest (66.67%) followed by dysgerminoma (18.53%). Out of 3 metastatic tumors observed (1.08%), 2 were from female genital tract and one was Krukenberg tumor as shown in TABLE 2.

Among total 278 ovarian tumors, benign were 217 (78.05%) and malignant 61 (21.95%). Out of 217 benign ovarian tumors, the serous tumors ranked first with a total of 141 (64.98%) followed by mucinous comprising of 47 tumor (21.66%) & ranked third is benign cystic teratoma with a total of 18 (8.30%) as shown in TABLE 3.

Among 61 malignant ovarian tumors, serous carcinomas (borderline & invasive together) ranked first (49.18%) followed by mucinous carcinomas both borderline & invasive (21.30%) and third most common is dysgerminoma (8.20%) as depicted in TABLE 4

There were 15 bilateral ovarian tumors in the present study. Among the primary tumors, serous carcinomas were observed to be bilateral in a large number of cases (25.92%), followed by mucinous carcinomas (9.09%). Benign serous tumors were bilateral in only 3.54%. Among the secondary tumors, 2 out of 3 were bilateral with an incidence of 66.66% as shown in TABLE 5.

Among 278 ovarian tumors recorded the age of patients ranged from 13-82yr. The maximum cases of benign epithelial tumors were observed in 3rd and 4th decade of life with a peak in 4th decade (32.26%). The type of benign tumor noted in the oldest patient of 82yr was mucinous cystadenoma. Most of the malignant ovarian neoplasms were found in between 41-60 years (27.86+27.32=49.18%). Germ cell tumors occurred relatively in a younger age group as compared to other malignant tumors. The secondary tumors were observed from 3rd to 5th decade of life as shown in TABLE 6.

IV. Discussion

The ovary is a complex structure from an embryological, anatomical and functional stand point. Therefore ovarian tumors aroused curiosity and problems to pathologists and clinicians regarding their abnormal contents and genesis. The value of detailed morphological study of ovarian tumors lies not only in systematic diagnosis but also in planning the modality of treatment and assessing the prognosis.

Surface epithelial tumors

In our study surface epithelial tumors (85.26%) constitute the most prominent type of ovarian tumors followed by germ cell tumors which is in agreement with other studies done by Misra.R.K. et al, Maheswari et al, Nasser A. Shaikh et al.[4,5,6] Benign serous tumors comprising 141 cases (50.72%) formed the largest group in the present study and our findings are identical to that of Misra R.K et al, but slightly higher than those of other authors Maheswari et al and Nasser A. Shaikh et al. This might be due to relative decrease in the occurrence of sex cord and germ cell tumors in our study. The incidence of borderline tumors in our study was 1.75% of total serous tumors, which is a lower figure when compared to 15% reported by Purola et al, Russel p et al.[7,8] In the present study the serous carcinomas constituted 17.54% of all serous tumors. The findings of other authors are slightly lower than that of ours. In our study we observed psammoma bodies in 3 cases (10%) of serous malignant tumors. It was observed that the behavior of serious carcinomas with psammoma bodies resemble that of borderline tumors.[9]

We used stromal invasion as criteria to distinguish borderline from serous carcinomas, the true invasion process is often associated with desmoplastic reaction and inflammatory response which are not seen in the

invasion of borderline tumors. We have not come across any foci of microinvasion and peritoneal implants in our study, though they have been described by many authors in the western literature.[10]

Second commonest group among all the ovarian tumors was of mucinous type consisting of 60 cases (21.52%) in the present study. Among these, the benign mucinous tumors formed 78.33%. Similar finding has been reported by Nasser. A. Shaikh et al, Misra R.K. et al Bennington, Kent & Mc kay.[4,6'11] The mucinous tumors are the largest with maximum size was 40x12x10cm, which is in accordance with other studies. Mucinous carcinomas formed 4.68% of all ovarian tumors which is almost similar to Misra. R.K. et al, Tandon et al & slightly lower than Maheswari et al & Nasser. A.Shaikh et al.[4,5,6,12] The occurrence of necrosis and hemorrhages were more common in invasive mucinous carcinomas than the borderline type. Microscopically when the invasion of the stroma is uncertain, the height of atypical epithelium has to be evaluated as suggested by Hart & Norris (1973). If the height of atypical epithelium is 4 cells or greater the tumor is considered to be carcinoma.[13]

We have one case of clear cell carcinoma in our study which is in close approximation with the incidence observed by others. This clear cell carcinoma has to be differentiated from dysgerminoma & metastatic renal cell carcinoma. Absence of lymphocytes and granulomas with positive PAS stain differentiates clear cell tumors from dysgerminomas. Renal cell carcinoma can be readily excluded by radiological studies & clinical data.

