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Adenocarcinoma of the Uterine Cervix : a Clinicopathological Study

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ABSTRACT

Objective To determine factors which correlated to the risk of recurrence for adenocarcinoma of the uterine cervix treated initially by surgery.

Design A retrospective study.

Setting University hospital.

Subjects The clinical information and pathologic specimens of adenocarcinoma of the uterine cervix were retrospectively reviewed for 74 patients who initially had been treated by radical hysterectomy with pelvic lymphadenectomy between 1983 and 1994.

Main outcome measures Significance of variables in relation to recurrence.

Results Significant differences in risk of recurrence were observed among the patients with and without lymph node metastasis (50% vs 15.2%, P = 0.03), and the tumours with increased histologic grade (grade 1 = 12.3% vs grade 2 + 3 = 41.2%, P = 0.01).

Conclusion Nodal metastasis and histologic grade were related to recurrence in surgically treated cervical adenocarcinoma.

Key words : adenocarcinoma, uterine cervix

There have been many studies undertaken to determine the treatment results and prognostic factors for adenocarcinoma of the uterine cervix.[1-16] The tumour stage and lymph node metastasis are considered to be the most accepted factors correlated with survival. The significance of histologic grade, depth of invasion, tumour size, and lymph-vascular space invasion are still not well-established especially to be factor that probably determine the type of treatment. We retrospectively reviewed the cervical adenocarcinoma treated by surgery in our institution with emphasis on the clinicopathologic features that remain controversial.

Materials and Methods

The computerized gynaecologic tumour registry of the Department of Obstetrics and Gynaecology, Faculty of Medicine, Chiang Mai University was searched for cases coded as cervical adenocarcinoma, adenosquamous carcinoma, anaplastic carcinoma, neuroendocrine carcinoma, and undifferentiated carcinoma between 1983-1994. Of the total 106 cases that we were able to locate the microscopic slides, pathology reports, and clinical records, there were 74 patients of invasive adenocarcinoma treated by radical hysterectomy with pelvic lymphadenectomy and constituted the present report.

In our institution, the patients with early cervical cancer (FIGO stage IB, IIA) routinely were treated by radical hysterectomy with pelvic lymphadenectomy. The patients with positive pelvic node were also received adjuvant radiation therapy.

The clinical data and follow-up information of each patients were accumulated from the gynaecologic tumour registry. Assessment of the tumour size and the tumour characteristics were also based on the clinical records.

Pathology review included confirmation of histologic subtype, grading, and presence of nodal metastasis. The histologic subtype was based on the new International Society of Gynecological Pathologists (ISGP) classification (Table 1).[13]

The histologic grading of mucinous adenocarcinoma was performed by architectural grade.[13] If less than 10 percent of the tumour was poorly differentiated with areas not forming glands or tubules, it was well-differentiated (grade 1). If 10 to 50 percent of the tumour did not form glands or tubules, it was moderately differentiated (grade 2). If the glands and tubules were not formed in more than half of the tumour, it was poorly differentiated (grade 3). All of the villoglandular adenocarcinoma and minimal deviation adenocarcinoma were placed in grade 1. The tumour of endometrioid cell type

Table 1. Histologic subtypes of the cervical adenocarcinoma

Mucinous (endocervical, intestinal, and signet-ring types)
Endometrioid
Clear cell
Minimal deviation (adenoma malignum, MDA)
Well-differentiated villoglandular
Serous
Mesonephric

were graded according to the FIGO grading system for endometrial carcinoma. Grading of the serous adenocarcinoma was followed the system for ovarian serous adenocarcinoma.

The number of microscopic slides available for review varied from 1 to 21 (mean 4.5) per cases. Haematoxylin and Eosin-stained slides were reviewed in each case. Immunostain for chromogranin A and histochemical stain for neurosecretory granule (Grimelius) were used to confirm the diagnosis of neuroendocrine carcinoma.

Descriptive statistical methods were used to present the data. Fisher's exact test was used to examine the significance of the variables in relation to recurrence. P values less than 0.05 were considered to be significant.

Results

The patients ranged in age from 22 to 55 years (mean, 40). Of 74 cases, 72 were FIGO stage IB and the other two were IIA. Most of patients had either exophytic (52.7%) or infiltrative (32.4%) mass. The size of the tumour were 3 cm. or less in 48 cases (64.9%) and larger than 3 cm. in 22 cases (29.7%). There was no description of the tumour size for the other 4 cases. The number of new cases per year increased from 2 (in 1983) to 13 (in 1994). Fourteen cases (18.9%) had recurrent disease developed after surgery, ranged from 4 to 26 months (mean 14, SD 6.7). For nonrecurrent patients, duration of follow-up ranged from 1 to 139 months (mean 51, SD 33).

