Endometrial cancer in polyps: A clinical study of 27 cases

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Summary

Purpose of investigation: To review risk factors, clinical presentation, diagnostic methods, and histopathologic findings in 27 cases of endometrial cancer in polyps.

Methods: A descriptive, retrospective study of 204 consecutive patients with endometrial carcinoma who were diagnosed at our institution between June 1998 to June 2001. Endometrial cancer arising in polyps occurred in 27 patients (13.2%) and accounted for 1.8% of 1,492 endometrial polyps diagnosed during this period.

Results: Patients had a mean age of 62 years. All except one woman were postmenopausal. Three breast cancer patients were currently given tamoxifen. Metrorrhagia was the presenting symptom in 74% of cases, although 22% of patients were asymptomatic at the time of diagnosis. Ultrasonography performed in 22 patients showed images compatible with an endometrial polyp in 50% of cases, myoma in 5%, and inconclusive findings in 45%. The median endometrial thickness was 11 mm (range 4-33 mm). Diagnosis was made by aspiration-biopsy in 13 patients and by hysteroscopic endometrial sampling in 13 (in one patient endometrial carcinoma was incidentally found in the surgical specimen). All patients were in FIGO Stage IA. Endometrioid carcinoma was found in 81.5% of cases. Retroperitoneal metastases were not found in 25 patients undergoing pelvic lymphadenectomy, nor neoplastic growth in the specimens of six polypeptomies performed during hysteroscopy. All patients are free of relapse after a mean follow-up of 30 months.

Conclusions: Postmenopausal women with endometrial polyps diagnosed by ultrasonography should undergo directed biopsies under hysteroscopic vision. The present series confirms the good prognosis of endometrial cancer in polyps.

Key words: Endometrial cancer; Endometrial polyps; Metrorrhagia; Ultrasonography.

Introduction

The true incidence of endometrial polyps is difficult to determine because many are removed piecemeal during curettage and are not recognized. However, currently outpatient evaluation methods including hysteroscopy and ultrasonography, have revealed that uterine polyps are a common finding, ranging in rate from 16 to 34% [1-6]. Endometrial polyps account for 6.8% of all cases of menometrorrhagia in women 20-40 years [7]. About 20% of postmenopausal bleeding is due to polyps [8, 9]. The etiology and pathogenesis of endometrial polyps are not fully understood but polyps are believed to be a risk factor for endometrial cancer [10]. Although malignant transformation of endometrial polyps is uncommon, it has been reported that 10-34% of endometrial cancers in postmenopausal women have been associated with polyps. It has been reported that the risk of endometrial carcinoma in patients with endometrial polyps is approximately double that in the non-polyp group [11]. The objective of this retrospective case series study was to assess risk factors, clinical presentation, diagnostic methods, and histopathologic findings in 27 cases of endometrial cancer in polyps.

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Patients and Methods

A descriptive, retrospective review of all medical records from consecutive patients with endometrial carcinoma who were diagnosed and treated at out institution between June 1998 and June 2001 revealed a total of 204 cases. Endometrial cancer arising in polyps occurred in 27 (13.2%) patients. These 27 patients constitute the basis of this report. During the same period of time, a total of 1,492 endometrial polyps were resected, with an incidence of endometrial carcinoma of 1.8%. In all patients neoplastic growth in the biopsied tissue was documented before surgery except for one patient who underwent vaginal hysterectomy due to uterine prolapse in which the diagnosis was made incidentally after histopathologic examination of the surgical specimen.

Transvaginal sonography with a 6.5 Mhz endovaginal transducer was performed as a diagnostic technique. An endometrial polyp was suspected in the presence of endometrial thickness > 5 mm in menopausal women, > 10 mm in postmenopausal women receiving hormone replacement therapy or tamoxifen, and > 15 mm in fertile women, as well as in the presence of hyperechoic areas that distorted the endometrial line without increased endometrial thickness. Transvaginal sonography was performed in most patients (81.5%, 22/27) except in those in which after aspiration-biopsy with a Cournier cannula carried out in the office and without local anesthesia, an endometrial carcinoma was found on histologic examination. These patients were referred directly to the Service of Gynecologic Oncology for treatment.