We have 2 cases of endometrioid adenocarcinoma with an incidence of 0.72% of all ovarian tumors which is slightly higher than the authors, but was equal to the findings of G.S.Pilli et al who observed 2 cases of endometrioid carcinoma comprising of 0.7% of total ovarian tumors.[14]

In our study we had 2 cases of benign Brenner tumors (0.72%) among total ovarian tumors, comparatively higher than other studies. We observed one case of malignant Brenner tumor with an incidence of 0.35% of all ovarian tumors. This is almost similar to that of Maheswari et al.[5] Adjacent areas of typical benign Brenner was observed, which is an important criterion to differentiate from primary ovarian transitional carcinoma as suggested by Idelson (1963), as the latter one is considered to have poorer prognosis. [15]

Among the serum markers, CA- 125 has been studied most extensively. Isolated values of CA-125 lack adequate sensitivity or specificity, but when monitored over time, serial CA-125 values can achieve a specificity of 99.6%. Multiple serum markers have been analyzed in women with early stage epithelial ovarian cancer. CA-125, CA 15-3, C19-9, CA 54-61, CA 72-4, CEA,

TAG72, TNF, TPA, and UGTF have been studied alone and in combination. The serial measurement of complementary serum markers can improve the use of marker screening for epithelial ovarian cancer.[16,17]

***Sexcord stromal tumors*:**

In our study we observed 11 cases of sex cord stromal tumors giving an incidence of 3.95%. Granulosa cell tumors and fibrotheoma are the most common variety of sex cord stromal tumors, which is lower than the observations made by other authors like Misra. R.K. et al (3.01%) and Nasser .A Shaikh et al (3.6%). Granulosa cell tumors constituted the majority of sex cord stromal tumors which is in accordance with that of Scully R.E.[18] We observed various patterns, but in our study the most common pattern is microfollicular type.

Granulosa cell tumors should be differentiated from undifferentiated carcinoma, malignant lymphoma, small cell carcinoma & carcinoid by the presence of typical call exner bodies, coffee bean nuclei of granulosa cells & reticulin stain.

Though associated pathology like endometrial hyperplasia and endometrial carcinoma has been reported in 2-13% of patients, we have not come across any such association in our study.

Juvenile granulosa cell tumor, Thecoma, Cellular fibromas & fibro sarcomas are not reported in our study. Combination of granulosa & theca cells, fibroma & thecoma were also seen in the present study which accounts for 1.08% & 1.43% of all ovarian tumors respectively. Similar observations were made by other studies.

Ge***rm cell tumors:***

Germ cell tumors constitute 15-20% of all ovarian tumors. In our study a total of 27 cases were observed (9.71%) which is slightly lower than the observations of other authors, but is almost similar to the findings of Nasser .A. Sheikh et al (10.67%). Dysgerminoma constitutes less than 1% of all ovarian tumors & about 5% of malignant ovarian tumors. In our study we observed 5 cases of dysgerminoma giving an incidence of 1.80% which is almost similar to the findings of other authors as Tandon et al, Misra R.K et al and Nasser A sheikh et al.

Benign cystic teratoma constituted 18 cases (6.47%) of all ovarian tumors and third commonest benign tumor after serous and mucinous cystadenomas. Identical reports are seen in other literatures. The common reported components are fat, cartilage & bone in all dermoid cysts. The other less common & rare elements like pancreas, retina, adrenal glands, thymus, kidney, breast & pituitary gland were not observed in our cases.

Immature elements were excluded by careful examination and proper sampling because of its behavior as a malignant neoplasm.

Malignant transformation in a mature cystic teratoma is a rare occurrence. The reported incidence was 2.8% by Krumerman & Chung.[19] In our series also we had one case of moderately differentiated squamous cell carcinoma, giving the incidence of 5.26%, which is comparatively a higher figure. But the Indian authors like Tyagi et al documented this change in 4% (1 out of 25 cases). [20] This might be due to less number of benign cystic teratomas in the present work.

We had one case of immature teratoma giving an incidence of 1.36% of all ovarian tumors. Grading of these tumors into 0 to III types according to the degree of differentiation & quantity of mature tissue has been proposed by Thurlbeck & Scully & subsequently adopted with elaboration of the criteria by Norris H.J et al.[21,22] In our case grade II differentiation was seen.

The incidence of struma ovarii was found to be 0.36% of all the ovarian tumors in the present study. No evidence of thyrotoxicosis or malignancy was seen though such changes have been reported by others. We have not observed any case of mixed germ cell tumor in the present work.

