Perivascular epithelial cell tumor arising from polypoid adenomyoma: a case report

T. Ishibashi[1], K. Nakayama[1], N. Nakayama[2], H. Katagiri[1], N. Ishikawa[3], K. Miyazaki[1]

[1]Department of Obstetrics and Gynecology, Shimane University School of Medicine, Izumo
[2]Department of Biochemistry, Shimane University School of Medicine, Izumo
[3]Department of Organ Pathology, Shimane University School of Medicine Izumo (Japan)

Summary

The present report describes a rare case of a uterine perivascular epithelioid cell tumor (PEComa) arising from a polypoid adenomyoma. The patient, a 44-year-old woman with tuberous sclerosis, was incidentally found to have a uterine mass with malignant-appearing features on a computed tomography (CT) scan. Pathological examination of the hysterectomy specimen demonstrated that the tumor was composed of pale, spindle-shaped, epithelioid tumor cells which were positive for SMA and HMB-45. These findings were consistent with a PEComa arising from a polypoid adenomyoma.

Key words: Perivascular epithelioid cell tumor (PEComa); Uterus; Polypoid adenomyoma.

Introduction

Primary uterine perivascular epithelioid cell tumors (PEComa) are rare [1-4]. PEComas are characterized by positive melanocytic markers, such as HMB-45 [5].
The authors report a rare case of a uterine PEComa arising from a polypoid adenomyoma.

Case Report

The patient, an institutionalized, 44-year-old female with mental retardation, tuberous sclerosis, and refractory epilepsy was admitted to Shimane University Hospital in October 2011 for the evaluation and management of a uterine tumor. She had a history of ER+, PR+, HER2-, invasive ductal carcinoma diagnosed at the age of 41 that had been treated with a right mastectomy and axillary lymph node dissection in January 2008 at another hospital. She was then treated with adjuvant lupron and nolvadex from April 2008 to February 2010, after which she was treated with nolvadex monotherapy. She was then followed with semi-annual computed tomography (CT) imaging and bone scintigraphy.

CT imaging performed in June 2011 was notable for uterine and right adnexal masses. The patient underwent a dilation and curettage, the pathology of which demonstrated proliferative epithelial cells and cystic, elongated, endothelial cells with no evidence of malignancy. Magnetic resonance imaging (MRI), however, suggested endometrial sarcoma or carcinosarcoma (Figure 1); therefore she was transferred to Shimane University Hospital for diagnosis and management. She then underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy in November 2011.

Pathological findings

On gross exam, the uterus, cervix, and bilateral adnexa weighed 280 g. The uterus measured 12 x 9 cm and had diffuse adenomyosis.

Two polypoid structures, measuring four cm and 2.5 cm, were present in the cavity and were histologically diagnosed as polypoid adenomyomas. These polyps consisted of clear cells in a ligulate pattern within the wall. Immunohistochemical staining revealed that these cells were SMA, HMB45, vimentin, desmin, Melan A and PR positive, and ER negative (Figure 2 A-H). These findings were compatible with a histological diagnosis of PEComa. There were no abnormal findings in the uterine cervix or left adnexa. The right ovary had a 10 x 6 cm endometrioma.

The malignant potential of a PEComa is determined with standard criteria. Two or more of the following six characteristics classify the tumor as malignant 1) Size > 5 cm, 2) Infiltrative, 3) High nuclear grade and cellularity, 4) Mitotic rate ≥ 1/50HPF, 5) Necrosis, and 6) Vascular invasion. The present

