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Original Article

Surface epithelial tumors of ovary - an analysis in a tertiary referral hospital

Ghartimagar D[1], Ghosh A[1] , KC G[1] , Ranabhat S[1], Talwar OP[1]

[1]*Department of Pathology, Manipal Teaching Hospital and Manipal College of Medical Science, Pokhara, Nepal*

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ABSTRACT

Background: Ovarian cancer accounts for 3% of all cancers in females. About 80% of these are benign, and they occur mostly in young women between 20 and 45 years. Borderline tumors occur at slightly older ages while incidence of malignant tumors increases with age, occurring predominantly in perimenopausal and postmenopausal women. About 190,000 new cases and 114,000 deaths from ovarian cancer are estimated to occur annually worldwide. The aim of the study was to find the incidence of surface ovarian tumor in a tertiary referral centre.

Materials and methods: This was a retrospective study carried out in the department of pathology, Manipal Teaching Hospital from January 2001 to December 2012. Specimens were received from the same and other hospitals. Records were retrieved from the departmental data bank and were analyzed.

Results: : A total of 310 cases of ovarian tumors have been reported in the same period. Among them, 180 cases were of surface epithelial origin and out of which 24 cases had bilateral tumors. Benign tumors comprised of 148 cases, 6 were borderline and 44 were malignant. Among these, the commonest was serous cystadenoma (98 cases) and the least common was malignant Brenner (2 cases). Combined or mixed tumor was seen in 9 cases.

Conclusion: : In our study surface epithelial tumors comprised 58% of all ovarian tumors. In both benign and malignant cases, serous tumor was the commonest followed by mucinous tumors.

INTRODUCTION

Ovarian masses are a common occurrence in women of all age groups, with approximately 8% of asymptomatic women aged 25 to 40 years.[1] About 80% of ovarian tumors are benign, and these occur mostly in young women between 20 and 45 years where as borderline tumors occur at slightly older ages. Incidence of malignant tumors increases with age, occurring predominantly in perimenopausal and postmenopausal women.[2,3] The age adjusted incidence rate of ovarian cancers vary between 2-15 per 100,000 women. It is least in the developing countries of South East Asia and Africa and highest in the industrialized developed countries of Europe and North America.[2,4] Ovarian carcinomas are the 6th most common cause of death from all cancers in women; 70% of patients with ovarian tumors present as advanced stage disease.[5,6] The aim of the study was to find the incidence of surface ovarian tumor in a tertiary referral centre.

Correspondence:
Dr. Dilasma Ghartimagar, MD
Assistant Professor, Department of Pathology Manipal College of Medical Science Pokhara, Nepal
E-mail: dilasmagm@hotmail.com

Table 1: Histopathological diagnosis along with their frequency.

Type		Number	Percentage
BENIGN	Serous	98	49.4%
	Mucinous	34	17.1%
	Brenner	07	3.5%
	Combined serous + Brenner	01	0.5%
	Combined serous + mucinous	02	01%
	Combined serous + teratoma	04	02%
	Combined mucinous + teratoma	02	01%
BORDERLINE	Mucinous	06	03%
CARCINOMA	Serous	32	16.6%
	Mucinous	10	05%
	Brenner	2	01%

MATERIALS AND METHODS

A hospital based, retrospective study was carried out in the department of pathology, Manipal Teaching Hospital. The study included all benign, borderline and malignant surface epithelial tumors of the ovary, diagnosed over a span of 12 years (Jan 2001 to Dec 2012). All the specimens received for histopathology from Manipal Teaching Hospital and other hospitals within Pokhara valley were included in the study. All the histopathological data were retrieved and collected from the departmental data bank and were analyzed.

RESULTS

A total of 310 patients of ovarian tumors have been reported, which included180 patients with surface epithelial tumors. Among them 24 patients had bilateral ovarian tumors. Among the 24 patients with bilateral tumors, 42 tumors were of epithelial origin and the rest 6 tumors were of non-epithelial origin (3 tumor deposits, 2 mature cytic teratoma and 1 mixed mullerian tumor). We have analyzed a total of 198 tumors of epithelial origin. The mean age was 43 year, ranging from 13 to 90 years. The tumor size ranged from 1.2 to 36cm (median size 9cm). Among all 198 tumors, 148 were benign, 6 were borderline and 44 were malignant cases. Table1 shows the incidence of surface epithelial tumors in our study. Among the benign surface epithelial tumors, the commonest was serous cystadenoma (98 cases; 49.4%) followed by benign mucinous tumors (34 cases; 17.1%). Among the malignant group, the commonest was of serous type (32cases; 16.6%) followed by mucinous type (10 cases; 5%).

