Scientific Research Publishing

Open Journal of Epidemiology, 2025, 15(3), 600-607
https://www.scirp.org/journal/ojepi
ISSN Online: 2165-7467
ISSN Print: 2165-7459

Perivascular Epithelioid Cell Tumor of the Cervix with Metastasis to the Brain

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How to cite this paper: Maro, K., Wang, C.L., Maro, H., Zhai, X.Q., Gao, Y.H., Gao, X., Msuya, L. and Zhou, B. (2025) Perivascular Epithelioid Cell Tumor of the Cervix with Metastasis to the Brain. *Open Journal of Epidemiology*, **15**, 600-607.
https://doi.org/10.4236/ojepi.2025.153039

Received: March 7, 2025
Accepted: August 12, 2025
Published: August 15, 2025

Abstract

Perivascular Epithelioid Cell tumors (PEComas) are rare mesenchymal neoplasms with distinctive histologic and immunohistochemical profiles that exhibit a predominantly perivascular distribution of neoplastic cells. The rarity and paucity of characteristic imaging features of PEComas, particularly in the gynecologic organs, pose a diagnostic challenge. PEComas have been reported at many anatomic locations including uterus, vulva, and retroperitoneum, with some cases associated with the tuberous sclerosis complex. PEComas of the uterus are especially difficult to diagnose preoperatively and are often found incidentally postoperatively. This case report represents the fourth reported case of a PEComa metastasizing to the brain, and the first case of a cervical PEComa diagnosed with brain metastasis. A 65-year-old postmenopausal woman presented to the clinic with postmenopausal vaginal bleeding, and she was found to have masses in the cervix and uterus. The patient had no known genetic predispositions such as tuberous sclerosis complex (TSC) and declined genetic testing. A cervical mass was eventually diagnosed as a PEComa, following histopathological and immunohistochemical analysis. While initially successful, the patient later developed neurologic symptoms, and imaging revealed a brain metastasis. Craniotomy with gross total resection of the metastatic lesion was performed, and the pathology confirmed that the brain lesion originated from the cervical PEComa. This report highlights the unpredictable metastatic behavior of PEComas, even to the brain, and the importance of rapid and accurate diagnosis, followed by extensive surgical resection of the primary tumor and any metastatic foci. Additional research is required to bet-

ter understand the biology of PEComas, to improve diagnosis, and to develop treatment strategies, especially for the group with evidence of metastatic disease.

Keywords

Perivascular Epithelioid Cell Tumor, PEComa

1. Introduction

PEComas are rare mesenchymal tumors distinguished by histologically and immunohistochemically peculiar perivascular epithelioid cells. Due to their heterogeneous clinical presentations and rarity, especially in the gynecological tract, these tumors pose a diagnostic challenge. PEComas may be found in the uterus, vulva, vagina, and retroperitoneum and are often associated with tuberous sclerosis complex [1]-[3].

These specific tumors include Angiomyolipomas (AMLs), clear cell sugar tumors, Primary Extrapulmonary Sugar Tumor (PEST), Lymphangioleiomyomatosis (LAM), Clear-Cell Myomelanocytic Tumor (CCMT) of the falciform ligament/ligamentum teres, primary cutaneous PEComa (CCCMT-Cutaneous Clear Cell Myomelanocytic Tumor) and PEComas not Otherwise Specified (NOS) [4]-[11].

In the gynecological field, uterine PEComas are particularly challenging to diagnose preoperatively. Studies have reported cases where these tumors were only identified postoperatively, highlighting the difficulties in clinical recognition and diagnosis [12].

We hereby report our findings to bolster the current knowledge concerning the clinicopathologic features, diagnostic pitfalls, and treatment strategies for PEComas within the gynecologic tract, owing to the yet-to-be settled controversies surrounding PEComas. Different previous articles will enable us to place an account on the fourth publication about PEComa with spread to central nervous system and the first one on cervical PEComa that tended to invade the brain. The patient has granted consent for publication of this case.