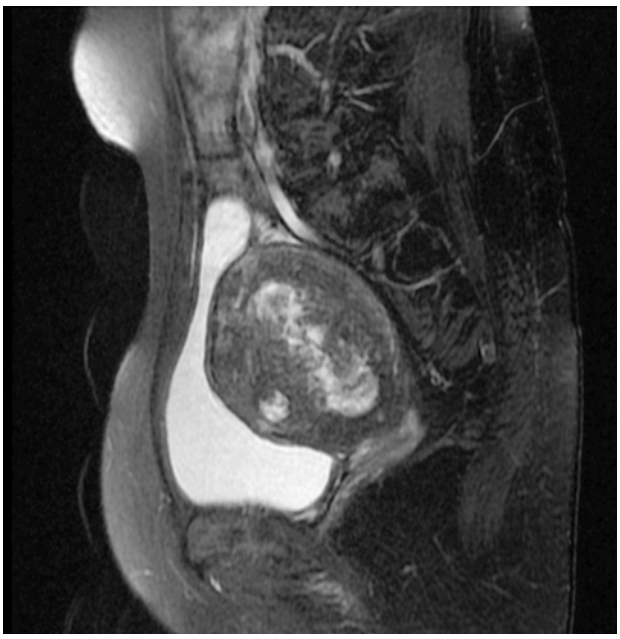

Figure 1. — MRI of preoperative axial and T2-weighted images. The submucosal tumor was identified in the uterine body. The tumor size was 7.0 x 6.4 x 4.3 cm.

