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A Clinicopathological Study of Postoperatively Upgraded Early Squamous-Cell Carcinoma of the Uterine Cervix

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Abstract

Objective: To investigate the clinicopathological backgrounds and diagnostic problems of postoperatively upgraded early squamous-cell carcinomas of the uterine cervix

Patients and Methods: A total of 23 patients with postoperatively upgraded early squamous-cell carcinomas who were treated at the Saitama Cancer Center during the period of January 1, 1976, through December 31, 1991, were analyzed clinicopathologically. We reexamined the Pap smears (ectocervix, endocervix), colposcopic findings, punch biopsies, and histological findings of the operative specimens. All patients were divided into one of 3 groups based on each patient's main location of the carcinoma of the cervix:

Type A: ectocervical type;
Type B: endocervical type; or
Type C: combined (ectocervical and endocervical) type.

Clinical staging of the uterine cervical carcinomas was done in accordance with the 1994 FIGO rules.

Results: The numbers of patients were: Type A, 2; Type B, 10; Type C, 11. Of the 23 patients, 21 (91.3%) had lesions in the endocervical portion at least. Fifteen patients (65.2%) complained of atypical vaginal bleeding. Colposcopic findings suggesting an invasive carcinoma appeared for only 6 patients (26.1%). A cytological reevaluation revealed that the endocervical findings were much stronger than the ectocervical ones in 10 (66.7%) of 15 patients whose smears of both sites could be rechecked.

Conclusions: Even if the preoperative diagnosis was early cervical carcinoma, CIS or Stage Ia1, the signs of atypical vaginal bleeding suggested that the final clinical stage would be upgraded after an operation. Furthermore, when the endocervical cytological findings were much more exaggerated than the ectocervical ones, the possibility of deeply invaded endocervical lesions should be considered.

Key words: cervical cancer, Pap smear, colposcopy, biopsy, distributions of carcinoma lesions

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Introduction

Most squamous-cell carcinomas of the uterine cervix can be diagnosed precisely using the combined methods of a cervical cytology, colposcopy, and biopsy.[1] However, even if a preoperative diagnosis is CIS or Stage Ia1, it is possible that after an operation it would be determined that the carcinoma lesions had invaded deeply into the cervical layer. If further postoperative treatment is needed in such cases,[2] undesired complications would result. Therefore, in consideration of a patient's quality of life, correct preoperative clinical diagnosis is necessary for appropriate therapy.[3]

In order to solve these preoperative diagnostic problems, we clinicopathologically analyzed stage-upgraded cases and compared their cytologic smears, colposcopic findings, and biopsies with postoperative histological specimens.

Patients and Methods

A total of 23 patients who had stage-upgraded squamous-cell carcinomas of the uterine cervix (Stage pTIa2–IIa), and who had undergone total, semiradical, or radical hysterectomies at the Saitama Cancer Center during the period of January 1, 1976, through December 31, 1991, were analyzed clinicopathologically. The patients were divided into one of 3 groups, based on each patient's distribution of carcinomatous lesions in the uterine cervix, as indicated below (Fig. 1).

1. Type A = ectocervical type; the carcinoma occupies mostly the ectocervical portion of the cervix;
2. Type B = endocervical type; the carcinoma occupies mostly the endocervical layer of the cervix; or
3. Type C = combined type; the carcinoma occupies both the ectocervical and endocervical portions of the cervix.

We used cotton swabs in taking ectocervical and endocervical smears. Before colposcopic observations, we applied a substantial amount of 3% acetic acid to the ectocervical portions. Surgical staging was done according to the FIGO rules.[4]