Out of 180 patients 84 (44.6%) were of <40 years of age, while 96 (53.4%) were above the age of forty. On gross examination 116 (58.6%) ovarian tumors were of <10cm in greatest dimension, where as 82 (41.4%) were larger than 10cm.

Table 2 summarizes the microscopic features of surface epithelial tumors. Among the patients with bilateral ovarian tumors and having surface epithelial tumors 19 tumors were of malignant serous cyst adenocarcinoma followed by15 benign serous cystadenoma, 4 benign mucinous cystadenoma, 3 malignant mucinous adenocarcinoma and 1 malignant Brenner tumor.

DISCUSSION

On the basis of four major types of tissue, primary ovarian neoplasm can be broadly classified as surface epithelial-stromal tumors, germ cell tumors and sex cord - stromal tumors.[2] Surface epithelial tumors are the most common neoplasm of the ovary. They originate from the ovarian

Table 2: Morphological features of surface epithelial tumors

No. of cases	
Necrosis (gross/ microscopy)	34
Increased atypical mitosis	30
Comedo pattern necrosis	02
Psammoma body	03
Focal mucin production in serous tumor	01
Emboli (vascular / lymphatic)	10
Peritoneal implant	11
Torsion	7
Metastasis to other sites	06 (FT 4 , U 2)

