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Letters to the Editor

The classification of a uterine sarcoma as 'High-grade endometrial stromal sarcoma' should be abandoned

We read with interest the epidemiologic data on a large sample of 2677 uterine sarcomas [1]. From Table 5 [1], it appears that the biologic behavior of high-grade endometrial stromal sarcoma parallels that of uterine adenosarcoma, but contrasts to the worse outcome in leiomyosarcomas and carcinosarcomas. We would like to ask Brooks et al. what criteria were used to define high-grade endometrial stromal sarcoma and how the epidemiologic data on low-grade endometrial stromal sarcoma compare to the other tumor types. Were the slides submitted to central review?

The following arguments are presented to motivate our hypothesis that the high-grade endometrial stromal sarcomas in Brooks' paper [1], in fact, might be low-grade endometrial stromal sarcomas, currently called endometrial stromal sarcomas.

Table 5 suggests survival of uterine adenosarcoma to be comparable to high-grade endometrial stromal sarcomas [1]. However, in the largest series of uterine adenosarcoma, the sarcomatous component consisted of (low-grade) endometrial stromal sarcoma alone in 56% and a mixture including (low-grade) endometrial stromal sarcoma in an additional 9% [2]. The similarity with (low-grade) endometrial stromal sarcoma is further enhanced by the presence of hormone receptors in a majority of uterine adenosarcomas [3]. Also, the observation that in one third of uterine adenosarcomas, recurrences appeared 5 or more years after hysterectomy [2], corresponding to the experience with (low-grade) endometrial stromal sarcoma [4]. In summary, since tumor biology of both (low-grade) endometrial stromal sarcoma [4] and uterine adenosarcoma [2,3] is characterized by a low-grade hormone-sensitive malignancy with an indolent growth pattern and tendency to recur, similar epidemiologic findings between both tumor types could be expected. However, in the absence of data on (low-grade) endometrial stromal sarcoma, 5-year survival rates of adenosarcoma strikingly paralleled that of high-grade endometrial stromal sarcoma [1].

The literature provides good arguments to assume that high-grade and low-grade endometrial stromal sarcomas are two separate entities. Estimated 5-year survival in high-grade endometrial stromal sarcoma varies from 30% to 47% [5,6], and rapidly progressive disease is frequently observed in high-grade tumors. Also, most reports (references are available on request) have failed to identify significant differences between high-grade endometrial stromal sarcoma and other high-grade uterine sarcomas such as leiomyosarcoma, pure heterologous sarcomas, undifferentiated sarcomas, and carcinosarcomas. These data contrast with an up to 80% 5-year survival in high-grade endometrial stromal sarcomas in Brook's paper [1].

In fact, pathologists suggest to abandon the term 'high-grade endometrial stromal sarcoma'. Instead, they prefer 'undifferentiated' or 'poorly differentiated uterine sarcoma' to designate this malignancy [7,8]. The term 'poorly differentiated endometrial sarcoma' was already introduced by Evans in 1982 [7]. Since these tumors do not demonstrate endometrial stromal differentiation, the author suggested not to use the mitotic rate to define 'poorly differentiated endometrial sarcoma' and suggests a similarity with carcinosarcomas rather than (low-grade) endometrial stromal sarcoma. Authorities on this subject suggest now that the division of endometrial stromal sarcomas into low-grade and high-grade categories has fallen out of favor and the designation endometrial stromal sarcoma is now considered best restricted to neoplasms that were formally referred to as 'low-grade' stromal sarcoma. Endometrial sarcomas without recognizable evidence of a definite endometrial stromal phenotype, designated poorly differentiated or undifferentiated endometrial sarcomas are almost invariably high grade [8].

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We thank the correspondent for giving us the opportunity to highlight an important consideration in the interpretation of SEER data. SEER data are not subjected to central pathology review. Rather, SEER data portray a relatively complete view of pathology practice in the US contemporary to the date the diagnosis was made. Consequently, they lack both the benefit of precise classification rendered by an expert review and the benefits that result from improved schemes of disease classification. For SEER data, the assignment of grade is dependent upon the diagnosis rendered by the local pathologists as coded by trained data abstractors. Nevertheless, SEER data offer many reports for the study of uncommon diseases. During the time period encompassed by our study, International Classification of Diseases for Oncology (ICD-0-2) coding was used.

We agree that the nomenclature of endometrial stromal sarcoma has evolved: the term "high-grade endometrial stromal" sarcoma (HGESS) has been replaced by the term "undifferentiated sarcoma". For the time period of our study—1989 to 1999—the ICD-O-2 employed the older classification of HGESS. Endometrial stromal sarcomas were then classified as either HGESS or low grade endometrial stromal sarcomas (LGESS), that is, endolymphatic stromal myosis (adenosarcoma was afforded a distinctly separate classification). Because there were few cases available for study, we did not present data for LGESS.

In our series, women with adenosarcoma had better survival than women with other histologic types. This is consistent with the low threshold previously used for he adenosarcoma diagnosis: adenosarcomas were biphasic tumors with a glandular component that appears bland and a mesenchymal component that typically is low-grade in appearance. Accordingly, the stage distribution for white women with adenosarcoma was predominantly Stage I (82%) compared to 61% of HGESS.

Recent single institution studies indicate that the 5-year survival rate for patients with low-grade (LGESS) disease was 92%, and 85% in high-grade (HGESS) disease [1]. We documented similar survival for women with HGESS. The importance of grade as a prognostic factor has been validated by Norris, Taylor, and others [2].

In summary, we agree that the classification system of endometrial stromal sarcomas has undergone evolution and that adenosarcomas as a whole portend a better prognosis than HGESS (now termed undifferentiated sarcoma). The relatively few cases of each subtype precluded extensive subgroup analysis; however, we did show that for selected patients with uterine sarcoma, adjuvant therapy may have a role. Moreover, through equitable referral for diagnosis and treatment, racial disparities in outcomes may be reduced if not eliminated.

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