Endometrial ablation (EA) has become one of the most commonly performed gynecologic procedures in the United States and other developed countries. Global endometrial ablation (GEA) devices have supplanted resectoscopic ablation primarily because they have brought with them technical simplicity and unprecedented safety. These devices, all of which received FDA approval between 1997 and 2001, are typically used to treat abnormal uterine bleeding (AUB) in premenopausal women. Several million women in the US who have undergone a previous EA procedure are about to enter the risk pool for the development of endometrial cancer (EC). Ours is the 18th reported case of post-ablation endometrial carcinoma (PAEC) in the English literature. This case underscores the diagnostic challenges faced in evaluating women with a history of a previous EA who cannot be properly evaluated with conventional techniques such as endometrial biopsy and sonohysterography.

**ABSTRACT**

Endometrial ablation (EA) has become one of the most commonly performed gynecologic procedures in the United States and other developed countries. Global endometrial ablation (GEA) devices have supplanted resectoscopic ablation primarily because they have brought with them technical simplicity and unprecedented safety. These devices, all of which received FDA approval between 1997 and 2001, are typically used to treat abnormal uterine bleeding (AUB) in premenopausal women. Several million women in the US who have undergone a previous EA procedure are about to enter the risk pool for the development of endometrial cancer (EC). Ours is the 18th reported case of post-ablation endometrial carcinoma (PAEC) in the English literature. This case underscores the diagnostic challenges faced in evaluating women with a history of a previous EA who cannot be properly evaluated with conventional techniques such as endometrial biopsy and sonohysterography.
Endometrial ablation (EA) has become a valuable tool in the management of AUB in the United States and other developed countries. Over 430,000 are performed annually in the US, where it has an anticipated growth rate of 4.7% for the next two years.\(^1\) Introduced in the late 1980s, the initial EA techniques—utilizing the Nd:YAG laser and the electrosurgical ball-end electrode—required somewhat cumbersome and expensive capital equipment and were associated with occasional dangerous and life-threatening complications (such as water intoxication and visceral injuries). By the late 1990s, these methods were largely supplanted by non-resectoscopic endometrial ablation (NREA) or “global” techniques whose relative safety and efficacy accelerated the acceptance and utilization of endometrial ablation.

While NREA techniques are responsible for a sharp reduction in the immediate complications that once plagued earlier EA techniques, it is now well-appreciated that nearly 25% of women undergoing all forms of EA develop late-onset endometrial ablation failures (LOEAFs) that result in hysterectomy.\(^2\) A rare late-onset complication of EA is post-ablation endometrial carcinoma (PAEC), which was first reported by Copperman et al. in 1993.\(^3\) Seventeen cases of PAEC have now appeared in the English-language literature—most of which have presented with abnormal uterine bleeding.\(^4\) The authors present an additional case of PAEC following a radiofrequency EA (NovaSure\(^6\) Hologic Inc., Bedford, Massachusetts) diagnosed in a pre-menopausal woman who presented with cyclic right pelvic pain two years following her procedure. This is the first report in which the diagnosis of EC was made utilizing ultrasound-guided re-operative hysteroscopy (UGRH).\(^7\) This case illustrates the importance and challenges of properly evaluating LOEAF-symptoms and the implications for a large cohort of women with a history of EA who are about to enter their sixth and seventh decades of life—the primary group at risk for developing the most common gynecologic cancer.

**CASE REPORT**

The patient is a 40-year-old gravida 5 para 3023 who was referred for evaluation of cyclic pelvic pain (CPP) following a bipolar radiofrequency endometrial ablation (NovaSure\(^6\)). Prior to her endometrial ablation in September 2013, the subject reported a two-year history of increasingly heavy, cyclic menses associated with moderate dysmenorrhea. Prior to her GEA procedure, her history included two Cesarean sections and a tubal ligation—there was no history of obesity, diabetes, or hypertension. Prior to her EA, a diagnostic hysteroscopy revealed a normal-appearing uterine cavity, and a concomitant endometrial biopsy disclosed only secretory endometrium.