Metastatic ovarian tumours:

Our study, showed 3 cases of secondary tumors (1.08%). Verma & Bhatia, reported a higher incidence of ovarian tumours (6.5%) where as Nasser A shaikh et al reported 1.58%.[23] Among the 3 cases only one case is Krukenberg with an incidence of 0.36% similar to that of other studies like Tandon et al & Misra R.K. et al, & remaining 2 were non krukenberg tumours (one is from adenocarcinoma endometrium and other from carcinoma cervix, each accounting for 0.36%).

***Incidence of bilaterality*:**

In our study we observed 15 cases (5.40%) of bilateral tumors of which 5 were benign and 10 were malignant on both sides. Our findings were similar to Misra.R.K. et al 4.52%

V. Conclusions

The ovary is a very common site of neoplasia in the female genital tract. The ovarian tumors manifest a wide spectrum of clinical, morphological and histological features. As the natural history, treatment modalities and prognosis of ovarian neoplasms differ, the histomorphological study remains the gold standard. However, it may be supplemented by newer techniques like IHC, morphometirc analysis, cytometric analysis of ploidy status to resolve the difficult, dilemmatic cases and to predict prognosis.

References

[1]. Jaun Rosai, "Rosai and Ackerman's Surgical pathology," 9th Edition, New delhi, Eslvier 2004.
[2]. Barber HRK: Ovarian carcinoma Etiology, Diagnosis & Treatment 2nd Edition, Masson, New York 1982
[3]. Novak, E.R., and Woodruff, J.D., In: Novak's Gynaecologic & Obstetric pathology.
[4]. Misra, R.K, Sharma, SP., Gupta V.Gaur, R., Mishra S.D., "Pattern of ovarian neoplasms in Eastern U.P:., Jorunal of OBG,1991, 241- 246
[5]. Rekha, V.kumar, Geetashree Mukherjee, Umadevi.K, Hazarika.D, Sclerosing stromal tumours of the ovary. Ind.Journal of cancer,1994, 31; 92-95.,
[6]. Naseer, A. Shaikh., Fazila, Hashmi., & Rukhsana, parveen, Samoo., " Pattern of ovarian tumours ; Report of 15 years experience at Liquat university".
[7]. Purola E. Serous papillary ovarian tumours. A study of 233 cases with special references to the histological type of tumours & its influence in prognosis Act OBG . 1963, scand 42 (supple 3):, 1-77. .
[8]. Russel, P. Bannatyne patricia. "Surgical pathology of ovaries", 1989.
[9]. Gilks C.B., Bell, D.A., Scully, R.E: serous psammocarcinoma of the ovary and peritoneum. International Journal of gynaec. Pathology , 1990,9:110-121.
[10]. Julian, C.G., Woodruff, J.D. The biologic, behavior of low grade papillary serous carcinoma of the ovary. Obstetrics & Gynaecology 1972, 40: 860-867.
[11]. Kent S.W., Mc kay D.G "Primary cancer of ovary" American Journal of OBG;1960, 80; 430. .
[12]. Tandon, R., Mathur, J.S., Mehram, M., Sharma, U.: pattern of ovarian tumours in Ajmeer/Rajasthan). J.Ind. med.Ass,1981,.77: 191-993
[13]. Hart, W.R., Norris H.J. Borderline & Malignant mucinous tumours of the ovary, cancer,1973, 31:1031-1045
[14]. Pilli G, Suneetha K.P, Dhaded, A V, Yenni V V, :Ovarian tumours JIMA; July,2002, 100(7).
[15]. Idleson, M.G: Malignancy in Brenner tumours of the ovary, with comments on histiogenesis & possible estrogen production. Obstetrics & Gynaecological survey.,1983, 18: 246-267.
[16]. Berek JS, Bast RC. Ovarian cancer screening: The Use of Serial Complementary Tumor Markers to Improve Sensitivity and Specificity for Early Detection. Cancer. 1995;76:2092-6.
[17]. Bast RC. Status of tumor markers in ovarian cancer screening. J Clin Oncol. 2003;21:200-5.
[18]. Scully R.E., In : Tumours of the ovary & maldeveloped gonads In: Atlas of tumour pathology, 2nd ser. Fascicle 16, Washington:1979, Armed forces Institute of Pathology.
[19]. Krumerman, M.S., Chung, A: Squamous cell carcinoma arising in a benign cystic teratoma of the ovary: A report of 4 cases & review of the literature. Cancer , 1977, 39:1237-1242.
[20]. Tyagi S.P., Maheswari, V., Tyagi, . N., Tewari, K., "Double malignancy in a benign cystic teratomas of the ovary " . Indian journal of cancer. 1993, Vol, 30; 140-142.

