Resectoscopic surgery may be an alternative to hysterectomy in high-risk women with atypical endometrial hyperplasia

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Abstract

STUDY OBJECTIVE: Endometrial hyperplasia is found in 2% to 10% of women with abnormal uterine bleeding (AUB). Up to 43% of patients with cytologic atypia harbor coexisting adenocarcinoma, and approximately 20% to 52% of atypical hyperplasias, if untreated, progress to cancer. The objective of this study was to estimate the incidence of atypical endometrial hyperplasia encountered during routine resectoscopic surgery in women with AUB and to evaluate the role of resectoscopic surgery in the management of women with AUB and atypical endometrial hyperplasia who refused and/or were at high risk for hysterectomy.

DESIGN: Prospective cohort study (Canadian Task Force classification II-3).

SETTING: University-affiliated teaching hospital.

PATIENTS: From January 1990 through December 2005, the senior author (GAV) performed primary resectoscopic surgery in 3401 women with AUB. Among these, there were 22 women with atypical (17 complex, 5 simple) endometrial hyperplasia.

INTERVENTIONS: All women underwent hysteroscopic evaluation and partial (n = 3) or complete (n = 19) endometrial electrocoagulation and/or resection. Subsequently, 6 women had hysterectomy and bilateral salpingo-oophorectomy (BSO).

MEASUREMENTS AND MAIN RESULTS: The median (range) for age, parity, and body mass index were 55 years (24 – 78 years), 2 (0 – 4), and 30.1 kg/m² (22.5 – 52.2 kg/m²), respectively. Among the 3401 women, there were 22 cases of atypical endometrial hyperplasia, 12 of which were incidentally diagnosed at the time of hysteroscopy (complex 10, simple 2, incidence 0.35%). After hysteroscopic diagnosis or confirmation of diagnosis, 6 women underwent hysterectomy and BSO. Of the remaining 16 women, followed for a median of 5 years (range 1.5 – 12 years), 1 was lost to follow-up, 1 had only a biopsy to preserve fertility, 1 died from lung cancer after 4 years, and 1 died from colon cancer after 5 years. One patient developed endometrial cancer after 10.5 years with postmenopausal bleeding. She remains alive and well 3.5 years after hysterectomy and BSO. The remaining 11 patients are amenorrheic at a median follow-up of 6 years (range 1.5 – 12 years).

CONCLUSIONS: Resectoscopic surgery in 3391 women with AUB detected 12 incidental cases of atypical endometrial hyperplasia (incidence 0.35%). Skillful resectoscopic surgery may be an alternative to hysterectomy in women with AUB and atypical endometrial hyperplasia, who refuse or are at high-risk for hysterectomy and who are compliant with regular and long-term follow-up.

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Endometrial hyperplasia is a noninvasive proliferation of the stromal and epithelial components of the endometrial tissue. Based on a variety of cytologic and architectural changes, endometrial hyperplasia constitutes a heterogeneous group of lesions that vary from simple exaggeration of the normal proliferative state at one extreme to changes closely resembling adenocarcinoma at the other. The International Society of Gynecological Pathologists and the World Health Organization classify endometrial hyperplasia as simple and complex, with or without atypia. Atypical hyperplasia designates proliferation of glands that is associated with cytologic atypia in which various degrees of nuclear atypia and loss of polarity are present.

Abnormal uterine bleeding (AUB) is experienced by 10% to 30% of reproductive-aged women. Endometrial hyperplasia is found in 2% to 10% of women with AUB. Traditionally, investigation of AUB included fractional dilation and curettage (D&C) in the operating room under general anesthesia. It has been reported that D&C provides adequate sampling in 75% of women, and misses up to 10% of pathology.

Hysteroscopic endometrial ablation was introduced in the 1980s, while nonhysteroscopic or global endometrial ablation was introduced in the 1990s. Both were designed as alternatives to hysterectomy for treatment of women with AUB of benign pathology. Before endometrial ablation, it is recommended that AUB be investigated in accordance with established clinical practice guidelines. Such guidelines recommend that office endometrial biopsy or D&C in the operating room be performed in all women with postmenopausal bleeding and in premenopausal women with certain risk factors, such as irregular bleeding, age greater than 45 years, obesity (weight > 90 kg or body mass index > 27 kg/m²), personal history of polycystic ovarian syndrome, infertility, nulliparity, or family history of endometrial or colon cancer. All of these have been shown to be independent risk factors for endometrial hyperplasia and carcinoma in women with AUB. Office endometrial biopsy is occasionally impossible to perform or provides an inadequate sample due to technical issues, cervical stenosis, or other patient conditions such as morbid obesity and discomfort. Under such circumstances, we have adopted the philosophy of performing hysteroscopic evaluation with directed biopsies or endometrial resection in the operating room under appropriate anesthesia and optimal medical conditions.

