Borderline Ovarian Epithelial Cancer

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Epidemiology

Ovarian tumors account for a considerable proportion of clinically important neoplasms in the female. 85% of them occur in women between ages of 20-65 years. Two-thirds (62%) occur in women of reproductive age while less than 3% occur in children age less than 15 years[1].

In general, 75-80% of ovarian tumors are benign in origin. Tumor registry based on 8 years period in King Chulalongkorn Memorial Hospital showed that patient age is considered to be a strong factor related to tumor nature type. It was found that 78% of benign ovarian tumors occur in women age less than 45 years while 55% of ovarian cancer is detected in women after the age of 45 years. Chance of cancer declined in relation with age as less than 10% of our ovarian cancer was detected in women after the age of 65 years[1].

The chance that a primary ovarian epithelial tumor in a patient under the age of 45 years was of borderline or invasive cancer was 1 in 7 or 14%. The chance that a primary ovarian epithelial tumor in a patient above the age of 40 years was of borderline or invasive cancer was 1 in 2.5 or 40%

Approach to an adnexal mass

It is generally accepted that most palpable adnexal mass are ovarian in origin. Endometriotic cyst is the most common mass encountered, followed by epithelial stromal tumor and tumor originated from germ cell type. Other tumor-like conditions such as hydrosalpinx, parovarian cyst or pseudocyst can mimic and present as an adnexal mass and required surgical attention indifferent from prevously mentioned tumor. It is agreed that ultrasound is not only to confirm the presence of adnexal mass but also to classify tumor according to its nature, benign or malignant. According to our presurgical ultrasound finding, we were able to delineate role of ultrasound in differentiating benign and malignant mass.

Based on 440 adnexal masses, endometriotic mass accounted for 169, epithelial stromal tumor 196, germ cell tumor 73.

Criteria used for ultrasound were 1) unilocular or multilocular cystic mass. 2) Unilocular or multilocular cystic-solid mass. 3) Solid mass. All of these adnexal masses were operated and their histologic diagnosis was then correlated with previous ultra-

Table 1. Frequency of ovarian tumor type based on age[1]

	Age < 45	Age > 45
Benign	78%	12%
Malignant	45%	55%

P< 0.05

Table 2. Distribution of ovarian masses (N= 440 cases)

Endometrioma	169
Epithelial-stromal tumor	196
Benign	81
Borderline	23
Malignant	92
Germ cell tumor	73
Cystic teratoma	55
Malignant germ cell tumor	18

Table 3. Distribution of ultrasound finding related to surgical pathologic finding (N= 426 cases)

	Cancer	Benign	Cases
Cystic-solid	94	42	136
Cystic	39	251	290
	133	293	426

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sound finding.

In this calculation, borderline tumor was included into ovarian cancer. It appeared that ultrasound could have detected borderline or malignant tumor approximately 70% of cases. Subgroup analysis failed to improve sensitivity when cystic ovarian mass size was incorporated into calculation.

Borderline ovarian tumor[2]

World Health Organization classification system is currently used to classify ovarian tumors that originate from surface epithelium and the adjacent stroma based on:

1. Epithelial cell type
2. Histologic pattern
3. Degree of epithelial proliferation

Based on our retrospective review from 1990-2004, there were 140 cases of borderline ovarian tumor. Less than 10% occur in women age less than 20 years. Half occur in women of reproductive age. 40% of borderline tumors are detected in women after the age of 45 years and 20% of them are detected in women after the age of 65 years.

A borderline mucinous tumor is much more common in Thailand as in Japan compared to other western countries. Only one-forth are of serous type. Borderline mucinous tumor was classified into a more common intestinal type and endocervical or mullerian type. Likewise, bilateral involvement of borderline serous tumor is more common than of mucinous type.

Management of borderline ovarian tumor

It is prudent to note that diagnosis of borderline ovarian tumor may arise after exploratory laparotomy. Frozen section seemed to be unreliable and difficult to differentiate borderline and malignant status with highest accuracy. In clinical practice, a surgeon who takes command of that particular surgery will be the one who has to navigate necessary surgi-

Table 4. Diagnostic ultrasound accuracy

Sensitivity	94/133	70.7%
Specificity	251/293	85.7%
Positive predictive value	94/136	69.1%
Negative predictive value	251/290	86.6%

Into

1. Serous	Borderline	Carcinoma
2. Mucinous	Borderline	Carcinoma
3. Endometrioid	Borderline	Carcinoma
4. Clear cell	Borderline	Carcinoma
5. Transitional	Borderline	Carcinoma
6. Squamous cell tumors	Borderline	Carcinoma

We used Scully's criteria to diagnose borderline ovarian tumor. [3]

Tumor of low malignant potential (LMP):
no obvious stromal invasion
1. with epithelial atypia
   1.1 classic LMP
   1.2 LMP with microinvasion
2. with intraepithelial carcinoma

Carcinoma: obvious stromal invasion
1. disorderly penetration of the cyst wall or the stromal component of a predominantly fibromatous tumor by carcinoma cells, with or without stromal reaction
2. confluence of carcinoma in the cyst wall or the stromal component of a predominantly fibromatous tumor

Table 5. Borderline ovarian tumor classified into mucinous, serous, clear cell and endometrioid cell type, Chulalongkorn Hospital 1990-2004 (n = 140 cases)

Mucinous	104		75%
- Intestinal		78.0%	
- Endocervical		19.1%	
- Mixed type		2.7%	
Serous	32		25%
Clear cell	2		1
Endometrioid	1		1

