Preoperative and postoperative correlation of histopathological findings in cases of endometrial hyperplasia

G. Gundem[1], *Asso. Prof., M.D.*; **F. Sendag**[1], *Assist. Prof., M.D.*; **M. Kazandi**[1], *Assist. Prof., M.D.*; **F. Akercan**[1], *Assist. Prof., M.D.*; **L. Mgoyi**[1], *Resident, M.D.*; **M. C. Terek**[1], *Specialist, M.D.*; **O. Zekioglu**[2], *Specialist, M.D.*

[1]*Department of Obstetrics and Gynecology;*
[2]*Department of Pathology, Ege University Faculty of Medicine, Izmir (Turkey)*

Summary

Objectives: To determine the preoperative and postoperative correlation of histopathological findings in cases of endometrial hyperplasia.

Material and Methods: One hundred and three patients with endometrial hyperplasia detected by surgical curettage performed due to various gynecologic pathologies were treated by hysterectomy. We compared retrospectively the histopathological diagnoses found on curettage with those found on hysterectomy specimens. The classification scheme endorsed by the International Society of Gynecological Pathologists was used to classify the endometrial hyperplasia. The histologic findings found on the endometrial tissue of curettage specimens were correlated with those from hysterectomy specimens. Histopathologic evaluation was performed by a single skilled gynecologic pathologist.

Results: A total number of 103 women – 76 (73.8%) premenopausal and 27 (26.2%) postmenopausal – were determined to have endometrial hyperplasia on histopathological evaluation of endometrial tissues obtained by endometrial curettage performed for evaluation of various bleeding abnormalities. These included 94 patients with simple hyperplasia without atypia (91.3%), two patients with simple hyperplasia with atypia (1.9%), five patients with complex hyperplasia without atypia (4.9%), and two patients with complex hyperplasia with atypia (1.9%). Histopathological evaluation of endometrial tissue obtained from hysterectomy specimens (of patients diagnosed with hyperplasia on curettage) revealed a total number of 65 cases (63.1%) with endometrial hyperplasia, and 38 cases (36.9%) with various histopathological findings. The correlation between preoperative and postoperative endometrial histologic findings was found to be statistically insignificant ($r = 0.105$, $p = 0.29$). Among 94 patients who were found to have simple hyperplasia without atypia on curettage specimens, 55.3%, were found to have simple hyperplasia without atypia, 1.1% simple hyperplasia with atypia, 5.3% complex hyperplasia without atypia, 9.6% secretory endometrium, 4.3% proliferative endometrium, 21.3% disorganized proliferative endometrium, 1.1% corpus luteum persistency, 1.1% basal endometrium, and 1.1% endometrium cancer on final hysterectomy specimens.

Conclusion: Postoperative diagnosis of endometrial pathology might be different from that of preoperative especially in cases with simple endometrial hyperplasia without atypia.

Key words: Endometrial hyperplasia; Histopathology; Atypia.

Introduction

Endometrial hyperplasia represents a spectrum of morphologic and biologic alterations of the endometrial glands and stroma, ranging from an exagerated physiological state to carcinoma in situ. Clinically significant hyperplasias usually evolve within a background of proliferative endometrium as a result of protracted estrogen stimulation in the absence of progestin influence. Endometrial hyperplasias are important clinically because they may be associated with estrogen-producing ovarian tumors, may result from hormonal therapy, and may precede or occur simultaneously with endometrial cancer.

Progestin therapy is the treatment of choice in the management of endometrial hyperplasia in the appropriate settings. Progestin therapy is very effective in reversing endometrial hyperplasia without atypia but is less effective for endometrial hyperplasia with atypia [1-4]. For women with endometrial hyperplasia without atypia, ovulation induction, cyclical or continuous progestin therapy seem to be effective medical therapies. Continuous progestin therapy with megestrol acetate is probably the most reliable treatment for reversing complex or atypical endometrial hyperplasia [2-5].

Endometrial hyperplasia is not uncommon in gynecological practice. All gynecologists should be familiar with the pathophysiology and the natural history of this disorder. The preoperative and postoperative diagnoses of cases with endometrial hyperplasia might not be well correlated and the course of treatment changes significantly.

The aim of the present study was to determine the preoperative and postoperative correlation of histopathological findings in cases of endometrial hyperplasia.