FT = fallopian tube , U = Uterus body

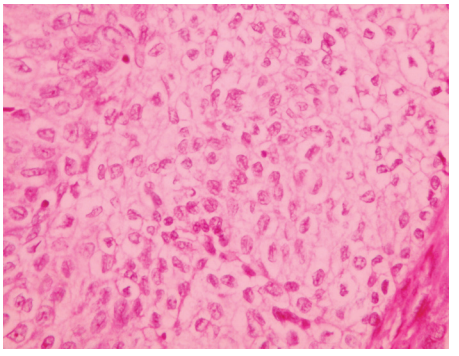

Figure 1: *Benign Brenner tumor (HE Stain, X100).*

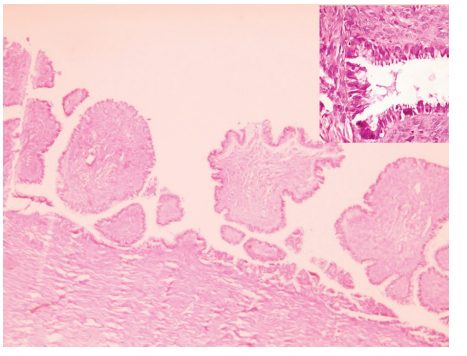

Figure 2: *Borderline mucinous tumor (HE Stain, X40), inset (HE Stain, X100).*

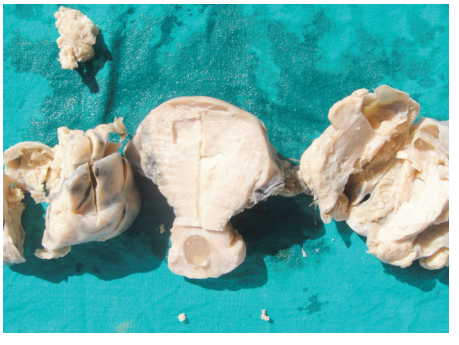

Figure 3: *Bilateral serous carcinoma.*

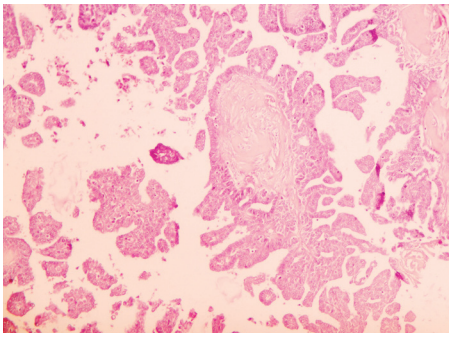

Figure 4: *Papillary serous cyst adenocarcinoma (HE Stain, X40).*

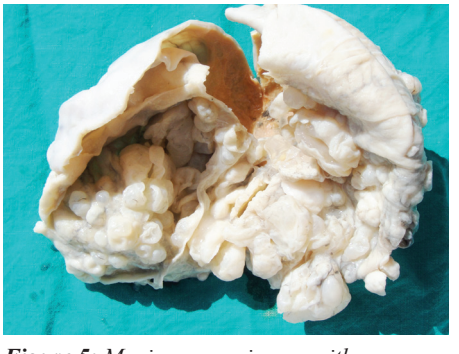

Figure 5: *Mucinous carcinoma with multiloculated cysts.*

Figure 6: *Malignant Brenners tumor with extensive necrosis.*

surface epithelium or its derivatives and occur in women of reproductive age and beyond. The epithelial tumors arise mostly from the inclusion glands leading to its cystic nature.[4] They are histologically composed of one or more distinctive types of epithelium, admixed with a variable amount of stroma. Their biological behavior varies with histological type.[2] In the diagnosis of ovarian tumor, clinical data and gross features and detail microscopic examination is required. One of the most important clinical features is the age of the patient. About 80% of ovarian tumors are benign and occur in age between 20-45 years, the remaining 20% are malignant and are more common in older women between 45-65 years.[2]

Surface epithelial tumors comprise 58% of all ovarian neoplasms and about 90% of malignant tumors in the Western world. But their frequency is less in the East.[4,7,8] Surface epithelial tumors form the main histological group not only in this analysis but also in other international studies.[9-12] The classification of ovarian epithelial tumors currently used by pathologists is based entirely on tumor cell morphology, architectural pattern, nuclear atypia and stromal invasion.[8,13,14] The cell type may be serous, mucinous, endometroid, Brenner/transitional, clear cell and undifferentiated. These cell types bear strong resemblance to the normal cell lining of different organs in the female genital tract.[13] Each can be again of benign, borderline and malignant type.[2] More than one cell type is often seen. If the secondary cells type involve less than 10% of the tumor, it

is classified according to the predominant cell type, while if it is more than 10% , it is classified as mixed epithelial tumor.[4] Among all the subtypes, only Brenner tumor shows a predominant stromal component. Our study of 12 years duration included 180 patients with 198 surface epithelial tumors.

Benign epithelial tumors

In serous tumors, approximately 75% are benign, 5-10% are borderline and 20-25% are malignant in current literature.[2] Our study showed 74.7% of benign, 3% borderline tumors and 22.2% malignant tumors. Benign serous tumors occur at any age, but are most common in the reproductive age group and account for 16% of all ovarian epithelial neoplasms in literature.[2,4] In the present study, benign serous tumors (98 cases) comprised 49.4% of all epithelial tumors. Grossly, benign serous tumors are composed of one or more thin walled cysts filled with watery fluid. Tumors are either lined by ciliated or less commonly by non-ciliated cuboidal and columnar epithelium.[2,15] The epithelial cells may show occasional mucin production and it was noticed in only 1 case of our study. Psammona bodies are however mostly absent.[4] The cysts may bear polypoidal excresences composed entirely of stroma. If the polypoidal excresences are firm in consistency, it shows dense fibrous stroma and if soft in consistency, it comprises of edematous storma.[15] They are usually 1-10cm but may be up to 30 or more in size.[2] In our study, 65% benign serous tumors were less than 10 cm and 35% were larger. Torsion was noted in 7 cases of benign serous tumors.

