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**Original Research**

# The incidence and extent of Müllerian metaplasias in ovarian surface epithelial tumors

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**Keywords:** Ovarian cancers, metaplastic changes, Müllerian system, ovarian carcinogenesis.

**Abstract**

**Objectives:** Most ovarian surface epithelial tumors emerge from a background of Müllerian metaplasias. The incidence and extent of Müllerian metaplasias were examined in ovarian surface epithelial tumors.

**Methods:** The incidence of Müllerian metaplasias was evaluated according to the presence of the metaplasias in all cases. The extent of these metaplastic changes was scored from (1+) to (4+) according to the extended area in all tumoral slide sections.

**Results:** Ciliated cell metaplasia was found in 80.4 % of benign tumors, 100 % of borderline tumors and 93.3 % of malignant tumors. Eosinophilic cell metaplasia was present in 13 % of benign tumors, 70 % of borderline tumors and 93.3 % of malignant tumors. Clear cell metaplasia was observed in 17.4 % of benign tumors, 20 % of borderline tumors and 40 % of malignant tumors. While ciliated cell metaplasia was more frequent and extensive in benign tumors, eosinophilic and clear cell metaplasias were more frequent and extensive in borderline and malignant tumors ($p<0.05$).

**Conclusions:** Our findings suggest that the incidence and extent of Müllerian metaplasias in ovarian surface epithelial tumors may not be homogeneous. This should be taken into account when their biological significances and relation with tumorigenesis are investigated.



## INTRODUCTION

The ovarian surface epithelium and Müllerian duct epithelium share a common origin, which is the mesoderm lining of the celomic cavity [1]. At various ages, but particularly in the reproductive, menopausal and postmenopausal women, this surface epithelium may migrate into the ovarian stroma to form inclusion cysts. The epithelium of inclusion cysts has the potential to differentiate into epithelia resembling those of normal Müllerian derivations (tubal, endometrial and endocervical epithelia) and the tumors are similar to those of the fallopian tube, endometrium and endocervix [2-4].

Most ovarian malignant surface epithelial tumors probably arise from the mesothelial surface epithelium or inclusion cysts [2-7]. Inclusion cysts have a greater potential to undergo neoplasia than does the surface itself. It has been suggested that most epithelial ovarian tumors are intraparenchymal, rather than being situated on the ovarian surface [3]. Immunohistochemically, some studies have demonstrated that various ovarian carcinoma antigens are far more frequent in the inclusion cyst epithelium than in the surface epithelium [5, 12, and 9]. This proportion is even higher in metaplastic areas of the inclusion cyst epithelium. These metaplastic changes may be seen in tumors or inclusion cysts of the contralateral ovary without the presence of tumors. It has been suggested that most of the ovarian surface epithelial tumors emerge from a background of these Müllerian metaplasias, and may initiate a neoplastic process in these cysts [4-6].

Although the histogenesis of ovarian epithelial cancers is still controversy, it is widely believed that most of them arise from the ovarian surface epithelium as mentioned above [10]. However, recent histopathologic and molecular genetic studies regarding ovarian

carcinogenesis have led to the development of a new paradigm for the pathogenesis and origin of ovarian epithelial cancers based on a dualistic model of carcinogenesis that divides ovarian epithelial cancers into two categories designated types I and II [11-14]. Several studies have shown that high grade or low grade serous, endometrioid, and clear cell carcinomas are characterized by several mutations, such as TP53, K-ras/BRAF, CTNNB1, and PIK3CA genes, respectively. Type I carcinomas (low-grade serous, mucinous, and endometrioid) commonly arise from precursor lesions. These tumors manifest as large adnexal masses with early-stage disease and have a relatively indolent clinical course. Contrary, type II carcinomas (high-grade serous, endometrioid, and undifferentiated carcinomas) arise de novo from the adnexal epithelia. They often have chromosomal instability, and aggressive biologic behavior. As a result of these developments, recent studies strongly suggest that fallopian tube epithelium, either benign or malignant, is the source of low-grade and high-grade serous carcinoma rather than the ovarian surface epithelium as previously believed [14].

