Endometrial polyps

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INTRODUCTION — Endometrial polyps are one of the most common etiologies of abnormal genital bleeding in both premenopausal and postmenopausal women [1-3]. They are hyperplastic overgrowths of endometrial glands and stroma that form a projection from the surface of the endometrium (lining of the uterus). They may also be asymptomatic. The great majority of endometrial polyps are benign, but malignancy occurs in some women [2].

The epidemiology, diagnosis, and management of endometrial polyps are reviewed here. General principles of the evaluation of uterine bleeding are discussed separately. (See "Approach to abnormal uterine bleeding in nonpregnant reproductive-age women" and "Postmenopausal uterine bleeding".)

HISTOPATHOLOGY — Endometrial polyps are localized hyperplastic overgrowths of endometrial glands and stroma around a vascular core that form a sessile or pedunculated projection from the surface of the endometrium (picture 1) [3,4]. Smooth muscle is sometimes present.

Single or multiple polyps may occur and range in diameter from a few millimeters to several centimeters (picture 2) [5]. Polyps can develop anywhere in the uterine cavity.

PATHOGENESIS — Several molecular mechanisms have been proposed to play a role in the development of endometrial polyps. These include monoclonal endometrial hyperplasia [6], overexpression of endometrial aromatase [7,8], and gene mutations [9,10]. Like uterine leiomyomas, polyps have characteristic cytogenetic rearrangements. Rearrangements in the high-mobility group (HMG) family of transcription factors appear to play a pathogenic role [9,11,12].

Endometrial polyps express both estrogen and progesterone receptors [13]. In polyps, as in normal endometrial tissue, progesterone may serve an antiproliferative function. This has been demonstrated in a subset of women with polyps, ie, those on tamoxifen therapy [14]. While androgens have been found to cause endometrial atrophy, similar to progestins, data suggest that testosterone does not substitute for progestational activity for polyps [15].

EPIDEMIOLOGY — Endometrial polyps are rare among adolescents [16]. The frequency of polyps is difficult to establish, since there are few data and some polyps are asymptomatic. Among clinically recognized polyps, the prevalence appears to rise steadily with increasing age, and to be higher in premenopausal than postmenopausal women (6 versus 12 percent in one study) [17]. Among women undergoing endometrial biopsy or hysterectomy, the prevalence of endometrial polyps is 10 to 24 percent [18,19].

RISK FACTORS — Endometrial polyps express both estrogen and progesterone receptors, although studies differ on whether these appear to have pathogenic importance [13,20]. Most risk factors for endometrial polyps involve increased levels or activity of endogenous or exogenous estrogen.

Tamoxifen — Polyps develop in 2 to 36 percent of postmenopausal women treated with tamoxifen [21,22]. Polyps in these women may be large (>2 cm), multiple, or show molecular alterations [11,21,23,24]. Data from a large randomized trial of breast cancer chemoprophylaxis in postmenopausal women found that the incidence of polyps was higher in women treated with tamoxifen compared with raloxifene (2.1 versus 0.6 percent; relative risk 0.30, 95% CI 0.25-0.35) [22].

Obesity — Endometrial polyps appear to be associated with obesity [25-27]. As an example, in a retrospective cohort study of 223 women planning to undergo in vitro fertilization, those with a BMI ≥30 had a significantly higher rate of polyps than other women (52 versus 15 percent) [26]; however, these data may not be generalizable to other women.

Other risk factors — Data suggest that postmenopausal hormone therapy is associated with endometrial polyps, particularly regimens with a high dose of estrogen and/or a progestin with low antiestrogenic activity [25,28].

Women with Lynch and Cowden syndrome may have an increased incidence of endometrial polyps compared to the general population, possibly accompanied by increased risk of associated endometrial cancer [29-31]. (See "Clinical features and diagnosis of Lynch syndrome (hereditary nonpolyposis colorectal cancer)".)

CLINICAL PRESENTATION — Endometrial polyps are typically identified in association with abnormal uterine bleeding. Many polyps are asymptomatic and are discovered as the result of an evaluation for infertility, a finding of endometrial cells on cervical cytology, or as an incidental finding on endometrial sampling, pelvic imaging, or hysteroscopy. In some women, prolapse of the polyp occurs and it can be visualized at the external cervical os during pelvic examination.

