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Original article

A novel hysteroscopic pattern of microvascular architecture in uterine endometrioid adenocarcinoma: Initial clinical experience

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ABSTRACT

Objective: To establish a specific hysteroscopic pattern—the "glomerular pattern"—to diagnose high-grade endometrial cancer and evaluate the accuracy rate of the pattern, based on final histology.
Materials and methods: From 2008 to 2011, 30 patients for whom pathology indicated endometrial cancer, based on the office hysteroscopy study, were included in the study. We reviewed the hysteroscopic pictures to determine the specific hysteroscopic pattern in high-grade endometrial cancer.
Results: Thirty patients who had endometrial cancer under hysteroscopy were included to the study. The study population had a mean age of 49.9 years. All patients had abnormal uterine bleeding. Office hysteroscopy was completed in all patients without anesthesia. The findings of the office hysteroscopy suggested endometrial cancer in 30 patients. Fifteen patients had the specific hysteroscopic pattern, called the "glomerular pattern." All 15 patients had grade 2 or grade 3 disease. Among patients who had a glomerular pattern, 53.3% (8/15) of patients had grade 2 endometrioid adenocarcinoma and 46.7% (7/15) patients had grade 3 endometrioid adenocarcinoma. Among the nonglomerular pattern group patients, 66.7% (10/15) patients had grade 1 endometrioid adenocarcinoma, 26.7% (4/15) patients had grade 2 endometrioid adenocarcinoma and 6.7% (1/15) patients had grade 3 endometrioid adenocarcinoma.
Conclusion: Our conclusion is that patients with the glomerular pattern have a high percentage of moderate or high-grade endometrioid adenocarcinoma. The glomerular sign may provide information on preoperative pathohistology and decrease the possibility of histology upgrade after hysterectomy. However, large series, prospective, and comparison studies are still needed.

Introduction

Hysteroscopic examination is a gold standard tool with high sensitivity and high specificity (94.2% and 88.8%, respectively) for evaluating endometrial hyperplasia and endometrial cancer, especially type I endometrioid adenocarcinoma.[1] In the past, several hysteroscopic features of endometrial hyperplasia or cancer have been established such as an uneven surface, irregularity of the endometrial glands, a polypoid pattern, a papillomatous pattern, and abnormal endometrial vessels.[1–3] However, very few studies have focused on using a specific pattern or picture in making a diagnosis or have discussed the accuracy of this method. By contrast, gastrointestinal tract studies have already determined a specific microvascular pattern with magnified endoscopy as a recognized feature in early stage gastric cancer.[4] Nakayoshi et al[4] described a "corkscrew pattern" under magnified endoscopy combined with narrow band imaging (NBI) to identify undifferentiated adenocarcinoma. Nakayoshi et al[4] discovered that this pattern exists in 85.7% of patients with undifferentiated adenocarcinoma. To date, no specific patterns or similar references exist in the gynecologic hysteroscopy field. The purpose of our study was to investigate a precise morphological pattern in hysteroscopy to

diagnose high-grade endometrial cancer, based on final hysterectomy histology.

Materials and methods

Patients

We reviewed 3043 cases of office hysteroscopy from 2008 to 2011, which were all performed by author H. Su. Patients who were diagnosed with endometrioid adenocarcinoma by endometrial biopsy or by hysterectomy pathology were included in the study. Patients excluded were those who had undergone endometrial biopsy or curettage for uterine bleeding within 1 month of office hysteroscopy or who had endometritis, pelvic inflammatory disease, or type II endometrial cancer (nonendometrioid) on final hysterectomy pathology.

Hysteroscopy procedure

Office hysteroscopy study

All patients were placed in the Trendelenburg position without anesthesia. All patients underwent office hysteroscopy with a 3.1 mm flexible hysteroscope (Olympus, Tokyo, Japan) with liquid medium distension under white light without NBI magnification. We reviewed office hysteroscopic pictures and videos, and recorded the endometrial characteristics and patterns for all patients.