Revised manuscript accepted for publication July 31, 2012

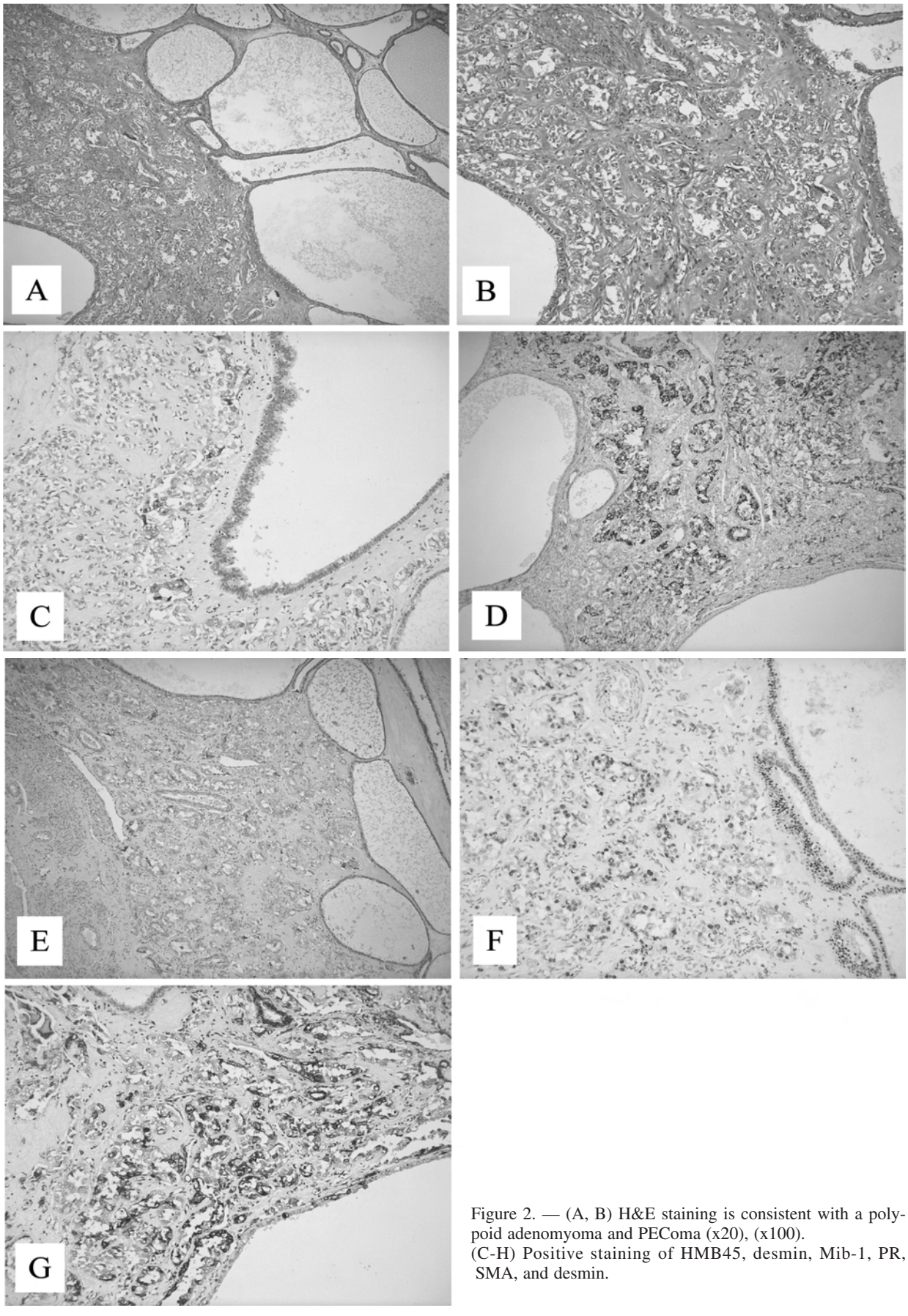

Figure 2. — (A, B) H&E staining is consistent with a polypoid adenomyoma and PEComa (x20), (x100).
(C-H) Positive staining of HMB45, desmin, Mib-1, PR, SMA, and desmin.

tumor demonstrated an infiltrative pattern, high cellularity, and nuclear grade. Vascular invasion was also suggested on hematoxylin and esoin (H&E) staining but was not confirmed by immunostaining of podoplanin. The tumor was classified as a PEComa with uncertain malignant potential.

Immunohistochemistry

Formalin-fixed and paraffin-embedded sections were dewaxed in xylene and hydrated in graded alcohol. After antigen retrieval in a sodium citrate buffer, slides were incubated overnight at 4°C with antibodies to vimentin (DAKO, Grostrup, Denmark, clone V9), SMA (DAKO, clone A4), desmin (DAKO, clone D33) ER (DAKO, clone 1D5), PR (DAKO, clone PgR636) and melanoma-associated antigen (DAKO, clone HMB-45), Melan A(DAKO, clone A103) at dilutions of 1:100, 1:100, 1:100, 1:100, 1:100, 1:50, and non-dilution, respectively. This was followed by incubation with a biotinylated linker and streptavidin-horseradish peroxidase (LSAB2 system-HRP, DAKO Cytomation, Carpinteria, CA). The signals were visualized using ABC$^+$ (DAKO Cytomation) as the substrate-chromagen at room temperature for 10 min. Sections were counterstained with hematoxylin and mounted.

Postoperative course

Given the patient's history of refractory epilepsy, the decision was made to not treat the patient with adjuvant chemotherapy. She has remained without evidence of recurrence as of the last follow-up.

Discussion

PEComa are mesenchymal tumors which stain positive for melanocyte markers such as HMB-45 [5]. PEComas include angiomyolipomas (AML), clear cell "sugar" tumors of the lung (CCST), and lymphangioleiomyomatosis (LAM). Since the pancreatic PEComa was first reported in 1996, PEComas have been identified elsewhere. Uncommon locations include the uterus, falciform ligament of liver, peritoneum, and heart [6]. Among these less common PEComas, 30% occur in the uterus, with 50 cases being reported in the literature [2-4, 7, 8]. In general, uterine PEComas present with abnormal vaginal bleeding. According to the review of 44 uterine PEComas published by Fadare *et al*., the average patient age was 45 years old (range 9-79) and 43% of presented with metastatic disease that was ultimately fatal [1].

Common sites of metastasis include the lung, liver, bone, and ovary. There appears to be a relationship with tuberous sclerosis and PEComas as 9.1% of the reviewed 44 cases (four cases), as well as the present case showed concurrent tuberous sclerosis [1]. It is possible that both arise from an alteration in tumor suppressor gene (*TSG)* function [9].

