
GYNAECOLOGY

Outcome of The Management of Women with “Atypical Squamous Cells” in Cervical Cytology after Colposcopy

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ABSTRACT

Objective: To study and compare the outcomes of the management of women with cervical cytology interpreted as atypical squamous cells of undetermined significance (ASC-US) and atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H) after colposcopic evaluation.

Study design: Retrospective descriptive study.

Setting: Nakornping Hospital, Chiang Mai, Thailand.

Materials and Methods: Medical records of 254 women with cervical cytology of ASC-US and 75 women with cervical cytology of ASC-H, who underwent colposcopy at colposcopy clinic of Nakornping hospital from October 2003 to September 2007 were retrospectively reviewed. The data was analyzed and compared between two groups of abnormal cervical cytology.

Results: Of 254 patients, who had ASC-US and 75 patients, who had ASC-H in cytology, the biopsy procedures were taken for histopathologic diagnosis in 133 patients (52%) of ASC-US group and 56 patients (75%) of ASC-H group. On histopathologic results, 30 patients (40.0%) had high-grade squamous intraepithelial lesion (HSIL) and 15 patients (20.0%) had invasive lesions in ASC-H group which was significantly higher than those with ASC-US group (47 patients; 18.5% had HSIL and 20 patients; 7.9% had invasive lesions; p value < 0.0001).

Conclusion: This study reaffirms the substantially risk of underlying significant lesions especially invasive cervical cancers in women with ASC-US and ASC-H smear, ASC-H group is at significant higher risk for high-grade and invasive lesions than ASC-US group. Therefore, women with ASC-US and ASC-H cytology should undergo immediate colposcopy in order to early detect and treat high-grade and invasive lesions.

Keywords: atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H), cervical cytology, colposcopy

Introduction

The Pap smear is the most successful cancers screening method to reduced the incidence of invasive cervical cancers in developed countries in a

direct consequence of well established screening programs.⁽¹⁾ The cervical cytology was refined in The Bethesda 2001 System and created the diagnostic category of “atypical squamous cells (ASC)”. The

category of ASC was divided into 2 subcategories: 1) undetermined significance (ASC-US) and 2) cannot exclude high-grade squamous intraepithelial lesion (ASC-H).⁽²⁾

Development of the ASC-H subcategory was stimulated by cross-sectional data indicating that individual cytologists are capable of identifying a personally defined subset of ASC cytology that is more strongly associated with underlying cervical intraepithelial neoplasia 2 or 3 (CIN2 or CIN3) than ASC-US but less strongly associated than cytology to HSIL.⁽³⁻⁹⁾ Based on the Bethesda subcategorization of ASC, different guidelines for the management of ASC-US and ASC-H have been proposed.⁽¹⁰⁾ For the women with ASC-US, decisions regarding colposcopy referral may be based on human papilloma virus (HPV) testing (which is considered the “preferred” method) or repeat cytology (which is considered “acceptable”), whereas for women with ASC-H finding, colposcopy is recommended. The studies for Thai women that evaluated the outcome of ASC-US and ASC-H have been limitedly established.

The purpose of the present study was to evaluate and compare the outcomes of the management of women with cervical cytology interpreted as ASC-US and ASC-H.

Materials and Methods

All of 1922 patients were referred and underwent colposcopy at colposcopy clinic in Nakornping hospital from October 2003 to September 2007. A total of 1649 patients, who had abnormal cervical cytology including 254 patients of ASC-US and 75 patients of ASC-H were counseled about colposcopy and the biopsy procedure for diagnosis and informed consent was obtained from each of them. Two hundred and sixty-seven patients (81.2%) had cervical smear at other hospitals and were interpreted by outside pathology laboratories. The biopsy procedure for histopathologic diagnosis were performed by staff and based on colposcopic finding according to standard guidelines. The biopsy procedure were

colposcopically directed biopsy (CDB), endocervical curettage (ECC), loop electrosurgical excision procedure (LEEP) and cold knife conization (CKC). The histopathologic diagnosis used for analysis were most severity results from any biopsy procedure. Colposcopic impression on the severity of intraepithelial lesions is based on abnormal colposcopic finding: acetowhite epithelium, punctuation, mosaic, border, iodine negativity, vascular patterns and atypical vessels.⁽¹¹⁾ All patients, who had the histopathologic results, were given a weekly follow-up appointment for reevaluation.

