



Histopathologic Correlation of ASC-US and ASC-H

Jidapa Thammasiri

Abstract

This descriptive study was designed to study the histopathologic correlation of atypical squamous cell in cervical smear at the National Cancer Institute from October 1,2005 to September 30,2007. Sixty-three cases of ASC-US were performed colposcopic biopsy and/or LEEP. The histologic diagnosis revealed low grade lesion or LSIL in 11 cases (17.4%), high grade lesion (HSIL or worse) 16 cases (25.4%), atypical squamous metaplasia 1 case (1.6%), and inflammation 35 cases (55.6%). In the category of ASC-H, 105 cases were performed colposcopy, which the histologic diagnosis revealed low grade lesion or CIN 1 in 21 cases (20 %), high grade lesion (CIN 2 or worse) 45 cases (42.9%), atypical squamous metaplasia 7 cases (6.7 %), and inflammation 32 cases (30.5 %). Cases classified as ASC-H are associated with a significant risk of high grade lesion than ASC-US category. However, this study assumed that patients with atypical squamous cell either ASC-US or ASC-H according to the 2001 Bethesda System classification should receive the proper management since they have an increase risk of underlying cervical intraepithelial neoplasia and rarely carcinoma. (*Thai Cancer J 2008;28:44-47.*)

บทคัดย่อ

การศึกษาผลตรวจชิ้นเนื้อจากปากมดลูกในผู้ป่วยที่ผลตรวจ Pap smear เป็นชนิด ASC-US และ ASC-H โดย จิดาภา ธรรมศิริ

สถาบันมะเร็งแห่งชาติ กรมการแพทย์ กรุงเทพมหานคร 10400

การศึกษานี้เป็นการวิจัยเชิงบรรยายเพื่อเปรียบเทียบผลการตรวจทางเซลล์วิทยาของปากมดลูกที่เป็นชนิด Atypical squamous cell (ASC) ในระบบ Bethesda 2001 กับผลการตรวจชิ้นเนื้อปากมดลูกที่ได้รับจากการทำคอลโปสโกปีในผู้ป่วยทั้งหมด 166 ราย ที่สถาบันมะเร็งแห่งชาติตั้งแต่วันที่ 1 ต.ค. 2548 ถึง 30 ก.ย.2550 พบว่าผู้ป่วยที่เป็น ASCUS ที่มีผลชิ้นเนื้อ มีจำนวน 63 ราย ส่วนผู้ป่วยที่เป็น ASC-H ที่มีผลชิ้นเนื้อ มีจำนวน 105 ราย ซึ่งจากการศึกษานี้พบว่ากลุ่ม ASC-US 63 รายมีผลการตรวจชิ้นเนื้อเป็น LSIL 11 ราย (17.4 %), เป็น HSIL หรือพยาธิสภาพที่รุนแรงกว่าจำนวน 16 ราย (25.4%), เป็น Atypical squamous metaplasia 1 ราย (1.6%) และเป็น Inflammation 35 ราย (55.6%) ส่วนในกลุ่ม ASC-H พบว่ามีผลการตรวจชิ้นเนื้อเป็น LSIL 21 ราย (20 %), เป็น HSIL หรือพยาธิสภาพที่รุนแรงกว่าจำนวน 45 ราย (42.9%), เป็น Atypical squamous metaplasia 7 ราย (6.7%) และเป็น Inflammation 32 ราย (30.5%) สรุปว่าผู้ป่วยที่มีผลการตรวจทางเซลล์วิทยาของปากมดลูกที่เป็นชนิด ASC มีโอกาสที่จะมีพยาธิสภาพของปากมดลูกได้ทุกชนิด แต่กลุ่มที่เป็น ASC-H จะมีโอกาสเสี่ยงที่จะเป็น HSIL ได้มากกว่า ASC-US (*วารสารโรคมะเร็ง 2551;28:44-47.*)

