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Original article

The role of pathologic evaluation of endometrial ablation resections in predicting ablation failure and adenomyosis in hysterectomy

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ABSTRACT

Endometrial ablation is commonly performed to manage heavy menstrual bleeding. However, failure in symptom control eventually requiring hysterectomy is frequent. Adenomyosis is common in such failure cases. Ablations using a resectoscope will produce an Endo-Myometrial Resection (EMR) specimen. The value of histopathologic examination of EMRs in predicting treatment failure and adenomyosis has not been addressed. We retrieved histologic material from subjects with failed ablation (persistent symptoms requiring hysterectomy) and subjects with ablation followed by clinical improvement and no hysterectomy (control group). Material was evaluated for features of an abnormal endometrial distribution suggestive of adenomyosis: myometrial fragments with endometrium on opposite edges, myometrium with endometrium in ≥3 edges and areas of endometrium completely surrounded by myometrium (endometrial islands). Hysterectomy specimens from the study group were evaluated for the presence of adenomyosis and its distribution (superficial/deep). Both study and control groups consisted of 18 patients each. The number of fragments with endometrium on opposite sides was significantly higher in the study group: 2.11 vs 0.94 in the control group ($p = 0.005$). Conversely, maximum aggregate dimension (2.3 cm vs 2.79 cm), number of fragments with endometrium on three sides (4.5 vs 2.78) and number of fragments with endometrial islands (4.5 vs 4.11) did not significantly differ between groups. Adenomyosis was seen in 72.2% hysterectomies from the study group; 27.8% involved deep myometrium. None of the EMR features were statistically associated with adenomyosis. Certain endomyometrial distribution patterns in EMR specimens correlate with future ablation failure and need for definitive surgery. This may be explained by residual endometrial tissue not resected due to a markedly irregular endomyometrial interface. Adenomyosis is frequent in cases of ablation failure. However, a significant association between EMR patterns studied and adenomyosis was not observed.

1. Introduction

Abnormal uterine bleeding is a prevalent women's health problem with significant physical, social and psychological burdens. It usually manifests with heavy menstrual bleeding (HMB), associated pain (dysmenorrhea) and/or intermenstrual bleeding. First-line therapy with pharmacologic agents has variable efficacy, and in the best scenario it reduces menstrual blood loss by only 50% [1]. Definitive treatment by hysterectomy is most effective in achieving symptom control and has high satisfaction rates; however, it carries complications associated with major surgery and it is costly [2–4].

Valid conservative treatments include Levonorgestrel-releasing intrauterine system and endometrial destruction (ablation) techniques [5]. The latter are less invasive than hysterectomy, have high efficacy, lower cost and low rates of adverse effects; thus, they have become widely popular in the last two decades and are usually preferred by patients over hysterectomy [6]. However, intervention is not always successful with failure rates requiring hysterectomy ranging from 12% [7] to 30% [4].

Predicting the likelihood of treatment failure after endometrial ablation is important for patient counselling, management and follow-up. Several studies have identified clinical independent risk factors associated with ablation failure including young age [7–10] and history of prior tubal ligation [8,9,11]. Likewise, anatomic lesions such as endometriosis, leiomyomata and adeno-

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myosis are frequent in hysterectomy specimens performed after endometrial ablation failure [11–13].

Several types of endometrial ablation are currently performed. First-generation ablation techniques include laser photovaporization, rollerball ablation and transcervical resection of the endometrium (TCRE). The latter procedure, still routinely performed in many practices, includes visualization of the uterine cavity and resection of the endometrium and superficial myometrium using a resectoscope. This intervention generates an Endo-Myometrial Resection (EMR) specimen that is routinely analysed in the surgical pathology laboratory. Anecdotally, we have observed complex and irregular endometrial distribution patterns in EMR specimens, similar to those seen in adenomyosis. This prompted us to hypothesize that certain features in EMR tissues can be predictive of adenomyosis and/or clinical ablation failure.

The aim of our study was to evaluate the endo-myometrial architecture of EMR specimens and its potential predictive association with treatment outcome (namely, ablation failure), as well as presence of adenomyosis on hysterectomy.

