Malignant Uterine Perivascular Epithelioid Cell Tumor: A Case Report

Dina J. Chamsy,[1] Scott C. Purinton,[1] Kelley S. Carrick,[2] Debra L. Richardson[1]

Clinical Practice Points

- Perivascular epithelioid cell tumors (PEComas) are mesenchymal neoplasms composed of perivascular epithelioid cells that coexpress myoid and melanocytic markers.
- They can arise in virtually any anatomic site.
- We describe the case of a 46-year-old woman with a malignant uterine PEComa.
- We conclude that surgical staging should be considered in the setting of all malignant PEComas because of their unpredictable metastatic potential.
- Adjuvant therapy is still experimental and should be considered only in case of metastasis.

Clinical Ovarian & Other Gynecologic Cancer, Vol. 5, No. 1, 37-9
Keywords: Malignant perivascular epithelioid tumors, Surgical staging, Uterine sarcoma

Introduction

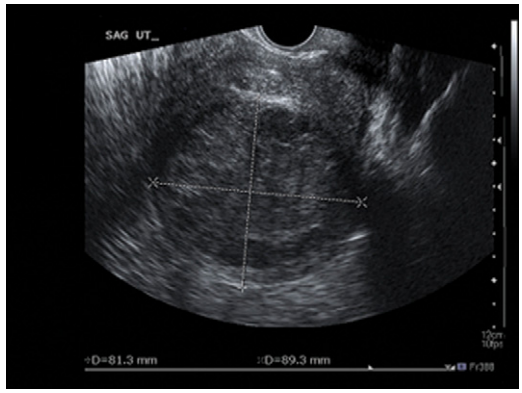
Perivascular epithelioid cell tumors (PEComas) are mesenchymal neoplasms that comprise angiomyolipoma, lymphangioleiomyomatosis, clear cell "sugar" tumor of the lung, and similar tumors arising in visceral sites, bones, and soft tissues termed PEComas not otherwise specified (PEComas-NOS). Many are related to the inherited syndrome of tuberous sclerosis complex (TSC), which is caused by mutations in either of 2 tumor suppressor genes, *TSC1* or *TSC2*, and can manifest with a variety of neoplasms in different organs, such as the kidneys, heart, eyes, lungs, and skin. PEComas-NOS are rare, with around 100 cases reported in the English literature.[1] Although 40 cases were described within the uterus, there were only 15 uterine PEComas that exhibited malignant behavior.[2] This report describes a rare case of malignant uterine PEComa arising within the myometrium.

Case Report

A 46-year-old woman presented with menorrhagia and pelvic pain. Pelvic examination and the ultrasonogram were consistent with a 14-week fibroid uterus. Papanicolaou smear and endometrial biopsy results were negative for malignancy. The patient was initially given leuprolide acetate. She presented 2 months later with worsening pelvic pain. The ultrasonogram showed an increase in the size of the largest fibroid from 7.3 to 9.2 cm (Figure 1). She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy.

Gross pathologic examination of the uterus demonstrated a 9.0-cm circumscribed, solid yellow-brown intramural mass filling the uterine cavity. Microscopic examination demonstrated a mesenchymal neoplasm composed of pleomorphic epithelioid cells with moderately abundant, lightly eosinophilic to clear cytoplasm; moderate to marked atypia; extensive necrosis; and 4 mitotic figures per 10 high power fields (HPFs) (Figure 2A). Tumor cells were radially

Figure 1 Uterine Perivascular Epithelioid Cell Tumor (PEComa) Appearing as a Discrete Mass in the Posterior Wall of the Uterus Measuring 81 × 89 × 92 mm. Mass Distorts the Serosal and Endometrial Contours



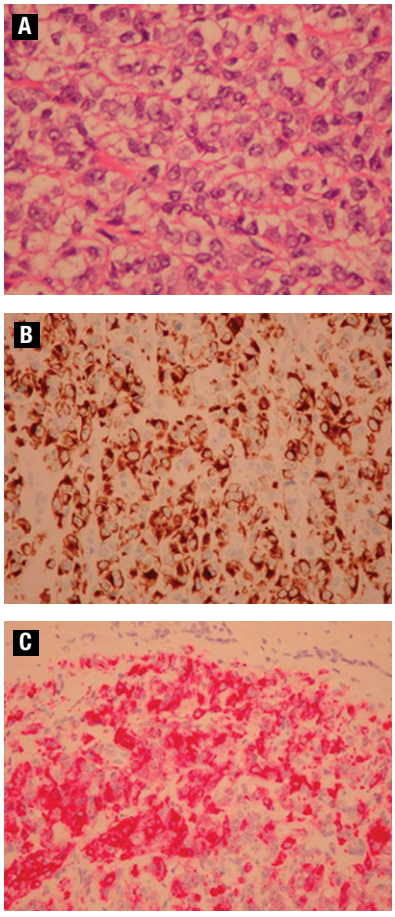
[1]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology
[2]Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX

Submitted: Jan 13, 2012; Revised: Mar 20, 2012; Accepted: Apr 13, 2012; Epub: May 31, 2012

Address for correspondence: Debra L. Richardson, MD, 5323 Harry Hines Boulevard MC 9032, Dallas, TX 75390-9032
Fax: 214-648-8408; e-mail contact: debra.richardson@utsouthwestern.edu

1941-4390/$ - see frontmatter
http://dx.doi.org/10.1016/j.cogc.2012.05.002

Figure 2 (A) Tumor Cells With Round Nuclei and Lightly Eosinophilic to Clear Cytoplasm (H&E Staining; Original Magnification ×40). (B) Positive Immunohistochemical Stain for Desmin; Brown Chromogen (Immunohistochemical Staining; Original Magnification ×20). (C) Positive Immunohistochemical Stain for HMB-45; Red Chromogen (Immunohistochemical Staining; Original Magnification ×20)



distributed around blood vessels and were infiltrating within the myometrium. Immunostaining showed strong diffuse positivity for desmin and HMB-45 (Figure 2B, 2C) and multifocal positivity for caldesmon, Melan-A, and MITF. The tumor was focally positive for estrogen receptor. Immunostaining for smooth muscle actin (SMA), S100, and pan keratin were negative. After expert pathologic review, the final diagnosis was malignant PEComa.

