Atypical endometrial lesions: hysteroscopic resection as an alternative to hysterectomy

P. Litta, C. Bartolucci, C. Saccardi, A. Codroma, A. Fabris, S. Borgato, L. Conte

Department of Health of the Woman and Child, Obstetrics and Gynecology Clinic, University of Padua (Italy)

Summary

Background: Endometrial hyperplasia is a precursor to endometrial carcinoma: the risk of progression to invasive endometrial cancer is increased in postmenopausal women and much more in cases of atypical endometrial hyperplasia (25%-30%). In addition, in 12.7% to 42.6% of cases according to various studies, endometrial cancer coexists in patients with diagnosis of atypical endometrial hyperplasia. The aim of this study was to evaluate the correlation between radical hysteroscopic resection of atypical endometrial lesions and the histopathological examination of the uterus. *Materials and Methods:* The authors collected 25 patients referring to the Department of Woman and Child Health, in the University of Padua (Italy) from January 2008 to June 2012, undergoing hysteroscopic resection for atypical polyps and focal atypical endometrial hyperplasia, and following hysterectomy within 30 days. Average age, menopausal status, hormone replacement therapy, body mass index (BMI), presence of hypertension and diabetes, and taking tamoxifen were reported. *Results:* After hysteroscopic resection in all patients atypical polyps and focal endometrial hyperplasia were confirmed. The hystopathologic evaluation of the uterus reported: in only two (8%) cases, the persistence of atypical endometrial lesion, whereas in 23 (92%) cases the endometrial tissue was negative for atypia or malignancy. *Conclusions*: Radical endometrial resection by hysteroscopy may serve as an alternative to hysterectomy in selected patients with atypical focal endometrial lesions, not only in fertile women, but also in patients who refuse hysterectomy or present high anesthesiologic and surgical risks, regardless of the risk of recurrence, and with the necessity of undergoing hysteroscopic close follow-up.

Key words: Resectoscope; Atypical endometrial hyperplasia; Atypical endometrial polyps; Conservative management.

Introduction

Endometrial hyperplasia represents a pre-malignant lesion of the endometrium which has a greater risk of progression into an invasive endometrial cancer in postmenopausal women who may often present atypical lesions [1]. Atypical hyperplasia shows greater short-term risks of progression into endometrial cancer within four years [2] in approximately 25%-30% of cases, whereas simple or complex hyperplasia without atypia is likely to progress in < 5%, within ten years [3, 4]. Without persistent estrogen stimulation, endometrial hyperplasia without atypia can, in many cases, revert spontaneously to a normal endometrium. In addition, according to literature, 12.7% to 42.6% of the cases with endometrial cancer also present atypical endometrial hyperplasia lesions [5]. Endometrial hyperplasia or polyps do not always cause symptoms, although abnormal uterine bleeding is common [6]. More than 90% of endometrial malignancies occur in women over 50 years who suffer from abnormal uterine bleeding. An early diagnosis is therefore highly recommended [7]. Curettage of the uterine cavity was considered for years the gold standard for abnormal uterine bleeding, although most focal lesions in the uterine cavity remained undetected (58% polyps, 50% hyperplasia, 60% atypical hyperplasia, and 11% cancers) [8], yielding false negative rates of 3% to 7% [9]. The risk that an atypical endometrial lesion may transform itself into an endometrial carcinoma involved performing a hysterectomy, even in young women. Currently, hysteroscopic resection has become the novel route for removing any intrauterine lesion, thus not only benign pathologies, but also minimal malignant lesions regardless of the risk. The aim of this study was to evaluate the hysteroscopic resection as an alternative to hysterectomy to completely remove an atypical endometrial focal lesion and compare it to the histopathology of the uterus.

Materials and Methods

In the period from January 2008 to June 2012, out of 2,900 women referred to Hysteroscopic Unit of the Department of Health of Woman and Child of the University of Padua (Italy), for abnormal uterine bleeding and endometrial thickening in postmenopause, the data of 25 (0.8%) patients with a hystopathological diagnosis of atypical polyp or focal atypical endometrial hyperplasia were collected.

An office hysteroscopy with endometrial biopsy was performed, without anesthesia and/or analgesia, in the early days after the menstrual cycle, according to the method previously described in other papers by the same authors [10-12].

Twenty-five patients with atypical endometrial lesions underwent operative hysteroscopy as an inpatient day surgery under general anesthesia using a nine-mm resectoscope with a 12° forward-oblique lens, with a monopolar 90° loop, and glycine as distension medium, with the aim of entirely removing the endometrial lesions. In premenopausal women the procedure was performed during the proliferative phase of the menstrual cycle. The same patients were then submitted to total laparoscopic hysterectomy [13] within 30 days.

Specimens removed by hysteroscopic resection (endometrial polyps and focal endometrial areas) and by laparoscopic surgery (uterus), were sent to the Institute of Pathological

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Anatomy of the University of Padua for histopathological examination.

Patient age, body mass index (BMI), menopausal status, hormone replacement, tamoxifen therapy, hypertension, and diabetes were recorded. Patients exceeding a year since the last menstrual period and age above 40 years were defined as postmenopausal.

Results

Twenty-five patients were included in the study. Mean age: was 60.8 years (range 39 – 74), and the demographic characteristic are described in Table 1.

Only seven (28%) women had hormone replacement therapy with average of 13.5 years (range 1-25) and three (12%) patients with previous breast cancer had tamoxifen (20 mg/day) for five years. No patient had a family history of bowel, breast, and endometrial cancer.