Mucinous tumors are those which contain intra-cytoplasmic mucin. They may resemble cells of the endocervix, gastric pylorus or intestine. In some tumors only scattered goblet cells are present in an epithelium that is otherwise non-mucinous.[2] Mucinous tumors account for 15% of all ovarian tumor in the West but more in the East due to less prevalence of other tumors like serous tumors.[4] In the current study, 25.2% of all epithelial tumors were of mucinous type (50 cases) of which benign, borderline and malignant tumors are 34 cases(68%), 6cases(12%) and 10 cases (20%) respectively. In literature, 75% of mucinous tumors are benign, 20% borderline and 5% malignant.[4,14] So, compared to international data, we had more benign subtype in serous tumors and more malignant ones in mucinous tumors. Mucinous neoplasm tend to be the largest of all ovarian tumors and many of them are known to be 30-55 cm in diameter and weigh 2 to 4kgs.[16] The mucinous cystadenoma may be unilocular, but more often has many locules with thin walls and contain thick to watery mucinous fluid.[16] Microscopically, this tumor is composed of glands and cysts that occasionally contain papillae with fibrovascular cores.[16,17] The epithelial lining typically resemble endocervical epithelium consisting of single row of uniform mucin producing cells with basal nuclei.[8,16] They are associated with dermoid cysts in up to 5%.[8] Our study showed 2 cases of combine mucinous cystadenoma with mature cystic teratoma. We also had 2 cases of combined serous and mucinous tumor (Table 1).

Brenner tumors are composed of epithelial elements histologically resembling urothelium.[18] Brenner tumors comprise less than 5% of all benign epithelial tumors.[2] Most of them are found incidentally and are of less than 2cm in size.[4,19] These tumors were seen in all age groups and 3.6% cases were seen in the pediatric age group.[20] Microscopically, they show well defined small nests of transitional cells with intervening fibromatous stroma. Nuclei show typical grooved coffee bean appearance (fig.1). In our study, we had 7 Brenner tumors and 1 cases of mixed serous tumor with Brenner areas. All 7 pure cases were less than 10cm in size and 1 case of mixed serous and Brenner was more than 10cm.

Borderline epithelial tumors

Mucinous borderline ovarian tumors have low malignant potential and exhibit an epithelial proliferation of mucinous type cells greater than that seen in their benign counterparts but without evidence of stromal invasion.[16] Mucinous borderline tumors are further subdivided into endocervical and intestinal type. In endocervical type, the epithelial cells lining the papillae are columnar mucinous cells and rounded cells with eosinophilic cytoplasm; the latter are often markedly stratified with detached cell clusters. The epithelial component may resembles intestinal type containing goblet cells, or may contains neuroendocrinecells and rarely contains paneth cells.[2]

We reported 6(3%) cases of mucinous borederline tumor in the study period. Microscopically, cells formed 3 or less layers with or without papillae over a continuous extent of at least 5mm.[4,21,22] Out of 6 cases, 5 cases were more than 40 years age and one case was below 40 years, all were unilateral and four cases were of size more than 10cms. In our study, three cases showed endocervical type of lining epithelium (fig.2). Borderline tumors may show peritoneal implants and lymphatic metastasis and these findings should not lead to an erroneous diagnosis of carcinoma in a morphologically borderline tumor.[14,22] Our cases however did not show any implants or metastasis.

Serous borderline tumor are of low malignant potential exhibiting an atypical epithelial proliferation of serous type cells greater than that seen in their benign counter parts but without destructive stromal invasion.[2] In our study, we did not come across any serous borderline tumor.

Malignant epithelial tumors

Cancers of the ovary represents about 30% of all malignancy of female genital tract.[16] And approximately 90% of primary malignant ovarian tumors arise from the ovarian surface epithelium.[13] We had 44 cases of carcinomas comprising 22.2% of all surface tumors.The mean age was 43.23 years

and almost the same age incidence (42 to 48) is reported in other studies as well.[11,21,23-25].