In this study, it was investigated the relationship between malignant transformation and the incidence and extent of Müllerian metaplastic changes in various ovarian surface epithelial tumors. The current study is the first report suggesting that distribution of the metaplastic changes in ovarian surface epithelial tumors is heterogeneous.

## MATERIALS AND METHODS

This retrospective study included 86 ovarian epithelial tumors consisting of 46 benign tumors, 10 borderline tumors and 30 malignant tumors. Benign tumors consisted of 13 serous cystadenofibroma, 15 serous cystadenoma, 3 serous papillary cystadenoma 1 mucinous cystadenofibroma, 13 mucinous cystadenoma and 1 mucinous papillary cystadenoma. Müllerian metaplastic changes in ovarian inclusion cysts of 15 control cases with hysterectomy due to uterine leiomyoma were also examined (Table 1-3). The age of two cases (one of cases benign, the other malignant tumor) and tumor diameter of one of malignant tumors could not be determined. The bilaterality was 13.3 % (2/15) in control group, 21.7 % (10/46) in benign tumors, 20 % (2/10) in borderline tumors, and 46.6 % (14/30) in malignant tumors. The inclusion cyst in the control groups was 46% (7/15) in the right ovary and 26% (4/15) in the left ovary. The Müllerian metaplastic changes in the endocervix and endometrium of malignant ovarian surface epithelial tumors were also evaluated.

The extent of Müllerian metaplastic changes was scored using following scale: 1-25% (1+), 26-50% (2+), 51-75% (3+) and 76-100% (4+) according to the proportion of the extended area in cystic or glandular lining epithelium of tumor and inclusion cysts (Table 3). It was evaluated about 2-10 tumoral slide sections in each case and about 5-90 microscopic fields in each section. Each slide consisted of 2-3 sections. Distribution and incidence of *ciliated cell metaplasia* in ovarian surface epithelial tumors were shown in Table-4. Extraovarian *ciliated cell metaplasia* in endocervix and endometrium of malignant ovarian tumors was also examined (Table-5). All these changes were evaluated by two experienced observers.

In the evalution of ciliated cell metaplasias, intercalary (or intercalated or peg) cells have been useful in the determination of ciliated cells, because they are usually found near these cells. In particular, these cells are helpful as indicators of ciliated cell metaplasias, when their cilia are exfoliated into the lumen due to autolysis.

Statistical analysis was performed using SPSS 11.0. The incidence of ovarian and extraovarian Müllerian metaplasias was compared using chi-square test. The extent of Müllerian metaplasias was presented by number of cases.

**Table 1**. The incidence of Müllerian metaplasias in ovarian surface epithelial tumors and control group

| Characteristics | Ciliated cell metaplasia | Eosinophilic cell metaplasia | Clear cell metaplasia |
|---|---|---|---|
| | # of cases (%) | | |
| **Control group (n=15)** | 8(53.3) | 0(0) | 0(0) |
| **Benign tumors (n=46)** | 37(80,4) | 6 (13) | 8 (17.4) |
| ***Borderline tumors (n=10)*** | *10(100)* | 7(70) | 2(20) |
| ***Malignant tumors (n=30)*** | *28(93.3)* | 28 (93.3) | 18 (40) |
| | $\chi^2$ = 13.773 p = 0.003 | $\chi^2$ = 62.916 p = 0.000 | $\chi^2$ = 12.980 p = 0.005 |