Abnormal uterine bleeding — Abnormal uterine bleeding , which is usually described by the patient as vaginal bleeding, is the most common presenting symptom and occurs in 64 to 88 percent of women with polyps [17,32,33]. Bleeding due to polyps is referred to as AUB-P in the nomenclature recommended by the International Federation of Gynecology and Obstetrics (FIGO) [34].

Metrorrhagia is the most frequent symptom in premenopausal women with endometrial polyps [35]. The volume of bleeding is usually small, and may be just spotting. Some women experience heavier bleeding between menstrual cycles or menorrhagia. Postmenopausal bleeding is another common presentation; some postmenopausal women with polyps have breakthrough bleeding during hormonal therapy. (See "Approach to abnormal uterine bleeding in nonpregnant reproductive-age women".)

Women with abnormal uterine bleeding may require evaluation for endometrial cancer. (See "Endometrial carcinoma: Clinical features and diagnosis", section on 'Abnormal uterine bleeding'.)

Incidental finding on imaging or hysteroscopy — Endometrial polyps are often identified incidentally on a pelvic ultrasound performed for other indications. In addition, some polyps are discovered at time of hysteroscopy, if this study is performed without a prior ultrasound.

Endometrial cells on cervical cytology — Cervical cytology is not a useful method for diagnosing endometrial polyps. Studies have shown an association between the finding of benign endometrial cells on liquid cervical cytology testing and both benign and malignant endometrial neoplasms. In a large retrospective chart review of women age 40 years or older with a cervical cytology report that included the presence of endometrial cells and underwent endometrial sampling, 12 percent of women had endometrial polyps alone and 2 percent had polyps with a coexistent diagnosis (ie, hyperplasia or endometritis) [36]. Among the women with polyps alone, 72 percent were asymptomatic. The evaluation of endometrial cells on cervical cytology is discussed separately. (See "Cervical and vaginal cytology: Interpretation of results", section on 'Benign-appearing endometrial cells in a woman ≥40 years'.)

Prolapsed polyp — Rarely, an endometrial polyp prolapses and is visible at the time of speculum examination at the external cervical os. Prolapsed polyps may be symptomatic or asymptomatic.

DIAGNOSTIC EVALUATION — Women with a suspected endometrial polyp are typically evaluated with pelvic imaging or hysteroscopy.

Diagnostic studies — Transvaginal ultrasound (TVUS) is the first line imaging study of choice of evaluation of women with abnormal uterine bleeding. This modality is effective at characterizing uterine and adnexal lesions and is less expensive than other modalities.

For women with an uncertain finding on ultrasound alone or who are candidates for expectant management, we suggest sonohysterography, also referred to as saline infusion sonogram (SIS) or diagnostic hysteroscopy. A systematic review of over 5000 women reported a similar performance for the diagnosis of polyps for all three modalities: sensitivity (TVUS: 91 percent; SIS: 95 percent;

hysteroscopy: 90 percent) and specificity (90 and 92 and 93 percent) [17]. Both SIS and hysteroscopy give a better sense of the shape of the lesion than TVUS alone. The advantage of SIS compared with hysteroscopy is that the adnexa are also visualized, so this modality is useful in women with suspected adnexal pathology (image 1 and image 2 and image 3). On the other hand, diagnostic hysteroscopy allows direct visualization of the lesion. (See "Saline infusion sonohysterography" and "Overview of hysteroscopy", section on 'Procedure'.)

Physical examination — In the absence of a prolapsed polyp, there are no physical examination findings associated with an endometrial polyp. A prolapsed polyp can be visualized during a speculum examination, typically as a globular, friable, pedunculated lesion protruding from the external cervical os.

