RESEARCH COMMUNICATION

Northern Thai Women with High Grade Squamous Intraepithelial Lesion on Cervical Cytology Have High Prevalence of Underlying Invasive Carcinoma

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Abstract

The aim of this study was to determine the underlying pathology of women with high grade squamous intraepithelial lesion (HSIL) on cervical cytology. A total of 681 women with HSIL cytology undergoing colposcopic examination at Chiang Mai University Hospital (CMUH) between January 2000 and December 2005 were evaluated for the underlying cervical pathology. The final pathology was diagnosed from the most severe lesions obtained by punch biopsy, loop electrosurgical procedure, cold knife conization or hysterectomy. Underlying high grade cervical lesions including cervical intraepithelial neoplasia grade 2, 3 and adenocarcinoma in situ were noted in 502 (73.7%) women. Invasive cervical carcinoma was identified in 141 (20.7%). The remaining 38 (5.6%) had either low grade or no intraepithelial lesions. No significant difference in the prevalence of underlying high grade and invasive lesions was noted between women with cytologic diagnosis of HSIL from CMUH and other hospitals. In conclusion, northern Thai women with HSIL cytology are at significant risk of having underlying severe cervical lesions, and especially invasive carcinoma which is detected in approximately one-fifth of the cases.

Key Words: High grade squamous intraepithelial lesion - Pap smear - cervical cytology - cervical carcinoma

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Introduction

Worldwide, approximately 500,000 new cases of cervical cancer are diagnosed each year, about 80% occur in developing countries, and over 50% occur in Asia. Among 250,000 women who die of cervical cancer annually, approximately 80% are from developing countries, where cervical cancer is the most common among female cancers (Ferlay et al., 2000). Among cancer in Thai women, cervical cancer is the most common with the age standardized incidence rate (ASR) of 19.5 per 100,000 person-years. The incidence is highest in Chiang Mai, the northern province of Thailand with an ASR of 25.6 followed by Lampang (ASR=23.6), Bangkok (ASR=20.7), Songkhla (ASR=16.1) and Khon Kaen (ASR=15.0) (Pengsaa et al., 2003).

The aims of cervical cancer screening are to reduce the incidence of cervical cancer, and thereby the morbidity associated with treatment, including loss of fertility, and the related mortality . One of the main problems of the high incidence of cervical cancer in Thailand is the screening coverage of populations at risk. Subsequent appropriate management for abnormal cervical cytology is also an important problem caused by the lack of colposcopists in provincial hospitals. The objectives of colposcopy in management of abnormal cytology are to rule out invasive cancer, to detect high-grade lesions and to guide appropriate treatment.

Immediate colposcopy is recommended for women with a high grade squamous intraepithelial lesion (HSIL). Underlying significant lesions, including high grade cervical lesions and invasive carcinoma are detected in 60-84% and 1-3%, respectively in affected women (Kinney et al., 1998; Jone et al., 2000; Massad et al., 2001; Szurkus ., 2003; Boman et al., 2004; Berdichevsky et al., 2004; Numnum et al., 2005; Sadan et al., 2006; Chute et al., 2006). However, such reports are from developed countries where the incidence of cervical cancer is relatively low. This study was accordingly undertaken to evaluate the underlying pathology of women in the northern region of Thailand who had HSIL on cervical cytology.

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Materials and Methods

Between January 2000 and December 2005, 618 women with HSIL cytology underwent colposcopy at Chiang Mai University Hospital. Colposcopic examination was performed following application of 5% acetic acid solution to the cervix and upper vagina. Cervical biopsies were carried out from the most abnormal appearing area of each lesion. Endocervical sampling using cytobrush was routinely performed in cases of satisfactory colposcopy, but was skipped in patients with unsatisfactory findings in whom diagnostic excision was indicated. Loop electrosurgical excision procedure (LEEP) or cold knife conization (CKC) was performed in cases of unsatisfactory colposcopy, pathologic diagnosis of less than high grade lesions and adenocarcinoma in situ or microinvasive carcinoma on cervical biopsy. Immediate LEEP after colposcopy or "see and treat" approach was performed in women with HSIL cytology after January 2002.

Women with biopsy-confirmed cervical intraepithelial neoplasia (CIN) grade 2, 3 were treated with either LEEP or CKC. Simple hysterectomy was performed for patients with stage IA1 cervical carcinoma. Radical hysterectomy with pelvic lymph node dissection was carried out for patients with stage IA2-IB cervical carcinoma. The final pathologic diagnosis was based on the most severe lesions obtained from biopsy, LEEP, CKC or hysterectomy. This study was conducted under the approval of the Research Ethics Committee of Chiang Mai University Hospital.

The data were entered into a database and analyzed for the prevalence of cervical lesions in women with HSIL cytology using the SPSS program for Window version 11. Comparisons between groups were performed using student's t test, chi square test or Fisher exact test as appropriate. P value of <0.05 was considered to be statistically significant.

Results

Mean age of the 681 women with HSIL cytology was 44.5 years with a range of 23-80 years. Twenty five (3.7%) women were nulliparous, 519 (76.2%) women were premenopausal women. Satisfactory colposcopy was noted in 177 (26.0%) women. Immediate LEEP after colposcopy was carried out in 526 (77.2%) patients, the remaining 155 (22.8%) underwent colposcopically directed biopsy for pathologic evaluation before planning appropriate treatment.