Table 1. Clinicopathological findings of postoperatively

Carcinoma occupational lesion	Cases	Patient age	Vaginal bleeding	Surgical staging		Operation performed	Conization
				Preoperation	Postoperation (muscle invasion)		
A	2	62	○	0	Ia2	SRH	
		45	○	Ia1	IIa (2 mm)	SRH	
B	10	49	○	0	Ia2	SRH	
		40	○	0	Ia2	ATH	
		74		0	Ia2	SRH	
		65	○	0	IIa (12 mm)	VTH	
		74		Ia1	Ia2	ATH	
		51		Ia1	Ib1 (5 mm)	SRH	
		43	○	Ia1	Ib1 (12 mm)	SRH	
		60	○	Ia1	IIa (13 mm)	SRH	
		59	○	Ia2	Ib1 (4.5 mm)	RH	○
		58	○	unknown	Ib1 (11 mm)	ATH	
C	11	41	○	0	Ib1 (8 mm)	ATH	
		39	○	0	Ia1	RH	
		34	○	0	IIa (2 mm)	RH	
		67		0	IIa (5 mm)	ATH	
		38		0	IIa (2 mm)	ATH	
		59	○	Ia1	Ia2	RH	○
		44		Ia1	Ia2	SRH	
		50	○	Ia1	Ib1 (7 mm)	SRH	○
		39	○	Ia1	Ib1 (10 mm)	SRH	
		46		Ia1	Ib1 (12 mm)	SRH	
		67		Ia1	IIa (13 mm)	SRH	

RH: radical hysterectomy, SRH: semiradical hysterectomy, ATH: abdominal total hysterectomy, VTH: vaginal total hysterectomy, W: acetowhite epithelium, P: punctation, M: mosaic, aV: atypical vessels

Results

Clinicopathological, cytohistological, and colposcopic details are shown by Table 1. The numbers of patients were: Type A, 2; Type B, 10; Type C, 11. The mean ages were 53.5, 57.3, and 47.6 years for Type A, Type B, and Type C patients, respectively. There was no significant difference with respect to mean age among the 3 types. A total hysterectomy was performed in 7 cases. A semiradical hysterectomy was performed in 12 cases; 1 of these patients had already received conization before the abdominal operation. A radical hysterectomy was performed in 4 cases; 2 of these patients had had conization. Because of the condition of the removed lesion — such as tumor volume, and vaginal and cervical marginal cut-ends — additional radiotherapy was needed for these 13 patients.

Among Type A patients, the preoperative sur-

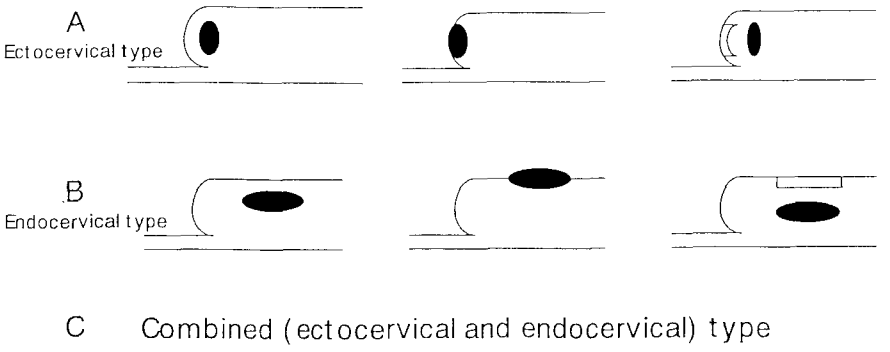

Fig. 1. Classification due to carcinomatous lesion in the uterine cervix.

upgraded early squamous-cell carcinoma of the uterus

Radiation therapy after operation	Colposcopy		Cytology	
	Abnomal findings W, P, M, aV	Invasive carcinoma	Strongly suggestive of or conclusive for malignancy	Endcervical finding stronger than ectocervix
			○	○
○	M	○	○	
		○		
	P. aV		○	○
○			○	
○	W			
			○	○
			○	○
○	aV		○	○
	aV			
	M. W		○	
○		○	○	○
○				
	W		○	○
○		○	○	
○				
○			○	○
○	P			
	M	○	○	
○	P			
○			○	○
○		○	○	○

gical stages were Stage 0 (1 patient) and Stage Ia1 (1 patient). They were later upgraded to Stage Ia2 and IIa, respectively. Among Type B patients, 4 were preoperatively Stage 0, 4 were Stage Ia1, 1 was Stage Ia2, and the stage was unknown for 1 patient. These patients were upgraded to Stage Ia2 (4), Ib1 (4), and IIa (2). Among Type C patients, 5 were preoperatively clinical Stage 0 and 6 were Stage Ia1. These patients were changed to Stage Ia1 (1), Ia2 (2), Ib1 (4) and IIa (4). This Stage Ia1 patient had prominent vessel permeation, so she formerly had been diagnosed as Stage Ib.