Table 6. Differences between endocervical and intestinal type mucinous borderline tumors[4]

	Intestinal	Endocervical
Age (yrs)	41	34
Bilaterality (%)	6	40
Diameter (cm)	19	8
Multiloculated	72	20
Argyrophil cells (%)	91	3
Acute inflammation (%)	22	100
Endometriosis (%)	6	30
Pseudomyxoma peritonii (%)	17	0

Table 7. Bilateral involvement of ovarian tumor[$]

	Mucinous	Serous
Benign	2.4	4.6
Borderline	3.3	16.7
Malignant	11.1	34.3

cal procedure and bear full responsibility when final diagnosis is made couple days later. If proper ultrasound reading is implemented, we can achieve a 70% of probability to correctly diagnose borderline and malignant tumor while 87% of benign masses are excluded. In fact this is merely a preoperative setting and different story occurs as of in real life. In the hands of experienced gynecologists, operative diagnosis can be made easily with great accuracy for endometriotic cyst and mature cystic teratoma. After excluding these two big players, endometriotic cysts and cystic teratoma, a proportion of epithelial-stromal tumor will be left for scrutiny. Our pathologists from Chulalongkorn hospital showed that among these ovarian cystic masses, benign tumor account for 83.8%, borderline tumor 4.9% and cancer of 11.5% if endometriotic cysts were excluded. Since mature cystic teratoma accounted for nearly half of total cases, after exclusion, odd ratio for malignancy sharply surged to 17.8%.

This is roughly estimated that after exclusion of both endometriotic cyst and cystic teratoma, 17.8% of ovarian mass which surgeons are confronting are possessing malignant risk including a borderline tumor.

It is noteworthy that mucinous and serous tumor share equal proportion of tumor masses. Borderline tumor is more common in mucinous tumor than in serous type while malignancy is commonly found in serous tumor as shown in Table 11.

Table 8. Age distribution relative to ovarian neoplasm type, Chulalongkorn Hospital 1999-2003 (n = 924)

Years	Dermoid	Malignant germ cell	Sex-cord	Benign epithelial	Border-line	Malignant
11-20	19	13	-	19	4	1
21-30	152	9	2	48	6	4
31-40	125	2	12	69	10	10
41-50	66	-	9	86	6	28
51-60	23	-	5	50	11	19
61-70	8	-	8	33	4	13
>70	9	-	2	17	4	5
	402	24	38	333	45	82

Table 9. Ovarian neoplasm after excluding mature cystic teratoma

Ovarian epithelial stromal tumor	460 cases
Benign	72.4%
Borderline	9.8%
Malignant	17.8%

Most of mucinous tumors contain mucin-like material. If mucinous content was found at the time of adnexectomy, a more conservative approach is possible since the chance that the tumor will be borderline and malignant is quite equal. In contrast, if the

Table 10. Age distribution relative to ovarian neoplasm type after exclusion of mature cystic teratoma (n = 460)

Years	Benign	Borderline	Malignant
11-20	19	4	1
21-30	48	6	4
31-40	69	10	10
41-50	86	6	28
51-60	50	11	19
61-70	33	4	13
> 70	17	4	5
	333	45	82

Table 11. Distribution of tumor type based on mucinous or serous tumor (n= 439)

Epithelial-stromal tumor		Mucinous n = 179	Serous n = 207
Benign	72.4.%	73.7%	86.9%
Borderline	9.8%	18.4%	4.8%
Malignant	17.8%	7.8%	8.2%

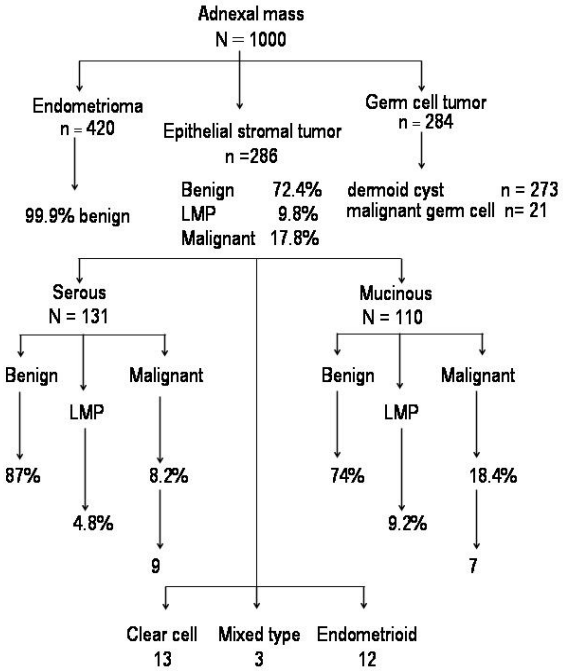

Fig. 1 Shematic flow chart of 1000 apparent adnexal masses

content is serous, then a more aggressive approach is unavoidable since one third of them finally turned out to be malignant. The above statement is skeptic and quoted with intention to enlighten the way we can approach the ovarian mass in the operating room. Since intracystic serous or mucinous content is not well accepted as a tool to predict likelihood of serous or mucinous tumor type. Whenever borderline ovarian tumor is suspected, appendectomy should be done. Undoubtedly, its presence is strongly correlated with microscopic finding in the appendix. Borderline ovarian tumor may arise from the appendix or lesion in the appendix metastasized from the ovary. It is then advocated that ovarian tumor contaning mucin should be remove along with appendectomy. Definitive surgery, total hysterectomy and bilateral salpingoophorectomy should be reserved in women who have strong evidence of cancer such as intracystic papillary structure or solid component.

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