**Table 2.** The incidence of Müllerian metaplasias according to age, tumor diameter, bilaterality, histological type and subtype, differentiation of ovarian surface epithelial tumors

| Characteristics | | Ciliated cell metaplasia | Eosinophilic cell metaplasia | Clear cell metaplasia |
|---|---|---|---|---|
| | | # of cases (%) | | |
| **Age [decades] (n=99)** | *2-5 (n=49)* | 39 (79.6) | 16 (32.7) | 9 (18.4) |
| | *6 and above (n=50)* | 42 (84.0) | 24 (48.0) | 13 (26.0) |
| | | $\chi^2$ = 0.095 p = 0.758 | $\chi^2$ = 1.825 p = 0.177 | $\chi^2$ = 0.451 p = 0.502 |
| **Tumor diameter (n=85)** | *1-5 cm (n=30)* | *21 (70.0)* | *7 (23.3)* | 6 (20.0) |
| | *6-10 cm (n=33)* | *31 (93.9)* | *18 (54.5)* | 9 (27.3) |
| | *>11 cm (n=22)* | *22 (100.0)* | *15 (68.2)* | 8 (36.4) |
| | | *$\chi^2$ = 13.754 p = 0.001* | *$\chi^2$ = 11.461 p = 0.003* | $\chi^2$ = 1,723 p = 0,422 |
| **Bilaterality (n=28)** | *Control group (n=2)* | 1 (50) | *0 (0.0)* | *0 (0.0)* |
| | *Benign tumors (n=10)* | 10 (100.0) | *2 (20.0)* | *0 (0.0)* |
| | *Borderline tumors (n=2)* | 2 (100.0) | *2 (100.0)* | *0 (0.0)* |
| | *Malignant tumors (n=14)* | 13 (92.9) | *13 (92.9)* | *6 (42.8)* |
| | | $\chi^2$ = 6.462 p = 0.091 | *$\chi^2$ = 30.582 p = 0.000* | *$\chi^2$ = 15.016 p = 0.002* |
| **Benign tumors (n=46)** | *Serous (n=31)* | *28 (90.3)* | 4 (13.3) | 6 (20.0) |
| | *Mucinous (n=15)* | *9 (60.0)* | 2 (13.3) | 2 (13.3) |
| | | *$\chi^2$ = 4.136 p = 0.042* | $\chi^2$ = 0.000 p = 1.000 | $\chi^2$ = 0.019 p = 0.890 |
| **Borderline tumors (n=10)** | *Serous (n=5)* | 5 (100.0) | *5 (100.0)* | 0 (0.0) |
| | *Mucinous (n=4)* | 4 (100.0) | *2 (50.0)* | 2 (50.0) |
| | *Endometrioid (n=1)* | 1 (100.0) | *0 (0.0)* | 0 (0.0) |
| | | No statistics possible | *$\chi^2$ = 6.672 p = 0.036* | $\chi^2$ = 4.463 p = 0.107 |
| **Malignant tumors (n=30)** | *Serous (n=26)* | 24 (92.3) | *26 (100.0)* | 10 (38.4) |
| | *Mucinous (n=2)* | 2 (100.0) | *1(50.0)* | 1 (50.0) |
| | *Endometrioid (n=2)* | 2 (100.0) | *1 (50.0)* | 1 (50.0) |
| | | $\chi^2$ = 0.594 p = 0.743 | *$\chi^2$ = 9.151 p = 0.010* | $\chi^2$ = 0.189 p = 0.910 |
| **Malignant tumors* (n=30)** | *Well differentiated (n=4)* | 4 (100.0) | 3 (75.0) | 0 (0.0) |
| | *Moderately differentiated (n=16)* | 15 (93.7) | 15 (93.7) | 6 (37.5) |
| | *Poorly differentiated (n=10)* | 9 (90.0) | 10 (100.0) | 6 (60.0) |
| | | $\chi^2$ = 0.713 p = 0.700 | $\chi^2$ = 2.716 p = 0.257 | $\chi^2$ = 5.750 p = 0.056 |

* According to histological grading

## RESULTS

The incidence of Müllerian metaplasias in benign, borderline and malignant ovarian surface epithelial tumors and control group was presented in Table-1. *Ciliated cell metaplasia was* more frequent in ovarian surface epithelial tumors than control cases ($p<0.05$). *On the contrary, Eosinophilic* and *clear cell metaplasia* ($p<0.01$, $p<0.05$ respectively) was more frequent in borderline and malignant tumors than benign tumors and control group. *Eosinophilic* and *clear cell metaplasias* were not observed in the control group.