Atypical vaginal bleeding appeared in 2 of 2 Type A patients, in 7 of 10 Type B patients, and in 6 of 11 Type C patients. A total of 65.2% (15/23) of the patients complained of atypical vaginal bleeding at their first visits.

Abnormal colposcopic findings such as aceto-white epithelium, punctation, mosaic and/or atypical vessels were also seen in 1 Type A patient, in 5 Type B patients, and in 4 Type C patients. Colposcopic findings suggesting an invasive carcinoma could be detected in 1 Type A patient, in 2 Type B patients, and in 3 Type C patients. Two patients had both abnormal colposcopic findings and findings suggesting an invasive carcinoma. We could detect abnormal colposcopic findings and/or an invasive carcinoma in 7 patients (53.8%) of 13 Type A and Type C patients, and in 7 patients (70.0%) of 10 Type B patients having a pure endocervical-type of carcinoma. In 5 Type C patients whose colposcopic analyses were within normal findings, a carcinoma of the ectocervical portion was covered by ectocervical epithelium, which looked like normal epithelium (Fig. 2). Colposcopic findings suggesting an invasive carcinoma appeared for only 6 patients (26.1%).

Cytological reexamination revealed that there were abnormal cytological findings strongly suggestive of or conclusive for malignancy in 2 Type A patients, in 7 Type B patients, and in 6 Type C patients. In the other 8 patients, we could not detect major abnormalities, i.e., those strongly suggestive of malignancy. Because cytological findings are different from site to site, we separately reexamined ectocervical and endocervical smears taken at the same time. Among the 15 patients for whom we could compare ectocervical and endocervical smears, there were 10 patients whose endocervical cytological findings were stronger than their ectocervical ones. In the endocervical smears of these 10 patients, the backgrounds were dirtier; that is, with much more debris from necrotic cells, hemorrhaging, and exudate. And cancer cells, which were very numerous, appeared much more in aggregates. Each cancer cell had a higher N/C ratio and a coarse chromatin pattern (Fig. 3). These findings were found in 50% (1/2) of the Type A patients, in 71.4% (5/7) of the Type B patients, and in 66.7% (4/6) of the Type C patients. Thus, with respect to cytological findings, 66.7% (10/15) of the endocervical smears were stronger than the ectocervical ones.

Discussion

Usually an appropriate diagnosis of uterine

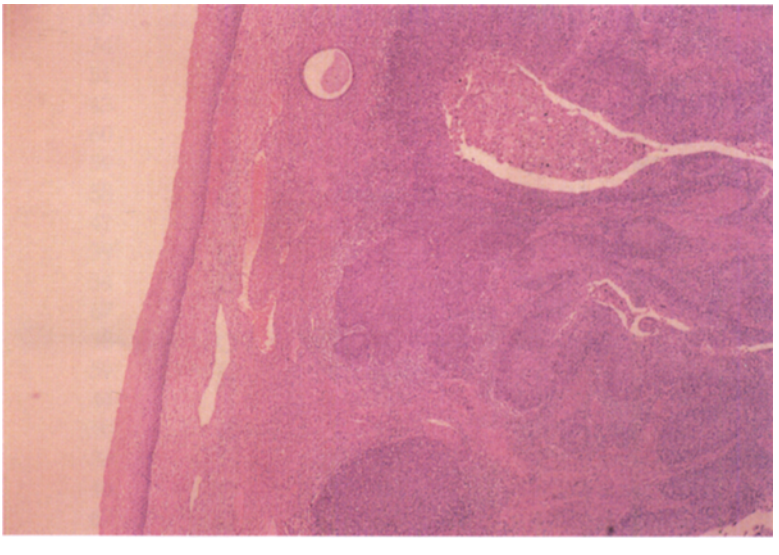

Fig. 2. In 5 Type C (5/11; 45.5%) patients, the carcinoma of the ectocervical portion was situated under the ectocervical epithelium, which looked like normal epithelium.