Serous adenocarcinoma comprises 80% to 84% of all ovarian carcinoma in Western world.[26] Seidman et al in their study of 220 ovarian carcinomas found that 70% were of serous origin.[26] We had 32 cases of serous adenocarcinoma comprising 72.7% (32/44) of all malignant surface epithelial tumors. Serous carcinomas range from predominantly cystic papillary tumors to entirely solid, soft or hard masses, often having papillary surfaces.[8,15] Two third of these tumors are bilateral .We had 8 cases (out of 32) of malignant serous tumors with bilateral involvement (fig.3). Microscopically, serous carcinomas are characterized by more extensive cellular budding, more confluent cellular growth and almost always with greater nuclear atypia (fig.4). The extent of papillarity and psammoma bodies varies greatly in serous carcinomas.[13,15] Serous carcinomas show a very wide spectrum of morphological appearances which contrasts with most other primary ovarian carcinomas in which morphologic variation is considerably less. The morphologic and genetic heterogeneity suggests that serous carcinomas may represent transformation or progression from other tumor types.[27] Most serous carcinomas demonstrate papillary and micropapillary architecture with evident of slit like spaces. Focally glandular, cribriform, solid, microcystic and trabecular pattern can also predominate.[27-29] They can be graded according to nuclear atypia, atypical mitosis and the extent of papillae/ glands.[8] Papillae and solid sheets of malignant cells, increased atypical mitosis, necrosis were seen in large number of our cases. Lymphovascular emboli and tumor deposits on the ovarian surface, fallopian tubes, uterine surfaces and peritoneal/omental implants were also noted (Table 2). Apporximately 30% of this type are known to show psammoma bodies, we found it only in 3 cases (19%).[14]

Mucinous adenocarcinomas are very uncommon and composed fewer than 3% of primary ovarian carcinomas in the Seidmanand other series.[26,29] Our study showed 10 mucinous carcinomas. Grossly, they are more often multilocular with mucoid material.[17,27] Mucinous carcinomas display a limited range of histologic appearances. Although, identifying intracytoplasmic mucin is mandatory, many mucinous tumor lack apical mucin in large parts of tumor, thereby imparting endometrioid appearance. Most primary mucinous carcinomas display transition from mucious borderline to carcinoma.[27] The malignant area may be quite small and hence a generous sampling of all mucinous tumors are advised.[2] In our study, among 10 cases, 6 showed multiloculated cyst on gross examination (fig.5). If frank stromal invasion (>10mm^2 area) is not seen, papillary areas or back to back malignant glands with even little stroma may be assumed as invasion.[2] Many mucinous tumors may show overt gland formation with less intracytoplasmic mucin mimicking endometrioid carcinoma.[13,27] The main differential diagnoses include endometrioid carcinoma, serous carcinoma with intraluminal mucin and metastatic adenocarcinoma. Coexisting mucinous borderline tumor, absence of endometriosis and squamous metaplasia favor a mucinous neoplasm instead of an endometrioid tumor.[27]

The great majority of malignant Brenner tumors occur in 50-70 years age group.[30] Only 5% of Brenner tumors are malignant.[2,30] Malignant Brenner tumors typically have both solid and cystic components grossly, with the cysts containing papillary or polypoidal masses or solid nodules in their wall.[18] Twelve percent of malignant Brenner tumors are bilateral.[31-32] Transitional cell carcinomas grossly resemble other carcinomas of epithelial–stromal type, but differ from malignant Brenner tumors by lacking gritty areas of calcification, which are evident in half cases of malignant Brenner tumors.[18,33] Obviously invasive components of malignant Brenner show predominantly malignant appearing transitional cells or squamous cells and may contain mucinous cells as well.[18] Occasionally tumors composed of crowded, irregular islands of malignant transitional cells with low grade features.[34] In our study, we found 2 cases of malignant Brenner in 43 and 66 years old females and the size were 12 and 25cm respectively. In both the cases extensive areas of necrosis along with high grade transitional cell carcinoma was noticed. In the first case, right side showed mature cystic teratoma and the left side showed malignant Brenner tumor (fig.6).

Endometrioid adenocarcinoma is the 2nd common ovarian carcinoma subtype in the West accounting for 7 to 20% of ovarian carcinoma in different international studies.[26,27] Although rare, clear cell carcinoma is the 3rd most common ovarian carcinoma in North America and accounts for approximately 5% of all ovarian tumors.[27] In our study, we did not come across both of these tumor types.

CONCLUSION

In our study, surface epithelial tumors comprised 58% of all ovarian tumors. Among both benign and malignant tumors, serous type was the commonest followed by mucinous type. They are unique in exhibiting significant heterogeneity in cell populations and morphological patterns with combination of more than one histological type. The histopathological findings and age distribution of these tumors corroborated well with other contemporary studies.

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