Patients with apparently normal colposcopy, no intraepithelial lesion from surgical procedure and those with pathologic diagnosis of low-grade squamous intraepithelial lesion (LSIL) were followed with Pap smears every 6 months for 2 years and then with annual examination if four consecutive Pap smears appear normal. Furthermore, women with pathologic diagnosis of HSIL for histologic result were managed according to American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines⁽¹⁰⁾ while patients with invasive cervical cancer were clinically staged and managed according to the International Federation of Gynecology and Obstetrics (FIGO).

Tissue specimens for histopathologic diagnosis were interpreted by the Department of Pathology, Faculty of Medicine, Chiang Mai University. During the study period, dermographic, abnormal cervical cytology or clinical situation, colposcopic and histopathologic data were prospectively stored on colposcopic data sheets.

The data were retrospectively analyzed using the statistical package for the social science (SPSS). The descriptive data were assessed using mean \pm SD, range, number of patients and percentage. Comparison of means between two independent groups was performed using the independent sample t-test and assessed categorical variable using Chi-square test. P values less than 0.05 were considered statistically significant.

Results

During the study period, 254 patients with cervical cytology reported as ASC-US and 75 patients with ASC-H abnormal cervical cytology were eligible for the present study. Clinical characteristics of each patient group was presented in table 1. The average age of all patients was 45.2 ± 8.9 years and the age range was 18-72 years. The mean parity was 2.0 ± 1.4 and most of the patients (76%) had 1 or 2 children. The recently contraception were tubal resection (28.9%), non-contraception (27.7%), oral contraceptive pills (21.6%) and depot medroxyprogesterone acetate (12.8%).

Univariable analysis showed that a parity of ASC-H group was statistically significant less than ASC-US group (1.6 ± 0.8 vs 2.1 ± 1.5 , $p = 0.015$) but age and contraceptive methods were not statistically significant in difference between two groups (Table 1).

Table 2 demonstrates the colposcopic data and histopathologic results for the group of ASC-US and ASC-H in cervical cytology. The colposcopic satisfactory revealed no statistically significant differences between two groups ($p = 0.070$).

Colposcopic impression of HSIL or invasive cancer were significantly higher in ASC-H group as compared with ASC-US group (57.4% vs 27.6%, $p = 0.002$). One hundred and twenty-one patients (47.6%) in ASC-US group and 19 patients (25.3%) in ASC-H group had normal and satisfactory colposcopy, these patients do not perform biopsy procedures and were followed with Pap smear every 6 months for 2 years.

The pathologic results of LSIL were two patients (2.7%) in ASC-H group and twenty-four patients (9.5%) in ASC-US group. The detection of pathologically confirmed HSIL (40.0%) or invasive cancer (20.0%) in women with ASC-H was significantly higher than in those with ASC-US (18.5%, 7.9%; respectively, $p < 0.0001$). Twenty patients (7.9%) with ASC-US cytology had invasive squamous cell carcinoma on subsequent histological evaluation (13 stage IA1 and 7 stage IB1). In ASC-H group, 15 patients (20.0%) had invasive carcinoma on pathologic results (13 patients had squamous cell carcinoma and 2 patients had adenocarcinoma, 10 stage IA1; 1 stage IA2; 3 stage IB1; 1 stage IB2).

Table 1. Clinical characteristics of patients with cytologic diagnosis of ASC-US and ASC-H.

| Characteristics | ASC-US | ASC-H | p-value |
|------------------------------------|----------------|----------------|---------|
| Age – Mean \pm SD, years | 45.3 ± 9.2 | 44.9 ± 7.7 | 0.705 |
| - Range, years | 18-72 | 27-62 | |
| Parity – Mean \pm SD, years | 2.1 ± 1.5 | 1.6 ± 0.8 | 0.015* |
| - Range | 0-10 | 0-4 | |
| Recently contraception, number (%) | | | 0.213 |
| Non-contraception | 72 (28.3) | 19 (25.3) | |
| Tubal resection | 77 (30.3) | 18 (24.0) | |
| Oral contraceptive pills | 54 (21.3) | 17 (22.7) | |
| DMPA | 28 (11.0) | 14 (18.7) | |
| Others | 23 (9.1) | 7 (9.3) | |

ASC-US = Atypical squamous cells of undetermined significance,

ASC-H = Atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion,

SD = standard deviation,

DMPA = depot medroxyprogesterone acetate

Table 2. Colposcopic impression and histopathologic result of patients with cytologic diagnosis of ASC-US and ASC-H.

