Histologic Types of Ovarian Tumors in Maharaj Nakorn Chiang Mai Hospital

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Abstract : *Based on histopathologic study, the relative frequency of ovarian tumors in Maharaj Nakorn Chiang Mai Hospital from January to December 1993 was analysed. Among 221 cases, 212 were primary neoplasms. Mature cystic teratoma was most commonly encountered (34%), followed by mucinous cystadenoma (19%) and serous cystadenoma (10%). For each histogenetic group, 51% of all primary tumors were common epithelial tumors, 7% were sex cord-stromal tumors, and 41% were germ cell tumors. In contrast to reports from western countries, mucinous tumor was more common than serous type with a ratio of 1.9:1 for benign group and 14:1 for borderline group. The relative frequency of granulosa cell tumor and malignant germ cell tumor was also higher than that of western countries. (Thai J Obstet Gynaecol 1995;7: 41-49.)*

Key words: ovary, tumor, histology

Histological typing of ovarian tumors, which was proposed by the World Health Organization (WHO) in 1973[1], has provided an internationally acceptable classification that can be used to investigate epidemiology and compare therapeutic results from different institution. Most of the published data, however, were from western studies[2-6] and only a small numbers were carried out in Asian countries including Thailand[7-9].

The purpose of this study was to analyze the frequency of various histologic types of ovarian tumors in Maharaj Nakorn Chiang Mai Hospital and to compare our findings with those presented in the International Union Against Cancer (UICC) Technical Report Series Volume 75[2].

Materials and Methods

The Maharaj Nakorn Chiang Mai Hospital (1500 beds) is the sole university hospital in Northern Thailand. The hospital serves not only as a primary health care center for

people in Chiang Mai province but also a referral center for other regional and community hospitals in the Northern region.

The cases included in this study were all ovarian tumors diagnosed in the department of Pathology between January and December 1993. Almost all cases (97.3%) had an adequate tissue sampling defined as minimum of 4 sections for benign tumors and 1 section per 1 cm. of the greatest dimension of the tumor particularly solid or papillary area for borderline and malignant tumors.

Hematoxylin and eosin stained (H&E) sections were performed routinely in each case. While special stains would be provided if necessary either histochemical stains (Mayers's mucicarmine, periodic acid Schiff and Grimelius) or immunohistochemical studies (antibodies for cytokeratin, carcinoembryonic antigen, alphafetoprotein, estrogen and progesterone related receptor protein, chromogranin, serotonin and myoglobin).

Each tumor was classified according to the standard nomenclature for ovarian tumors by the WHO classification. Ovarian endometriosis, simple cyst and tumor like lesions were excluded. Among the epithelial group, the borderline tumor (BT) or tumor of low malignant potential (LMP) was defined using the following criterion, presence of unusual proliferative activities characterized by nuclear atypia with stratification, increased mitotic activity, and tendency of separation of cellular buds floating in the lumen or on the surface. Presence of stromal invasion distinguished the malignancy or carcinoma from the BT or LMP. Another criteria for diagnosis of mucinous carcinoma, despite no evidence of stromal invasion, was nuclear atypia with stratification for 4 or more layers. Mixed epithelial tumor was diagnosed if more than one histologic type was seen in the same specimen and the minor element accounted for at least 10% of the representative tissue.

Additional information including age, laterality, and size of tumor were obtained from the pathology reports. The result of this study was compared to the comparative data of ovarian neoplasms from different geographic areas reported by Stalsberg et al[2]. To compensate the difference in age structure of the studies population, age standardized relative frequencies using the same unweighted mean percentage as Stalsberg's report were applied for statistical analysis.

Results

A total of 221 cases of ovarian neoplasms was histologically diagnosed during a one year period, of which 212 were primary and 9 were metastatic tumors. Table 1 listed the relative frequency of primary ovarian neoplasms. The most common tumor was mature cystic teratoma (73 cases or 34.4%). The next three most common tumors were mucinous cystade-

noma (41 cases or 19.3%), serous cystadenoma (21 cases or 9.9%) and mucinous LMP (14 cases or 6.6%). Among the 47 truly malignant tumors, endometrioid carcinoma (9 cases or 19%) was most commonly seen followed by serous carcinoma (8 cases or 17%) and granulosa cell tumor (6 cases or 12.8%).

