Endometrioid adenocarcinoma treated by hysteroscopic endomyometrial resection

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Abstract: A 53-year-old multiparous woman, with no identifiable risk factor for endometrial cancer, presented with menorrhagia. She had been treated with oral contraceptives for 3 years. Office endometrial biopsy indicated well-differentiated villoglandular adenocarcinoma of the endometrium. The patient refused hysterectomy and would consent only to hysteroscopic resection. She remains alive and well, with no clinical evidence of recurrence 5 years after resection. We propose that skillful resectoscopic surgery, under specific circumstance, may be an appropriate alternative treatment to hysterectomy for some early uterine malignancies.

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Endometrial cancer is the most common malignancy of the female genital tract. It has been estimated that 2.8% of white women in the United States will develop cancer of the uterus during their lifetime, with a 0.48% lifetime mortality risk. Approximately 90% of women with endometrial cancer have abnormal uterine bleeding (AUB), which initiates investigation, such as office endometrial biopsy, dilation and curettage, or hysteroscopy, and facilitates early diagnosis. Early diagnosis identifies approximately 72% of cases in stage I of the disease, leading to a 5-year survival rate of 90% after hysterectomy and bilateral salpingo-oophorectomy (BSO). In women wishing to retain their uterus and/or fertility, early endometrial cancer has been treated with large doses of progestins with variable success.

In this report, we describe a woman with a solitary, sessile, well-differentiated endometrioid adenocarcinoma with focal villoglandular differentiation who refused hysterectomy and was treated only by hysteroscopic resection. The patient remains alive and well after 5 years of follow-up.

Case report

A 53-year-old, gravida 2, para 2 woman presented with menorrhagia. She previously had a tubal ligation and had been taking a combined oral contraceptive pill (Minestrin 1/20, Galen Chemicals, Rockaway, NJ) for the last 2.5 years to treat her menorrhagia. Her menstrual flow lasted 6 days, 2 of which were described as heavy. She had a height of 1.55 m, a weight of 49 kg (body mass index [BMI] 20.4 kg/m²), and no risk factors for endometrial neoplasia. The uterus was antverted, mobile, and of normal size, and there were no adnexal masses. After reviewing treatment options, she agreed to hysteroscopic evaluation and possible endometrial ablation/resection. An office endometrial biopsy was performed, and she was prescribed 100 mg of danazol (Sanofi Synthelabo, Markham, Ontario, Canada), once daily to thin her endometrium before ablation.
A week later, the endometrial biopsy was reported as well-differentiated villoglandular adenocarcinoma. It could not be determined if the cancer cells were of endometrial or endocervical origin. In consultation with pathology and oncology services, it was recommended to perform hysteroscopic evaluation to obtain directed biopsies and to determine the origin of her cancer and its extent.

The patient was referred to our oncology service but she was adamantly opposed to hysterectomy and BSO, and consented only to hysteroscopic evaluation and endomyometrial resection. Examination under anesthesia revealed a normal-size uterus, sounding to 8 cm. The cervix was dilated to 10 mm, and a 26-F (9 mm) Storz resectoscope was introduced (Storz, Tuttlingen, Germany). The uterine cavity was distended with 1.5% glycine solution, using the Endomat pump (Storz) set at 300 mL/min infusion rate, 70 mm Hg infusion pressure, and 0.2 Barr negative pressure.

The endocervical canal and uterine cavity appeared normal except for a 1.5-cm, well-defined, exophytic, broad-based lesion, starting below the left tubal ostium and extending halfway down the left posterolateral wall of the uterine cavity. The rest of the endometrium was quite thin and had a normal appearance. The right tubal ostium appeared normal.

Using cutting waveform of 125 W of power and an 8 mm–diameter loop electrode, the lesion and the entire endometrium were resected in long strips all the way down to the cervical canal. Each strip was numbered and submitted separately for histologic orientation and evaluation. The tubal ostia and uterine fundus were also resected. At the end of the procedure, there was no visible residual endometrium. Additional myometrial tissue was resected from the lateral and deep margins of the resected lesion and submitted to pathology to assess the margins of the lesion.

The gross specimen of the resected endometrial strips were numbered by the surgeon (GAV) and submitted separately. The strips were oriented and measured by the pathologist (HE) as shown in Table 1. Figure 1 shows whole mount of 2 segments of strip No. 1, labeled as left lateral wall. The microscopic description was as follows: Specimens 1 & 5 confirm the presence of a well-differentiated adenocarcinoma. Most of the carcinoma is present in specimen 1. The adenocarcinoma is growing in a complex glandular and papillary architecture. The constituent cells show only minimal cytologic atypia. There is focal squamous metaplasia and secretory change. The features are those of a well-differentiated endometrioid adenocarcinoma with focal villoglandular differentiation. There are focal areas suggestive of very superficial myometrial invasion. The diagnosis is shown in Table 1 and Figure 2.

Once again, the patient refused hysterectomy and BSO, as well as postoperative prophylactic treatment with progestins. She has been followed by semi-annual assessments (history and physical examination) and transvaginal ultrasound, and annual pelvic magnetic resonance imaging. She remains alive and well, with no evidence of recurrence, 5-years after her surgery.