| Characteristics | ASC-US Number (%) n = 254 | ASC-H Number (%) n = 75 | p-value |
|------------------------------------|---------------------------------|-------------------------------|-----------|
| Colposcopic satisfactory | | | 0.070 |
| Satisfactory | 168 (66.1) | 41 (54.7) | |
| Unsatisfactory | 86 (33.9) | 34 (45.3) | |
| Colposcopic impression | | | 0.002* |
| No lesion | 141 (55.5) | 22 (29.3) | |
| LSIL | 43 (16.9) | 10 (13.3) | |
| HSIL | 65 (25.6) | 40 (53.4) | |
| Invasive carcinoma | 5 (2.0) | 3 (4.0) | |
| Histopathologic diagnosis | | | < 0.0001* |
| No lesion | 42 (16.5) | 9 (12.0) | |
| LSIL | 24 (9.5) | 2 (2.7) | |
| HSIL | 47 (18.5) | 30 (40.0) | |
| Invasive carcinoma | 20 (7.9) | 15 (20.0) | |
| Normal and satisfactory colposcopy | 121 (47.6) | 19 (25.3) | |

LSIL = low-grade squamous intraepithelial lesion,

HSIL = high-grade squamous intraepithelial lesion,

ASC-US = Atypical squamous cells of undetermined significance,

ASC-H = Atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion

Discussion

The previous studies had consistently demonstrated that the detection rate of clinically significant lesions in women with ASC-H was higher than in those with ASC-US cytology, and such a prevalence was intermediate between ASC-US and HSIL smears.⁽³⁻⁹⁾ This study showed that a histopathologic diagnosis of ASC-H cytology seems to confer a higher risk for HSIL or invasive cervical cancers than ASC-US cytology (60% vs 26.4%, $p < 0.0001$). The pathologically confirmed high-grade lesions or invasive cancers were identified in 26.4% of women with ASC-US cytology, which is higher than those reported in several studies (2% to 19%).⁽¹²⁻¹⁶⁾ Furthermore, an extraordinary high prevalence of invasive cancer (7.9%) was found in our study as compared to less than 0.8% in previous reports.⁽¹²⁻¹⁶⁾

In another group of women with ASC-H cytology, the prevalence of pathologically confirmed

high-grade lesions or invasive cancers were identified in 60%, which is nearby the detection rate of clinically significant lesions in other studies varied from 15% to 80%.⁽³⁻⁹⁾ However, the prevalence of invasive cancers in other studies were less than 3.5%⁽³⁻⁶⁾ which was much lower than in this study (20.0%).

In the literature, almost studies⁽³⁻⁷⁾ on the histopathologic result of ASC-US and ASC-H smear were reported from North America, where the incidence of cervical cancer appears to be relatively low. Based on our finding, women with ASC-US and ASC-H cytology had pathologically confirmed invasive cancers higher than the previous studies. This may reflect inadequate smear due to difference in the sampling devices or the techniques of sampling influence the quality of Pap smear⁽¹⁷⁾ and a high incidence of invasive cervical cancer in our country, cervical cancer is the most common cancer

in female with the age standardized incidence rate (ASR) of 19.5 per 100,000 person-year.⁽¹⁸⁾ The incidence is highest in Chiang Mai, a northern province with an ASR of 25.3, followed by Lampang (ASR = 23.6), Bangkok (ASR = 20.7) and Khon Kaen (ASR = 15.0).⁽¹⁸⁾ In this study, all women with ASC-US cytology from the first Pap screening were performed colposcopic examinations because there were the problems of quality control of Pap smear, the high incidence of cervical cancer, poor compliance and psychologic distress of these women. Furthermore, the cost of human papillomavirus (HPV) testing is much higher than of colposcopy and repeat cervical cytological test in our country.

A program of repeat cervical cytological testing, colposcopy immediately or after DNA testing of high-risk types of HPV are all acceptable methods for managing woman with ASC-US and each of these approaches has advantage and disadvantage.⁽¹⁰⁾ Referring women with ASC-US cytology for immediate colposcopy allows women with significant lesions to be readily identified and could reduce the risk of follow-up. The disadvantages of colposcopy are that many women consider the procedure to be uncomfortable, more expensive and it has the potential for overdiagnosis and overtreatment.⁽¹⁹⁾

The recommended management of women with ASC-H cytology is referral for colposcopic evaluation.⁽¹⁰⁾ Based on our findings, women with ASC-H should undergo immediate colposcopic and histopathologic evaluation in order to early detect and treat high-grade and invasive cervical lesions. If no lesion is identified at colposcopy, it is recommended that a review of cytology, colposcopy and histologic results be performed.

