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Endometrial polyps

A clinical study of 245 cases

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Abstract. *Objectives:* Endometrial polyps (EPs) are among the common cases of abnormal uterine bleeding. Hormonal factors may be involved in the pathogenesis as indicated by endometrial abnormalities in patients treated with tamoxifen. This study was designed to analyse the patient characteristics which may be associated with polyp occurence and assess the diagnostic and therapeutic difficulties. Group of 245 patients was formed of 152 postmenopausal and 93 premenopausal women with EP diagnosed hysteroscopically and confirmed histologically. Evaluated factors were as follows: 1) patient characteristics: age, body mass, systemic hypertension, diabetes mellitus, nulliparity, late menopause, estrogen replacement therapy, and tamoxifen treatment; 2) clinical features of EPs, and 3) the number of curettage's (D&C) and hysteroscopies. *Results:* Hypertension associated with obesity appears to be an important factor in combination which may play role in the pathogenesis of EPs like the late menopause which was noted in 30% of examined postmenopausal women. An association between EPs and tamoxifen was found in 8% patients with breast cancer. 2. Postmenopausal uterine bleeding and menstrual disorders were prominent clinical symptoms in 44% post- and in 82% of premenopausal women. The other 56% post- and 18% premenopausal patients were asymptomatic. 3. The multiple EPs were present in 26% of postmenopausal and in 15% premenopausal women. 4.Transvaginal ultrasonography supplemented by sonohysterography in cases with abnormal ultrasonographic finding should be the main diagnostic method. 5. Hysteroscopical polypectomy is regarded as the optimal therapy and the removal of the endometrial basalis in the EP origin area prevents persistence or recurrence of EP.

Key words: Endometrium – Polyp – Estrogens – Tamoxifen – Hysteroscopy

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Introduction

Endometrial polyps (EPs) are among the common causes of abnormal uterine bleeding. Hormonal factors may be involved in the EP pathogenesis as indicated by endometrial abnormalities in patients treated with tamoxifen. Despite being an estrogen antagonist, tamoxifen has been shown to have estrogen agonist effects on the endometrium. The partial agonist activity of tamoxifen in postmenopausal women may thus produce a hormonal environment of low levels of unopposed estrogen similar to that in perimenopausal women [2, 15, 19, 20].

Dilatation and curettage has long been considered the standard method for investigation of abnormal uterine bleeding and for obtaining a sample of endometrium for histological examination. However, as it is a "blind" procedure, it has well-recognized limitations and a large number of endometrial polyps is missed because of their mobility [7, 8]. The addition of hysteroscopy yielded more information and potentially serves both a diagnostic and therapeutic purpose [16].

Our study had two objectives: first, to analyze the patients characteristics which may be associated with polyp occurrence, and second, to assess the diagnostic and therapeutic difficulties.

Material and methods

This prospective study was performed in time period between March 1995 and April 1998. The criteria for inclusion of the patients into the study were histological confirmation of EP together with vaginal ultrasonographic examination three months after EP resection and half a year later.

EPs were diagnosed hysteroscopically and confirmed morphologically in a set of 245 patients divided into two groups according to the menopause, i.e.,

- premenopausal group of 93 women aged from 23–58 years (mean, 44 years).
- postmenopausal group of 152 patients between ages from 39–87 years (mean, 62 years).

Menopause was defined as cessation of the menstruation for longer then one year.

The evaluated factors were as follows:

- Patient characteristics: Age, body mass (BMI: body mass index calculated according to the general accepted formula: W/H^2, where W is the weight in grams and H is the height in centimeters, and divided into three classes; <25 normal body mass, 26–29 overweight, >29 obesity), systemic hypertension and diabetes mellitus (both defined according to WHO classification), nulliparity, late menopause (later than age 52), estrogen replacement therapy (ERT), and tamoxifen treatment. All regarded as factors which may be associated with unopposed estrogen environment.
- Clinical features of the EPs.
- The number of curettage's (D&C) or hysteroscopies. Time of their performance related to the reproductive period.