Due to possible progression of atypical endometrial hyperplasia to endometrial carcinoma, or their coexistence, the most appropriate treatment for atypical endometrial hyperplasia is considered to be hysterectomy and bilateral salpingo-oophorectomy (BSO).

In our current study, we present 22 women with AUB and atypical endometrial hyperplasia. In 12 women, prehysteroscopy office endometrial biopsy was inadequate; technically impossible; or reported as normal, proliferative endometrium or endometrial hyperplasia without atypia.

Atypical endometrial hyperplasia was known preoperatively in 10 women. The purpose of the study was to estimate the frequency of atypical endometrial hyperplasia encountered during hysteroscopic endometrial ablation and to determine if hysteroscopic surgery can be used as an alternative to hysterectomy for patients with atypical endometrial hyperplasia when hysterectomy is difficult, risky, or refused.

Material and methods

From January 1990 through December 2005, the senior author (GAV) performed primary resectoscopic surgery using electrocautery with rollerball, resection with a loop electrode, or a combination of both in 3401 women with AUB. A 26F (~9 mm) diameter resectoscope (Storz, Tutlingen, Germany) and 3- to 5-mm rollerballs or 8-mm diameter loop electrodes were used to coagulate or cut tissue at 100 ± 20 W of power. The uterus was distended/irrigated with 1.5% glycine solution at 100 cm H2O (~75 mm Hg) pressure with 100 ± 20 mm Hg suction to evacuate air bubbles, clots, and debris from the uterus. As a rule, resection rather than rollerball ablation of the entire endometrium was performed in the absence of a recent (<6 months) negative endometrial biopsy; in the presence of intruterine polyp(s), myoma(s), or suspicious lesion(s); and in women with any of the risk factors for endometrial neoplasia, as described above. Having adopted the above principles, we incidentally identified 12 atypical endometrial hyperplasia cases (10 complex [Table 1] and 2 simple [Table 2]).

Results

The characteristics of the patients, preoperative endometrial biopsy, hysteroscopic findings and treatment, post-hysteroscopy pathology and treatment, and clinical outcomes are also listed in the corresponding tables. Case histories of the first 7 patients of Table 1 and first 3 patients of Table 2 have been previously published.