A polypoid lesion at the external cervical os is most commonly a cervical polyp, but may be a prolapsed endometrial polyp or leiomyoma. In general, a cervical polyp is identified by visualizing or palpating a stalk originating from the endocervical canal, while the stalk of an endometrial polyp originates from the uterine cavity. Prolapsed leiomyomas typically have a firm consistency, while polyps are soft and friable. (See "Congenital cervical anomalies and benign cervical lesions", section on 'Polyps' and "Prolapsed uterine leiomyoma (fibroid)", section on 'Incidental finding on pelvic examination'.)

DIAGNOSIS — The diagnosis of an endometrial polyp is a histologic diagnosis based upon the evaluation of the specimen after it has been removed. Histologic evaluation can also exclude malignancy.

The specimen is usually collected at time of polypectomy. In some women, an endometrial polyp is diagnosed on an office endometrial biopsy performed to evaluate abnormal uterine bleeding. In such cases, polypectomy should still be performed if indicated (for symptom relief or to exclude malignancy), since the entire polyp may not have been removed with the endometrial biopsy. (See 'Polypectomy' below.)

DIFFERENTIAL DIAGNOSIS — The differential diagnosis of an endometrial polyp includes other structural lesions of the uterine cavity, primarily intracavitary leiomyomas. It is usually, but not always, possible to differentiate between these lesions with sonography. In addition, polyps and fibroids typically have different appearances when visualized with hysteroscopy. Polyps often have a beefy red appearance, and are usually thinner and less likely to be sessile. In addition, they are soft and friable when touched with an instrument. In contrast, myomas are firm and are mainly white in color with small surface blood vessels. The final determination is made with histology. (See "Epidemiology, clinical manifestations, diagnosis, and natural history of uterine leiomyomas (fibroids)", section on 'Diagnosis'.)

An endometrial lesion on ultrasound may also represent endometrial hyperplasia or cancer. At hysteroscopy, polyps are generally well-demarcated, in contrast with endometrial neoplasia. (See "Endometrial carcinoma: Clinical features and diagnosis", section on 'Pelvic sonography'.)

The differential diagnosis of a prolapsed endometrial polyp includes a cervical polyp and a prolapsed leiomyoma. The approach to differentiating between these lesions is discussed above. (See 'Physical examination' above.)

CLINICAL COURSE

Continued growth or regression — A prospective study on the course of endometrial polyps performed two saline infusion sonograms 2.5 years apart on 64 initially asymptomatic women (mean age 44 years) [37]. Seven women had polyps on the first examination. Four of these women had spontaneous regression of their polyps at the second scan, while seven women developed new polyps over the 2.5-year interval. Polyps larger than 1 cm were least likely to regress. Hormone use did not appear to affect the natural history of the polyps, but the study sample was small.

Risk of malignancy — Approximately 95 percent of endometrial polyps are benign [38]. A systematic review of 17 observational studies including over 10,000 women reported that the incidence of polyps that were malignant or hyperplastic was significantly higher in postmenopausal compared with premenopausal women (5.4 versus 1.7 percent; RR 3.86; 95% CI 2.9–5.1) and those with bleeding compared to those without bleeding (4.2 versus 2.2 percent; RR 2.0; 95% CI 1.2–3.1) [2]. Of note, these characteristics are also associated with an increased risk of endometrial malignancy without polyps.

The systematic review found that data were inconsistent regarding whether increased polyp size was associated with malignancy [38]. Studies of 400 or more women that support this association have reported that premalignant or malignant histology was associated with polyps greater than 1.5 cm in diameter [39,40].

Tamoxifen — Malignant transformation of an endometrial polyp appears to occur more frequently in women on tamoxifen (up to 11 percent) than in other women [21]. There is no evidence for an association between malignancy and polyp size or duration of tamoxifen therapy. Likewise, tamoxifen use is associated with an increase in the overall risk of endometrial cancer [22]. (See "Endometrial carcinoma: Epidemiology and risk factors", section on 'Tamoxifen'.)

Treatment of women with malignant endometrial polyps is discussed in detail separately. (See "Endometrial carcinoma: Histopathology and pathogenesis", section on 'Carcinoma involving an endometrial polyp'.)

