RESEARCH COMMUNICATION

Histopathological Outcomes of Women with Squamous Cell Carcinoma on Cervical Cytology

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Abstract

The aim of this study was to determine the final histopathological outcome for women with a squamous cell carcinoma (SCCA) diagnosed by cervical cytology. The medical records and computerized colposcopic database of patients with SCCA on cytology who underwent colposcopy at Chiang Mai University Hospital between February 2003 and December 2005 were reviewed and 48 women with SCCA cytology were identified (mean age 50 years, range 31-73). Nineteen (39.6%) women were postmenopausal. Unsatisfactory colposcopy was noted in 42 (87.5%). Thirty one (64.6%) of the patients had a final pathological diagnosis of high-grade squamous intraepithelial lesions (HGSIL), whereas only 16 (33.3%) had invasive cancer. The remaining one patient had a low-grade squamous intraepithelial lesion. Sensitivity and specificity of colposcopic examination for predicting invasive cancer was 50% and 78%, respectively. In conclusion, most women with a SCCA on cervical cytology have high-grade cervical lesions on final pathology, with only one third demonstrating invasive cancer. The loop electrosurgical excision procedure (LEEP) remains an important measure for combined treatment and diagnosis.

Key Words: Cervical squamous cell carcinoma - Pap smear cytology - colposcopy - histopathological diagnosis

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Introduction

The Bethesda System for reporting the results of cervical cytology has been adopted as a uniform terminology system that provides explicit guidance for clinical management (Solomon et al., 2002). Squamous cell carcinoma (SCCA) is a distinctive diagnostic subcategory in the 2001 Bethesda System within the epithelial cell abnormalities category, characterized by more pronounced malignant features as compared with high-grade squamous intraepithelial lesion (HGSIL). These include marked nuclear irregularity, presence of great numbers of large and irregular nucleoli, and tumor diathesis (Garcia and Goulart, 2002). However, a cytological diagnosis of SCCA appears quite uncommon with the prevalence of only 0.01% of cytology interpretations (Jones et al., 2000). Despite the tendency toward more progressive disease, a specific consensus guideline for the management of women with SCCA on Pap smear has not been established. Currently, the management scheme for this condition follows that recommended for cytological diagnosis of HGSIL, including immediate colposcopy with colposcopically-directed biopsy (CDB), endocervical sampling, or loop electrosurgical excision procedure (LEEP) when considered appropriate.

The aims of the present study were: i) to determine the final histological diagnosis of women presented with SCCAs on cervical Pap smears; and ii) to examine the role of colposcopy in evaluating the correlation with histopathological diagnosis.

Materials and Methods

After approval of the Ethical Committee, the medical records and computerized colposcopic database of patients with SCCAs on cervical cytology who underwent colposcopy at Department of Obstetrics and Gynecology, Chiang Mai University Hospital between February 2003 and December 2005 were reviewed. Thorough examination of the cervix was carried out followed by colposcopic examination. Colposcopic impression on severity of the lesions was based on the acetowhite changes, the margins and the vascular patterns. If invasive cancer was suspected, CDB was performed to confirm the diagnosis. If the colposcopic appearance was less than invasive, diagnostic LEEP was carried out. Diagnostic LEEP was also performed in case of unsatisfactory colposcopy and pathology on CDB of less than frankly invasive cancer. Endocervical curettage (ECC) was routinely performed after LEEP. If the surgical

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margins were involved or the ECC was positive, and the lesion was less than frankly invasive cancer, re-excision of the cervix or hysterectomy, when deemed appropriate, was performed 6-8 weeks later to evaluate the final pathology.

Results

During the study period, 959 women underwent colposcopy for abnormal cervical cytology or related conditions. Among these 48 (5%) had SCCA cytology. Their mean age was 50 years with a range of 31-73 years. Nineteen (39.6%) were menopausal. Three (6.3%) were seropositive for HIV. Unsatisfactory colposcopy was noted in 42 (87.5%), with unidentifiable extent of the lesions in 30, unseen squamocolumnar junction in 10, and contact cervical bleeding in 2. Half of the patients had colposcopic features of HGSIL and 16 (33%) patients had a colposcopic diagnosis of invasive cancer. There was no identifiable cervical lesion on colposcopy in 8 (16.7%) patients. However, the colposcopic examinations in all of these cases were unsatisfactory (6 from inability to visualize the entire squamocolumnar junction, 1 from bleeding, and 1 from severe cervical atrophy). The final histological diagnosis for these 8 patients was HGSIL in 4 (50%), frankly invasive cancer in 3 (37.5%), and LGSIL in 1 (12.5%).