Hysteroscopy classifications

Endometrial cancer

Patients who met the following hysteroscopic findings in this study were suspected of having endometrial cancer: a polypoid endometrium with a white or gray color shift; absence of endometrial glands; a cerebroid pattern (Figure 1); and the specific pattern, the "glomerular pattern."
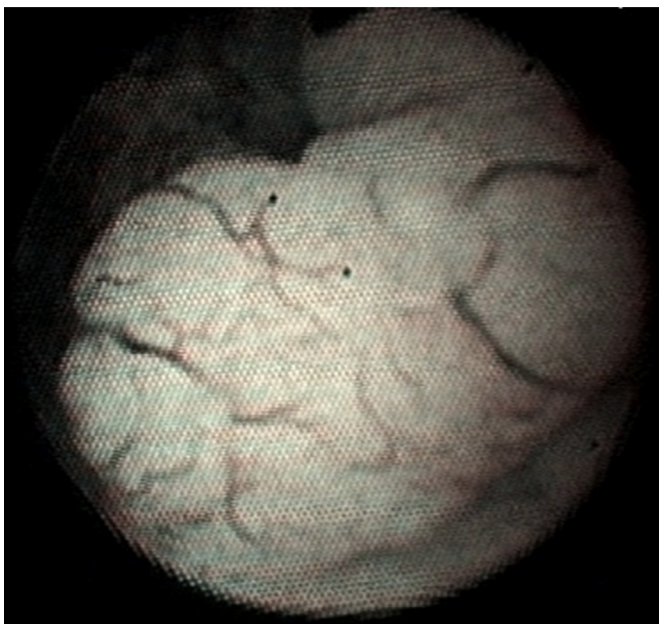
Definition of glomerular pattern

The glomerular pattern consists of a polypoid endometrium with a papillary-like feature, and most importantly, the endometrium has an abnormal neovascularization feature with intertwined neovascular vessels coated by a thin layer of endometrial tissue (Figure 2). To us, this vascular finding appeared similar to the glomerular capillary system of the kidney; thus, we named it the "glomerular pattern." We hypothesized that the hysteroscopic finding of the glomerular pattern is highly suggestive of high-grade endometrial cancer.

Data analysis

The patients' demographics, hysteroscopic patterns, glomerular pattern, and pathologic reports were recorded. All photography, videos, and pathology results were reviewed. Patients who were suspected of having endometrial cancer were categorized into two groups: Group 1 comprised patients with the glomerular pattern and Group 2 comprised patients without the glomerular pattern.

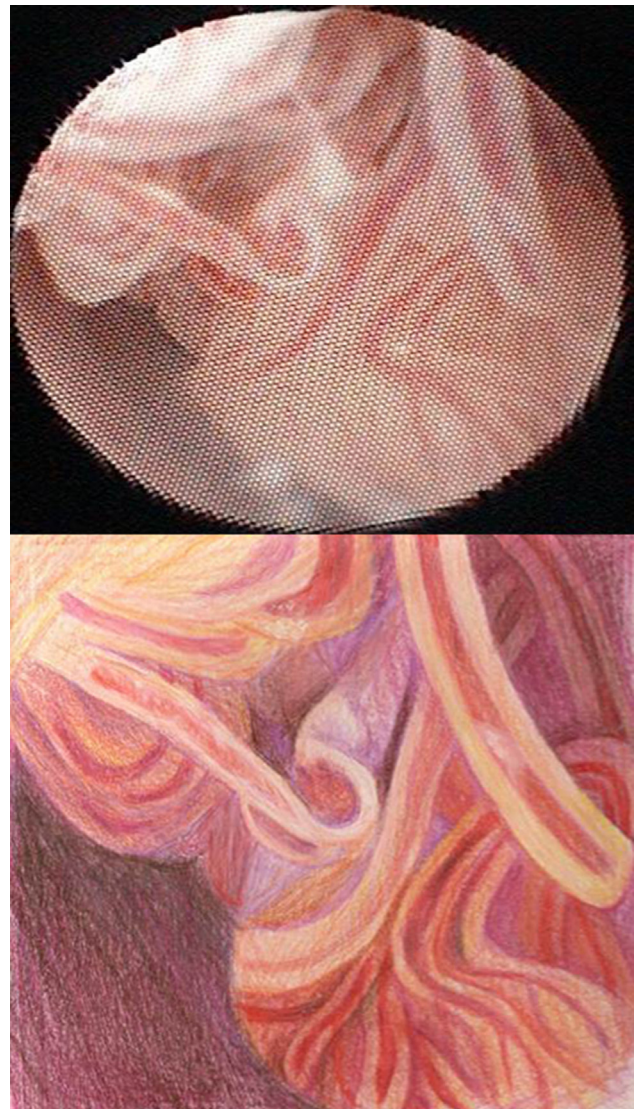**Figure 1.** The cerebroid pattern. Polypoid endometrium with white or gray color shift and the absence of endometrial glands.

Figure 2. The glomerular pattern. Intertwined neovascular vessels are coated by a thin layer of endometrial tissue.

Table 1
Clinical characteristics of patients in the office hysteroscopy study.

n	30
Mean age (y)	49.9 (range, 25—72)
Histological type	
Endometrioid	
Grade 1	10
Grade 2	12
Grade 3	8

Pathological references were based on the results of operative hysteroscopy excision biopsy and hysterectomy. Operative hysteroscopies were performed under general anesthesia and all endometrial tissues were excised comprehensively. All patients underwent staging surgery, according to the histopathological results.

