CARCINOMA OF THE ENDOMETRIUM:

ESSENTIALS OF DIAGNOSIS

Abnormal bleeding is the presenting sign in 90% of cases.
Papanicolaou smear is frequently negative.
After a negative pregnancy test, endometrial tissue is required to confirm the diagnosis.

General Considerations:

Adenocarcinoma of the endometrium is the second most common cancer of the female genital tract. It oc curs most often in women 50 70 years of age. Obesity, nulliparity, diabetes, and polycystic ovaries with pr olonged anovula- tion, unopposed estrogen therapy, and the extended use of tamoxifen for the treatment of breast cancer are also risk factors. Women with a family history of colon cancer (hereditary nonpolypos is colorectal cancer, Lynch syn- drome) are at significantly increased risk, with a lifetime incidence as high as 30%.

Abnormal bleeding is the presenting sign in 90% of cases. Any postmenopausal bleeding requires investi ga- tion. Pain generally occurs late in the disease, with metas- tases or infection.

Papanicolaou smears of the cervix occasionally show atypical endometrial cells but are an insensitive dia gnostic tool. Endocervical and endometrial sampling is the only reliable means of diagnosis. Simultaneou s hysteroscopy can be a valuable addition in order to localize polyps or other lesions within the uterine ca vity. Vaginal ultrasonog- raphy may be used to determine the thickness of the endo- metrium as an indicat ion of hypertrophy and possible neoplastic change. The finding of a thin endometrial lining on ultrasound i s clinically reassuring in cases where very little tissue is obtainable through endometrial biopsy.

Pathologic assessment is important in differentiating hyperplasias, which often can be treated with cyclic oral progestins.

Prevention

Prompt endometrial sampling for patients who report abnormal menstrual bleeding or postmenopausal ut erine bleeding will reveal many incipient as well as clinical cases of endometrial cancer. Younger women with chronic anovulation are at risk for endometrial hyperplasia and subsequent endometrial cancer; they can significantly reduce the risk of hyperplasia with the use of oral contra- ceptives or cyclic progestin ther apy.

Staging

Staging and prognosis are based on surgical and pathologic evaluation only. Examination under anesthes ia, endome- trial and endocervical sampling, chest radiography, intra- venous urography, cystoscopy, sig moidoscopy, transvaginal sonography, and MRI will help determine the extent of the disease and its appr opriate treatment.

Treatment

Treatment consists of total hysterectomy and bilateral salpingo-oophorectomy. Peritoneal washings for cy tologic examination are routinely taken and lymph node sampling may be done. If invasion deep into the myometrium has occurred or if sampled lymph nodes are positive for tumor, postoperative irradiation is in dicated. Patients with stage III endometrial cancer are generally treated with surgery fol- lowed by chemot herapy and/or radiation therapy. A review by the Society of Gynecologic Oncology Clinical Practice Com mittee concluded the use of adjuvant chemotherapy to treat stage I or II endometrial carcinoma is not sup - ported by the available evidence. Palliation of advanced or metastatic endometrial adenocarcinoma may be accomplished with large doses of progestins, eg, medroxyproges- terone, 400 mg weekly intramuscul arly, or megestrol acetate, 80 160 mg daily orally.

Prognosis

With early diagnosis and treatment, the overall 5-year sur- vival is 80 85%. With stage I disease, the depth of myome- trial invasion is the strongest predictor of survival, with a 98% 5-year survival with less than 66 % depth of invasion and 78% survival with 66% or more invasion.

When to Refer

All patients with endometrial carcinoma should be referred
to a gynecologic oncologist.

ENDOMETRIOSIS

ESSENTIALS OF DIAGNOSIS

Dysmenorrhea.
Dyspareunia.
Increased frequency among infertile women.
Abnormal uterine bleeding.

General Considerations

Endometriosis is an aberrant growth of endometrium out- side the uterus, particularly in the dependent pa rts of the pelvis and in the ovaries, whose principal manifestations are chronic pain and infertility. While re trograde men- struation is the most widely accepted cause, its pathogen- esis and natural course are not f ully understood. The overall prevalence in the United States is 6 10% and is four- to fivefold greater amon g infertile women. Endome- triosis is associated with an increased risk of coronary heart disease.

Clinical Findings

The clinical manifestations of endometriosis are variable and unpredictable in both presentation and cours e. Dys- menorrhea, chronic pelvic pain, and dyspareunia, are among the well-recognized manifestations. A significant number of women with endometriosis, however, remain asymptomatic and most women with endometriosis have a normal pelvic examination. However, in some women, pelvic examination can discl ose tender nodules in the cul- de-sac or rectovaginal septum, uterine retroversion with decreased uterine mobility, cervical motion tenderness, or an adnexal mass or tenderness.

