Histopathologic Consistency between Endometrial Hyperplasia Diagnosis from Endometrial Curettage and Pathologic Diagnoses from Hysterectomy Specimens

Somneuk Jesadapatrakul, MD*
Siriwan Tangjitgamol, MD**, Sumonmal Manusirivitaya,MD**

** Department of Pathology, Bangkok Metropolitan Administration Medical College and Vajira Hospital*
*** Department of Obstetrics and Gynecology, Bangkok Metropolitan Administration Medical College and Vajira Hospital*

Objectives: *To evaluate the consistency between histopathology of endometrial hyperplasia (EMH) from endometrial curettage and those from the subsequent hysterectomy specimen. The co-incidental finding of endometrial carcinoma in patients with EMH was also studied.*
Material and Method: *All patients who had a diagnosis of EMH from the curettage procedure and underwent hysterectomy, between January 1995 and December 2004, were identified. The histopathology of the curettage specimens were compared to those of the hysterectomy specimens.*
Results: *The histopathologic subtypes of EMH from the curettage specimens of 46 patients included in the study were: simple or complex hyperplasia in 30 cases and atypical simple or complex hyperplasia in 16 cases. The consistency rate of endometrial tissue from curettage and hysterectomy specimens was 41.3%. The consistency rates were 62.5% and 30.0% in patients with atypical EMH and EMH without atypia respectively. Eight cases (17.4%) of EMH also had co-incident endometrial carcinoma.*
Conclusion: *The consistency rate of endometrial tissue from curettage and hysterectomy specimens was only modest. This rate was lower in EMH without atypia.*

Keywords: *Endometrial hyperplasia, Fractional curettage, Hysterectomy, Consistency*

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Endometrial hyperplasia (EMH) is a pathological condition of endometrium which carries both clinical and pathological significance. It is one of the most important predisposing factors for the development of endometrial carcinoma (EMC) [1]. This risk is especially seen in atypical EMH which carries the risk of associated EMC more than EMH without atypia [2,3]. In the pathological point of view, discrimination between EMH, especially atypical complex EMH, and EMC can sometimes cause a diagnostic problem to the pathologist [1,4]. Although many recent studies reported the use of more sophisticated techniques such as various immunohistochemistry to distinguish these two conditions [5,6], histology remains an important basic diagnostic tool [1,4]. Many histologic criteria have been suggested to differentiate between atypical complex EMH and well-differentiated EMC. However, the decision is frequently difficult to make. Reproducibilty of atypical EMH diagnosis by the pathologists is also a problem; it was reported to be less than 50% in one study [7]. The under- or over-diagnoses might be encountered and either of these circumstances can mislead a surgeon to an inappropriate management. EMH may be treated medically or surgically with simple hysterectomy while the atypical EMH requires a meticulous intra-operative assessment of the gross pathology or frozen section, and the EMC requires a more extensive procedure of surgical staging.

We studied the consistency between endometrial hyperplasia primarily diagnosed from endometrial curettages and the endometrial histopathology from the subsequent hysterectomy specimens. Various clinico-pathological characteristics were studied to

Correspondence to : Tangjitgamol S, Department of Obstetrics and Gynecology, Bangkok Metropolitan Administration Medical College and Vajira Hospital, 681 Samsen Rd, Dusit district, Bangkok, 10300, Thailand. Phone: 0-2244-3405, Fax: 0-2243-7907, E-mail:siriwanonco @yahoo.com

evaluate the association with the consistency or non-consistency. The co-incidental finding of EMC in the hyperplastic endometrium and their possible associated factors were also studied.

Material and Method

Between January 1995 and December 2004 in Bangkok Metropolitan Administration Medical College and Vajira Hospital, 386 women who had abnormal vaginal bleeding and had histopathology of EMH from fractional or endometrial curettage were identified. All patients who had diagnoses of EMH from the curettage specimens and underwent subsequent hysterectomy were included in the study. The patients whose curettage specimens had or were suspicious to have only few foci of EMC in the background of EMH were also included. While those who had an overt or outgrowth of EMC over that of EMH from the curettage specimen, and the pathologists gave the primary diagnosis of EMC were excluded from the study. Any patients who had any hormonal treatment after endometrial curettage and prior to hysterectomy were also excluded. Data collected were: age, parity, menopausal status, histological subtype of EMH, endometrial histology of the hysterectomy specimens, time interval from the curettage and the hysterectomy. The histologic diagnoses from the curettage specimens were compared to those from the hysterecetomy specimens. Consistency in this study means the tissue from endometrial curettages and the subsequent hysterectomy specimens had the same histologic subtype of EMH. Consistency rate was obtained from the number of all patients who had the same histology from the curettage and the hysterectomy specimens divided by the number of all patients included in the study.