Pathology Division, National Cancer Institute, Bangkok, Thailand

Introduction

It has been known that the use of the Papanicolaou classification was no longer acceptable medical practice and it is replaced by The Bethesda System (TBS). The TBS for reporting cervical vaginal cytologic diagnosis have been used by The National Cancer Institute of Thailand since 2001. One of the basic tenets of TBS is the division of preneoplastic squamous lesions into two categories: low-grade squamous intraepithelial lesions (LSIL) and high-grade squamous intraepithelial lesion (HSIL). This division is intended to reflect the current understanding of cervical carcinogenesis, and it is the basis for the recently published clinical guidelines for the treatment of women with cytologic abnormalities. Categories of abnormality broadly similar to borderline nuclear change-atypical squamous cells of undetermined significance (ASCUS) and atypical glandular cells of undetermined significance (AGUS) cells – are recognized. The 2001 Bethesda System has classified the category of atypical squamous cell (ASC) into ASC-US (Atypical squamous cells of undetermined significance) and ASC-H (Atypical squamous cell cannot exclude HSIL). ASC does not represent a single diagnostic entity, but it encompasses a spectrum of cellular changes and reflects a variety of pathologic processes including reactive changes as well as lesion which suggest the possible presence of underlying cervical intraepithelial neoplasia (CIN) and rarely carcinoma¹. The interpretation and precise classification of abnormal squamous cell changes in cervicovaginal smear (Pap test) are challenging and controversial. This study is a retrospective investigation of the histopathologic finding in women with ASC-US and ASC-H diagnosed on Pap test of conventional

method.

Materials and Methods

The cytology files (October 1, 2005–September 30, 2007) were searched for cervicovaginal Pap tests interpreted as ASC-US and ASC-H. Cases were included for study only if there was a subsequent cervicovaginal tissue sample within one year of the cytologic interpretation.

Results

Among 605 patients with ASC-US, 63 cases met the inclusion criteria of the study and of 200 patients with ASC-H, 105 cases met the inclusion criteria for the study. The interval between the cytologic interpretation and cervicovaginal tissue examination ranged from 8 day to 6 months. The patients' ages ranged from 29 to 75 years (mean 49.4) in the ASCUS category and ranged from 22–74 years (mean 47.3) in the ASC-H category.

In the group of ASC-US category (Table 1), the histologic follow-up demonstrated evidence of squamous cell carcinoma in 3 cases (4.8%), HSIL 13 cases (20.6%), LSIL 11 cases (17.5%) and atypical squamous metaplasia 1 case (1.6%) The other 35 cases (55.6%) showed chronic cervicitis with reactive changes and endocervical polyp.

In the group of ASC-H category, 2 cases of adenocarcinoma (1.9%), 5 cases of squamous cell carcinoma (4.8%), 38 cases of HSIL (36.9%), 21 cases of LSIL (20%), and 7 cases of atypical immature squamous metaplastic change (6.7%) were observed. The other 32 cases (31.1%) showed chronic cervicitis without evidence of cervical intraepithelial neoplasia. The two cases

Table 1 Histological outcome of the case classified as ASC-US and ASC-H

Histopathologic diagnosis	ASC-US		ASC-H	
	(No. of case)	%	(No.of case)	%
LSIL	11	17.46	21	20
HSIL (CIN 1 + CIN 2)	13	20.63	38	36.19
Atypical	1	1.59	7	6.66
Squamous cell carcinoma	3	4.76	5	4.76
Adenocarcinoma	-		2	1.90
Inflammation	35	55.55	32	30.47

Abbreviations: ASC-US, atypical squamous cell of undetermined significance; ASC-H, atypical squamous cell cannot exclude HSIL; LSIL, low grade squamous intraepithelial lesion; HSIL, high grade squamous intraepithelial lesion.

Table 2 Histopathologic diagnosis of 63 patients with ASC-US category stratified by age

Age range (years)	LSIL	HSIL*	Negative**
29	-	-	1
30-39	3	3	1
40-49	2	6	20
50-59	6	3	11
60-69	-	3	2
70-75	-	1	1

*HSIL includes CIN 2, CIN 3 and a few cases worse than HSIL e.g. squamous cell carcinoma and adenocarcinoma.

**Negative includes inflammation and a few cases of atypical immature squamous metaplasia.

Table 3 Histopathologic findings of 105 patients with ASC-H category stratified by age.

Age range (years)	LSIL	HSIL*	Negative**
22-29	1	2	2
30-39	2	9	4
40-49	13	17	23
50-59	2	8	6
60-69	3	5	3
70-75	-	4	1

*HSIL includes CIN 2, CIN 3 and a few cases worse than HSIL e.g. squamous cell carcinoma and adenocarcinoma.