The incidence of Müllerian metaplasias according to clinical features, histopathological subtype and differentiation of ovarian surface epithelial tumors was presented in Tables-2. Between groups by tumor diameter, there were statistically significant differences for *ciliated* and *eosinophilic cell metaplasias* ($p<0.01$). As tumor diameter increased, the incidence of *clear cell metaplasia* relatively increased. But this increase was not statistically significant ($p>0.05$). However, when bilateral cases were compared, statistically significant differences were found for *eosinophilic* and *clear cell metaplasias* ($p<0.01$). The incidence of *ciliated cell metaplasia* in bilateral cases was relatively higher in all types of ovarian surface epithelial tumors than control group. But this difference was not statistically significant ($p>0.05$). *Ciliated cell metaplasia* was more frequent in serous benign tumors than mucinous ones ($p<0.05$). *Eosinophilic cell metaplasia* was more frequent in serous borderline and malignant tumors than mucinous ones ($p<0.05$). There were no statistically significant difference between age groups, subtypes of benign tumors, histological differentiation of malignant tumours for the incidence of Müllerian metaplasias ($p>0.05$). But the incidence of *clear cell metaplasia* was relatively higher in poorly differentiated malignant tumors than moderately

differentiated malignant tumors. But the difference was not statistically significant (p>0.05). This metaplasia was not seen in well differentiated malignant tumors.

In benign ovarian tumors, *ciliated cell metaplasia* was more extensive than *eosinophilic* and *clear cell* metaplasia (Table 3). On the contrary, in malignant ovarian tumors, e*osinophilic and clear cell metaplasias* were more extensive than *ciliated cell metaplasia. The eosinophilic and clear cell metaplasia* in bilateral cases was more extensive malignant tumors than borderline and benign tumors. The *eosinophilic cell metaplasia* was relatively frequent and extensive in moderately and poorly differentiated malignant tumors than well differentiated malignant tumors. C*lear cell metaplasia* was only seen in moderately and poorly differentiated malignant tumors.

*Ciliated cell metaplasia* was usually seen in serous area of mucinous tumors. It was observed in papillary structures, cystic and luminal surfaces (Table 4). Distribution of *ciliated cell metaplasia* was not homogeneous in ovarian surface epithelial tumors.

The incidence and extent of *extraovarian ciliated metaplasia* in patients with malignant ovarian surface epithelial tumors are shown in Table 5. *Ciliated cell metaplasia* was observed in two synchronized ovarian and endometrial malignant tumors (endometrioid type). The incidence of *extraovarian ciliated cell metaplasia* in endocervix and endometrium of patients with malignant ovarian tumors was relatively increased, as tumor diameter was increased. But this was not statistically significant (p>0.05). It was more frequent in endometrium of patient with endometrioid malignant ovarian tumors than serous ones (p<0.05). While it was relatively more frequent in endocervix of patient with endometrioid malignant ovarian tumors than serous ones, there was not statistically significant difference (p>0.05). It was not seen in endometrium and endocervix of patient with mucinous malignant ovarian tumors. It was more frequent in well differentiated malignant ovarian tumors than the others. But this was not statistically significant (p>0.05).