Table 1 includes 17 women with atypical complex endometrial hyperplasia. Seven of these were known to have atypical hyperplasia before hysteroscopic surgery. These women declined or were at high risk for hysterectomy and BSO. They consented only to hysteroscopic evaluation and possible endometrial resection. One of seven women (No. 11, TC) wished to preserve her fertility. Complete resection was done in 6 women, and the seventh (TC) had only a biopsy. Except in 1 woman (No. 7, SM), histopathologic evaluation confirmed atypical endometrial hyperplasia. Of the 6 women who had complete endometrial resection, 1 was lost to follow-up (No. 5, FH), and the other 5 remain amenorrheic after a median follow-up of 4 years (range 1.5–6 years). The woman who wished to retain fertility also remains alive and well after 4 years of follow-up. She had...
<table>
<thead>
<tr>
<th>Patient No./initials</th>
<th>Age (yrs)/parity</th>
<th>BMI kg/m²</th>
<th>Preoperative endometrial biopsy</th>
<th>Hysteroscopic findings</th>
<th>Hysteroscopic treatment</th>
<th>Hysteroscopic pathology</th>
<th>Post-hysteroscopic management</th>
<th>Clinical outcome/years</th>
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<tbody>
<tr>
<td>1/CM 45/1</td>
<td>32</td>
<td>SH</td>
<td>Thick endometrium</td>
<td>*Rollerball/resection</td>
<td>FACH</td>
<td>Endometrial Ca/10.5 A&amp;W/14</td>
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<tr>
<td>2/AC 65/4</td>
<td>38</td>
<td>SH</td>
<td>2-cm polyp</td>
<td>Resection</td>
<td>ACH</td>
<td>Amenorrheic/8</td>
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<tr>
<td>3/SL 57/3</td>
<td>29.6</td>
<td>FSH</td>
<td>Normal endometrium/polyt</td>
<td>*Rollerball/resection</td>
<td>FACH/benign polyp</td>
<td>Amenorrheic/8</td>
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<tr>
<td>4/AS 65/1</td>
<td>24.6</td>
<td>Unable to do</td>
<td>Thick endometrium/ large polyp</td>
<td>Resection</td>
<td>FACH/benign polyp</td>
<td>Amenorrheic/7</td>
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<td>5/FH 74/3</td>
<td>28.5</td>
<td>FACH</td>
<td>Thick endometrium</td>
<td>Resection</td>
<td>FACH</td>
<td>Lost to follow-up</td>
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<td>ACH</td>
<td>Normal endometrium/ polypoid</td>
<td>*Rollerball/resection</td>
<td>Normal</td>
<td>Amenorrheic/6</td>
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<td>Unable to do Thicke ndometrium</td>
<td>Resection</td>
<td>ACH</td>
<td>TAH + BSO/no residual endometrium</td>
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<td>FACH</td>
<td>Amenorrheic/5</td>
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<td>Normal</td>
<td>Normal endometrium/myomas</td>
<td>Resection</td>
<td>FACH</td>
<td>LAVH + BSO/no residual hyperplasia Conceived after ART Amenorrheic/4</td>
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<tr>
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<td>ACH</td>
<td>Unable to do Thick endometrium</td>
<td>Resection</td>
<td>ACH</td>
<td>TAH + BSO/No residual hyperplasia Amenorrheic/4</td>
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<td>15/CK† 78/0</td>
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<td>ACH</td>
<td>Thick endometrium/ polypoid</td>
<td>Partial resection/polyectomy</td>
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<td>Amenorrheic/4</td>
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<td>ACH</td>
<td>Amenorrheic/1.5</td>
<td></td>
<td></td>
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<tr>
<td>17/ML 52/1</td>
<td>27.6</td>
<td>CH</td>
<td>Thin endometrium/ 3 polyps</td>
<td>Resection</td>
<td>ACH</td>
<td>TAH + BSO/CH</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A&W = alive and well; ACH = atypical complex hyperplasia; ART = assisted reproductive technology; BMI = body mass index; Ca = cancer; CH = complex hyperplasia; FACH = focal atypical complex hyperplasia; FSH = focal simple hyperplasia; LAVH = laparoscopic-assisted vaginal hysterectomy; SH = simple hyperplasia; TAH + BSO = total abdominal hysterectomy and bilateral salpingo-oophorectomy.

*Rollerball of the cornua and fundus and resection of the remaining endometrium.
†On Tamoxifen.
a twin pregnancy after assisted reproductive technology. She delivered the twins at 24 weeks. One twin survived and is doing well. She is currently being treated with progestins and followed regularly by endometrial biopsies, as she is trying to conceive again.

Ten women were diagnosed with atypical endometrial hyperplasia after resectoscopic surgery. These women had complete endometrial resection with or without rollerball coagulation of the fundus and cornua, except 1 (No. 15, CK), who had only a polypectomy and partial resection because of increased endomyometrial vascularity, intraoperative bleeding, and excessive fluid absorption. Four of these 10 women consented to hysterectomy and BSO including CK (No. 15). Histopathologic evaluation of the hysterectomy specimens confirmed absence of hyperplasia in 3 uteri and the presence of complex hyperplasia with no atypia in the fourth. Of the remaining 6 women, 4 are amenorrheic after a median follow-up of 6 years (range 4–8 years). One died from colon cancer after 5 years of amenorrhea. One patient developed endometrial carcinoma after 10.5 years. She presented with postmenopausal bleeding (age 57), and office biopsy indicated well-differentiated endometrial adenocarcinoma. The hysterectomy specimen indicated endometrioid adenocarcinoma (grade 1) with focal invasion of the outer half of myometrium, and cervical stroma. Complex atypical hyperplasia also was noted. She remains alive and well 3.5 years after hysterectomy, BSO, and adjuvant radiation therapy.

Table 2 includes 5 women with atypical simple hyperplasia. Three of these women were known to have atypical hyperplasia. They declined or were at high-risk for hysterectomy and BSO. They consented to hysteroscopic evaluation and possible endometrial resection. Complete resection was done, and histopathologic evaluation confirmed focal atypical simple hyperplasia in 1 woman, simple hyperplasia with no atypia in the second, and normal proliferative endometrium in the third. The woman with focal atypical hyperplasia consented to hysterectomy and BSO. No endometrial pathology was found in the hysterectomy specimen. The other 2 women remain amenorrheic after 8 and 12 years of follow-up, respectively. Two women were diagnosed with focal atypical simple hyperplasia after resectoscopic surgery. One had complete endometrial resection, but died of lung cancer after 4 years of amenorrhea. The other woman had partial endometrial resection because of uterine perforation at hysteroscopy. Two years later, she consented to hysterectomy and BSO. Except for endometriosis, no endometrial pathology was found in the hysterectomy specimen.