Previously undetected gross cervical lesions were found at the time of colposcopy (during pre-colposcopic naked-eye examination) in 7 (14.6%) patients. Six of them had a subsequent CDB performed which confirmed frankly invasive carcinoma in 4 and HGSIL in 2. For the latter, HGSIL and frankly invasive carcinoma were found in subsequent LEEP specimens. The remaining patient who had a 1 centimeter erythematous nodule discovered at the time of colposcopy underwent immediate LEEP instead of CDB. HGSIL was finally diagnosed.

Of the 48 patients, 10 (20.8%) had CDB performed for diagnosis at the time of colposcopy; 6 with gross visible lesions as mentioned above, and 4 with colposcopic findings suspicious for invasion. A diagnosis of invasive carcinoma was made without the need for further LEEP in 4 patients, all of them with grossly visible lesions. Of the 38 patients who underwent immediate LEEP for diagnosis without intervening CDB, 8 (21.05%) had negative excision margins. Sixteen (42.1%), 6 (15.79%), and 8 (21.05%) were found to have positive endocervical, ectocervical, and both margins, respectively.

Colposcopic features and the final histological diagnosis of the 48 patients are compared in Table 1. Approximately two-thirds (64.6%) of the patients had a final histological diagnosis of HGSIL, whereas one-third (33.3%) had histologically-confirmed invasive carcinoma. However, there were 2 patients with the diagnosis of HGSIL who had positive LEEP margins. Repeat LEEP was planned to obtain definite diagnoses but both of them were lost to follow-up. Of the 16 patients with invasive carcinoma, 15 had squamous cell carcinoma and 1 had poorly differentiated neuroendocrine carcinoma. The FIGO stage distribution was 6 (12.5%) IA1, 2 (4.2%) IA2, 7 (14.6%) IB1, and 1 (2.1%) IIA. The final histological diagnosis of the 3 patients with HIV immunopositivity was LGSIL, HGSIL, and FIGO stage IA1 invasive carcinoma in one each.

From the correlation of colposcopic impression and final histological diagnosis presented in Table 1, sensitivity and specificity of colposcopic examination in predicting invasive carcinoma was 50% and 78%, respectively. The sensitivity of colposcopy in detecting frankly invasive carcinoma (FIGO stage IB and IIA) appeared higher than that for microinvasive carcinoma (FIGO stage IA1 and IA2), at 62.5 versus 37.5%, respectively (Table 2).

Table 1. Correlation of Colposcopic Features and Histopathological Diagnosis

Colposcopic Features (%)	Histological diagnosis (%)*			
	LGSIL	HGSIL	Invasive	Total
Normal (No lesion)	1	4	3	8 (16.7)
HGSIL	0	19	5	24 (50.0)
Microinvasive	0	1	0	1 (2.1)
Invasive	0	7	8	15 (31.3)
Total	1 (2.1)	31 (64.6)	16 (33.3)	48 (100)

*LGSIL: Low-grade squamous intraepithelial lesion, HGSIL: High-grade squamous intraepithelial lesion

Table 2. Correlation of Colposcopic Features and Stage of Histopathologically-confirmed Invasive Carcinoma

Colposcopic Features	FIGO Stage of invasive carcinoma			
	IA1	IA2	IB1	IIA
No lesion	0	2	1	0
HGSIL*	3	0	2	0
Invasive	3	0	4	1
Total	6	2	7	1

* HGSIL: High-grade squamous intraepithelial lesion

Discussion

We demonstrated in the present series that the majority (approximately two-thirds) of patients with a cytological diagnosis of SCCA have a final histological diagnosis of HGSIL. Almost all of the remaining one-third was found to have invasive carcinoma with the exception of only one patient who had LGSIL as a final diagnosis. Of note, the proportion of patients with the final diagnosis of invasive carcinoma appeared lower than what might be expected given the alarming cytology results. Two studies were identified in the literature that addressed similar issues in part of their reports. The College of American Pathologists Q-Probes study showed that in 186 patients with SCCA on cervical cytology, approximately 68% and 24% had final histological diagnosis of invasive carcinoma and HGSIL, respectively (Jones et al., 2000), providing a clear contrast with our data. However, in the study by Massad et al, the underlying pathology of SCCA was noted in only 4 (15%) of 26 patients with SCCA cytology. The reported rate of invasive carcinoma diagnosis in the patients with HGSIL

Pap smear was 1-2% in the literature (Jones et al., 2000; Massad et al., 2001; Wright et al., 2002). The 33.3% rate of invasive carcinoma diagnosis in our study thus appears substantial.