### Discussion

Endometrial cancer, like other epithelial cancers, occurs after a single cell mutation (a monoclonal event) due to alterations in oncogenes and tumor-suppressor genes. Two pathogenetic types (I and II) of endometrial carcinomas have been described.\(^7\) Type I is a low-grade, slow-growing cancer on a background of endometrial hyperplasia. It is frequently found in younger women with certain risk factors or in menopausal women taking unopposed estrogen. This cancer carries a better prognosis. Type II is less common, occurring in approximately 10% of cases. It is thought to arise de novo in older women and is unrelated to hyperplasia or estrogenic stimulation. It has a much more virulent course and carries a worse prognosis.\(^7,8\) Histologically, type

<table>
<thead>
<tr>
<th>Site of endometrial tissue</th>
<th>Measurement (mm)</th>
<th>Histopathology (grade)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left lateral wall</td>
<td>37 × 6 × 7</td>
<td>Endometrioid adenocarcinoma* (1) + features suggestive of adenomyosis</td>
</tr>
<tr>
<td>Right lateral wall</td>
<td>43 × 7 × 7</td>
<td>Negative for malignancy</td>
</tr>
<tr>
<td>Anterior wall</td>
<td>43 × 6 × 5</td>
<td>Negative for malignancy</td>
</tr>
<tr>
<td>Posterior wall</td>
<td>43 × 6 × 5</td>
<td>Negative for malignancy</td>
</tr>
<tr>
<td>Fundal aggregates</td>
<td>40 × 25 × 6</td>
<td>Small focus of endometrioid adenocarcinoma (1) + features suggestive of adenomyosis</td>
</tr>
<tr>
<td>Tumor depth margin</td>
<td>25 × 6 × 5</td>
<td>Negative for malignancy</td>
</tr>
</tbody>
</table>

\(^*\)Adenocarcinoma with villoglandular differentiation and focal area suggestive of superficial myometrial invasion.

Figure 1 Whole mount of 2 segments of strip No. 1 (left lateral wall) showing the papillary sessile lesions on the right-hand side.
II cancer can be found in a background of atrophic endometrium without preceding stages of progressively more severe forms of endometrial hyperplasia.9

It appears that our patient does not fall into either group. A similar case report of a solitary endometrial lesion, unresponsive to medroxyprogesterone acetate, was confirmed by hysteroscopic endometrial resection to be endometrial cancer. Following traditional hysterectomy and BSO, no residual malignancy was found.10

Our case raises three important issues for clinicians encountering patients with a uterine cancer. The first issue is what to do for those women who refuse traditional hysterectomy and BSO, in whom hysterectomy is difficult to perform or who are at high risk for complications, or who wish to maintain their fertility. Under such circumstances, chemotherapy and/or radiotherapy have been used with various degrees of success and clinical outcomes.3–5

The second issue is whether or not it is actually feasible to ablate/resect the entire endometrium. It has been shown that total endometrial ablation/resection is possible. Several reports indicate that no residual cancer was found in hysterectomy specimens after hysteroscopic electrocoagulation/resection of endometrium harboring unsuspected cancers.11–17

From our own experience of 10 incidental cancers treated inadvertently by endometrial ablation/resection, only 2 had residual cancer in the hysterectomy specimen.17 It must be pointed out however, that 1 of the 2 women had none of the risk factors for endometrial cancer. She was 38 years of age, gravida 1, para 1, with a BMI of 26.4 kg/m². Office endometrial biopsy was not performed, and endometrial cancer was not suspected hysteroscopically. Furthermore, the presence of residual cancer may reflect a degree of surgical inexperience, because endometrial ablation/resection in that case was performed 14 years ago. It also may have been the consequence of a non-deliberate attempt to ablate/resect the entire endometrium because that woman was not suspected to harbor endometrial cancer at the time of surgery. The second case of residual cancer was a 57-year-old, gravida 2, para 2 woman with a BMI of 31 kg/m². Preoperative endometrial biopsy indicated atypical simple hyperplasia. The patient was at high risk for surgical complications due to moderate cardiopulmonary dysfunction. Hysteroscopic endometrial resection was completed hastily because she absorbed 800 mL of 1.5% glycine solution.

The third issue is whether or not hysteroscopic treatment should ever be considered an appropriate alternative to hysterectomy for the treatment of stage I endometrial carcinoma. In the present case, we demonstrated that this solitary lesion was resected safely, the tissue was oriented and quantitated appropriately, and the margins were identified as free of disease. The patient remains alive and well with no evidence of recurrence 5 years after resection. The problem, of course, remains our limited ability to accurately determine early recurrence. Hindsight indicates that removal of only the lesion and additional strips at its margins, without removing the rest of the endometrium, may have been a better choice. This would have allowed us to perform routine hysteroscopic evaluation, similar to cystoscopic surveillance by urologists for bladder tumors. In this patient, the endometrial cavity was completely obliterated, and hysteroscopic surveillance is not possible.

**Conclusions**

We propose that, under certain clinical conditions and circumstances, hysteroscopic resection of certain uterine cancers may be appropriate, provided we apply the same principles urologists use when treating urinary bladder transitional cell carcinoma. These principles are:

1. The lesion is focal, well demarcated, and distinguished from the surrounding normal endomyometrial tissue;
2. Resection of the lesion itself is performed, as opposed to a total endomyometrial resection; removal of additional strips of tissue from the periphery of the lesion will determine tumor margins;
3. Subsequent hysteroscopic evaluation of the uterus, and biopsy if indicated, can be performed to rule out recurrence. Complete endomyometrial resection results in total obliteration of the endometrial cavity, depriving the opportunity for hysteroscopic surveillance.

**References**