The above mentioned data were evaluated in all examined patients.
Vaginal sonography (HDI 3000, ATL, Bothel, vaginal transducer C9–5, ICT 9–5 MHz) was used as a main diagnostic method. Saline contrast sonohysterography was indicated in cases with abnormal sonographic appearance.

Direct endometrial cavity visualization was performed by hysteroscopy (diameter 5.5 mm, 30′ angle, Olympus) followed by polypectomy (resectoscope in 9 mm diameter, 12′ angle, Olympus). The uterine cavity was distended with Clear Flex solution (Bieffe Medital). Wire loop or knife electrodes were used according to EP localization. Each polyp resection was completed by curettage. EP and endometrial tissue were fixed separately for subsequent morphology. The first sonographic control was performed three months after the EP resection, the next one half a year later.

All patients fulfilled inclusion criteria and completed the study.

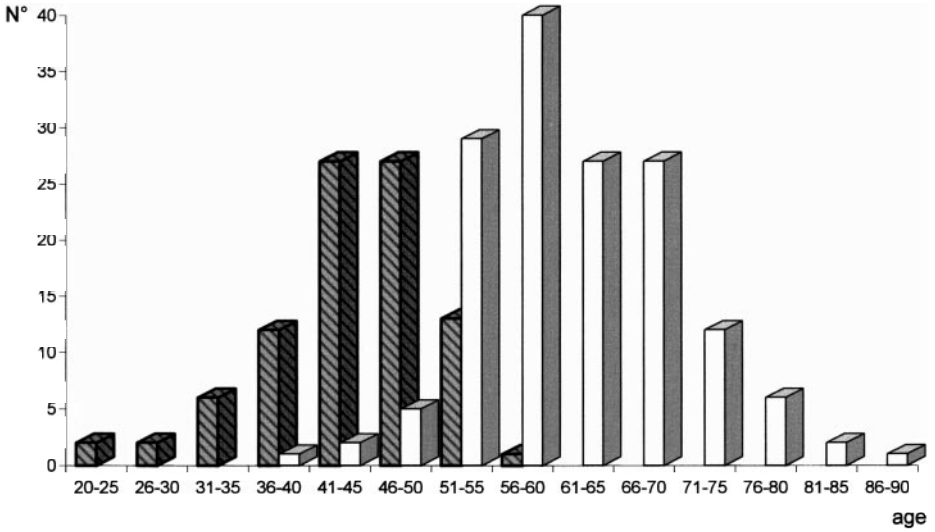

Fig. 1. Age distribution of examined patient groups, *white columnes* postmenopausal group, *black columnes* premenopausal group

Results

Evaluated factors of premenopausal group (n=93)

Patient characteristics

Patient age shown in Fig. 1 was between 41 and 50 years with 57 (61%) cases as the most frequent age period.

Body mass. Normal *body mass*, overweight, and obesity were encountered in 48 (52%), 36 (39%), and 9 (9%) patients, respectively.

Hypertension was diagnosed in 11 (12%) women and was associated with obesity in 8 (9,6%) cases.

Diabetes mellitus. Noninsulin-dependent *diabetes mellitus* (type II) was noted in one (1.1%) obese woman.

Nulliparity. There were 5 *nulliparous* patients in this group. 2 of them, aged 29 and 37 years, had been treated for chronic anovulation and abnormal bleeding.

Menstruation after 52 years of age was present in 6 (12%) women.

Clinical symptomatology

76 (82%) patients were symptomatic. Type of the abnormal bleeding is shown in Table 1.

EP number and recurrence. Solitary EP was diagnosed in 79 (85%) patients. 2 EPs were found in 9 (10%) women. 3 or more EPs were encountered in 5 (5%) patients. The EP recurrence was present in 1 patient 10 months after the polypectomy. In 7 cases only, the EPs were originated in the fundus.

Table 1. Type of abnormal uterine bleeding in premenopausal group

Type	*n*	%
Hypermenorrhoea	36	38.7
Polymenorrhoea	5	5.4
Intermenstrual	11	11.8
Premenstrual	3	3.2
Metrorrhagia	17	18.3
Asymptomatic	21	22.6

Hormonally treated menstruation disturbances. 19 (17%) patients with EPs were hormonally treated and the abnormal uterine bleeding was normalized in 9 cases inclusive 1 patient with malignant transformation in 1 of 3 resected EPs.