SCCAs discovered on Pap smear are rare. Management usually follows the guidelines for the more commonly diagnosed HGSIL, which include immediate colposcopy with CDB, endocervical sampling, or LEEP as considered appropriate. At our institution where risk of loss to follow-up is a concern, performance of immediate LEEP of the transformation zone after colposcopy (the so called "see and treat") has been adopted for this group of patients (Charoenkwan et al., 2004). This technique has been proven to be safe, efficacious, and cost-effective (Wright et al., 2002; Bigrigg et al., 1994; Denny et al., 1995; Santos et al., 1996; Holschneider et al., 1999). While there is concern that a significant number of the excised specimens might lack histologically confirmable cervical intraepithelial lesions (Luesley et al., 1990; Bigrigg et al., 1990), 97.9% of our cases had at least high-grade intraepithelial lesion on final histological diagnosis.

Generally with the "see and treat" approach, the role of colposcopy is to identify suspicious lesions for which intervening colposcopically directed biopsy is still worthwhile and unnecessary LEEP can be avoided. In addition, when LEEP is needed, colposcopy can aid in marking the extent of excision and selecting the proper-size electrosurgical loop to obtain clear excision margins. Of note, however, these proposed benefits of colposcopy could not be proven in the setting of this study. In the 10 patients that had lesions suspicious for invasive carcinoma at the time of colposcopy and had CDB performed for diagnosis, definite diagnosis had been reached by CDB without the need of further LEEP in only 4 patients. All of them already had gross visible lesions on naked-eye examination before performing colposcopy and thus would have undergone biopsy regardless. Of the 38 patients who underwent LEEP subsequent to colposcopy without intervening CDB, only one-fifth had negative excision margins while almost 40% had positive ectocervical margins.

The correlation of colposcopic and final histological diagnosis was not impressive which could be due to the fact that the rate of unsatisfactory colposcopic evaluation in the present study was quite high. Accuracy rate of colposcopy in the detection of microinvasive carcinoma and occult invasive carcinoma in patients with a satisfactory colposcopic examination were 73% and 87%, respectively in one retrospective review of 180 patients. (Benedet et al., 1985). The limitation of colposcopy in detecting microinvasive and invasive disease has been recognized with the reported sensitivity of only 50% in identifying microinvasive disease (Paraskevaidis et al., 1992; Hopman et al., 1998). The rate of underdiagnosis of microinvasive carcinoma with colposcopy was 100% in one report (Edebiri et al., 1990). Furthermore, a lack of abnormal colposcopic findings does not always indicate an absence of cervical pathology. HGSIL and invasive carcinoma were found in 50% and 37.5% of patients with no visible lesion on colposcopic examination, respectively.

The usual interval between initial pelvic examination with Pap smear and colposcopy visit was less than 1 month which is, in most instances, insufficient for a microscopic lesion to progress to a grossly visible lesion. The rate of discovering a previously undetected gross invasive carcinoma at the time of colposcopy was approximately 10% (5 out of 48 patients) in this study. The punch biopsy of the lesions could have readily been performed for these patients and unnecessary referral for colposcopy could have been avoided. This has brought into our attention a need for more careful evaluation at initial pelvic examination.

Certain limitations were present in this study. There was the lack of central cytological review of the referral Pap smear. However, this reflects the real-life situation in the region where effective system of slide tracking and transfer is not widely available. In addition, if the cytological review was conducted in these cases, the reproducibility rate would probably be satisfactory considering the prominent cytological features that lead to the cytological diagnosis of SCCA. The other apparent limitation was a small sample size. A larger study might be able to provide a more clinically meaningful conclusion regarding the role of colposcopy.

In conclusion, women with SCCA on cervical cytology should undergo careful pelvic examination. If no gross lesion can be identified, colposcopy followed by biopsy and LEEP when indicated remains an important diagnostic approach. Most of the women with SCCA cytology in this study have underlying HGSIL; only one-third has invasive carcinoma.

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