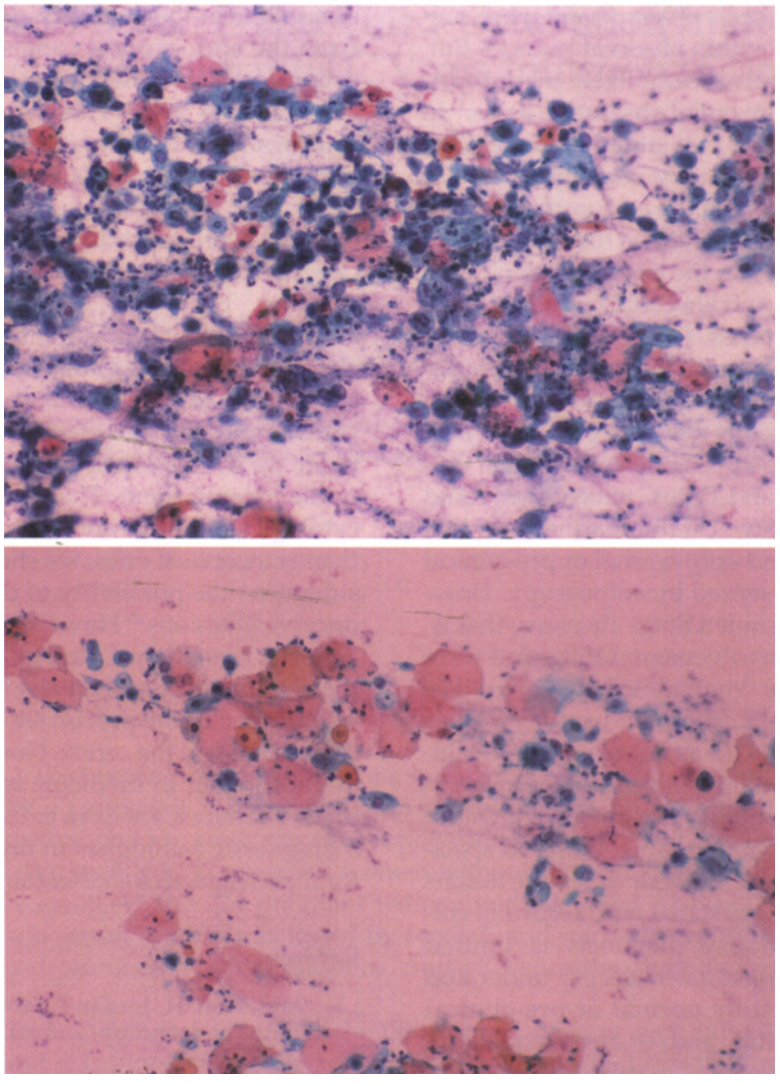

Fig. 3. Among 15 patients for whom we could compare ectocervical and endocervical smears, there were 10 whose endocervical cytological findings (Top) were stronger than their ectocervical findings (Bottom). In the endocervical smears of these patients, the backgrounds were dirtier, that is, containing more necroticcell debris. Also, the cancer cells, whose numbers were very numerous, appeared much more in aggregates.

cervical carcinoma can be made by a combination of cytology, colposcopy, and punch biopsy.[1] However, when cancer lesions are not in areas that can be reached by these methods, in some cases an incorrect diagnosis cannot be avoided. Although ultrasound sonography or magnetic resonance imaging (MRI) is now available for detecting such lesions, these methods are not always useful for endocervical lesions and are not applied in all cases because of cost-benefit considerations. In order not to miss such lesions, it is necessary to make an effort to detect them precisely by using every technique and all clinicopathological findings possible.