2. Case

A 65-year-old woman with a history of three pregnancies with three living children had postmenopausal bleeding and no history of fever, palpitation, chest tightness or abdominal pain. Her medical history included hypertension managed with amlodipine and she denied prior malignancies or TSC-associated symptoms like seizures or cognitive deficits. Family history revealed no neoplasm or genetic disorders. On gynecological examination, senile changes in the vulva, a small amount of dark brown vaginal secretion without a peculiar smell, atrophied and smooth cervix and forward tilted, atrophied uterus with no tenderness or mass. Cervical TCT and HPV tests were normal. A pelvic MRI showed a mass seen in

the cervical canal (Figure 1). She underwent hysteroscopic surgery where two masses were resected, one from the cervix at 12 o'clock and the other from the proximal uterine wall. The first pathological results on the first mass of the cervix showed a heterotypic cell with an occasional mitotic Figure 1/50 hpf, and it was concluded in the immunohistochemical staining that they were finally excluded. epitheliogenic, neurogenic and lymphohematopoietic tumors while the second mass at the uterine wall was confirmed as an endometrial polyp. Considering the rarity of this malignancy and the high capacities for extreme complications, the current patient was vigilant about her condition. In view of the diagnosis of Perivascular Epithelioid Cell tumor (PEComa) with malignant potential unknown and tumor thrombus in the right iliac vein, the patient received laparoscopy-assisted abdominal hysterectomy and bilateral salpingioophorectomy. Histological examination revealed a tumor measuring 1 cm × 1 cm × 0.5 cm on the serosal surface and 1/3 < 2/3 infiltrating the cervical wall. In addition, 1 in 50 high-power fields exhibited mitotic figures. Definite neoplastic necrosis or lymphangiogenesis could not be identified. In addition, the cervical body junction, uterine and bilateral fallopian tubes were not affected by the tumor. Immunohistochemically, the tumor stained positive for MelanA, SMA and HMB45, focally positive for vimentin and Ki-67, but negative for CK7, S-100, CD99, Desmin, CKpan, CD38 and LCA. The patient was counseled for genetic testing, but she refused. The tumor thrombus as a result of immobilization in the right external iliac vein was removed. The D-dimer levels on the third postoperative day were 6171 ng/L. She was treated with enoxaparin and discharged from the hospital on the seventh postoperative day, once the pathology results were available. A review 2 weeks postoperative revealed slurred speech and right limb weakness without an obvious cause. She was able to grasp things by her right upper limb but was only able to walk slowly with her right foot dragging on the floor. The MRI of the brain (Figure 2) showed severe metastasis, a diameter of 4 cm

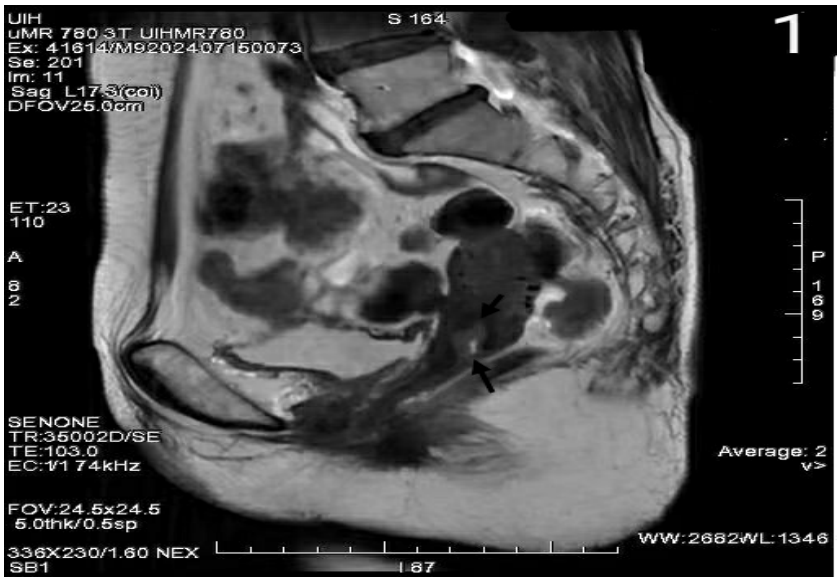

Figure 1. Pelvic MRI showing a mass in the cervix pointed with the black arrows.