**Table 3.** The extent of Müllerian metaplasias in ovarian surface epithelial tumors

| Characteristics | | Ciliated cell metaplasia | | | | Eosinophilic cell metaplasia | | | | Clear cell metaplasia | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | # of cases | | | | | | | | | | | |
| | | 1+ | 2+ | 3+ | 4+ | 1+ | 2+ | 3+ | 4+ | 1+ | 2+ | 3+ | 4+ |
| **Age [decades] (n=99)** | *2 – 5 (n=49)* | 12 | 13 | 6 | 8 | 6 | 2 | 7 | 1 | 6 | 3 | 0 | 0 |
| | *6 and above(n=50)* | 18 | 11 | 7 | 6 | 9 | 10 | 2 | 3 | 5 | 7 | 1 | 0 |
| **Tumor diameter (n=85)** | *1-5 cm (n=30)* | 3 | 5 | 4 | 9 | 4 | 2 | 1 | 0 | 5 | 1 | 0 | 0 |
| | *6-10 cm (n=33)* | 13 | 8 | 7 | 3 | 7 | 4 | 4 | 3 | 2 | 7 | 0 | 0 |
| | *>11 cm (n=22)* | 9 | 8 | 5 | 0 | 4 | 6 | 4 | 1 | 5 | 2 | 1 | 0 |
| **Bilaterality (n=28)** | *Control group (n=2)* | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | *Benign tumors (n=10)* | 1 | 5 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | *Borderline tumors (n=2)* | 0 | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | *Malignant tumors (n=14)* | 8 | 3 | 1 | 1 | 4 | 2 | 6 | 1 | 1 | 4 | 1 | 0 |
| **Benign tumors (n=46)** | *Serous (n=31)* | 5 | 6 | 5 | 12 | 4 | 0 | 0 | 0 | 5 | 1 | 0 | 0 |
| | *Mucinous (n=15)* | 3 | 4 | 2 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| **Borderline tumors (n=10)** | *Serous (n=5)* | 0 | 1 | 4 | 0 | 1 | 1 | 1 | 2 | 0 | 0 | 0 | 0 |
| | *Mucinous(n=4)* | 2 | 2 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | *Endometrioid (n=1)* | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Malignant tumors (n=30)** | *Serous (n=26)* | 15 | 7 | 2 | 0 | 7 | 9 | 8 | 2 | 2 | 7 | 1 | 0 |
| | *Mucinous (n=2)* | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| | *Endometrioid (n=2)* | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| **Malignant tumors* (n=30)** | *Well differentiated (n=4)* | 1 | 1 | 2 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 |
| | *Moderately differentiated (n=16)* | 9 | 5 | 1 | 0 | 4 | 5 | 5 | 1 | 3 | 3 | 0 | 0 |
| | *Poorly differentiated (n=10)* | 7 | 2 | 0 | 0 | 4 | 3 | 2 | 1 | 5 | 1 | 0 | 0 |

* According to histological grading

**Table 4.** Distribution and incidence of ciliated cell metaplasia in ovarian surface epithelial tumors

| Characteristics | | Papillary structures | Cystic luminal surfaces | Papillary structures and cystic luminal surfaces | Glandular luminal surfaces | Glandular and cystic luminal surfaces |
|---|---|---|---|---|---|---|
| | | No. of cases (%) | No. of cases (%) | No. of cases (%) | No. of cases (%) | No. of cases (%) |
| **Benign tumors (n=46)** | *Serous (n=30)* | 3 (10) | 11 (36.6) | 11 (36.6) | 1 (3.3) | 1 (3.3) |
| | *Mucinous (n=15)* | 1 (6.6) | 7 (46.6) | 0 (0.0) | 0 (0.0) | 1 (6.6) |
| | *Endometrioid (n=1)* | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (100) | 0 (0) |
| **Borderline tumors (n=10)** | *Serous (n=5)* | 0 (0.0) | 0 (0.0) | 5 (100.0) | 0 (0.0) | 0 (0.0) |
| | *Mucinous (n=4)* | 0 (0.0) | 0 (0.0) | 3 (75.0) | 0 (0.0) | 1 (25.0) |
| | *Endometrioid (n=1)* | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (100.0) |
| **Malignant tumors (n=30)** | *Serous (n=26)* | 22 (84.6) | 0 (0.0) | 2 (7.6) | 0 (0.0) | 0 (0.0) |
| | *Mucinous (n=2)* | 2 (100) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | *Endometrioid (n=2)* | 1 (50) | 0 (0.0) | 1 (50) | 0 (0.0) | 0 (0.0) |

**Table 5.** The extent and incidence of extraovarian ciliated metaplasia in patients with malignant ovarian surface epithelial tumors.

