Endometrial Cancer

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Question 1:
What do you think can be done to address the racial disparity in prognosis for white and black women? Is it a matter of poor patient education leading to delayed diagnosis, limited access to care, or other factors of which a general obstetrician–gynecologist should be aware and may potentially be able to affect? In light of the effect of race on prognosis, do you consider a woman’s race when developing recommendations for her treatment?

Response from Dr. Sorosky:
The incidence of endometrial cancer is approximately twice the rate in white women when compared to black women. Despite the higher incidence, the survival rate is higher in white women when compared to black women. The Gynecologic Oncology Group evaluated these disparities and found that black women had disease diagnosed at an older age than did white women, and a greater proportion of type II disease, which is more aggressive. Black women also had more advanced disease, higher tumor grade, and more lymph node metastases when compared to white women. Black women with low income present at an advanced stage and have a lower survival rate compared with non-Hispanic white women. Education of women regarding the symptoms of endometrial cancer and improved access to medical care will eliminate delay in diagnosis and treatment in all women with endometrial cancer. The difference in survival is not solely based upon access to care issues, and biologic differences among races require more research and investigation. Race should not be considered in developing recommendations for treatment of endometrial cancer.

Question 2:
The epidemic of obesity in this country seems to be the primary epidemiologic factor driving the disturbing increase in incidence of endometrial cancer. Do you think that there should be a more concerted effort to counsel diabetic and obese women about their increased risk for endometrial cancer so that symptoms of abnormal bleeding will be brought to the attention of a gynecologist sooner? Is there evidence to support your opinion? Will the new recommendations for less frequent Pap tests lead to fewer women presenting for examinations annually, delaying evaluation for abnormal periods in at-risk women?

Response from Dr. Sorosky:
Obesity is an established risk factor for endometrial cancer. Thus, we are seeing an increased incidence in endometrial cancer cases as the population becomes increasingly more obese. Also, age is a risk factor and as the life expectancy for women increases, the incidence of endometrial cancer is higher. Diabetes may occur secondary to obesity. Women with
endometrial cancer more commonly die from medical comorbidities rather than the endometrial cancer. Heart disease is the most common cause of death in women. Obesity may result in diabetes and hypertension. Obesity may contribute to limited mobility, slips and falls, and wear and tear on joints. As part of routine health maintenance, obesity should be discussed and evaluated. Recommendations in 2012 for Pap test screening have not called for elimination of the regular health care maintenance. As these recommendations came out several months ago, it would be speculative to assume that less frequent Pap tests would lead to fewer women presenting for evaluation of abnormal menses. There are no data available to refute or substantiate that assumption. The annual examination is an excellent opportunity to provide women with health care maintenance, primary care services, education, and the opinions and recommendations from a physician educated in women’s health.

Question 3:

A premenopausal woman presents with dysfunctional uterine bleeding. Office endometrial biopsy is performed and is negative for malignancy and hyperplasia. She chooses expectant management. At what interval should endometrial biopsy be repeated if her symptoms persist? Should these intervals be altered based on risk factors such as obesity and previous tamoxifen therapy? Does dilation and curettage (D&C) with or without hysteroscopy need to be considered rather than repeat office biopsy? If D&C cannot be afforded in a high-risk patient, can sequential biopsies be considered sufficient?

Response from Dr. Sorosky:

The evaluation of abnormal uterine bleeding in reproductive-aged women should follow the acronym PALM-COEIN: polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified. The American College of Obstetricians and Gynecologists (the College) supports this nomenclature, which was developed by the International Federation of Gynecology and Obstetrics (FIGO) in 2011 to standardize the terminology used to describe abnormal uterine bleeding. Persistent bleeding with a previous benign pathology requires further testing to rule out nonfocal endometrial pathology or a structural pathology such as a polyp or a submucosal leiomyoma. Hysteroscopy or sonohysterography should be performed in a premenopausal woman with persistent dysfunctional uterine bleeding who has a biopsy negative for malignancy and hyperplasia to evaluate for polyps and structural abnormalities. If hysteroscopy or sonohysterography does not provide additional information, medical therapy to regulate the bleeding may be instituted. If the woman has risk factors for hyperplasia, biopsy should be repeated in 6 months. Previous tamoxifen therapy would not alter these recommendations. Sequential biopsies can be considered sufficient in a woman who cannot undergo a D&C. D&C is recommended if endometrial biopsy reveals complex hyperplasia with atypia. Both endometrial biopsy and D&C are appropriate to diagnose hyperplasia and cancer but are not as sensitive as hysteroscopy in determining the etiology of vaginal bleeding.

Question 4:

In a postmenopausal woman with persistent bleeding after office biopsy demonstrating atrophic endometrium, at what interval should her biopsy be repeated? Again, is repeat biopsy sufficient, or is D&C with or without hysteroscopy preferred?