[21]. Thurlbeck , W.M ., Scully R.E : Solid teratomas of the ovary. A clinicopathological analysis of 9 cases . 1960, 13, 804 -811.
[22]. Norris, H.J., Zirkin, H.J., Benson W.L., Immature (Maignant) teratoma of the ovary. A clinical & pathological study of 56 cases, 1976, cancer,37:2359-2372,.
[23]. Verma K ., Bhatia, A: Ovarian neoplasms . A study of 403 tumours . J .OBG,1981, 31 : 106-111

TABLES AND FIGURES

TABLE 1 – FREQUENCY DISTRIBUTION OF HISTOGENETIC GROUP OF ORIGIN

Sl.No	Type of Tumor	Benign		Malignant		Total	
		No	%	No	%	No	%
1.	Surface epithelial tumors	190	87.56	47	77.05	237	85.25
2.	Sexcord stromal tumors	80	3.69	3	4.92	11	3.95
3.	Germ cell tumors	19	8.75	8	13.11	27	9.72
4.	Metastatic	-		3	4.92	3	1.08
		219	100.00	61	100.00	278	100.00

TABLE-2: INCIDENCE OF SPECIFIC CATEGORY OF OVARIAN NEOPLASMS

S.NO	Type of tumor	No of tumor	% of specific Category	% of specific tumor
	I. Surface epithelial tumors	237		85.25
1.	Serous	171	72.15	
2.	Mucinous	60	25.32	
3.	Endometrioid	2	0.84	
4.	Clear cell	1	0.43	
5.	Brenner	3	1.26	
6.	Mixed epithelial	-		
	II Sex cord stromal tumors	11		3.95
1.	Granulosa cell tumors			
2.	Pure granulosa type	3	29.28	
3.	Granulosa theca cell tumor	1	9.08	
4	Pure theca cell	-		
5.	Fibrothecoma	4	36.36	
6.	Fibroma	3	27.28	
	III .Germ cell tumor	27		9.71
1.	Dysgerminoma	5	18.53	
2.	Yolk sac tumor	1	3.70	
3.	Immature teratoma	1	3.70	
4.	Benign cystic teratoma	18	66.67	
5.	Malignant dermoid	1	3.70	
6.	Monodermal (Struma ovarii)	1	3.70	
7.	Mixed Germ Cell tumor	-	-	
	IV Metastatic	3	-	1.09
	Total	278		100.00

TABLE 3: FREQUENCY DISTRIBUTION OF BENIGN OVARIAN TUMORS

S.NO	Name of tumor	No	%among total benign tumors (219)	%among total ovarian tumors(278)
1.	Serous type	141	64.98	50.72
2.	Mucinous cystadenoma	47	21.66	16.90
3.	Brenner tumors	2	0.92	0.72
4.	Fibroma	4	1.84	1.44
5.	Fibrothecoma	4	1.84	1.44
6.	Benign cystic teratoma	18	8.30	6.48
7.	Struma ovarii	1	0.46	0.38

TABLE 4: INCIDENCE OF VARIOUS OVARIAN MALIGNANCIES

S.NO	Type of tumor	Tumor of Low malignant potential	Malignant	Total	%among total malignant tumors(61)	%among total ovarian tumors (278)
1.	Serous type	3	27	30	49.18	10.79
2.	Mucinous type	2	11	13	21.30	4.68
3.	Endometrioid type		2	2	3.28	0.73
4.	Clear cell type		1	1	1.64	0.36
5.	Brenner type		1	1	1.64	0.36
6.	Granulosa cell type		3	3	4.92	1.08
7.	Dysgerminoma		5	5	8.20	1.79
8.	Yolk sac tumor		1	1	1.64	0.36
9.	Immature teratoma		1	1	1.64	0.36
10.	Malignant dermoid		1	1	1.64	0.36
11.	Metastatic		3	3	4.92	1.08
	Total	5	56	61	100.00	21.95

TABLE 5: DISTRIBUTION OF VARIOUS BILATERAL OVARIAN TUMOURS

S.NO	Type of tumor	No of Bilateral tumors	%among total of individual tumor
1.	Benign serous tumors	5	3.54(141)
2.	Malignant serous tumor	7	25.92(27)
3.	Malignant mucinous tumors	1	9.09(11)
4.	Metastatic	2	66.66(3)