All patients with polyps diagnosed sonographically were scheduled for hysteroscopy. Hysteroscopy was performed in the office with cervical anesthesia and paracervical block or in the

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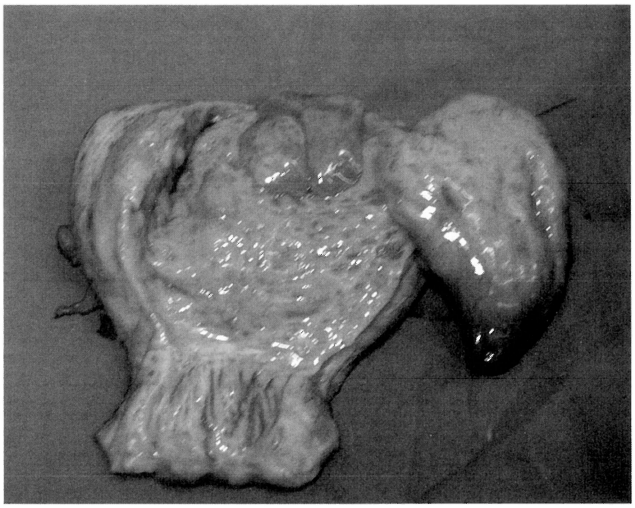

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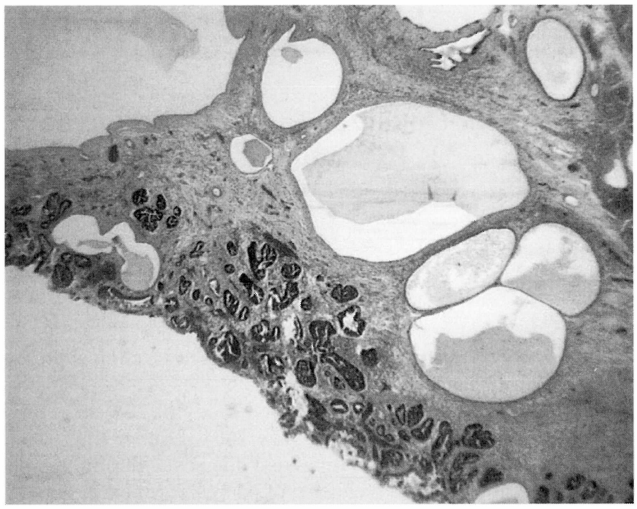

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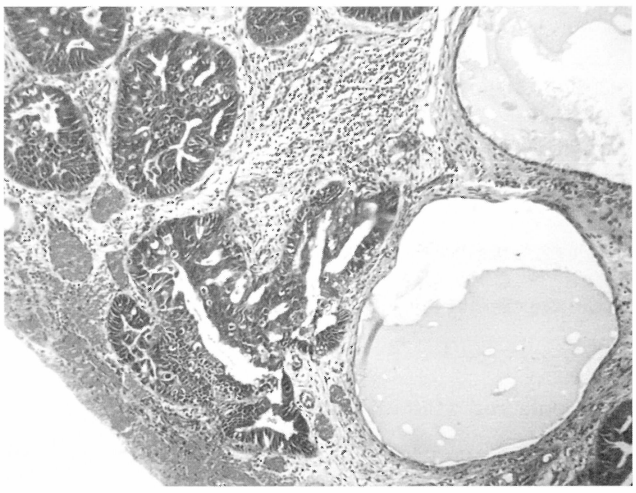

Figure 1. — Gross appearance of a large polypoid mass in a hysterectomy surgical specimen with the implantation base in the fundus. The external surface is smooth and brilliant with hemorrhagic areas in the tip.

Figure 2. — Microscopic image of an endometrial polyp with cystic glands on a vessel-rich stroma. The lower portion shows malignant changes characteristic of an adenocarcinoma (hematoxylin & eosin x 25).