2. Materials and methods

This study was approved by the Ottawa Health Science Research Ethics Board.

2.1. Case selection and review

EMR samples corresponding to ablation procedures performed in a three-year period were retrieved from the anatomic pathology database at The Ottawa Hospital. Cases available were separated in study (failed ablation) and control groups. Failed endometrial ablation was defined as persistent symptoms such as pain or bleeding after the procedure requiring definitive management by hysterectomy. Only cases with EMR and subsequent hysterectomy material available for review were included. The control group consisted of subjects who had endometrial ablation, clinical improvement at follow-up and no hysterectomy. Electronic medical records were consulted for patients' age, medical follow up after the endometrial ablation and time elapsed between the ablation and the hysterectomy.

2.2. Histopathologic evaluation

Hematoxylin and eosin-stained slides from EMR and hysterectomy specimens were reviewed by one gynecologic pathologist (CPH) and one pathologist in training (AB). The total number of EMR fragments in each sample was recorded. The aggregate tissue measurements at the time of grossing were retrieved from the pathology reports. All EMR fragments were evaluated for patterns of irregularity in the endo-myometrial interface. We specifically looked for patterns of unevenness in the distribution of endometrium and myometrium across the sample, which mirror those seen in adenomyosis. The following patterns were recorded:

- Endometrium on opposite edges of an EMR fragment (separated by myometrium)
- Endometrium on 3 or more edges of a single EMR fragment
- Areas of endometrium within a single EMR fragment completely surrounded by myometrium (endometrial islands)

The number of EMR fragments displaying these patterns was recorded in each case.

Hysterectomy specimens of the study group were evaluated for the presence of adenomyosis. When present, adenomyosis extent was documented as superficial (confined to the inner myometrial half) or deep (extending to outer myometrial wall). Other histopathologic features were recorded, including presence of leiomyomas (with largest dimension in cm) and the functional status of the endometrium (secretory vs proliferative).

2.3. Statistical analysis

Statistical tests were performed using GraphPad Prism version 5.0 for Windows (GraphPad, La Jolla California USA). Unpaired Student *t*-test was used for comparison between the study and the control groups. Kruskal-Wallis test was used to compare cases with superficial adenomyosis, deep adenomyosis and no adenomyosis within the study group. A p value of <0.05 was considered statistically significant.

3. Results

Our study and control groups consisted of 18 patients each (36 patients in total). Patient characteristics are summarized in Table 1. The average time interval between ablation and hysterectomy in the study group was 20.8 months. The documented duration of follow-up in the control group ranged from 3 months to 47 months, with a mean of 29 months.

Histopathologic findings in EMR specimens are summarized in Table 2 and illustrated in Figs. 1 and 2. Among all characteristics

Table 1
Patient age and follow-up periods in the study and control groups.

	Study group N = 18		Control group N = 18	
	Age at time of ablation (years)	Time until hysterectomy (months)	Age (years)	Follow up (months)
Average	40.2	20.8	44	29
Maximum	49	74	52	47
Minimum	27	4	34	3

Table 2
Histopathologic characteristics of EMR specimens in the study (endometrial ablation failure) and control groups.

	Study group (N = 18)	Control group (N = 18)	p value
Total No. of EMR fragments*	12.72 (5.08)	10.56 (5.3)	0.232
Maximum aggregate dimension (cm)*	2.3 (0.76)	2.79 (1.39)	0.222
No. of EMR fragments with endometrium*	10.72 (4.27	9.56 (5.5)	0.494
No. of EMR fragments with endometrium on opposite sides*	2.11 (1.37)	0.94 (0.85)	0.005
No. of EMR fragments with endometrium on three sides or more*	4.5 (4.49)	2.78 (2.32)	0.169
No. of EMR fragments with endometrial islands*	4.5 (3.52)	4.11 (2.28)	0.704
No. of EMR fragments with >3 endometrial islands*	0.17 (0.37)	0.28 (0.93)	0.651

* Mean (standard deviation).