**Negative includes inflammation and a few case of atypical immature squamous metaplasia.

of adenocarcinoma were concluded to be endometrial origin. Two cases of squamous cell carcinoma were proved to be the recurrent case of squamous cell carcinoma. HSIL was the most frequent histopathologic type found in patients aged 40–49 years in both ASC-US and ASC-H. (Table 2, 3)

Discussion

The diagnosis of ASC-US and ASC-H often causes worrying among the clinicians because it may reflect an exuberant benign change or a potentially serious lesion, which can not be

unequivocally classified². Laboratory rates of ASC vary depending on the patient population, the diagnostic criteria utilized, and the experience and skill of the cytotechnologist or cytopathologist. While there is no ‘correct’ percentage rate of ASC in a low-risk population, the rate of ASC should be less than 5% of total specimen³. For laboratories that serve high risk population, than the rate of ASC may be higher, but should not exceed 2–3 times than the rate of SIL in the laboratory. From this study, it was found that the ASC rate was 1.28%.

The major finding in this study is that 25.4 %

of case diagnosis of ASC-US are associated with an underlying high-grade intraepithelial lesion although the negative rate is rather high (55.6%). Follow-up of a large number of patient with ASCUS from different laboratories has revealed 10.3–43% with SIL^{4,5}. But in case of ASC-H, 42.9% of cases are found to be high grade lesion which includes CIN2, CIN3 or worse. This confirms that ASC-H is associated with a significant risk of HSIL. Triage approach using a combination of review cytological diagnosis and HPV DNA testing would produce the best results. A small number of cases in this study reveal histopathologic diagnosis of atypical immature squamous metaplastic cells (AIM). The current evidence suggests that approximately 50% of AIM are HPV-related squamous proliferation of immature metaplastic epithelium⁶. Some lesions are benign, some are LSILs and HSILs. The study by Park et al⁷ suggests that biology is not predicted by morphology, nor will it identify cases that are HPV positive. Thus, there may be a role for HPV testing and Ki-67 labeling to separate the benign lesions and confirm or predict the SILs.

In conclusion, the finding from this study of ASC-US and ASC-H on a Pap test correlated with the presence of an underlying SIL or invasive carcinoma in approximately 25.4% and 42.9%

respectively. The cytologic finding warrants further investigation in order to exclude SILs and/or carcinoma.

Acknowledgements

The author thanks Miss Akarane Korn K. and Mrs. Suparat P. for fruitful collaboration.

Reference

1. Sherman ME, Solomon D, Schiffman M (for the ALTS Group). Qualification of ASCUS. A comparison of equivocal LSIL and equivocal HSIL cervical cytology in The ASUS LSIL Triage Study. *Am J Clin Pathol* 2001;116:386-94.
2. Sherman ME, Abdul-Karin FW, Berek JS, et al. Atypical squamous cells. In: Solomon D, Nayar R, editors. *The Bethesda System for reporting cervical cytology*. 2nd ed. New York: Springer-Verlag Inc.; 2004. p.67-85.
3. Loffe OB, Henry MR. The uterine cervix. In: Silverberg SG, editor. *Silverberg's principles and practice of surgical pathology and cytopathology* 4th ed, Churchill Livingstone Elsevier; 2006. p.1864-5.
4. Davey DD, Naryshkin S, Nielsen ML, Kline TS. Atypical squamous cells of undetermined significance : interlaboratory comparison and quality assurance monitors. *Diagn Cytopathol* 1994;11:390-6.
5. เจริญ วิภูภิญโญ ความสำคัญทางคลินิกของผลการตรวจมะเร็งปากมดลูกที่รายงานผลเป็น ASCUS และ AGUS วารสารโรงพยาบาลราชวิถี 2544;12:25-31.
6. Maire AD. Cytologic and histologic diagnosis and significance of controversial squamous lesion of the uterine cervix. *Mod Pathol* 2000;13:250-60.
7. Park IJ, Genest DR, Sun D, Crum CP. Atypical immature squamous metaplastic-type cervical proliferations : a histologic spectrum of uncertain etiology. *Mod Pathol* 1998;11:111A.