The subject became amenorrheic and enjoyed excellent results for nearly two years—until August 2015—when she experienced her first episode of suprapubic and right lower quadrant pain, described as “labor-like”, varying in intensity from 5–7/10 and associated with mild vaginal spotting. The pain became cyclic, increasing in both duration and intensity over the ensuing five months. By December of 2015 she reported a seven-day episode of light vaginal bleeding associated with incapacitating (10/10) pain and was referred to one of the authors (MW).

The patient was 5’2” tall, weighed 133 pounds, and was normotensive (BP 117/78). Her TVUS revealed a retroverted uterus measuring 86.2 mm long x 56.5 mm AP x 65.9 mm transverse with a total uterine volume of 168.1 cc. The ovaries were normal-appearing bilaterally. There was clear evidence of a moderate-size central hematometra measuring 22.0 mm long x 12.0 mm AP x 20.6 mm transverse. The hematometra was lined by a prominent hyperechoic layer of varying thickness (Fig. 1a and b).

The subject was taken to our operating room and underwent an ultrasound-guided reoperative hysteroscopic...
(UGRH) surgery\(^9\) (Fig. 2) on January 14, 2016. Her procedure involved the resection of thick lower segment adhesions, incision and drainage of a central hematometra, and exploration of the entire uterine cavity. Her UGRHHS involved resection to within 10 mm of the serosal surface except at the cornua where it was explored to within 3 mm of the serosa. There was active-appearing endometrial tissue lining the central hematometra. However, further dissection revealed thick fibrotic bands partially obstructing access to the right cornua. Excision of the adhesive bands allowed complete exploration of the right cornua and revealed a large nest of endometrial tissue that was resected and sent separately from the main specimen (Fig. 3a and b).

During the course of the patient’s procedure, a total of 6 grams of tissue was excised which included endometrial adenocarcinoma, endometrioid type, and FIGO Grade 1 (Fig. 4a and b). The tumor cells were positive for immunostain ER and were negative for immunostains P16, carcinoembryonic antigen, and vimentin. The subject was referred to a gynecologic oncologist and underwent a robotically-assisted laparoscopic hysterectomy, bilateral salpino-ophorectomy, and lymphadenectomy on February 24, 2016. Histologic examination of the uterus revealed no residual evidence of endometrial carcinoma.

**DISCUSSION**

Endometrial ablation and endometrial cancer—a demographic time-bomb

Endometrial ablation is a minimally invasive approach for managing benign causes of intractable uterine bleeding in women who respond poorly or are not candidates for conventional medical therapy. EA is now one of the most common gynecologic procedures in the United States with 430,000 performed annually.\(^1\) The widespread use of EA is attributable to several FDA-approved NREA devices—brought to market between 1997 and 2001\(^1,10\)—which have sharply reduced the complications once associated with resectoscopic approaches. The bipolar radiofrequency ablation system (NovaSure\(^8\)) utilized in our case is the most frequently used GEA device in the US, enjoying a 55% market share.\(^11\) Between 2001 and 2014 over two million NovaSure\(^8\) procedures were performed.\(^12\)

In 1987, DeCherney et al.\(^13\) warned of the possibility that failing to excise or destroy a nest of endometrial tissue might later result in a blind pocket of endometrial carcinoma (EC). Wortman et al.\(^10\) and McCausland et al.\(^6\) have also expressed concerns that the combination of persistent endometrium and obstructive intrauterine synechiae could hinder or delay the diagnosis of endometrial cancer—the most common gynecologic malignancy in the United States.\(^14\)

Endometrial cancer typically presents with postmenopausal bleeding, staining or discharge, and affects 2.8% of women. The average age at the time of diagnosis is 60 years with only 7% of EC occurring before the age of 45.\(^14\) The American Cancer Society estimates that there will be 60,050 new cases of endometrial cancer in 2016, with 10,470 deaths attributed to the disease.\(^14\) Importantly, the incidence of new cases of endometrial cancer diagnoses in the US has slowly increased between 1988 and 2013 according to the Surveillance, Epidemiology, and End Results (SEER) database.\(^15\)
In a demographic contrast, intractable uterine bleeding affects a younger cohort of women. The average age of American women who undergo EA, according to numerous studies, varies from 41–45 years—a nearly a decade-and-a-half younger than the average age of women who develop EC. This has led some authors to speculate on how EA might affect the subsequent incidence and presentation of post-ablation endometrial cancer (PAEC).