A postoperative computed tomographic scan revealed 2 small soft tissue masses at the vaginal cuff but no distant metastasis. The patient underwent repeated exploratory laparotomy and pelvic and paraaortic lymph node dissection. Forty-two lymph node and vaginal cuff biopsy results were negative for malignancy. The patient had no evidence of disease at her 12-month follow up.

Discussion

PEComas-NOS predominantly occurs in women with a mean age of 54 years at diagnosis. It can occur in almost any organ system; however the uterus appears to be the most common site. Uterine PEComas commonly present with vaginal bleeding. They are typically localized and well circumscribed. They can vary in size and may have focal areas of hemorrhage and necrosis. Microscopically, PEComa is composed of spindled and/or epithelioid cells with lightly eosinophilic to clear cytoplasm, which may be arranged in sheets, nests, or fascicles and may appear to "spill off" radially from vascular walls. They generally display slight atypia and sparse mitotic activity; however a subset can have marked atypia and elevated mitotic activity.[3] PEComas typically express both myoid markers (desmin, SMA, caldesmon) and melanocytic markers (HMB-45, Melan-A, tyrosinase, and microphthalmia transcription factor). Desmin produces positive staining. In the study by Folpe et al[4], 33% of cases stained positive for S-100. Folpe[4] concluded that HMB-45 was the most sensitive marker for PEComa.

The differential diagnosis of a uterine PEComa includes endometrial stromal sarcoma and the much more common true smooth muscle tumors, with which PEComa shares overlapping gross, microscopic, and occasionally immunohistochemical staining features. Diagnosis of this rare entity may be challenging and rests on the identification of certain histologic features, typically round to ovoid nuclei and lightly eosinophilic to clear cytoplasm devoid of paranuclear vacuoles, the coexpression of myoid and melanocytic markers, and often the presence of estrogen and progesterone receptors and the tumor cells' focal radial arrangement around blood vessels.

Most PEComas-NOS follows a benign course; however one third exhibit locally aggressive behavior and/or metastasis. Our patient exhibited all the tentative malignancy criteria described by Folpe et al[4] that predict a subsequent aggressive behavior, including tumor size $>$ 5 cm, infiltrative growth pattern, high nuclear grade, necrosis, and mitotic activity $>$ 1/50 HPFs.

Thus far among the limited number of cases reported, no single criterion or set of criteria has been found to reliably predict the behavior of this tumor in all cases. PEComas may present with distant metastasis many years after their initial diagnosis. Fadare[2] reviewed 40 cases of uterine PEComas, 15 (38%) of which exhibited malignant behavior. Of these, 7 (47%) had advanced disease at initial presentation, including 2 patients with lymph node involvement. The other 8 (53%) patients had disease recurrence to the lung (2 patients), pelvis (2), pelvis and lymph nodes (1), pelvis, bone and lung (1), bone and lung (1), and liver and lung (1). The majority of recurrent cases (87.5%) were clinically confined to the uterus at initial presentation, as they were diagnosed after a simple hysterectomy and were not surgically staged. This suggests that lymph node involvement might be diagnosed more often if surgical staging is performed at initial presentation. It is our opinion that until long-term data on a larger number of patients become available, PEComas-NOS should be considered tumors of uncertain malignant potential. Thus we recommend surgical staging of all PEComas that exhibit any of Folpe's tentative malignancy criteria.

Surgery is the mainstay of treatment for primary lesions as well as local and metastatic recurrences. Its aim is to obtain negative surgical margins. Since most PEComas are benign, primary resection is curative. The role of adjuvant chemotherapy and radiation therapy in the management of locally advanced or metastatic disease remains experimental.

Conclusion

PEComas-NOS are most often benign; however a malignant course has been documented. Criteria for malignancy are currently tentative because of the rarity of this diagnosis. Surgical staging should be considered in patients diagnosed with malignant PEComas. In the setting of a nonmetastatic tumor, resection alone is the mainstay of treatment. When treating metastatic or local spread, adjuvant chemotherapy and radiation therapy are still experimental and of uncertain benefit.

Disclosure

The authors have stated that they have no conflicts of interest.

References

1. Armah HB, Parwani AV. Malignant perivascular epithelioid cell tumor of the uterus with late renal and pulmonary metastasis: a case report and review of literature. *Diagn Pathol* 2007; 3:2-45.
2. Fadare O. Uterine PEComa: appraisal of a controversial and increasingly reported mesenchymal neoplasm. *Int Semin Surg Oncol* 2008; 5:7.
3. Armah HB, Parwani AV. Perivascular epithelioid cell tumor. *Arch Pathol Lab Med* 2009; 133:648-54.
4. Folpe AL, Mentzel T, Lehr HA, et al. Perivascular epithelioid cell neoplasms of soft tissue and gynecologic origin: a clinicopathologic study of 26 cases and review of the literature. *Am J Surg Pathol* 2005; 29:1558-75.