Table 1 shows the final pathologic diagnoses of the 681 patients with HSIL cytology. Overall, 643 (94.4%) patients had significant cervical lesions. Of note, invasive carcinoma was found in 141 (20.7%) women. Stage IA1 and stage IA2 cervical carcinoma were identified in 79 (11.6%) and 12 (1.8%) patients, respectively. Frankly invasive carcinoma was detected in 50 (7.3%) patients. Thirty eight (5.6%) patients had no significant lesions despite undergoing diagnostic LEEP. Among 526 women who underwent immediate LEEP after colposcopy, 37 (7%) had no significant lesions. When separately analyzed between 241 women with cytologic diagnosis of HSIL from Chiang Mai University Hospital and 440 women with HSIL cytology diagnosed from other hospitals, no statistically significant difference in the prevalence of high grade lesions and invasive carcinoma was found (P=0.51).

Table 1. Underlying Lesions for 681 Women with HSIL on Cervical Cytology

Underlying lesion	CMUH (%)	Others (%)	Total (%)
None	5 (2.0)	24 (5.5)	29 (4.3)
CIN 1	4 (1.7)	5 (1.1)	9 (1.3)
CIN 2, 3 & AIS	179 (74.3)	323 (73.4)	502 (73.7)
Invasive carcinoma	53 (22.0)	88 (20.0)	141 (20.7)
Total	241 (100)	440 (100)	681 (100)

CIN = Cervical intraepithelial neoplasia; AIS = Adenocarcinoma in situ; CMUH = Chiang Mai University Hospital

Discussion

Our study showed that histologically confirmed high grade lesions were detected in 73.7% of women with HSIL cytology which is similar those reports of 60-84% in the previous studies (Kinney et al., 1998; Jone et al., 2000; Massad et al., 2001; Szurkus, 2003; Boman et al., 2004; Berdichevsky et al., 2004; Numnum et al., 2005; Sadan et al., 2006; Chute et al., 2006). Of significant difference was the high prevalence of underlying invasive carcinoma which was 20.7% in this study compared to those of 1-3% in the previous reports. This may reflect the high incidence of cervical cancer in the northern region of Thailand. No significant difference in the prevalence of high grade lesions and invasive carcinoma was identified when women with HSIL cytology in our hospital were compared with those from the other hospitals.

Women with HSIL cytology are at increased risk of having CIN 2, 3 or invasive cancer. Immediate colposcopy is recommended for managing these patients. The patients are treated after cervical lesions are histologically confirmed. This three-step approach is costly and time consuming. Previous studies showed that the two-step protocol, i.e. the "see and treat" approach decreased the time interval between diagnosis and treatment with a similar accuracy of diagnosis compared to the traditional three-step protocol (Berdichevsky et al., 2004; Sadan et al., 2006). With the "see and treat" approach, the overtreatment rate in our study was 7% which was much lower than those of 16-33% in the previous reports (Berdichevsky et al., 2004; Numnum et al., 2005; Sadan et al., 2006). This reflects the higher prevalence of underlying significant lesion, i.e. CIN 2, 3 or invasive carcinoma in women with HSIL cytology in our region which is 94.4% compared to those of 70-85% in the other studies (Berdichevsky et al., 2004, Numnum et al., 2005, Sadan et al., 2006).

The potential benefits of the "see and treat" protocol include a more accurate histologic diagnosis due to a larger cervical specimen compared with that obtained from punch

biopsy, a reduction of patient visits, a decrease in cost and a shorter diagnosis to treatment interval (Luesley et al., 1990). This approach appears to be encouraging particularly for developing countries where lacks of experienced colposcopists, loss to follow-up and health care costs are of major concern. However, the drawbacks of such approach are the problem of thermal damage interfering pathologic evaluation, the concern of overtreatment and the risk of postoperative complications. Although a small amount of epithelial disruption at the surgical margins has been observed, this does not generally interfere with pathologic evaluation (Wright et al., 1992; Mathevet et al., 1994). The over treatment rate in our study was low at 7%. When performed by expert colposcopists, this procedure has been shown to be safe and effective in treating women with cervical lesions (Kietpeerakool et al., 2006).

The disadvantages of this study are the retrospective by nature. The majority of cytologic slides of patients referred from other hospitals could not be reviewed. However, it represents the real situation of women with HSIL cytology who need further diagnostic workup for definite treatment. The advantage of this study is the considerably high number of women. Furthermore, these patients were managed by expert colposcopists in a single institution. In our hospital, women with HSIL cytology who have no gross invasive tumor identified by visual inspection will undergo colposcopy followed by LEEP or the so-called "see and treat" approach. Since LEEP will be subsequently performed in nearly all women with HSIL cytology, we are currently conducting a study to evaluate the accuracy, the clinical and histological outcomes in women with such cytologic result comparing between the "colposcopy and LEEP approach" versus the "visual inspection and LEEP" approach.

In conclusion, northern Thai women with HSIL cytology have a substantially high prevalence of severe cervical lesions, and especially invasive carcinoma which is identified in about one-fifth of the patients.

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