| Characteristics | | Endocervix | | | | | Endometrium | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Incidence | Extent | | | | Incidence | Extent | | | |
| | | No. of cases (%) | 1+ | 2+ | 3+ | 4+ | No. of cases (%) | 1+ | 2+ | 3+ | 4+ |
| **Age [decades] (n=44)** | *2 - 5 (n=14)* | 3 (21.0) | 2 | 0 | 1 | 0 | 5 (35.7) | 4 | 1 | 0 | 0 |
| | *6 and above (n=30)* | 7 (23.3) | 7 | 0 | 0 | 0 | 16 (53.3) | 12 | 3 | 1 | 0 |
| | | $\chi^2 = 0.000$ $p = 1.000$ | | | | | $\chi^2 = 0.586$ $p = 0.444$ | | | | |
| **Tumor diameter (n=29)** | *1-5 cm (n=3)* | 0 (0.0) | 0 | 0 | 0 | 0 | 0 (0.0) | 0 | 0 | 0 | 0 |
| | *6-10 cm (n=13)* | 2 (15.3) | 1 | 1 | 0 | 0 | 3 (23.0) | 2 | 1 | 0 | 0 |
| | *>11 cm (n=13)* | 3 (23.0) | 2 | 0 | 1 | 0 | 5 (38.4) | 5 | 0 | 0 | 0 |
| | | $\chi^2 = 1.454$ $p = 0.483$ | | | | | $\chi^2 = 2.794$ $p = 0.247$ | | | | |
| **Malignant tumors (n=30)** | *Serous (n=26)* | 4 (15.3) | 2 | 1 | 1 | 0 | *6 (23.1)* | *6* | *0* | *0* | *0* |
| | *Mucinous (n=2)* | 0 (0.0) | 0 | 0 | 0 | 0 | *0 (0.0)* | *0* | *0* | *0* | *0* |
| | *Endometrioid (n=2)* | 1 (50.0) | 1 | 0 | 0 | 0 | *2 (100.0)* | *1* | *1* | *0* | *0* |
| | | $\chi^2 = 1.936$ $p = 0.380$ | | | | | $\chi^2 = 6.704$ $p = 0.035$ | | | | |
| **Malignant tumors * (n=30)** | *Well differentiated (n=4)* | 1 (25.0) | 1 | 0 | 0 | 0 | 2 (50.0) | 2 | 0 | 0 | 0 |
| | *Moderately differentiated (n=16)* | 3 (18.7) | 1 | 1 | 1 | 0 | 5 (31.2) | 4 | 1 | 0 | 0 |
| | *Poorly differentiated (n=10)* | 1 (10.0) | 1 | 0 | 0 | 0 | 1 (10.0) | 1 | 0 | 0 | 0 |
| | | $\chi^2 = 0.591$ $p = 0.744$ | | | | | $\chi^2 = 2.873$ $p = 0.238$ | | | | |

* According to histological grading

## DISCUSSION

Ovarian epithelial tumors are heterogeneous with several histologic subtypes that have cytogenetic and molecular features, oncologic signaling pathways, and biologic behaviors. Ovarian epithelial cancers are one of the most common gynecologic malignancies. The fact that ovarian epithelial cancers were derived from the ovarian surface epithelium or cortical inclusion cysts is commonly acceptable hypothesis [11-13]. Although it is generally purposed that these cysts develop by invagination of ovarian surface epithelium, there is reason to believe that during ovulation, as the fimbria come into close contact with the ovary, tubal epithelial cells implant on the disrupted ovarian surface to form a cortical inclusion cyst. However, recent studies suggested that these cysts could be derived not from the ovarian surface epithelium but from implanted fimbrial tubal epithelium [12, 14]. Ovarian inclusion

cysts or embryological remnants of Müllerian ducts (secondary Müllerian system) undergo to Müllerian Metaplasia [11, 13]. The development of ovarian cancers from embryological remnants that have already undergone Müllerian differentiation could explain the manifestation of different histologic subtypes of ovarian cancer that are identical to fallopian tube (serous), endometrial (endometrioid), endocervical (mucinous), and vaginal (clear cell) epithelia [11, 13].