Benign, LMP Malignant Tumors

The relative frequency of benign, LMP and malignant tumors is shown in Table 2. Benign tumors (149 cases) accounted for 70.3% while the LMP (16 cases) and malignant (47 cases) were 7.5% and 22.2% respectively. The total epithelial tumors (including 16 LMP) were 108 cases (50.9%), whereas, the sex cord stromal tumors were 15 cases (7%) and germ cell tumors were 88 cases (41.5%). Among the tumors classified as ovarian cancer (including LMP), 68% were epithelial type, 9.5% were sex cord stromal tumors and 20.6% were malignant germ cell tumors. If only truly malignant tumors were considered, epithelial tumors (27 cases) accounted for 57.4%. Sex cord stromal tumors (6 cases) and germ cell tumors (13 cases) shared 12.8% and 27.7% respectively.

Sixteen epithelial tumors were classified as LMP, of which 14 were intestinal mucinous LMP. The remaining two were serous and endometrioid type.

Table 1 *Relative frequency of primary ovarian neoplasms*

Primary ovarian neoplasms	No. of cases	%
Mature cystic teratoma	73	34.4
Mucinous cystadenoma	41	19.3
Serous cystadenoma	21	9.9
Mucinous borderline tumor (MLMP)	14	6.6
Endometrioid carcinoma	9	4.2
Fibroma/thecoma	9	4.2
Serous carcinoma	8	3.7
Gramulosa cell tumor	6	2.8
Clear cell carcinoma	4	1.9
Immature teratoma	4	1.9
Dysgerminoma	4	1.9
Endodermal sinus tumor	4	1.9
Mucinous carcinoma	3	1.4
Struma ovarii	2	0.9
Brenner tumor, benign	2	0.9
Carcinosarcoma	2	0.9
Other	6	2.8
	212	100

Table 2 *Relative frequency of types of primary ovarian neoplasms*

Type	No. of cases	%
Benign	149	70.3
Epithelial	65	
Sex cord stromal	9	
Germ cell	75	
Borderline (LMP)	16	7.5
Malignant	47	22.2
Epithelial	27	
Sex cord stroma	6	
Germ cell	13	
Other	1	

Table 3 *Frequency of subtypes of serous and mucinous tumors*

Type	serous	%	mucinous	%	Ratio of serous/mucinous
Benign	21	70.0	41	67.8	0.5
Borderline	1	3.3	14	25.4	0.1
Malignant	8	26.7	3	6.8	2.0
Total	30	100	58	100	

Comparison between serous and mucinous tumors was presented in Table 3. In the benign group, the number of mucinous tumor was almost twice that of serous tumor. This held true for LMP which the mucinous LMP was much more common than serous LMP (14:1). On contrary, the serous carcinoma was seen more frequently than mucinous carcinoma (8:3).

AGE

The frequency of primary ovarian tumors relating to the age distributions was shown in Table 4. It is notable that 73% of all benign tumors and 50% of all LMP occured in patients under the age of 45 years, while 33% of malignant epithelial tumors were seen in patients under 45 and only one of 27 cases (3.6%) was under 35. Malignant nonepithelial tumors were commonly encountered in patients under 45 (15 of 20 cases or 75%) and 76.9% of malignant germ cell tumors (10 of 13 cases) were seen in women younger than 35.

Table 4 *Types of tumors related to patient age*

Age	Benign	Borderline	Malignant		
			Epit.	Non-Epit.	Total
< 15	1	0	0	4	4
15-24	21	1	0	4	4
25-34	42	3	1	3	4
35-44	42	4	8	4	12
45-54	19	6	4	4	8
55-64	11	2	9	1	10
65-74	11	0	5	0	5
>74	1	0	0	0	0
unkown	1	-	-	-	-
Total	145	16	27	20	47

Bilaterality

Bilaterality of the tumors was found in 68.5% of serous carcinoma, 55% of endometrioid carcinoma, and 33% of mucinous carcinoma. Among the benign group, 13.7% of mature cystic teratoma as well as one Brenner tumor and one mucinous cystadenoma showed bilateral involvement. None of the serous cystadenoma had bilateral tumors.

Metastatic Tumor

Of all 9 metastatic tumors to the ovary, 7 were adenocarcinoma, one was squamous cell carcinoma, and one was high grade stromal sarcoma.

Comparative Data

Based on the same unweighted mean percentage as Stalsberg's report, the age standardized relative frequencies were calculated and compared to data from different geographic areas including Sendai (Japan), Bombay (India), Recife (Brazil), New Orleans (USA), Birmingham (England) and Norway.