Data were analyzed by parametric and non-parametric statistics using SPSS statistical software version 11.5 (SPSS, Chicago, IL). Descriptive statistics were used for demographic data and summarized as mean with standard deviation (SD) or median with range. Categorized variables were compared with the chi-squared test or Fisher's exact test as appropriate. Differences between continuous variables were evaluated with unpaired t-test for variables that were normally distributed and the Mann-Whitney U test for variables that were not normally distributed.

Results

During the study period, 55 patients who had diagnoses of EMH from endometrial curettage and subsequently underwent total abdominal hysterectomy were included in the study. Nine patients were later excluded because four of them received hormonal treatment prior to hysterectomy and five patients had incomplete pathological data regarding the specific type of EMH, remaining 46 patients included in the study. Mean age of the 46 patients was 49.9 $\pm$ 9.1 years. Less than one third of the patients were in postmenopausal state. After uterine curettage, all patients underwent hysterectomy at the median interval of 6.7 weeks (range, 1.4-35.9 weeks). The patients' clinical and pathological features are listed in Table 1. The histopathologic subtypes of EMH revealed from the curettage specimens were simple or complex hyperplasia in 30 cases. Sixteen cases were atypical hyperplasia; one as simple hyperplasia with atypia and 15 as complex hyperplasia with atypia. The endometrial histology from the hysterectomy specimen varied from hyperplasia, endometrioid carcinoma, proliferative, secretory, or inactive pattern. The correlation of histopathology of endometrium from the curettage and hysterectomy specimen are shown in Table 2. The consistency rate between the curettage and the hysterectomy specimen in our study was 41.3% (19/46 cases). The characteristic features of the patients with consistent and inconsistent histologic findings between the curettage and hysterectomy specimens are shown in Table 3.

Overall, eight cases (17.4%) had co-incidental EMC in association with EMH. Microscopic foci of EMC were readily discovered in association with complex hyperplasia with atypia from the curettage specimens in 6/8 cases. Three out of these six patients

Table 1. Clinical characteristic features of patients with endometrial hyperplasia and underwent subsequent hysterectomy

Clinical characteristics	
Age (mean $\pm$ SD) (years) (N=46)	49.9$\pm$9.1
Parity (median and range) (N=25)	2 (0-14)
Menopausal status (N=46)	
Premenopause (n, %)	33 (71.7)
Postmenopause (n, %)	13 (28.3)
Interval from curettage to hysterectomy (median and range) (weeks) (N=46)	6.7 (1.4-35.9)

underwent complete surgical staging. One of them had grade 3 tumor, myometrial invasion > 1/2, and involvement of lower uterine segment and received postoperative radiotherapy while the other two patients had grade 1 tumors with only minimal myometrial invasion. The other three patients in this group did not have any gross pathology in the hysterectomy specimens, and were later found histologically to have only complex hyperplasia with atypia without residual cancer in two cases, and inactive endometrium in another case.

The other 2/8 EMC (25%) were not detected in the curettage specimens. They were the only two cases which their pathology from curettage specimens were upgraded as evidenced from the hysterectomy (from complex hyperplasia with and without atypia to invasive cancer). Both cases were grade 1 tumor, with minimal myometrial invasion, and without any poor prognostic factors.

The only clinical feature which was significant different between the EMH patients who had cancer or had not was the number of parity, while the age and menopausal status were not significantly different between the two groups (Table 4). EMC was more commonly found in patients who had atypical hyperplasia in the curettage specimen, 7/16 patients (43.8%) compared to 1/30 patients (3.3%) with hyperplasia without atypia (P=0.001).

Table 2. Correlation of endometrial histopathology from the curettage and hysterectomy specimen (n = 46)

Histopathology from curettage \ Histopathology from hysterectomy	Same type of hyperplasia				Upgraded as cancer	Downgraded as normal endometrium			Total
	Simple hyperplasia	Complex hyperplasia	Atypical complex hyperplasia	Atypical complex hyperplasia with carcinoma	Carcinoma	Inactive	Proliferative	Secretory	
Simple hyperplasia	4	0	0	0	0	3	11	2	20
Complex hyperplasia	0	5	0	0	1	1	3	0	10
Atypical simple hyperplasia	0	0	0	0	0	0	1	0	1
Atypical complex hyperplasia	0	0	5	0	1	3	0	0	9
Atypical complex hyperplasia with carcinoma	0	0	2	3	0	1	0	0	6
Total	4	5	7	3	2	8	15	2	46