The indications for office hysteroscopy were: abnormal uterine bleeding in 12 (48%) patients and postmenopausal endometrial thickening in 13 (52%) patients (Table 2).

The histopathological diagnosis of atypical polyp was confirmed in 16 (64%) women, and in nine (36%) women, atypical focal endometrial hyperplasia after resectoscopic surgery was found. Moreover, in case of polyps, an endometrial biopsy at the basal area of the polyp was added and only in three (12%) cases was an additional transcervical resection of the endometrium performed.

No complications such as uterine perforation, excessive absorption of distension medium, endometritis or failed procedure occurred.

After laparoscopic hysterectomy, histopathological examination of the uterus did not show the persistence of endometrial atypia in 23 (92%) cases, whereas in two (8%) cases endometrial atypical tissue was still present. No case of endometrial carcinoma was reported. There were no intra- or post-operative complications after laparoscopic surgery.

Table 1. — *Demographic data of 25 patients*.

	Number	Percentage
Premenopausal	7	28%
Postmenopausal	18	72%
Hormone replacement therapy	7	28%
Nulliparous	5	20%
Multiparous	20	80%
Overweight (BMI ≥ 25 - < 30 Kg/m^2)	10	40%
Obesity (BMI ≥ 30 Kg/m^2)	8	32%
Hypertension	10	40%
Diabetes mellitus	2	8%
Family history of bowel/breast/ endometrial cancer	0	0%
Tamoxifen (20 mg/day)	3	12%

Table 2. — *Indications to hysteroscopy*.

	Abnormal uterine bleeding	Endometrial thickening (≤ 4 mm)	Total
Premenopause	7 (28%)	–	7 (28%)
Menopause	5 (20%)	13 (52%)	18 (72%)

Discussion

The most important risk factor of progression of endometrial hyperplasia into endometrial cancer is more closely related to the presence of cytological atypia. There are still debates regarding the possibility of conservative management in these patients. The risk of progression to endometrial adenocarcinoma for atypical hyperplasia occurs in 25%-30%, with a time span of four years [2, 14]. Previous studies reported that, in cases of untreated atypical hyperplasia, the regression, persistence, and progression to endometrial carcinoma over a mean period of 13.4 years was 60%, 17%, and 23%, respectively [5].

In women who have completed their families or who are postmenopausal, the therapy of choice for atypical endometrial hyperplasia is hysterectomy, whereas in younger patients conservative medical or minimally invasive surgical treatments could be offered.

Currently there are no standardized treatment protocols, but the choice depends on the severity of the lesion, the patient's age, medical history, and the preferences of the patient. Medical treatment in young women with diffuse atypical endometrial hyperplasia could lead to regression of the lesion; instead surgical treatment, such as hysteroscopic resection, can be suggested in cases of atypical lesions as polyp or focal endometrial hyperplasia, even if hysteroscopic surveillance is mandatory.

Some authors have conducted studies with experimental protocols with hysteroscopic resection as conservative treatment for atypical polyps, with benign polyp base, and surrounding endometrium, both in young patients who wish to preserve their fertility, and in postmenopausal patients not undergoing hysterectomy under general anesthesia because of high anesthesiologic risk for important co-morbidity. In all patients, the follow-up period was five years, with an outpatient hysteroscopic assessment with endometrial sampling every six months during the first two years and subsequently every year thereafter [15]. In the fertile group, the patients were divided in two subgroups: the first in which the patients were subjected to insertion of levonorgestrel intrauterine device (LNG-IUD) and the second as control group; after five-years follow-up, there was no significant difference between women in the two subgroups. At the end of the trial, there were no recurrences of atypical polyps in both subgroups [16].

The results of the present retrospective study showed that in women treated with resectoscopic excision of atypical endometrial lesions, the therapeutic efficacy occurred in 92% of the patients and only in 8% of patients there was persistent atypical lesions. The authors believe that the limit of this procedure occurs when the lesion is close to the antrum of the uterine tube with a thickness < one cm because, beyond the excision of the lesion, there is a high risk of uterine perforation while performing a large biopsy of the surrounding tissue.

In a recent study [17], six young women with focal endometrial adenocarcinoma (grade G1) were conservatively treated with hysteroscopic resection followed by hormone therapy with megestrol acetate (160 mg/day) for six months. The radical excision of the lesion was confirmed by the absence of atypia in the surrounding tissue, while medical therapy had only the aim of consolidation.

The conservative management of Stage I endometrial carcinoma in young women is accepted as a reasonable short-term alternative to definitive surgical treatment. The risk of disease progression during conservative management is 5%-6% [18], while in cases of persistent disease, total hysterectomy is mandatory.

Considering the findings from this retrospective study, which are in accordance with others present in the literature regarding hysteroscopic resection for atypical endometrial hyperplasia, the authors can state that this procedure is safe, and a skillful surgeon is able to completely remove the intracavitary lesions. Furthermore this procedure could be suggested as a treatment alternative to hysterectomy in fertile women who desire to become pregnant or when hysterectomy is refused, or with high anesthesiologic and surgical risks. In these selected patients, it is necessary to perform a strict follow-up through an office hysteroscopy with endometrial biopsy.

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Address reprint requests to:
P. LITTA, M.D.
Department of Health of the Woman and Child
Obstetrics and Gynecology Clinic
University of Padua, Italy
Via Giustiniani, 3
35128 Padova (Italy)
e-mail: pietro.litta@unipd.it