Effect on fertility and pregnancy — Women undergoing evaluation for infertility may have a finding of an endometrial polyp on ultrasound or hysteroscopy; the reported prevalence in those undergoing in vitro fertilization is 6 to 8 percent [41,42]. There are few data regarding the impact of removal on fertility. A systematic review based upon limited data concluded that removing polyps was beneficial in infertile women [1]; this conclusion was based primarily on a single randomized trial (n = 204) that showed a higher pregnancy rate in women undergoing intrauterine insemination who underwent polyp removal compared with hysteroscopy alone (63 versus 28 percent) [43,44]. (See "Evaluation of female infertility" and 'Symptomatic women' below.)

Endometrial polyps do not appear to be associated with an increased risk of spontaneous abortion or adverse obstetric outcomes. In studies performed in women with a recent miscarriage, the prevalence of polyps was the same as in the general population [45,46]. (See 'Epidemiology' above.)

CHOOSING A MANAGEMENT APPROACH — Symptomatic endometrial polyps should be removed in all women. The goal of polypectomy is both relief of symptoms and detection of malignancy, since symptomatic polyps are more likely to be malignant. (See 'Risk of malignancy' above.)

Management of asymptomatic polyps depends upon the likelihood of malignancy associated with a polyp and whether removal is indicated due to infertility. There are no data from randomized trials to guide therapy of asymptomatic polyps.

Premenopausal women

Symptomatic women — Symptomatic polyps should be removed, regardless of menopausal status.

Asymptomatic women — For premenopausal women, we suggest removal of asymptomatic polyps for women with risk factors for endometrial hyperplasia or cancer (table 1). (See "Endometrial carcinoma: Epidemiology and risk factors", section on 'Risk factors'.)

For other asymptomatic women, we perform polypectomy if the following characteristics are present:

- Polyp >1.5 cm in diameter
- Multiple polyps
- Polyp prolapsed through the cervix
- Infertility (see 'Infertile women' below)

Some studies report that polyps >1.5 cm in diameter are associated with an increased risk of malignancy or hyperplasia, although the data are inconsistent regarding polyp size (see 'Risk of malignancy' above).

Multiple polyps and prolapsed polyps are unlikely to regress and are likely to become symptomatic, in our clinical experience. In addition, prolapsed polyps are typically removed easily in an outpatient setting.

If symptoms develop, polypectomy should be performed.

For women managed expectantly, there are studies regarding the need for continued surveillance. In our practice, we don't perform further surveillance in these patients.

Infertile women — The data regarding the impact of removal of an endometrial polyp on fertility are limited, as discussed above. Current evidence is insufficient to make a recommendation, although most clinicians perform polypectomy in infertile women. (See 'Effect on fertility and pregnancy' above.)

Postmenopausal women — For postmenopausal women, we recommend removal of all endometrial polyps. The risk of malignancy in a polyp is highest in postmenopausal women and the risk of complications associated with polypectomy is low. (See 'Risk of malignancy' above and 'Polypectomy' below.)

Women with recurrent polyps — In rare cases, endometrial polyps recur after removal. In such cases, care should be taken to completely remove the polyp(s) in a repeat polypectomy procedure. There are no data regarding management of recurrent endometrial polyps. One option is a levonorgestrel-releasing intrauterine device, given its reported efficacy in women receiving tamoxifen treatment [14]. Endometrial ablation is also an option for women who have completed their childbearing.

Women on tamoxifen therapy — Use of the 20 mcg per day levonorgestrel-releasing intrauterine device (Mirena; LNg20 IUD) decreases the incidence of endometrial polyps in women on tamoxifen. However, further study is needed to determine whether such treatment results in a decrease in endometrial carcinoma in general or malignant transformation in polyps and whether use of levonorgestrel, particularly in women with progesterone receptor-positive breast cancer, increases the risk of breast cancer recurrence [47,48]. A decrease in the incidence of polyps in women on tamoxifen has been demonstrated in two randomized trials [49,50]. The trial with the longest follow-up included pre- and postmenopausal women with mostly stage I or II breast cancer on tamoxifen (n = 113) and found that use of the LNg20 IUD compared with no treatment resulted in a statistically significant decrease in the rate of polyps at one (2 versus 16 percent) and five years (4 versus 33 percent) [14,50]. Hysteroscopy and endometrial sampling was performed at 12, 24, 45, and 60 months. All polyps were removed upon detection and were benign; the authors noted that the prompt removal of polyps in the study may have masked the risk of malignant transformation (up to 11 percent in women on tamoxifen [21]). There were no cases of endometrial carcinoma and no significant difference in the rate of endometrial hyperplasia between the two groups at five years, but there were few events (0 of 58 women in the LNg20 group; 1 of 60 in the control group). No difference in the breast cancer recurrence rate was found, but there was insufficient statistical power to assess this outcome.