Revised manuscript accepted for publication January 16, 2003

Materials and Methods

One-hundred and three patients with endometrial hyperplasia detected by surgical curettage performed due to various gynecologic pathologies were treated by hysterectomy. We retrospectively compared the histopathological diagnoses found on curettage with those found on hysterectomy specimens.

All of the patients who were admitted to Ege University Faculty of Medicine Department of Obstetrics and Gynecology during the period of July 1996 through September 1999 were taken into the study. All the patients had undergone hysterectomy as indicated by various gynecological pathologies. The classification scheme endorsed by the International Society of Gynecological Pathologists was used to classify the endometrial hyperplasia [3]. The histologic findings found on endometrial tissues of curettage specimens were correlated with those found from hysterectomy materials. Histopathologic evaluation was performed by a single skilled gynecologic pathologist.

The normal distribution of values were determined by Liliefors test accepting a p value higher than 0.05 as the homogeneous distribution. The correlation of the variables was assessed using Spearman's correlation test. The chi-square test and Fisher's exact test were also used to compare the data; a p value lower than 0.05 was accepted as significant.

Results

The mean age of patients diagnosed with endometrial hyperplasia was 48.7 years (range 36 to 78 years, SD 6.9). The mean age at menopause was 48.8 years (range 40 to 57 years, SD 4.1), with a mean time in menopause of 7.5 years (range 1 to 28 years, SD 7.8). The patients were found to have a considerable degree of endometrial thickening, obtained by transvaginal ultrasonography measurement of endometrial lining, with a mean endometrial thickness of 12 mm (range 5 to 23 mm, SD 5.4) (Table 1).

A total number of 103 women, 76 (73.8%) premenopausal and 27 (26.2%) postmenopausal, were found to have endometrial hyperplasia on histopathological evaluation of endometrial tissues obtained by endometrial curettage performed for evaluation of various bleeding abnormalities. These included 94 patients with simple hyperplasia without atypia (91.3%), two patients with simple hyperplasia with atypia (1.9%), five patients with complex hyperplasia without atypia (4.9%), and two patients with complex hyperplasia with atypia (1.9%). Histopathological evaluation of endometrial tissues obtained from hysterectomy specimens (of patients diagnosed as having hyperplasia on curettage) revealed a total number of 65 cases (63.1%) with endometrial hyperplasia including 54 patients with simple hyperplasia without atypia (52.4%), one patient with simple hyperplasia with atypia (1%), eight patients with complex hyperplasia without atypia (7.8%), and two patients with complex hyperplasia with atypia (1.9%). Thirty-eight cases (36.9%) were found to have various histolopathological findings including: secretory endometrium 9/103 (8.7%), proliferative endometrium 4/103 (3.9%), disorganized proliferative endometrium 21/103 (20.4%), corpus luteum persistency 1/103 (1.0%), basal endometrium 1/103 (1.0 %), and endometrial neoplasia 2/103 (1.9%) (Table 2). Using the Spearman correlation coefficient, correlations between preoperative and postoperative endometrial histologic findings were found to be statistically insignificant (correlation coefficient = 0.105, p = 0.29).

Among 94 patients who were found to have simple hyperplasia without atypia on curettage specimens, 52 (55.3%) were determined to have simple hyperplasia without atypia, one (1.1%) simple hyperplasia with atypia, five (5.3%) complex hyperplasia without atypia, nine (9.6%) secretory endometrium, four (4.3%) proliferative endometrium, 20 (21.3%) disorganized proliferative endometrium, one (1.1%) corpus luteum persistency, one (1.1%) basal endometrium, and one (1.1%) endometrium cancer on final hysterectomy specimens (Table 3) ($X^2 = 3.6$, Fisher's exact p = 0.082). Two patients with simple hyperplasia with atypia on curettage specimens were found to have simple hyperplasia with atypia in one, and complex hyperplasia without atypia in the other. Five patients with complex hyperplasia without atypia on their endometrial curettings were found to have complex hyperplasia without atypia in three, simple hyperplasia without atypia in one, and carcinoma in one patient. Both patients with complex hyperplasia on curettage materials were found to have the same histopathologic findings

Table 1. — *Demographic variables of the patients.*

	Minimum	Maximum	Mean	SD
Age (years)	36	78	48.7	6.9
Age at menopause (years)	40	57	48.8	4.1
Time since menopause (years)	1	28	7.5	7.8
Endometrial thickness (mm)	5	23	12	5.4

SD: Standard deviation.