The primary endpoint of our study was to evaluate the relationship between the two groups, based on their corresponding pathological grades. Sensitivity and specificity were calculated and descriptive statistics were performed using SPSS for Windows version 17.0.0 (2008; IBM-SPSS, Inc., Chicago, IL, USA).

Results

From 2008 to 2011, 30 patients were included in the study. The study population had a mean age of 49.9 years. All patients had abnormal uterine bleeding. Table 1 presents the detailed patients' characteristics.

Office hysteroscopy was completed in all patients without anesthesia. Fifteen patients had the glomerular pattern and all patients had either grade 2 or grade 3 disease. Table 2 presents a comparison of the tumor grade at final hysterectomy and the office hysteroscopic pattern. In the group without the glomerular pattern, 10 (66.7%) patients had grade 1 endometrioid adenocarcinoma and 5 (33.4%) patients had grade 2 or 3 endometrioid adenocarcinoma. Furthermore, among the patients with the glomerular pattern, 60% (9/15) patients had myometrium invasion, whereas only 20% (3/15) patients in the nonglomerular pattern group had myometrium invasion.

Discussion

Panoramic hysteroscopy has a high detection rate for endometrial cancer. Clark et al[5] published a systematic meta-analytic review and concluded that the diagnostic accuracy of office hysteroscopy is high for endometrial cancer but only moderately accurate for endometrial hyperplasia. However, the high detection rate for endometrial cancer is insufficient for clinical treatment. A physician requires histological grading of endometrial cancer before staging surgery because intraoperative lymph node assessment is necessary in high-risk patients.[6] Creasman et al[7] report that the incidence of lymph node spread of endometrial cancer was 3% in grade 1 tumors, 9% in grade 2 tumors, and 18% in grade 3 tumors. Among grade 2 tumors with inner, middle, and deep myometrium

invasion, 5%, 9%, and 19%, respectively, had pelvic lymph node metastasis. In grade 3 tumors with inner, middle, and deep myometrium invasion, 9%, 4%, and 34%, respectively had pelvic lymph node metastasis. According to another study,[8] 14.7% of grade 1 tumors diagnosed by office endometrial sampling are upgraded postoperatively. There are essentially numerous limitations in pre- and intraoperative methods in predicting the actual histological grade that could subsequently increase the risk of undertreatment in some histologically upgraded patients. Hysteroscopy is a good preoperative evaluation tool, although to date there are no publications of a useful scientific marker for endometrial cancer.

Uno et al[2] attempted to establish a morphologic criterion for endometrial hyperplasia; they have had limited results. Only the cystic pattern was statistically significant ($p < 0.05$) with a sensitivity of 15.79% and a specificity of 97.29%. Garuti et al[9] reported three hysteroscopic patterns (i.e., nodular, polypoid, and papillomatous) in 60 endometrial cancer patients. The three patterns were incapable of differentiating between tumor grading, and therefore incapable of predicting staging or survival. In colposcopy, studies of cervical cancer screening have already scientifically quantitatively analyzed descriptive appearances.[10,11] However, to our knowledge, no studies of a similar nature has been reported in hysteroscopy.

In a gastric cancer study, Yao et al[12] first reported a microvascular architectural pattern in distinguishing between differentiated and undifferentiated gastric cancer. Nakayoshi et al[4] also reported a correlation between vascular patterns and different histopathological grades: 85.7% of patients with undifferentiated adenocarcinoma had a microvascular corkscrew pattern. It appears as though the glomerular pattern identified in this series is comparable to the findings of studies of other systems and shows a direct correlation between tumor differentiation and myometrium invasion.

The purpose of our study was to provide a preliminary report to determine the scientific quantitative patterns in endometrial cancer and consequently increase the accuracy of histological grading before staging surgery. The glomerular pattern described in this article is apparently a quantitative morphological pattern in patients suspected of having endometrial cancer. It could be a useful tool aiding the prediction of tumor grade before staging surgery. Our study provides a preliminary outlook in aiding the diagnosis of endometrial cancer; however, multiple limitations exist such as the small case number, it involves a single doctor, and it is a single arm case series.

Our conclusion is that the glomerular pattern is present in a high percentage of patients with moderate or poorly differentiated endometrioid adenocarcinoma. This finding could provide information for preoperative histopathology. A large series prospective comparison study is still warranted to confirm these findings.

Table 2
Histopathological grading after hysterectomy with the glomerular pattern and no glomerular pattern.

Variable	Glomerular pattern (*n* = 15)	No glomerular pattern (*n* = 15)
Grade 1	0 (0)	10 (66.7)
Grade 2	8 (53.3)	4 (26.7)
Grade 3	7 (46.7)	1 (6.7)

Data are presented as *n* (%).

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