Figure 3. — Histologic appearance of the neoplastic glands infiltrating a polyp (hematoxylin & eosin x 250).

hospital with locoregional anesthesia. Instruments used were 5 mm and 9 mm operating hysteroscopes (Karl Storz, Tuttlingen, Germany) with normal saline and glycine as the distending media for outpatient and inpatient hysteroscopies, respectively. In polypoid lesions of less than 3-4 cm located in the anterior, posterior or lateral walls with a thin pedicle, polypectomy was performed with the Versapoint bipolar electrode or using a vaporizing electrode in premenopausal women due to the risk of bleeding. Patients with polyps of less than 3-4 mm in the fundus or greater than 4 cm were scheduled for elective surgery. Cervical preparation in postmenopasal women included the use of 17-beta-estradiol vaginally or TTS (one patch 4 days before the procedure), and two doses of GnRH analogues in cases of dysfunctional uterine hemorrhage or in premenopausal women with recent menstrual cycle alterations.

The definitive diagnosis of endometrial cancer arising in a polyp was made by histopathologic examination (Figures 1-3). Only those cases in which carcinoma was limited to the polypoid lesion were considered. Adjacent carcinomas that in their growth involved a polyp or tumors in which neoplastic growth exceeded the polypoid pedicle and spread to the adjacent endometrium-myometrium were excluded. All patients were in FIGO Stage IA. Tumor extension was assessed by magnetic resonance imaging.

Primary surgical treatment included extrafascial hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymphadenectomy and peritoneal washing samples for cytological examination. Operations were carried out by laparotomy or laparoscopy. Paraaortic lymphadenectomy was eventually performed depending on histologic findings in the previous biopsy and intraoperative inspection of the surgical specimen. Only in the patient in which endometrial carcinoma in a polyp was incidentally detected after a vaginal hysterectomy – and due to the absence of histopathologic risk factors – was no further treatment was indicated. All patients were followed at regular intervals at the outpatient clinics of the hospital.

Results

The mean age of the patients was 62 years (range 48-80 years). All except for one woman were menopausal. Six patients were nulligravid and 21 multigravid. Hypertension was present in 11 patients, diabetes mellitus in six, and history of endometrial hyperplasia in four (simple hyperplasia without atypia 2, complex atypical hyperplasia 2). None of the patients received hormonal replacement therapy and three breast cancer patients (intraductal carcinoma) were currently being treated with tamoxifen.

Metrorrhagia was the presenting symptom in 74% of cases (n = 20). Twenty-two percent of patients (n = 6)

were asymptomatic at the time of diagnosis. Pain was present in 4% of patients. Transvaginal ultrasonography performed in 22 patients showed images compatible with an endometrial polyp in 50% of cases (n = 11), myoma in 5% (n = 1), and inconclusive findings in 45% (n = 10). The median endometrial thickness was 11 mm (range 4-33 mm).

With regard to diagnostic techniques and excluding the patient in which endometrial carcinoma was incidentally found in the surgical specimen, endometrial carcinoma was diagnosed by aspiration-biopsy in 13 cases and by hysteroscopy in 13 (outpatient hysteroscopy 9, inpatient hysteroscopy 4). Hysteroscopic findings included polyps in nine patients, generalized polyposis in two, pearly mass in one, and unknown in one (hysterectomy performed elsewhere). Polyps ranged between 10 and 40 mm in size. Hysteroscopic polypectomy was performed in nine patients (Table 1). A directed biopsy was perfomed in three patients and a blind biopsy using a Novak's curette in one.