Table 2. — *The histopatholgical findings found on hysterectomy specimens of women with endometrial hyperplasia without atypia on endometrial curettage specimens.*

Histopathological type	Preoperative	Postoperative
Simple hyperplasia without atypia	94 (91.3%)	54 (52%)
Simple hyperplasia with atypia	2 (1.9%)	1 (1.0%)
Complex hyperplasia without atypia	5 (4.9%)	8 (7.8%)
Complex hyperplasia with atypia	2 (1.9%)	2 (1.9%)
Secretory endometrium		9 (8.9%)
Proliferative endometrium		4 (3.9%)
Disorganized proliferative endometrium		21 (20.4%)
Corpus luteum persistency		1 (1.0%)
Basal endometrium		1 (1.0%)
Endometrial neoplasia		2 (1.9%)

Table 3. — *Postoperative histopathologic findings in 94 patients diagnosed of having simple endometrial hyperplasia on curettage specimens.*

	No. of patients	Percentage of patients (%)
Simple hyperplasia without atypia	52	55.3
Simple hyperplasia with atypia	1	1.1
Complex hyperplasia without atypia	5	5.3
Secretory endometrium	9	9.6
Proliferative endometrium	4	4.3
Disorganized proliferative endometrium	20	21.3
Corpus luteum persistency	1	1.1
Basal endometrium	1	1.1

after evaluation of their hysterectomy specimens. Two patients, one with complex hyperplasia without atypia and the other with simple hyperplasia without atypia on their curettage materials, were found to have adenosquamous carcinoma and stromal sarcoma on their hysterectomy specimens, respectively.

Discussion

Endometrial hyperplasia is thought to be caused by prolonged, unopposed estrogen stimulation of the endometrium. It has been considered to be a precancerous lesion of well-differentiated endometrial carcinoma, especially the endometrioid type. Endometrial hyperplasia mostly presents clinically with abnormal uterine bleeding and more often at the climacteric period [6]. Medical attention has been focused on the early recognition and treatment of this benign condition before its progression into endometrial carcinoma. Women affected by breast cancer who have been treated with tamoxifen were found to have an increased risk of endometrial hyperplasia and subsequently, endometrial adenocarcinoma [7, 8]. In the present study a total number of 103 women, 76 (73.8%) premenopausal and 27 (26.2%) postmenopausal, were found to have endometrial hyperplasia on histopathological evaluation of endometrial tissues obtained by endometrial curettage performed for evaluation of various bleeding abnormalities. These included 94 patients with simple hyperplasia without atypia (91.3%), two patients with simple hyperplasia with atypia (1.9%), five patients with complex hyperplasia without atypia (4.9%), and two patients with complex hyperplasia with atypia (1.9%). Histopathological evaluation of endometrial tissues obtained from hysterectomy specimens (of patients diagnosed as having hyperplasia on curettage) revealed a total number of 65 cases (63.1%) with endometrial hyperplasia, and 38 cases (36.9%) were found to have various histopathological findings. The correlation between preoperative and postoperative endometrial histologic findings was found to be statistically insignificant ($r = 0.105$, $p = 0.29$).

The risk of endometrial hyperplasia to develop into invasive cancer according to criteria described by Kurman has been estimated to be 1%, 3%, 8% and 29% for patients with simple, complex, simple atypical, and complex atypical hyperplasia, respectively [9]. Nevertheless, most cases of endometrial hyperplasia, except for complex atypical hyperplasia, may disappear spontaneously within a short period of time [10].

Coexistent carcinoma has recently been reported to occur in up to 45% of patients with complex atypical endometrial hyperplasia. Reports have shown age to be the most identifiable predictor for risk of cancer [11, 12]. In contrast to the present study, Dunton *et al.* [13], by the use of computerized morphometric analyses of endometrial hyperplasia in the prediction of coexisting carcinoma, reported that 26.7% of patients (12 of 45) with endometrial hyperplasia by preoperative histopathologic classification showed coexistent carcinoma at hysterectomy, and all instances of carcinoma occurred in patients with atypical hyperplasia. Endometrial carcinomas associated with hyperplasia were found to have superficial myometrial invasion (invasion less than 1/2 of the myometrium), lower surgical stage disease, lower histopathologic grade, higher levels of progesterone receptors, lack of cervical involvement and lymphovascular space invasion, and no lymph node metastases [14, 15].