The limitations of this study were the retrospective by nature, a lack of central slide review of cervical smears, the use of a uniform management protocol (colposcopy) for women with ASC-US or ASC-H smears and relatively small sample size. Women with ASC-US or ASC-H smears who had normal colposcopic finding defaulted from adequate follow up and most women were referred and had

cytologic surveillance at other hospitals. However, this study does show that significant lesions including invasive cancers were identified in approximately one-fourth of women with ASC-US cytology and approximately 60% of women with ASC-H cytology in our institute.

In conclusion, the histopathologic diagnosis of ASC-H smear seems to confer a substantially higher risk for HSIL or invasive cervical lesions than ASC-US smear. Immediate colposcopic examination should be the appropriate management for women with ASC-US and ASC-H smear in order to early detect and treat high-grade and invasive lesion.

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ผลการดูแลรักษาสตรีที่มีผลตรวจเซลล์วิทยาของปากมดลูกชนิด atypical squamous cells หลังตรวจปากมดลูกด้วยกล้องขยายทางช่องคลอด

วัชรินทร์ สุนทรลัมศิริ

วัตถุประสงค์ : เพื่อศึกษาและเปรียบเทียบผลการรักษาในสตรีที่มีผลตรวจทางเซลล์วิทยาของปากมดลูกชนิด ASC-US และ ASC-H หลังการตรวจปากมดลูกด้วยกล้องขยายทางช่องคลอด

รูปแบบการศึกษา : การศึกษาแบบเก็บข้อมูลย้อนหลัง เชิงพรรณนา

สถานที่ศึกษา : โรงพยาบาลนครพิงค์ จังหวัดเชียงใหม่

วัสดุและวิธีการ : ได้ทำการรวบรวมข้อมูลจากบันทึกทางการแพทย์ของผู้ป่วยที่มีผลการตรวจทางเซลล์วิทยาของ ปากมดลูกชนิด ASC-US จำนวน 254 รายและชนิด ASC-H จำนวน 75 ราย ที่ได้รับการตรวจด้วยกล้องขยายทางช่องคลอด ณ โรงพยาบาลนครพิงค์ ระหว่างวันที่ 1 ตุลาคม พ.ศ.2546 ถึงวันที่ 30 กันยายน พ.ศ.2550 นำข้อมูลที่ได้มาวิเคราะห์และเปรียบเทียบผลการตรวจทางพยาธิวิทยาของปากมดลูกในทั้ง 2 กลุ่ม

ผลการศึกษา : ในกลุ่มผู้ป่วยที่มีผลการตรวจเซลล์วิทยาชนิด ASC-US จำนวน 254 รายและ ASC-H จำนวน 75 รายมีการตรวจทางพยาธิวิทยาจากการตัดชิ้นเนื้อบริเวณปากมดลูกในผู้ป่วยจำนวน 133 ราย (ร้อยละ 52) และ 56 ราย (ร้อยละ 75) ตามลำดับ ผลการตรวจทางพยาธิวิทยาพบว่าในกลุ่ม ASC-H มีความชุกของการเกิดรอยโรคภายในเยื่อบุสควมัสชั้นสูง (high-grade squamous intraepithelial lesion; HSIL) ร้อยละ 40 (30 ราย) และมะเร็งระยะลุกลามร้อยละ 20 (15 ราย) ซึ่งสูงกว่ากลุ่ม ASC-US ที่มีรอยโรคชนิด HSIL ร้อยละ 18.5 (47 ราย) และมะเร็งระยะลุกลามร้อยละ 7.9 (20 ราย) อย่างมีนัยสำคัญทางสถิติ ($p\text{-value} < 0.0001$)

สรุป : สตรีที่มีผลการตรวจทางเซลล์วิทยาของปากมดลูกชนิด ASC-US และ ASC-H มีความเสี่ยงชัดเจนต่อรอยโรคภายในเยื่อบุสควมัสชั้นสูงและระยะลุกลาม โดยกลุ่ม ASC-H มีความเสี่ยงต่อรอยโรสดังกล่าวสูงกว่ากลุ่ม ASC-US ในสตรีที่มีผลการตรวจทางเซลล์วิทยาชนิด ASC-US และ ASC-H ควรได้รับการตรวจด้วยกล้องขยายทางช่องคลอดทันที เพื่อให้สามารถตรวจหาความผิดปกติ และรักษามะเร็งปากมดลูกตั้งแต่ระยะเริ่มแรก