Discussion

The consistency rate between curettage and hysterectomy specimens in our study was relatively low at 41.3%. The clinical characteristics of patients with consistent or inconsistent histologic diagnoses were not significantly different, thus these would not be the explanation for this low rate of consistency. One observation of note was more numbers of premenopausal patients had inconsistent diagnoses while postmenopausal patients had the opposite finding, yet, these were not significantly different. The only feature which was significantly different between the two groups was the type of EMH. The EMH without atypia had lower consistency rate than the atypical EMH. The type of EMH as a factor for diagnostic accuracy or consistency of curettage was also seen in the study of Xie at al. [8]. However, their findings were in reverse direction from our study. The consistency of histologic diagnoses by curettage and hysterectomy specimens in their study was 62% [8]. They factored and reported the value of curettage procedure in term of accuracy for each subtype of EMH; 76.7% for complex

Table 3. Clinical and histologic characteristics of the patients with concordant and discordant histologyic diagnoses between curettage and hysterectomy (n=46)

Characteristic features	Concordant diagnoses (n =19)	Discordant diagnoses (n =27)	p value
Age (mean ± SD)	50.4±10.6	49.6±8.0	0.70*
Parity (median, range)	2 (0-6)	3 (1-14)	0.11**
Menopausal status			
Premenopause (n=33)	12 (36.4)	21 (63.6)	0.28***
Postmenopause (n=13)	7 (53.8)	6 (46.2)	
Interval from curettage to hysterectomy (median and range) (weeks)	7.9 (1.4-13.9)	6.6 (1.9-35.9)	0.66**
Type of endometrial hyperplasia			
Hyperplasia without atypia (n=30)	9 (30.0)	21 (70.0)	0.03***
Atypical hyperplasia (n=16)	10 (62.5)	6 (37.5)	

* p value by unpaired t-test
** p value by Mann-Whitney U test
*** p value by Chi-Square test

Table 4. Clinical and pathological characteristics of the patients with endometrial hyperplasia with and without cancer (n=46)

Characteristic features	Hyperplasia without cancer (n=38)	Hyperplasia with cancer (n=8)	p value
Age (mean ± SD)	50.1±8.7	49.3±9.1	0.82*
Parity (median, range)	3 (1-14)	0.5 (0-3)	0.03**
Menopausal status			
Premenopause (n=33)	27 (81.8)	6 (18.2)	0.82***
Postmenopause (n=13)	11 (84.6)	2 (15.4)	
Type of endometrial hyperplasia			
Hyperplasia without atypia (n=30)	29 (96.7)	1 (3.3)	0.001***
Atypical hyperplasia (n=16)	9 (56.3)	7 (43.8)	

* p value by unpaired t-test
** p value by Mann-Whitney U test
*** p value by Chi-Square test

atypical hyperplasia and 88% or 92% for simple hyperplasia and complex hyperplasia respectively [8]. The high percentages (approximately half) of complex hyperplasia with atypia cases in their study had co-incidental EMC and accounted for the low accuracy in this particular group. Although our study had similar co-incidence of EMC with atypical EMH as the study of Xie, however almost all of these cases were readily diagnosed from the curettage specimen and did not contribute to the low consistency rate. We tended to believe that the low proliferative activity of the EMH without atypia contributed to our finding. The abnormal hyperplastic endometrial tissue without atypia, which was not voluminous, might have been mostly removed by the curettage procedure, leaving only normal physiologic or inactive endometrium in the hysterectomy specimen. While the atypical hyperplasia with higher degree of proliferation were not totally scraped out, rendering more number of patients with consistent histologic findings.

Another possibility of the inconsistent diagnoses was the reproducibility of tissue diagnosis. One study by the Gynecologic Oncology Group on the agreement of atypical EMH diagnoses, from the curettage specimen reported in the community hospital and their review, were either downgraded to any benign disorders or upgraded to cancer in approximately half of all cases [7]. Furthermore, the diagnosis of atypical EMH were disagreed in 5.5%. We regarded the problem of reproducibility as minimal or nil in our study because the tissue diagnoses were made in our single institution with a few pathologists who always con-

ferred and agreed on the diagnoses. This should not be the reason for any inconsistency between the curettage and hysterectomy specimens.

We found coexisting EMC in 17% of patients with EMH; 6/8 or 75% of them were discovered from the curettage specimens. The relatively low incidence rate of EMC in our study might lie on the exclusion criteria. We primarily excluded those who had overt or dominated feature of EMC from the study, despite some or most of them might also have EMH. Based on the general practice in our hospital that all endometrial sampling were obtained by curettage instead of biopsy, this should obtain more tissue for diagnoses and higher chance for EMC detection from the curettage specimens, and were excluded from our study.