The incidence and presentation of PAEC

Incidence of PAEC: Neuwirth et al. assessed the incidence of endometrial cancer following EA in a low-risk population and detected neither an increased nor reduced risk of EC in EA-treated women compared to those in the US SEER database. However, given the limited size of his sample—509 women—and the relatively short duration of follow-up, this study provides insufficient reassurance as a very large cohort of women are presently entering the EC risk pool.

Clinical presentation of PAEC: Abnormal uterine bleeding is present in approximately 75–90% of women with endometrial carcinoma. AlHilli et al., in his review of 17 cases of PAEC, reported that irregular vaginal bleeding was the presenting complaint in 12 subjects. One subject presented complaining of pain accompanied by irregular bleeding, one reported only pelvic pain, while three others were entirely asymptomatic—the diagnosis of EC was made only as an incidental finding following hysterectomies performed for unrelated reasons. Our subject, a premenopausal woman who presented with severe cyclic pelvic pain and light vaginal bleeding, represents the 18th reported case of PAEC and only the second one following a radiofrequency EA (NovaSure®). Another case of endometrial cancer, FIGO Stage IIIC, occurring 10 years following a radiofrequency endometrial ablation, has not been reported, but is described on the American Cancer Society’s website.

The intersection of endometrial ablation and endometrial cancer—the critical time we face and what it means for screening

Now, less than 20 years since the approval of the first GEA devices, we are entering a critical period during which a large cohort of women with prior EAs and an unknown risk for developing endometrial cancer are gestating. The scant but available data reveal that EC-affected women may be entirely asymptomatic while others are likely to present with irregular vaginal bleeding and pelvic pain. This raises the question of how to adequately screen pre- and postmenopausal women with prior endometrial ablations who may or may not be symptomatic.
The role of transvaginal ultrasound examination

It has been our practice since 1991 to perform annual transvaginal ultrasound examinations on all women with a previous EA or endometrial resection (EMR). The finding of asymptomatic hematometra is common and noteworthy—the management of asymptomatic women can be complex and is beyond the scope of this article. Figure 5 demonstrates the presence of bilateral cornual hematometra in an asymptomatic 56-year-old woman with a history of a prior EMR.

Ultrasound-guided reoperative hysteroscopy (UGRH) is a surgical technique previously described by one of the authors (MW) to date, we have performed over 300 UGRH procedures. During UGRHS obstructive adhesions, often located at the internal os and in the cornual regions (Fig. 6a), are systematically excised, thereby allowing access and sampling of the entire uterine cavity (Fig. 6b). The advantages of UGRH include reliable evaluation of the entire uterus and the ability to obtain representative tissue for histologic diagnosis in women who require endometrial sampling. Additionally, it has proven to be effective in treating most cases of LOEAF.

Our index case demonstrates the importance of properly evaluating women with LOEAF—especially true in postmenopausal women who are at increased risk for the development of PAEC. UGRH, however, is a rarely performed procedure and unavailable to most practitioners. Although it is doubtful that this technique will be widely employed, it remains—with proper training and supervision—a safe and reliable tool. It would be wise for academic institutions to adopt this practice as a large cohort of women will doubtlessly benefit from what can be achieved both diagnostically and therapeutically.

CONCLUSION

As a large cohort of endometrial ablation-treated women enter their sixth and seventh decades of life, our specialty needs to consider how best to monitor and treat both asymptomatic and symptomatic women that are likely to present in an atypical fashion with endometrial carcinoma. The use of routine sonographic monitoring as part of annual gynecologic exam has long been our practice and is strongly recommended for women with previous ablative procedures. Academic institutions with the resources to perform ultrasound-guided reoperative hysteroscopy are strongly encouraged to learn this technique and position themselves to provide resources for a large cohort of women who have already undergone EA and require endometrial sampling.

AUTHORS’ DISCLOSURES

The authors have no conflicts of interest to disclose.

REFERENCES