**Frequency of atypical endometrial hyperplasia**

From Tables 1 and 2, the frequency of incidental atypical endometrial hyperplasia during hysteroscopic endometrial ablation is 0.35% (12/3391).
Resectoscopic surgery in atypical endometrial hyperplasia

In Tables 1 and 2, we list 16 women with atypical endometrial hyperplasia who declined hysterectomy and BSO. Except for 1 woman who wanted to preserve her fertility, all women were treated with resectoscopic surgery. Eleven women remain amenorrheic after a median follow-up of 6 years (range 1.5–12 years). One woman was lost to follow-up. Two other women were amenorrheic at 4 and 5 years of follow-up but died of unrelated causes. One developed endometrial carcinoma 10.5 years after hysteroscopic surgery. She remains alive and well 3.5 years after hysterectomy, BSO, and adjuvant radiation therapy.

Discussion

The prevalence of endometrial hyperplasia in women with AUB is 2% to 10%,7–11 and the prevalence of atypical hyperplasia in women with irregular menstrual cycles is 0.5% to 0.7%.11,17 Previous reports showed that when untreated, 20% to 52% of atypical hyperplasias progress to cancer, compared with 2% of hyperplasias lacking atypia.2,3,18–21 Furthermore, it has been shown that the majority of hyperplasias that progress into cancer do so in the first few years after the original diagnosis.21 We cannot determine at what interval our patient with the initial diagnosis of focal atypical hyperplasia progressed to endometrial cancer. Following hysteroscopic endometrial ablation, our patient reported occasional spotting. Transvaginal ultrasonic measurement of endometrial thickness was reported as 6 mm and 4.5 mm at 6 and 9 years after ablation, respectively. Office endometrial biopsies were reported as insufficient tissue for diagnosis. At 10.5 years, the patient presented with postmenopausal bright red bleeding, and biopsy confirmed well-differentiated endometrial adenocarcinoma.

It has also been reported that when untreated, 20% to 52% of atypical hyperplasias progress to cancer, compared with 2% of hyperplasias lacking atypia.2,3,18–21 Furthermore, it has been shown that the majority of hyperplasias that progress into cancer do so in the first few years after the original diagnosis.21 We cannot determine at what interval our patient with the initial diagnosis of focal atypical hyperplasia progressed to endometrial cancer. Following hysteroscopic endometrial ablation, our patient reported occasional spotting. Transvaginal ultrasonic measurement of endometrial thickness was reported as 6 mm and 4.5 mm at 6 and 9 years after ablation, respectively. Office endometrial biopsies were reported as insufficient tissue for diagnosis. At 10.5 years, the patient presented with postmenopausal bright red bleeding, and biopsy confirmed well-differentiated endometrial adenocarcinoma.

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Atypical endometrial hyperplasia is found in approximately 0.35% of women undergoing hysteroscopic endometrial ablation for AUB. Routinely performing endometrial resection, rather than rollerball ablation, in women at high risk for hyperplasia/neoplasia will identify these cases of atypical hyperplasia. Skillful endometrial resection may be an alternative treatment for women with atypical endometrial hyperplasia when hysterectomy is difficult, risky, or refused.

Editor’s Comments

It is important to note that the patients described here had endometrial resection rather than rollerball or “global” ablations in which endometrial sampling is not an integral part of the procedure (except for the thermal balloon as part of “endometrial preparation”). Because adenomatous hyperplasia seen on preablation sampling is usually a contraindication to the procedure, this situation may arise infrequently as these newer procedures gain in popularity. While resec-
tion as viewed through the hysteroscope is much more dramatic than rollerball ablation, no difference in amenorrhea rates has been demonstrable in the literature over the past decade. One could argue that it’s difficult to get endometrial cancer if the endometrium has been totally removed or destroyed, but, of course, that’s the rub. We all know of individual patients in whom, years after total amenorrhea, menstruation reappears with either a benign or malignant endometrium. Keep in mind that postablation insertion of a medicated intrauterine device may be an excellent ancillary measure in these high-risk patients.

References