Table 1. — *Hysteroscopic findings and histological characteristics in 27 patients with endometrial carcinoma in polyps.*

	No. of patients	Percentage
Diagnostic technique, n = 27		
Aspiration-biopsy, vaginal ultrasonography	13	48.1
Hysterectomy surgical specimen, incidental diagnosis	1	3.7
Hysteroscopy	13	48.1
Hysteroscopic findings, n = 13		
Polyp	9	69.2
Generalized polyposis	2	15.4
Pearly mass	1	7.7
Inconclusive	1	7.5
Hysteroscopic polypectomy, n = 9		
Scissors	4	44.5
Resectoscope	4	44.5
Versapoint electrode	1	10
Histological findings, n = 27		
Endometrioid carcinoma	22	81.5
Seropapillary adenocarcinoma	4	7.4
Adenosquamous carcinoma	1	3.7

In six patients in which the diagnosis of endometrial cancer was made by hysteroscopy, no cancer was found in the hysterectomy specimen. On the 25 patients undergoing pelvic lymphadenectomy, retroperitoneal metastases were not observed. Cytological examination of peritoneal washing samples were negative. After histopathologic examination, all patients were classified in FIGO Stage IA. Histological findings included endometrioid carcinoma in 22 cases (adenoacanthoma 2), seropapillary adenocarcinoma in four, and adenosquamous carcinoma in one (Table 1). The histologic grade was well differentiated carcinoma in 17 patients, moderately differentiated in six, and poorly differentiated in four. Adjuvant treatment after surgery was not indicated. No patient had tumor relapse after a mean follow-up period of 30 months.

Discussion

During a 3-year study period, the prevalence of endometrial cancer in polyps was 13.2% (27 of 204 patients). During the same period of time, a total of 1,492 endometrial polyps were resected, with an incidence of endometrial carcinoma of 1.8%. As far as we are aware, the present clinical series of 27 patients with endometrial cancer arising in polyps is the largest reported in the literature.

Although endometrial polyps can appear in menopausal women receiving hormone replacement therapy [10], none of our patients were taking hormones. In our population three patients were currently being treated with tamoxifen. Endometrial polyps and endometrial neoplasms are a recognized complication of chronic tamoxifen treatment [11-14], and it has been suggested that polymorphisms at the methylenetetrahydrofolate reductase gene could influence susceptibility to endometrial cancer [15, 16].

Hysteroscopy is a valuable tool in diagnosing structural intracavital pathology, very suitable for the outpatient clinic, but the value in diagnosing endometrial carcinoma is limited and even after guided biopsy a malignancy cannot be ruled out [17]. More polyps are being diagnosed with the widespread use of transvaginal ultrasound scanning and color Doppler sonography [18, 19]. In fact, Perez-Medina *et al.* [20] have shown that low Doppler resistance was highly predictive of atypia inside endometrial polyps. However, these techniques cannot replace hysteroscopic studies and surgical removal and pathologic evaluation to predict histologic type.

The present series indicate that endometrioid carcinoma is the most predominant histologic type because most of the study population corresponds to type I endometrial cancer [21], followed by seropapillary adenocarcinoma. Seropapillary adenocarcinoma in an aggressive neoplasm and in agreement with the study of McCluggage *et al.* [22], this type of tumor appears in women during the late postmenopausal period in association with negligible estrogenic exposure that characterizes endometrial carcinoma type II.

Although different studies have consistently indicated the risk of malignant pathology in endometrial polyps in postmenopausal women with abnormal uterine bleeding [23, 24], we have recorded endometrial cancer in polyps in one fertile woman as well as in six patients who were asymptomatic. In six of the patients in which diagnosis was made by hysteroscopy, neoplastic changes in the final histopathologic study were not observed. On the other hand, resected lymph nodes were free of disease in all cases. However, detection of polyps should be taken seriously reinforcing the need for their removal independently of the size or symptoms especially in menopausal women. In our opinion, the diagnosis, prognosis, and management of polyps require further evaluation in controlled studies.

Conclusion

Endometrial carcinoma in polyps is more frequent in postmenopausal women with abnormal uterine bleeding, but this malignancy may occasionally develop in fertile asymptomatic women. Detection of a polypoid mass by abdominal ultrasound should be confirmed by biopsy under hysteroscopic view. The present series confirm that endometrial cancer in polyps has a good prognosis and that lymph node metastasis is exceptional.

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