Previous D&C and resectoscopy

Curettage for abnormal bleeding was noted in 27 (29%) cases. It was performed twice in 8 women and 3 times in 1 patient. An abnormal ultrasonographic finding after the curettage was present in 17 (18%) patients which was found as an indication for hysteroscopy. Polypectomy was noted in one patient history.

Hysteroscopy complications. There were no complications of the hysteroscopy in the premenopausal patient group.

Evaluated factors of postmenopausal group (n=152)

Patient characteristics

Patient age is demonstrated in Fig. 1. The age peak was found between ages 51 and 70 years with 123 (81%) patients.

Body Mass. Normal body mass, overweight, obesity, and more then 40% excess body weight were encountered in 48 (32%), 60 (39%), 39 (26%), and 5 (3%) patients, respectively.

Hypertension was diagnosed in 55 (36%) women. 28 (18%) hypertonics were obese.

Diabetes mellitus. Insulin-dependent diabetes was noted in 5 (3%) and noninsulin-dependent diabetes in 11 (7%) patients. The noninsulin-dependent diabetes was associated with obesity in 6 (4%) cases.

Nulliparity. Infertility was present in 8 (5%) women, in 2 of them the septate uterus was noted. Male infertility: 1 case.

Late menopause was encountered in 46 (30%) patients.

Estrogen replacement therapy (E R T). ERT (50 μg/d of transdermal estradiol, Estraderm TTS 50, Ciba-Geigy Limited, Basel, Switzerland) was used in 3 patients for 8, 12, and 18 months with subsequent progestogens supplementation. After 9 months, ERT (0.6 mg/d of conjugated estrogens, Presomen, Kali-Chemie Pharma GmbH, Hannover, Germany) was discontinued because of breast carcinoma in the 4th patient. This woman was treated with tamoxifen and the EP was diagnosed 3 years later. Combined hormone replacement therapy (2 mg/d of estradiol and

1 mg/d of norethisterone acetate, Kliogest, Novo Nordisk A/S, Bagsvaerd, Denmark) was applied to 10 women for 1–42 months (mean, 14 months).

Tamoxifen or other types of hormonal therapy. Breast carcinoma had been treated with tamoxifen-citrate in 12 (8%) patients with EP. Tamoxifen was applied during 9–36 months (mean, 22 months). 2 other patients were treated with megestrol acetate for 24 and 36 months and 1 woman with medroxyprogesterone acetate for 24 months.

Clinical features

67 (44%) out of 152 postmenopausal patients presented with uterine bleeding.

EP number and recurrence. Solitary EP was found in 113 (74%) patients, 2 polyps in 21 (14%) women, 3 in 13 (9%) women, and more then 3 EPs were diagnosed in 5 (3%) patients. Hysteroscopy was repeated in 10 (7%) cases for abnormal ultrasonographic finding 5–28 months (mean,13 months) after polypectomy. Polyp recurrence was encountered in 9 (6%) patients, 1 shown atypical hyperplasia. The uterine fundus appeared to be the site of EP origin in 40 (26%) cases.

Hysteroscopy complications. Uterine perforation occurred in 3 (2%) patients and requiring hysterectomy in 2 of them.

Previous D&C or resectoscopy

84 (55%) patients in this group had an invasive diagnostic examination for uterine bleeding. There were 76 curettings and 8 hysteroscopies. 2 hysteroscopic polypectomies were noted in 6 women, 5 of them for EP recurrence. 34 (22%) patients have had more then 1 D&C in previous history.

Discussion

The relationship between estrogens and endometrium stimulation is well known and the factors which may be associated with unopposed estrogen environment had been intensively studied [18]. Some of them were evaluated in our study.

EPs usually occur in women between 40 and 50 years old and more frequently in the postmenopause [4]. Our results confirm this with age peak between 51 and 70 years (Fig. 1).