Note: Tumors of individual group are given in brackets

TABLE 6: AGE DISTRIBUTION

AGE	Benign		Malignant		Total	
	No	%	No	%	No	%
0-10	-	-	-	-	-	-
11-20	9	4.15	6	9.84	15	5.40
21-30	56	25.81	5	8.20	61	21.95
31-40	70	32.26	12	19.67	82	29.49
41-50	50	23.04	17	27.86	67	24.10
51-60	21	9.68	13	21.32	34	12.24
61-70	7	3.22	8	13.11	15	5.40
71-80	3	1.38	0	-	3	1.07
<90	1	0.45	0	-	1	0.35
	217	100.00	61	100.00	278	100.00

PHOTOMICROGRAPHS OF VARIOUS OVARIAN TUMORS

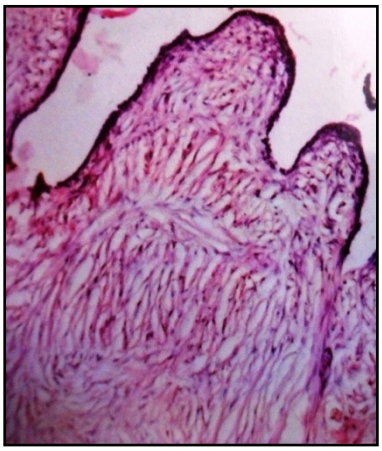

Figure 1 Cystadenofibroma

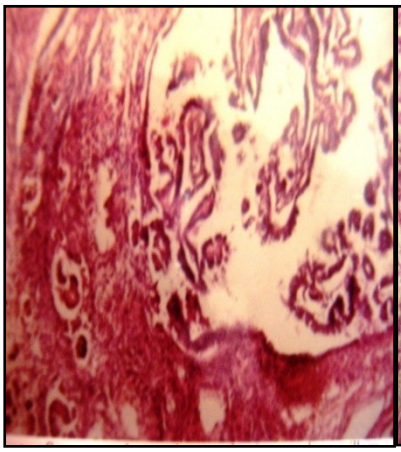

Figure2 Papillary cystadenocarcinoma

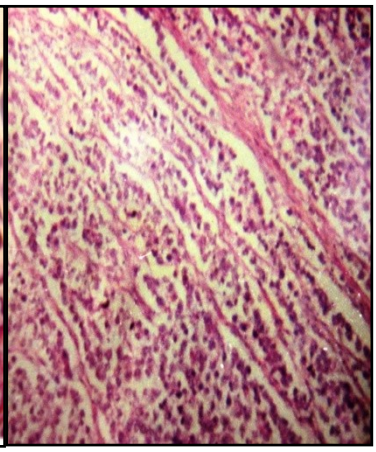

Figure 3 Granulosa cell tumor

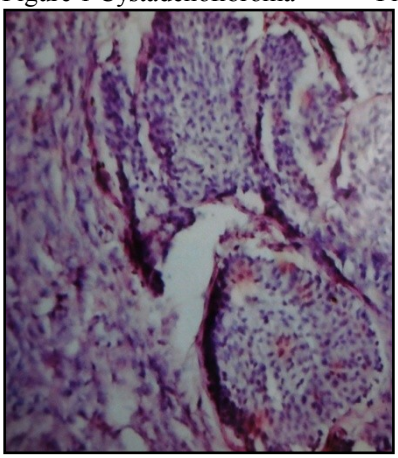

Figure 4 Immature teratoma

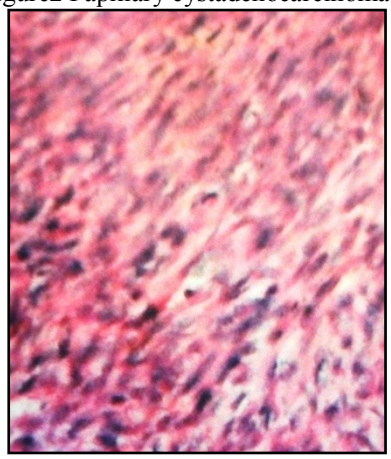

Figure 5 Fibroma

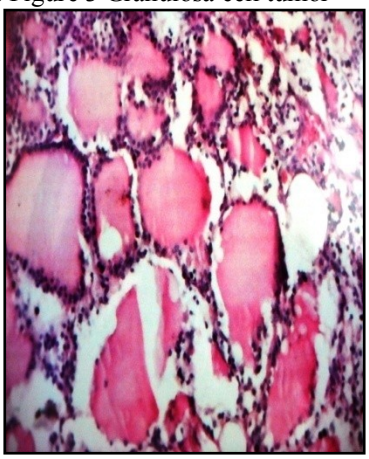

Figure 6 Struma ovarii