Figure 1 shows the proportion of benign, LMP and malignant epithelial neoplasms. Range of proportion from 2% (Bombay and N.O. black) to 16.3% (Chiang Mai) was observed in the LMP. Proportion

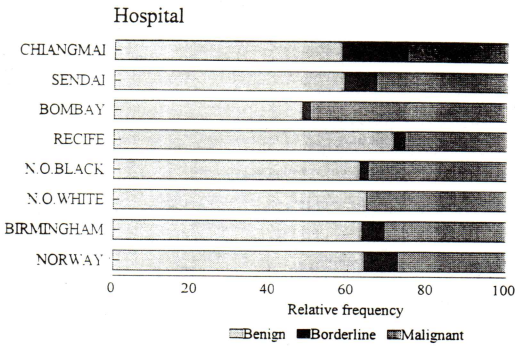

Fig. 1 Relative frequency of subtypes of epithelial tumors

of the two most common benign epithelial tumors, serous and mucinous, was presented in Figure 2. Serous cystadenoma was more frequently encountered than mucinous tumors in New Orleans (55:26.7 and 64:36) and Birmingham (54.8:43.6). In Sendai (43.8:49.7) and Chiang Mai (30.5:64.9), however, the serous type was less common than the mucinous. The highest proportion of serous cystadenoma was reported from Recife, but it was noted that non-neoplastic tumor like lesions were included in the same category.

Figure 3 shows the ratio of serous to mucinous tumor among benign, LMP and malignant subtypes. The lowest ratio for the LMP was 0.1 (Chiang Mai). The ratio was also lower in Sendai and Bombay than in Birmingham and Norway. These findings indicate that mucinous LMP was more common in Asian countries.

For the sex cord stromal tumors, the proportion of granulosa cell tumor and thecoma fibroma was presented in Figure 4. Higher proportion of the granulosa cell tumors (37.1 to 40.5%) was found in developing countries and African American while a lower frequency (5.4 to 20.4%) was seen in white and Japan (Sendai). Finally, Figure 5 indicate that the proportion

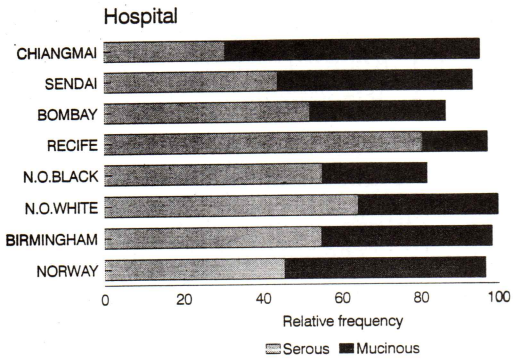

Fig. 2 Relative frequency of benign common epithelial tumors

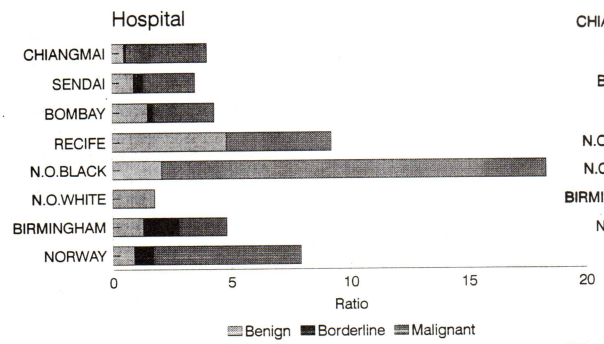

Fig. 3 Ratio of serous to mucinous tumors

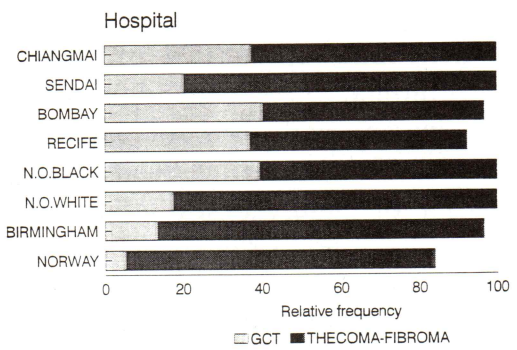

Fig. 4 Relative frequency of sex cord-stromal tumors

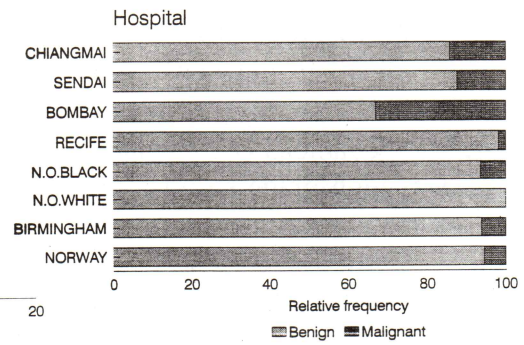

Fig. 5 Relative frequency of germ cell tumors

of malignant germ cell tumor was higher in Asian countries (12.5 to 33.0%) than that in western countries (0 to 6.3%).