Response from Dr. Sorosky:

In women with an atrophic endometrium and vaginal bleeding, transvaginal ultrasonography to evaluate the endometrial thickness is a useful adjunct to determine if additional biopsies are required. If the endometrial thickness is less than 4 mm, the likelihood of malignancy is very low and repeated biopsies are not warranted. If the endometrial stripe is greater than 4 mm, hysteroscopy to evaluate for other causes of bleeding, polyps, leiomyomas, etc is preferred.
Question 5:
In a premenopausal woman with complex atypical hyperplasia who desires childbearing, how long should progestin therapy be given before re-evaluating her endometrial pathology? Can she continue to attempt pregnancy as long as her biopsies are reassuring? For how long would you treat her conservatively if the pathology did not improve?

Response from Dr. Sorosky:
If complex hyperplasia with atypia is diagnosed with an endometrial biopsy, a D&C should be performed because of the risk of co-existent carcinoma. If the endometrium is thickened, operative hysteroscopy may be a useful adjunct to remove the hyperplastic endometrium. Endometrial biopsy should be repeated every 3–4 months after initiation of progestin therapy until amenorrhea is established or the atypical hyperplasia has resolved. Depending upon the response, the dose and type of progestin administration may be increased or altered. Progestin may be administered orally, intramuscularly, or via a progestin-releasing intrauterine device (IUD). Endometrial biopsy may be performed with an IUD in place, paying careful attention not to remove the IUD. If there is no response to increasing the dose or route of administration within one year, the lesion should be considered not responsive to therapy and I would recommend hysterectomy. Pregnancy may be attempted as long as the biopsies are reassuring. Assisted reproductive technologies may be required to achieve pregnancy.

Question 6:
In a premenopausal woman under the age of 35 years with risk factors for hyperplasia and malignancy (obesity, chronic anovulation, etc), what is the earliest age at which you would consider performing endometrial biopsy?

Response from Dr. Sorosky:
Risk factors including symptomatic bleeding, suspected chronic anovulation, anemia, and obesity mandate a biopsy in women less than 35 years of age. In younger women at menarche, hyperplasia may be the etiology of bleeding. Oral contraceptives or progestin may be used to treat these women. Age should not be the sole criteria for determining the need for an endometrial biopsy.

Question 7:
A 60-year-old woman who has had total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO) and staging for endometrial cancer with a history of normal cervical cytology returns to her general obstetrician–gynecologist for annual screening 5 years after treatment. Do you recommend obtaining yearly vaginal cuff cytology?

Response from Dr. Sorosky:
The literature is inconclusive regarding the value of annual cytology in detecting recurrent disease in the asymptomatic woman. In many instances cytology that led to the diagnosis of recurrence was performed in symptomatic (vaginal bleeding) women. Women treated for endometrial cancer should be counseled about symptoms of recurrent disease, vaginal bleeding, pain, lower leg edema, cough, and/or hemoptysis. Given the lack of evidence-based data supporting annual cytology of the vaginal vault, less frequent screening is acceptable, such as every 2–3 years. However, histories should continue to be taken and physical examination to be performed even if cytology is not performed. I examine women every 3–4 months for the first 2 years after treatment is completed, every 6 months for years 3 to 5, and annually thereafter.
**Question 8:**

Your article emphasized the high risk of coexistent endometrial cancer in women with complex atypical hyperplasia, and that it is unclear if these women should be surgically managed by general obstetrician–gynecologists or gynecologic oncologists. In your opinion, is it better care for these women to be referred to gynecologist oncologists? Do you routinely perform lymphadenectomy at the time of hysterectomy in these patients?

**Response from Dr. Sorosky:**

*Total hysterectomy with BSO is the treatment of choice for women not desirous of future child-bearing diagnosed with complex atypical hyperplasia. The route of surgery (vaginal, abdominal, laparoscopic, or robotic) is at the discretion of the surgeon. The hysterectomy specimen should not be morcellated as morcellation may hinder pathologic interpretation of depth of invasions and margins. These women certainly can be surgically managed by a general obstetrician–gynecologist. As the incidence of co-existent endometrial carcinoma is in excess of 40%, preoperative consultation with a gynecologic oncologist may be helpful if these women have questions about treatment options and prognostic variables with endometrial cancer that the general obstetrician–gynecologist is uncomfortable discussing. If the preoperative diagnosis is complex hyperplasia with atypia, the patient and surgeon should not be surprised if the final pathology returns as cancer. A postoperative diagnosis of endometrial carcinoma should not come as a surprise to a woman with a preoperative diagnosis of complex atypical hyperplasia. I do not routinely perform lymphadenectomy at the time of hysterectomy in women with complex atypical hyperplasia.*