The frequencies of various histologic

Table 2. The clinical and pathologic features : univariate analysis

Features	Total No.	No recurrence	Recurrence	P Value
Tumour size (clinical)				0.34
≤ 3 cm	48	40	8	
> 3 cm.	22	16	6	
NA	4			
Histology				-
Mucinous	49	36	13	
Endometrioid	9	9	-	
MDA	3	3	-	
Villoglandular	12	12	-	
Serous	1	-	1	
Differentiation				0.02
Grade 1	57	50	7	
Grade 2	7	4	3	
Grade 3	10	6	4	
Group data				0.01
Grade 1	57	50	7	
Grade 2 + 3	17	10	7	
Pelvic Lymph Node				0.03
Negative	66	56	10	
Positive	8	4	4	

NA = Not Available

subtypes of the tumour and histologic grade are shown in Table 2. Eight patients had metastatic carcinoma in the pelvic lymph nodes. Depth of invasion was very difficult to determine in this study, largely because the gross descriptions available for review generally did not mention the proportion of cervical wall invaded by tumour and the microscopic slides did not show the entire thickness from mucosal surface to the deepest point of invasion.

Statistical analysis showed that presence of nodal metastasis and histologic grade of tumour either separate into three groups (grade 1, 2, 3) or two groups (grade 1 and 2 + 3) were associated with increased risk of recurrence (Table 2). Although the patients with tumour larger than 3 cm. (27.3%) had higher rate of recurrence than those with tumour 3 cm. or less (16.7%), the difference was not statistically significant.

Discussion

This study did confirm most previous reports that lymph node metastasis significantly increased risk of recurrence.[5, 6, 8-12] Increased histologic grade (grade 2, 3) was the other pathologic feature correlated with risk of recurrence. Although eight of eleven previous reports demonstrated that histologic grade correlated with survival, only three stated clearly about grading system used in their studies.[1-6, 8-12] Berek et al and Matthews et al divided the tumour into three grades according to the growth patterns and degrees of nuclear anaplasia.[5, 12] Fu YS et al used nuclear grade in their study,[2] whereas architectural grade was used in our present report. However, Saigo et al found that histologic grading by nuclear grade did not correlate with survival.[6] Further studies are needed to determine that which grading system should be used for mucinous adenocarcinoma.

In our study, the tumour size was not significantly increased risk of recurrence. The results from previous reports were different. Some proposed that tumour larger than 4 cm. associated with increased risk of recurrence.[4, 5, 8] The tumour size was probably not a reliable factor because most of the records were based on subjective clinical estimation. To confirm the significant tumour size, prospective study stated clearly how to measure the lesion and immediately recorded before cut through or manipulate the tumour is probably the best way to get the best answer.

For the depth of invasion, there were two previous reports investigated about this factor. One measured the depth from mucosal surface,[5] the other measured from the highest adjacent epithelial-stromal basement membrane.[12] In the former report, there were no lymph node metastases in patients with a tumour that had depth of invasion less than 2 mm. For the latter, there were no tumour recurrence in patients with a tumour that had depth of invasion 3 mm. or less. For the tumour with superficial invasion, measurement either method would be helpful. For the larger tumour, percent of involvement of the cervical wall or distance from deepest point of invasion to the serosa should be reported.[13]

There were two previous reports demonstrated the significant of lymph-vascular space invasion. Metthews et al also purposed that alternate treatment should be considered if pretreatment biopsies demonstrate obvious lymph-vascular invasion.[12] Presence of lymph-vascular space invasion was found to be an indicator of poor prognosis even in the absence of nodal metastasis in the study by Saigo et al.[6] In the present report, we could not confirm this observation because we had only few patients

with lymph-vascular space invasion.

There were two important factors that may respond to the different results from various reports, types of treatment and histologic subtypes of tumour. Only two of fifteen previous reports that selectively studied only the patients who treated by surgery alone.[5, 12] In the remaining thirteen reports, the patients were treated either combination of surgery and radiation therapy or radiation alone or surgery alone. For histologic subtype of tumour included in the study, mixed types of malignancy especially adenosquamous carcinoma were included in most previous reports, whereas our study which followed the new ISGP classification excluded adenosquamous carcinoma.

In summary, nodal metastasis and histologic grade were the factors predictive of recurrence in surgically treated cervical adenocarcinoma. Further prospective studies are needed to define reproducible criterias for histologic grade, depth of invasion, and tumour size as well as the prognostic significance of these factors and lymph-vascular space invasion.

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