Ovarian conservation and hormone receptors in uterine Müllerian adenosarcomas

To the Editor:

We read with interest the proposed clinical implications of positive estrogen and progesterone receptors in endometrial adenosarcomas by Dr. Amant et al. [1]. All five tumors analyzed stained positive for estrogen and progesterone receptors in the epithelial component while stromal staining was positive for estrogen receptor in three of five and positive for progesterone receptor in four of the five tumors. A prior study demonstrated that most low-grade stromal sarcomas, the most common sarcomatous component of adenosarcomas, are positive for estrogen and/or progesterone receptors [2].

We determined the estrogen and progesterone receptor status in two additional cases, both of which were positive in the stromal component as well as the epithelial component. One of the cases has been published previously [3]. This patient, originally stage IB, is now 55 months out from definitive surgery and remains no evidence of disease. Although she desired fertility initially, she and her husband have decided to adopt instead of pursuing in vitro fertilization and surrogacy (personal communication, Chad Michener).

It is estimated that the initial ovarian involvement in patients with uterine adenosarcoma is approximately 2% [4]. We agree with Dr. Amant that patients who have completed their family should be advised to have both ovaries removed. However, hormone replacement therapy should be discussed, as there are no data to support withholding such treatment from these patients. The relative risk of endometrial cancer in the general population is 2.3 for unopposed estrogen users compared to estrogen nonusers [5]. Based on these data it seems logical that patients with a history of endometrial cancer be excluded from receiving estrogen therapy. However, an additional effect of estrogen is increased cell division of normal endometrial cells, making the patient vulnerable to DNA damage [6]. In this regard one could consider estrogen a tumor promoter of cells that have already become genetically altered [7]. In this case, we should consider recurrent disease, not the result of de novo hormonal stimulation and neoplastic transformation, but a result of occult residual disease.

Until now there have been no prospective data regarding the use of hormone replacement therapy in endometrial cancer patients. A review of the retrospective data indicates that there is an equal or lesser incidence of recurrence in endometrial cancer patients who begin estrogen therapy following treatment for their cancers compared to patients who were nonusers (2 versus 12.5%, respectively) [7,8]. Definitive answers will be given by Gynecologic Oncology Group Study 137. The latter is a prospective, randomized, double-blind, placebo-controlled study, started in June 1997 ($n = 2108$) that includes women with histologically confirmed endometrial adenocarcinomas (IA/B/C IIA/B) of all grades and treated initially with total hysterectomy and bilateral salpingo-ophorectomy. Unfortunately, data will not be available for another 1 to 2 years. Until then patients will have to be selected for hormone therapy based on their symptomatology and the risks they are willing to take.

In the era of informed consent and medico-legal pressures, patients must be educated about the advantages and disadvantages of all possible therapies. At the end of the day the physician should not decide on the therapy, but the patient should have the tools to make a well-informed decision. Similarly, a nonbiased discussion regarding ovarian conservation should take place with young patients interested in preserving their fertility. To date, there is one report in the literature of a successful pregnancy in a patient with a history of a Müllerian adenosarcoma [4]. Withholding hormonal treatment or excluding patients from pregnancy based only on assumptions and not sound scientific data should be limited as much as possible. We should encourage our patients to participate in good clinical trials so that patients and physicians can receive answers based on facts. Unfortunately, for rare tumors like endometrial adenosarcomas questions like this can be difficult if not impossible to answer.

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