Polypoid adenomyomas account for 2% of endometrial polyps [10]. It is unclear if the presence of this entity in the present case is also related to the PEComa or tuberous sclerosis, or is coincidental. This is the first report documenting a PEComa arising in a polyp of any type. In 2008, Frorio and colleagues documented a unique case of a PEComa arising in a background of endometriosis [2]. In their report, they observed HMB-45 positive cells surrounding ectopic endometrial glands. Histopathologically, PEComas are characterized by proliferation of eosinophilic epithelioid cells or smooth muscle cell-like spindle cells. PEComas also demonstrate neovascularization around the tumor cells that is similar to what is observed in renal clear cell carcinomas. Neovascularization is not a typical feature of uterine PEComas.

Prognostic factor for PEComas have not been clearly defined. Folpe et al. reported that tumor size (larger than eight cm in diameter), frequent nuclear fission (more than 1/50 HPF), and necrosis predicted local or distant metastasis [6]. None of these features were evident in the present case. As infiltrative growth was present the authors considered the present tumor to have uncertain malignant potential.

The present case describes a rare presentation of a uterine PEComa. PEComas should be differentiated from uterine abnormalities in tuberous sclerosis patients.

References

[1] Fadare O.: "Uterine PEComa: appraisal of a controversial and increasingly reported mesenchymal neoplasm". *Int. Semin. Surg. Oncol*., 2008, *5*, 7.

[2] Froio E., Piana S., Cavazza A., Valli R., Abrate M., Gardini G.: "Multifocal PEComa (PEComatosis) of the female genital tract associated with endometriosis, diffuse adenomyosis, and endometrial atypical hyperplasia". *Int. J. Surg. Pathol*., 2008, *16*, 443.

[3] Yavuz E., Cakr C., Tuzlal S., Ahskal B., Topuz S., Ilhan R.: "Uterine perivascular epithelioid cell tumor coexisting with pulmonary lymphangioleiomyomatosis and renal angiomyolipoma: a case report". *Appl. Immunohistochem. Mol. Morphol*., 2008, *16*, 405.

[4] Yamagata Y., Kawauchi S., Tamura H., Murakami A., Sasaki K., Sugino N.: "A case of HMB45-negative perivascular epithelioid cell tumor (PEComa) of the uterine corpus: a possible diagnostic application of molecular-cytogenetic analysis". *Eur. J. Gynaecol. Oncol*., 2009, *30*, 216.

[5] Folpe A.L.: "Neoplasms with perivascular epithelioid cell differentiation (PEComas)". In: Fletcher C.D.M., Unni K.K., Mertens F. (eds.). World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of Soft Tissue and Bone. Lyon, IARC Press., 2002, 221.

[6] Folpe A.L., Mentzel T., Lehr H.A., Fisher C., Balzer B.L., Weiss S.W.: "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.

[7] Zamboni G., Pea M., Martignoni G., Zancanaro C., Faccioli G., Gilioli E. *et al*.: "Clear cell "sugar" tumor of the pancreas. A novel member of the family of lesions characterized by the presence of perivascular epithelioid cells". *Am. J. Surg. Pathol*., 1996, *20*, 722.

[8] Pea M., Martignoni G., Zamboni G., Bonetti F.: "Perivascular epithelioid cell". *Am. J. Surg. Pathol*., 1996, *20*, 1149.

[9] Lim G.S., Oliva E.: "The morphologic spectrum of uterine PEC-cell associated tumors in a patient with tuberous sclerosis". *Int. J. Gynecol. Pathol*., 2011, *30*, 121.

[10] Silverberg S.G.: "Adenomyomatosis of endometrium and endocervix-a hamartoma". *Am. J. Clin. Pathol*., 1975, *64*, 192.

Address reprint requests to:
K. NAKAYAMA, M.D., Ph.D.
Shimane University School of Medicine
Enyacho 89-1, Izumo,
6938501 Shiman (Japan)
e-mail: kn88@med.shimane-u.ac.jp