Endometrial hyperplasia has the tendency to be overdiagnosed with a background of polyps, endometritis, artifacts and even normally cycling endometrium. Atypical hyperplasia may also be overdiagnosed when epithelial metaplasia changes occur in simple or complex hyperplasia without atypia [16].

Transvaginal ultrasonography was found to have a poor positive predictive value but a high negative pedictive value for detecting serious endometrial disease in asymptomatic postmenopausal women [17]. Langer *et al.* [17] reported that, at a threshold value of 5 mm for endometrial thickness, transvaginal ultrasonogaphy was found to have a positive predictive value of 9% for detecting any endometrial abnormality, with 90% sensitivity, 48% specificity, and a negative predictive value of 99%. In the present study, the endometrial thickness measured by transvaginal sonography ranged between 5 and 23 with a mean of 12 ± 5.4 mm.

Endometrial pathologies may be missed on routine endometrial sampling procedure. Cohen *et al.* [18] in a comparison between endometrial pathologies collected by hysteroscopy and hysterectomy in postmenopausal breast cancer tamoxifen-treated patients identified three new cancers by re-evaluating hysterectomy materials.

The progesterone challenge test was found to be a reliable, non-invasive, easy-to-use test that may be used in the screening of postmenopausal women at risk of endometrial hyperplasia and subsequently endometrial carcinoma. Pehlivanov *et al.* [19] reported that more than half of the patients with a positive progesterone challenge test who underwent curretage had endometrial hyperplasia. El-Maraghy *et al.* [20] found a sensitivity of 91.2% and specificity of 100% for the progesterone challenge test.

Endometrial hyperplasia is a commonly encountered pathology in gynecology. All gynecologists should be familiar with the pathophysiology and the natural course of this disorder. Unopposed estrogen stimulation should be investigated and corrected appropriately. The regression of hyperplasia back to normal endometrium is the main purpose of any conservative treatment in order to prevent development of adenocarcinoma. Treatment options should be individualised according to grade of the disease, age of the patient and desire of pregnancy [21-23]. Treatment with progestins appears to be a safe alternative to hysterectomy especially in women who desire future fertility [4]. Combined progesterone and gonadotropin-releasing hormone analogues were found to be an effective alternative in the treatment of selected patients with atypical endometrial hyperplasia [24, 25]. For patients who are managed conservatively, long-term follow-up is mandatory to prevent excessive uterine blood loss and progression to carcinoma.

In the present study the cases with endometrial hyperplasia tended to be overdiagnosed in endometrial curettings. Of the cases with simple endometrial hyperplasia without atypia 61.7% were diagnosed by histopathological examination of the hysterectomy specimen. Prominently, 21.3% of the cases were diagnosed as disorganized proliferative endometrium. In contrast to the current literature [26] endometrial cancer was detected in cases with endometrial hyperplasias without atypia.

Difficulty in establishing a correct diagnosis of endometrial hyperplasia by curettage may be explained firstly by, extreme variability of the morphological changes of the endometrium during the normal menstrual cycle and the great influence of numerous factors such as age and hormonal therapy, and consequently endometrial morphology may show a great number of overlapping features ranging from physiologic variability to true autonomous proliferation. Secondly, morphology can vary greatly throughout the endometrium: areas with a more or less normal appearance are found adjacent to simple cyctic alterations and/or complex proliferations. Moreover, the epithelial cells of any one endometrium may show areas with only slight pseudostratification and normal gland-lining cells next to areas with pseudopapillary buds, increased proliferation, and pleomorphism [27].

In conclusion, the postoperative diagnosis of endometrial pathology might be different from that of preoperative especially in cases with simple endometrial hyperplasia without atypia. In order to diagnose endometrial hyperplasia cases correctly, immunohistochemical markers may be preferred. In the future, the new categories in the diagnosis of endometrial hyperplasia as described by Dietel and Mutter [27, 28] and European studies [29] seem to be promising.

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Address reprint requests to:
F. SENDAG, M.D.
Department of Obstetrics and Gynecology
Ege University Faculty of Medicine
Bornova, Izmir 35100 (Turkey)