Generally, taking a patient's history is an important method and a first step in diagnosing a disease. Vaginal bleeding is the most common symptom occurring in patients with advanced lesions of the cervix. Most often this is postcoital, irregular, or postmenopausal bleeding.[5] In a preclinical or early stage, CIS or Stage Ia1, a few patients complain of abnormal vaginal bleeding. In this study, more than one-half of the patients whose stage was upgraded postoperatively complained of vaginal bleeding. This strongly suggests that a clinicopathological finding of vaginal bleeding is one of the important signs that should never be ignored. Even if the preoperative diagnosis is early cervical carcinoma, CIS, or Stage Ia, a sign of atypical vaginal bleeding suggests that the clinical stage will be upgraded after an operation.

Colposcopic diagnosis is very useful when malignant lesions are within observable areas. But, colposcopic diagnosis is completely inappropriate for lesions that are out of observable areas.[1] In this study, there were two situations where we could not apply colposcopy usefully. One was when the lesions were in the endocervical canal. In Type B and Type C patients, the main cancer lesions were situated in the upper portion of the endocervical canal, and we could not detect them through the external os. Few were detected by colposcopy because the majority were of the endocervical type. The other situation was when the main cancer lesions were deeply under normal or preinvasive-appearing ectocervical epithelium. In Type A and Type C patients, we could not detect an invasive carcinoma that was in a deep canal layer, and only normal or pre-clinical epithelium was observed by colposcopy. However, we had 7 upgraded Stage IIa cases; that is, they had vaginal involvement. Of the 7, 4 were upgraded by only vaginal involvement. We should meticulously check the vaginal wall as well as the ectocervix, so as not to miss any vaginal involvement and/or isolated lesions.

Usually a punch biopsy is done under colposcopic observation, and a punch-biopsied specimen can be diagnosed correctly when the lesions are accessible.[1] As was stated with regard to colposcopy, punch-biopsy diagnosis is limited when the lesions are situated deeply under and completely covered by normal or pre-clinical ectocervical epithelium, and/or are extended upwards in the endocervical canal.[6] Endocervical curettage or conization is recommended for patients whose lesions exist mainly in the cervical canal. But we did not prefer those methods, because endocervical curettage specimens cannot always clarify the complete histopathologic structure of a cervical carcinoma, and because cervical conization is too harmful for any unexpected deep cervical involvement. Our 3 conized specimens had residual carcinomas at their surgical margins, and they all required further radical operation.

Cytology is a powerful means of compensating these diagnostic limitations of colposcopies and biopsies. Of 23 patients who were upgraded, 21 had endocervical lesions beyond our observational inspections. Usually we took smears from both the ectocervical surface and the endocervical canal. In this study, when the main cancer lesions were in the endocervical canal, the smears from the endocervical canals were much more prominent and more exaggerated than the ectocervical ones were. These different cytological findings revealed that in endocervical smears, both the number of cells and their appearance in aggregates were more numerous, and the backgrounds were much dirtier, being smudgy with debris from necrotic cells, hemorrhaging, and exudate. They also had a high N/C ratio, clumped chromatin in the hyperchromatic nuclei, and a disordered architecture.[7] When we observe both the ectocervical and endocervical smears and can detect a discrepancy between them, we should consider additional possibilities in diagnosing them. That is, when endocevical cytological findings are much more exaggerated than ectocervical ones, we should take into consideration the possibility of deeply invaded endocervical lesions.[6] However, cytology has a diagnostic limitation. Cytology generally suggests that malignant lesions exist somewhere, but it cannot specify the precise site that the cancer lesions occupy in the cervix. None of the diagnostic methods used in medicine is perfect and complete. Therefore, we have to use adequately these 3 diagnostic techniques in order to compensate for their respective shortcomings.

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