The ovarian Müllerian metaplasias have been considered as precursor lesions, such as endocervical and endometrial Müllerian metaplasias [2-7, 11, 13]. The ovarian precursor lesions undoubtedly exist and may be histologically identified in the early stages [4, 5]. However, the detection of these precursor lesions in the ovary is more difficult in the early stages, when borderline and malignant ovarian tumors were compared with endocervical and endometrial tumors. Therefore, the majority of patients with malignant ovarian surface epithelial tumors are diagnosed at an advanced stage and the prognosis is usually poor. These metaplastic changes may be easily overlooked by pathologists [3, 5]. Therefore, they have been rarely reported.

The Müllerian metaplasias are frequently accompanied with ovarian surface epithelial tumors. In this study, it was determined that *ciliated cell metaplasia* was more frequent in benign, borderline and malignant tumors than control group ($p<0.05$) (Table 1). It was observed that *ciliated cell metaplasia* was more extensive in the benign tumors than the others. On the contrary, *eosinophilic and clear cell metaplasias* were more extensive in borderline and malignant tumors than the others. *Eosinophilic and clear cell metaplasias* were also more frequent in moderately and poorly differentiated ovarian tumors. They were never seen in control group. Therefore, it was considered that *eosinophilic and clear cell metaplasias* were close relation with malignant transformation.

*Eosinophilic cell metaplasia* or change may be seen in ciliated cells and squamous cells. It has been suggested that these metaplastic changes are degenerative and reparative alterations. These changes may be interpreted as nuclear atypia. It was determined that the incidence of *eosinophilic cell metaplasia* increased from benign tumors towards malignant tumors ($p<0.01$) (Table 1). *Eosinophilic cell metaplasia* may be a precursor or precancerous lesions rather than degenerative or reparative alteration.

*Ciliated, eosinophilic and clear cell metaplasias* are usually associated with serous and endometrioid tumors, while mucinous (endocervical type) metaplasias are associated with mucinous tumors [4]. Most mucinous tumors stem from the foci of mucinous metaplasia of either the ovarian surface mesothelium or cortical inclusion cysts [2-5]. Therefore, *ciliated, eosinophilic and clear cell metaplasias* may not be observed in mucinous areas, except in serous areas of mucinous tumors. In this study, it was determined that incidence and extent of *ciliated and eosinophilic cell metaplasias* were more frequent and extensive in serous ovarian tumors than mucinous ones ($p<0.05$) (Table 2-3).

Intercalary cells are similar to clear cells due to their glycogen content. This similarity makes us consider the possibility of a relation with clear cell metaplasia. However, this hypothesis needs to be confirmed with ultrastructural and molecular studies.

When cilia are exfoliated into cystic spaces, benign tumors may be confused with borderline tumors because of the atypical appearances of *ciliated cell metaplasia* [2-6, 9, 15, 16]. In this study, such appearances were found in three cases of benign tumors. These cases were reported as serous cystadenofibroma. In particular, when cystic adenofibroma is referred to the pathologist during the intraoperative consultation, this lesion may be interpreted as a borderline tumor. Therefore, the pathologist should consider the possibility of *ciliated cell metaplasia* and should look for intercalary cells.

In addition, it was determined that *eosinophilic* and *clear cell metaplasias* in bilateral cases was more frequent in borderline and malignant tumors than benign tumors ($p<0.01$). It was observed that the incidence of *ciliated* and *eosinophilic cell metaplasias* increased, as tumor diameter increased ($p<0.01$). It was determined that the incidence of Müllerian metaplasias was higher in advanced ages. But this difference was not statistically significant ($p>0.05$). *Extraovarian ciliated cell metaplasia* was only determined in endometrium and endocervix of patient with serous and endometrioid malignant ovarian tumors. It was not seen in endometrium and endocervix of mucinous ovarian tumors.

In conclusion, this current study is the first report in its kind and our findings are significant in appearing to indicate the existence of a close relationship between metaplastic changes and ovarian epithelial malignancies. In addition, this study indicates that the incidence and extent of Müllerian metaplasias in ovarian surface epithelial tumors may not be homogeneous. This should be taken into account when their biological significances and relation with tumorigenesis are investigated.

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