Obesity characterized by increased peripheral aromatization of androgens to estrogens in adipose tissue seems to be associated with an estrogenic state [12]. Obesity was most often noted in our postmenopausal patients, but was found to be an insignificant factor judging by the prevalence of obesity in the general population of our geographic region. However, age associated with obesity are regarded as likely factor combination inducing the endometrial abnormalities [3].

Systemic hypertension alone was present in 12% of the examined premenopausal and 36% of the postmenopausal patients with EPs, i.e., in 27% of all our patients. It was associated with obesity in 22%. Hypertension associated with obesity appears to be an important factor which may play the role in the pathogenesis of EPs. However, it is known, that systolic pressure and the prevalence of hypertension increase dramatically with age [1]. This is an important clinical problem

because of extremely high prevalence – up to 80% – of hypertension in elderly women.

In contrast, the examined diabetics showed no relationship to EPs. Noninsulin-dependent diabetes was noted in only 1.1% obese premenopausal and 4% postmenopausal women.

Infertility is another factor which may be associated with anovulatory cycles [5]. It was diagnosed in 3 pre- and 8 postmenopausal nulliparous patients, i.e., in 4.5% of all patients. This factor is difficult to analyze retrospectively. Only 2 premenopausal women were treated for chronic anovulation at the time of polypectomy.

Late menopause, as a factor inducing prolonged exposure of the endometrium to estrogens, was noted in 30% of examined postmenopausal women with EPs and was found to be an important factor probably involved in EP pathogenesis. Some recent studies have confirmed a relationship of ERT with endometrial abnormalities especially with endometrial cancer [9, 17]. ERT was applied in 4 our patients for 8 to 18 months. It is difficult to assess whether EPs diagnosed in these patients were hormonally induced because of the lack of vaginal sonography or biopsy before ERT. Uterine bleeding occurred in these patients when the combined therapy with progestogens was applied.

Tamoxifen, as an antiestrogen, is likely to be involved in the endometrial changes because of its estrogenic activity [6, 10, 11, 14]. An association between EPs and tamoxifen was found in 8% of our patients with breast cancer.

76 (82%) of premenopausal patients presented with menstrual disorders. In some these cases the abnormal uterine bleeding was normalized with progestagens. We can speculate about the coincidence of EP and anovulatory cycles.

According to some authors [13], the uterine fundus is the most frequent site of EP origin. In our series EPs occurred in fundus in only 19% out of 245 patients. We can offer no explanation for this discrepancy. The multiple EPs were present in 26% of our postmenopausal and in 15% of the premenopausal women.

2 morphological types of EPs may occur in the reproductive age. The hyperplastic EPs are derived from the basal endometrium layer which is dependent on estrogens but no on progesterone stimulation. The glandular component of the second type of EPs, i.e., the functional EPs respond to cyclic hormonal changes during the menstrual cycle and its morphology resembles that of the surrounding endometrium. It is the reason, why the tissue fragmentation during curretage may make the diagnosis of functional EPs difficult or even impossible.

In the postmenopause, the majority of EPs presents with a fibrotic transformation of the stroma (atrophic EP). We believe that the fibrosis is the cause of inadequately removed polyp by curettage. Persistence of the polyp had been noted in the history of 51 of our patients treated by curettage alone. We consider hysteroscopy as the optimal method for the examination of uterine cavity and for the focused treatment of EP.

In conclusion, menstrual disorders are prominent clinical symptoms in premenopausal women with EPs. However, our study indicates that in the presence of hyperplastic EPs the abnormal uterine bleeding may be normalized with progestagens. From this point of view, the symptomatology of EPs is questionable. We speculate about the coincidence of EP and anovulatory cycles, but the examination of serum progesterone levels is needed. On the other hand, the unopposed estrogens may contribute to the EP pathogenesis and the prompt therapeutic management of anovulation should be effective in the prevention of EP. Hysteroscopic polypec-

tomy is regarded as the optimal therapy and the removal of endometrial basalis in the EP origin area prevents not only persistence but also recurrence of EP, i.e., polypectomy would have to reach the superficial layer of the myometrium.

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