Discussion

An international comparison of histologic types of benign and malignant ovarian tumors in general hospital material reported by Stalsberg et al. has provided the relative frequencies of each histogenetic group that 54% of all ovarian neoplasms were common epithelial tumors, 10% were sex cord stromal tumors and 35% were germ cell tumors[2]. In our study, the common epithelial tumors accounted for 50.9% with 7% of sex cord stromal tumors and 41.5% of germ cell tumors. Although these proportions seemed to be comparable, remarkable dissimilar findings in five subtypes were also noted and each will be discussed separately.

For the benign epithelial tumor, western countries reported that the serous cystadenoma was more common than mucinous cystadenoma with a ratio ranging from 1.3:1 to 2.2:1[2-4]. Our study and another report from a university hospital in Bangkok (Thailand)[9] showed that the serous type was less common than the mucinous type with a ratio of 0.5:1 and 0.4:1 respectively. This histologic distribution may be influenced by geographic difference rather than the use of variable diagnostic criteria.

Within the group of tumors of low malignant potential (LMP), a higher proportion of the mucinous LMP than the serous LMP in our study was supported by another two reports from the university hospital in Bangkok (Thailand)[8-9] and a report from Japan[7]. The ratio of serous to mucinous LMP from these studies ranged from 0.1 to 0.5, whereas, such a ratio from the western countries ranged 1.4 to 2[3-4]. Although the different distribution may possibly be due to varied diagnostic criterion to distinguish between benign and LMP, and between LMP and malignant tumors, the geographic influence also, perhaps, played a significant role.

As shown in Figure 1, the proportion of LMP varied from area to area and ranged 2.0 to 16.3% of all epithelial neoplasms. The difference may be influenced partly by different distribution in each area and partly by variation in the diagnostic criteria used among each institution.

Diagnosis of LMP was a subject of variability among pathologists. Although diagnostic criteria to differentiate LMP from either benign or malignant type has already been described[10], diagnostic decision was mainly depended on an individual subjectivity which was affected by variation of threshold from person to person. This problem was a well-recognized cause of under report of LMP and less reliability of incidence LMP in the cancer registries. Some LMP may be diagnosed as benign tumor, whereas some may be diagnosed as malignant. In our study,

6 of 16 LMP were in-itially reported as benign tumors.

The proportion of the truly malignant epithelial tumors in our study was also different from western studies. In the present report, carcinoma of the ovary accounted for 57.4% of all malignant tumors. This percentage was comparable to the report from Japan (63.9%)[7] but lower than that of reports from Western countries (85.5 to 92.3%)[3-4]. In contrast, the malignant germ cell tumors were more commonly seen in Asian countries, accounted for 20.6% of ovarian cancer in our study and ranged from 17.2 to 25% in the report from Japan[7]. This proportion was only 2.5 to 7% in the Western series[3,4,6]. We agreed with Nakashima et al. that higher relative frequency of the malignant germ cell tumors was considered to reflect a much lower relative frequency of malignant epithelial tumors. Comparison between various histologic subtypes of both malignant epithelial and germ cell tumors was limited because our study had smaller numbers of malignant tumors.

Among the sex cord stromal group, the proportion of the granulosa cell tumor in our study (37.6%) as well as in other developing countries (40.5% in Bombay, 37.1% in Recife) and African American (39.6%) was higher than that of reports from Japan and other developed areas (5.4 - 20.4%)[2,3].

In conclusion, the present study report the histologic distribution of ovarian tumors during a one year period in Maharaj Nakorn Chiang Mai Hospital. Comparison between our data and other reports especially from western countries showed remarkable different findings including 1) in this study, the mucinous cystadenoma and mucinous LMP were more common than the serous type 2) the relative frequency of the malignant epithelial tumor was lower, whereas, that of the malignant germ cell tumor was higher than in western countries 3) the relative frequency of granulosa cell tumor was higher in developing countries and African American.

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