When we factored these EMC according to the clinical and pathological factors, we found the EMH patients, who had associated EMC or not, had no differences in age or menopausal status. Only the number of parity, which has long been known as one of the risk factors for EMC, was the only different clinical feature between the two groups. The patients who had higher parity appeared to have lesser number of associated carcinoma in the EMH condition. This was also found in the study of Karamursel et al who reported that number of parity was the only factor which was significantly different between the two groups while age, menopausal age, and menopausal status were not [3]. The pathological factor which we studied and showed significant difference between the two groups was the type of hyperplasia. The incidences of EMC in our study was 43.8% in atypical hyperplasia group versus 3.3% in the hyperplasia without atypia. Our results were concordant with other studies which reported the incidences of coexisting EMC with atypical EMH from biopsy or curettage specimen ranging from 17%-63% in atypical hyperplasia [2,3,7-10] and only 0-21% in hyperplasia without atypia [2,3].

The findings from this study were basic information to the physician regarding the possibilities of the inconsistency between the result from endometrial curettages and the hysterectomy specimens. The clinician should be aware of and counsel the patients of these possibilities and their lines of management. As two EMC cases from our study were discovered from the histologic examination of the hysterectomy specimen, the surgeon should initially by themselves, thoroughly assessed the resected uterus by opening and inspecting the gross pathology in the operating room. In case of a suspicious diagnosis, intraoperative frozen-section examination of the uterus might minimize an inappropriate surgical treatment.

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ความสอดคล้องของผลพยาธิวิทยาของเยื่อบุโพรงมดลูกหนาตัวที่พบจากการขูดมดลูกและผลที่พบจากการตัดมดลูก

สมนึก เจษฎาภัทรกุล, ศิริวรรณ ตั้งจิตกมล, สุมนมาลย์ มนัสศิริวิทยา

วัตถุประสงค์: *เพื่อศึกษาอัตราความสอดคล้องของผลพยาธิวิทยาที่เป็นเยื่อบุโพรงมดลูกหนาตัวผิดปกติในชิ้นเนื้อที่ได้จากการขูดมดลูกกับผลพยาธิวิทยาในชิ้นเนื้อของเยื่อบุโพรงมดลูกที่พบจากการตัดมดลูกและเพื่อศึกษาความชุกของมะเร็งเยื่อบุโพรงมดลูกที่พบในภาวะเยื่อบุโพรงมดลูกหนาตัวผิดปกติ*

วัสดุและวิธีการ: *รวบรวมข้อมูลจากเวชระเบียนของหน่วยพยาธิวิทยาและจากเวชระเบียนผู้ป่วยนอก เพื่อค้นรายชื่อผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นเยื่อบุโพรงมดลูกหนาตัวผิดปกติจากการขูดมดลูกและต่อมาได้รับการตัดมดลูกภายใน 1 ปี โดยไม่ได้รับการรักษาด้วยยาฮอร์โมนใดๆ ก่อนการตัดมดลูก ที่มารับการรักษาที่วิทยาลัยแพทยศาสตร์กรุงเทพมหานครและวชิรพยาบาล ตั้งแต่เดือนมกราคม พ.ศ. 2538-เดือนธันวาคม พ.ศ. 2547*

ผลการศึกษา: *มีผู้ป่วยจำนวน 46 ราย ที่มีภาวะเยื่อบุโพรงมดลูกหนาตัวผิดปกติจากการขูดมดลูกและตรงตามเกณฑ์การคัดเข้า พบว่าเยื่อบุโพรงมดลูกหนาตัวผิดปกติเป็นชนิด simple or complex hyperplasia 30 ราย และ atypical simple or complex hyperplasia 16 ราย อัตราความสอดคล้องของผลทางพยาธิวิทยาของชิ้นเนื้อที่ได้จากการขูดมดลูกและจากการตัดมดลูก คือ ร้อยละ 41.3 โดยอัตราความเข้ากันได้นี้ เท่ากับ ร้อยละ 62.5 และ ร้อยละ 30.0 ในชิ้นเนื้อชนิด atypical endometrial hyperplasia และ endometrial hyperplasia without atypia ตามลำดับ จากการศึกษานี้ พบว่ามีผู้ป่วย 8 รายที่มีเยื่อบุโพรงมดลูกหนาตัวผิดปกติ มีมะเร็งเยื่อบุโพรงมดลูกร่วมด้วย คิดเป็นร้อยละ 17.4*

สรุป: *ความสอดคล้องของผลพยาธิวิทยาของเยื่อบุโพรงมดลูกหนาตัวที่พบจากการขูดมดลูกและผลพยาธิวิทยาที่พบจากการตัดมดลูกค่อนข้างต่ำ โดยเฉพาะอย่างยิ่งในชนิด endometrial hyperplasia without atypia*