POLYPECTOMY — Polypectomy under hysteroscopic guidance is the treatment of choice for most endometrial polyps.

Hysteroscopic visualization of the polyp is the preferred approach, since blind curettage may miss small polyps and other structural abnormalities [51-53]. Hysteroscopic instruments that may be used to remove a polyp include: grasping forceps, microscissors, electrosurgical loop (ie, resectoscope), morcellator, or a bipolar electrosurgical probe [51,54,55]. Some surgeons visualize the polyp via hysteroscopy and then remove it using a blind approach (eg, using Randall polyp forceps or a Kelly clamp) [56]. If this approach is used, the hysteroscope should be used again after polypectomy to confirm complete removal of the polyp.

For women with symptomatic polyps, polypectomy results in improvement of symptoms in 75 to 100 percent of patients, based upon studies with follow-up intervals of 2 to 52 months [57].

Complications of hysteroscopic polypectomy are infrequent, and the risk is the same as for other hysteroscopic procedures. General principles of hysteroscopy are discussed separately. (See "Overview of hysteroscopy", section on 'Complications'.)

Rarely, an endometrial polyp prolapses through the cervix and can be removed vaginally. A polypoid lesion at the external cervical os is most commonly a cervical polyp, but may be a prolapsed endometrial polyp or leiomyoma (see 'Physical examination' above). The procedure for removal of a prolapsed endometrial polyp is the same as for a prolapsed leiomyoma. (See "Prolapsed uterine leiomyoma (fibroid)", section on 'Vaginal myomectomy'.)

Women who undergo removal of a prolapsed polyp without dilation of the cervix and visualization of complete removal should be counseled about the potential for recurrence. The risk of recurrence in this situation is not known.

SUMMARY AND RECOMMENDATIONS

- Endometrial polyps are hyperplastic overgrowths of endometrial glands and stroma that form a projection from the surface of the endometrium (lining of the uterus). (See 'Histopathology' above.)
- Among women undergoing endometrial biopsy or hysterectomy, the prevalence of endometrial polyps is 10 to 24 percent. (See 'Epidemiology' above.)
- Endometrial polyps are a common cause of abnormal uterine bleeding in both premenopausal and postmenopausal women. They may also be asymptomatic. (See 'Clinical presentation' above.)
- The great majority of endometrial polyps are benign, but malignancy occurs in some women. Endometrial polyps are more likely to be malignant in women who are postmenopausal and those who present with bleeding. (See 'Risk of malignancy' above.)
- Transvaginal ultrasound alone is typically sufficient for women who have an indication for surgical management with operative hysteroscopy. For women with an uncertain finding on ultrasound alone or who are candidates for expectant management, we suggest sonohysterography (saline infusion sonogram) or diagnostic hysteroscopy. (See 'Diagnostic studies' above.)
- The diagnosis of an endometrial polyp is a histologic diagnosis based upon the evaluation of the specimen after it has been removed. Histologic evaluation can also exclude malignancy. (See 'Diagnosis' above.)
- For premenopausal women, symptomatic polyps require removal. We also suggest removal of asymptomatic polyps in premenopausal women with risk factors for endometrial hyperplasia or cancer (**Grade 2C**). Polypectomy is also a reasonable option for women with polyps that are >1.5 cm, multiple, or prolapsed, or for women who are infertile. (See 'Choosing a management approach' above.)
- For postmenopausal women, we recommend removal of all endometrial polyps (**Grade 1B**). (See 'Choosing a management approach' above.)

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