Endometriosis must be distinguished from PID, ovar- ian neoplasms, and uterine myomas. Bowel invasio n by endometrial tissue may produce blood in the stool that must be distinguished from bowel neoplasm. Imaging is of limited value and is useful only in the presence of a pelvic or adnexal mass. Transvaginal ult ra- sonography is the imaging modality of choice to detect the presence of deeply penetrating endometrio sis of the rectum or rectovaginal septum, while MRI should be reserved for equivocal cases of rectovagin al or bladder endometriosis. Ultimately, a definitive diagnosis of endo- metriosis is made only by histology of lesions removed at surgery.

Treatment

A. Medical Treatment

Although there is no conclusive evidence that NSAIDs improve pain associated with endometriosis, these agents are reasonable options in appropriately selected patients. Medical treatment, using a variety of hor monal therapies, is effective in the amelioration of pain associated with endometriosis. However, there is no evidence that any of these agents increase the likelihood of pregnancy. Their preoperative use is of qu estionable value in reducing the difficulty of surgery. Most of these regimens are designed to inhibit ovulat ion over 4 9 months and lower hormone levels, thus preventing cyclic stimulation of endometriotic implants and inducing atrophy. The optimum duration of therapy is not clear, and the relative merits in terms of sid e effects and long-term risks and benefits show insignificant differences when compared with each other and, in mild cases, with placebo. Commonly used medical regimens include the following:

1. Low-dose oral contraceptives can be given cyclically or continuously; prolonged suppression of ovulatio n often inhibits further stimulation of residual endome- triosis, especially if taken after one of the therapies mentioned here. Any of the combination oral contra- ceptives, the contraceptive patch, or vaginal ring ma y be used continuously for 6 12 months. Breakthrough bleeding can be treated with conjugated estrogens, 1.25 mg orally daily for 1 week, or estradiol, 2 mg daily orally for 1 week.
2. Progestins, specifically oral norethindrone acetate and subcutaneous DMPA, have been approved by t he FDA for treatment of endometriosis-associated pain.
3. Intrauterine progestin, with the levonorgestrel intra- uterine system has also been shown to be effective in reducing endometriosis-associated pelvic pain, and it is recommended before surgery.

4. GnRH agonists are highly effective in reducing the pain syndromes associated with endometriosis. Ho wever, they are not superior to other methods such as combined oral contraceptives as first-line therapy. The GnRH analogs (such as long-acting injectable leu- prolide acetate, 3.75 mg intramuscularly monthly, used for 6 months) suppresses ovulation. Side effects of vaso- motor symptoms and bone demineralizatio n may be relieved by add-back therapy, such as conjugated equine estrogen, 0.625 mg, or norethindrone, 5 mg orally daily.
5. Danazol is an androgenic medication that has been used for the treatment of endometriosis-associated pain. It should be used for 4 6 months in the lowest dose necessary to suppress menstruation, usually 20

0 400 mg orally twice daily. However, danazol has a high incidence of androgenic side effects that are mor e severe than other medications available, including decreased breast size, weight gain, acne, and hirsuti sm.

6. Aromatase inhibitors (such as anastrozole or letrozole) in combination with conventional therapy have been evaluated with positive results in premenopausal women with endometriosis-associated pain and pa in recurrence.

B. Surgical Measures

Surgical treatment of endometriosis particularly exten- sive disease is effective both in reducing pain and in promoting fertility. Laparoscopic ablation of endometrial implants significantly reduces pain. Ablation of i mplants and, if necessary, removal of ovarian endometriomas enhance fertility, although subsequent preg nancy rates are inversely related to the severity of disease. Women with disabling pain for whom childbea ring is not a consider- ation can be treated definitively with total abdominal hys- terectomy and bilateral sa lpingo-oophorectomy. In premenopausal women, hormone replacement then may be used to relieve vaso motor symptoms. However, hor- mone replacement may lead to a recurrence of endome- triosis and asso ciated pain.

Prognosis

There is little systematic research regarding either the pro- gression of the disease or the prediction of clin ical out- comes. The prognosis for reproductive function in early or moderately advanced endometriosis a ppears to be good with conservative therapy. Hysterectomy, with bilateral salpingo-oophorectomy, often i s regarded as definitive therapy for the treatment of endometriosis associated with intractable pelvic pain, adnexal masses, or multiple previ- ous ineffective conservative surgical procedures. However, symptoms may recur even after hysterectomy and oophorectomy.

When to Refer

Refer to a gynecologist for laparoscopic diagnosis or treatment.

When to Admit

Rarely necessary except for acute abdomen associated with ruptured or bleeding endometrioma.