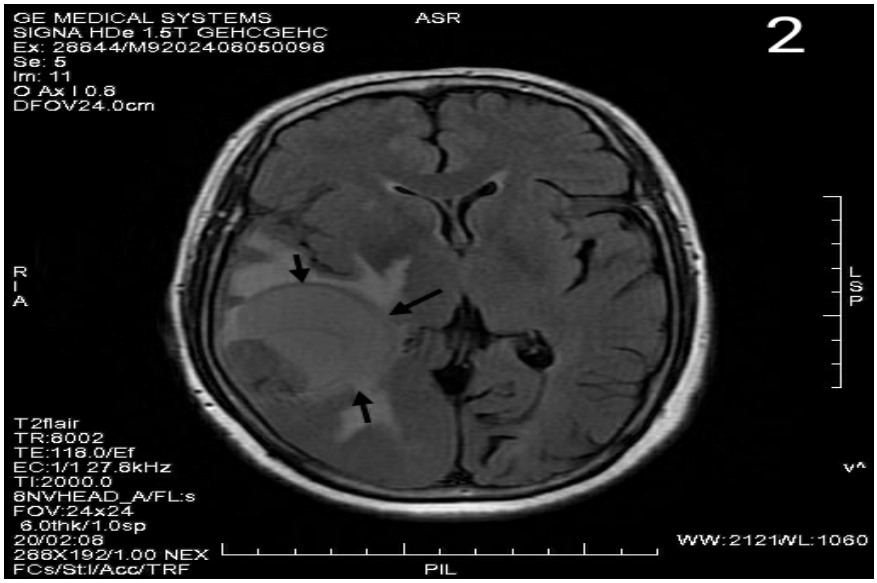

Figure 2. Brain MRI showing a mass in the left posterior temporal lobe pointed by the black arrows.

in the right posterior temporal lobe. A craniotomy was performed under general anesthesia through a right temporal approach. A curvilinear incision was made over the right temporal region followed by elevation of a bone flap. The dura was opened in a cruciate manner, revealing a 4 cm lesion in the posterior temporal lobe. Gross total resection was achieved using microsurgical techniques and neuronavigation assistance, ensuring preservation of surrounding functional cortex. Hemostasis was secured and the dura closed primarily. The bone flap was replaced, and the wound was closed in anatomical layers. Histology confirmed the brain lesion as metastatic cervical PEComa.

Postoperative follow-up care included neurological monitoring, physiotherapy for right-sided weakness, and periodic imaging to assess for recurrence. The patient was referred for oncologic evaluation, including consideration of targeted therapy with mTOR inhibitors based on the known pathway involvement in PEComa. Although initial genetic testing was declined, repeat counseling was provided, emphasizing the potential benefits of identifying TSC1/TSC2 mutations for guiding systemic treatment options and familial risk assessment.

3. Discussion

The malignancy of PEComa is dependent on cellular characteristics irrespective of the site of origin. Sites of prominent metastasis include lung, bone, liver, intestine, and lymph nodes, whereas cases of isolated CNS metastases have been observed in only three instances due to the protective nature of the CNS, arising from the presence of the blood-brain barrier which restricts the unhindered transference of tumor cells [13]-[15]. Herein we discuss a case of metastatic malignant PEComa to the brain, being the fourth incident documented in a middle-aged female.

PEComas are a type of tumor that is characterized by the presence of genetic alterations constituting tuberous sclerosis complex (TSC); specifically, they show the loss of TSC1 and TSC2 gene functions in 27% and 73% of cases, respectively. The TSC genes are important in the regulation of the Rheb/mTOR/p70S6K pathway. Electron microscopy shows multiple granules with the ultrastructural characteristics of promelanosomes within a cytoplasm that displays features similar to those of smooth muscle cells [13].

PEComas are defined as tumors characterized by the presence of myoid markers (SMA, desmin, caldesmon) and the melanocytic markers (HMB-45, Melan-A, MiTF) by means of immunohistochemical coexpression. Their mode of expression is variable with morphology: tumors that are mainly spindle show strong muscle marker expression with limited melanocytic marker expression; predominantly epithelioid tumors may show strong expression of melanocytic markers with limited muscle marker expression [4] [5] [10] [11] [16] [17].

Immunohistochemical results showed positivity with Melan A, SMARCA4, HMB45 and negativity with CK7, S-100, CD99, Desmin, CKpan, CD 138, LCA work, showing the tumor showed much stronger expression of melanocytic markers than muscle markers which was consistent with studies reporting varied marker expression in cervical PEComas where HMB-45 was positive in all samples, Melan-A in 83%, and desmin in 66% [8].

PEComa occurring at "non-classic" anatomic distributions is known as PEComa-not otherwise specified (PEComa-NOS) and has been reported in gynecological, genitourinary, gastrointestinal, extremities, skin, heart, breast, oral cavity, and orbit with uterus as the most prevalent site. In our case report the patient had tumor size of 1 × 1 × 0.5 cm in diameter, with mitotic rate of 1/50 hpf, without nuclear pleomorphism, no neoplastic necrosis or lymphovascular invasion seen which is supportive of a benign/uncertain malignant classification of the PEComas as in (**Table 1**) [16]-[18].

Based on the risk stratification guidelines proposed by Bleeker *et al.*, primary tumor size greater than 5 cm and a high mitotic rate of 1/50 hpf were identified as significant factors associated with recurrence in malignant PEComa cases [14]. For instance, a primary tumor exceeding 5 cm in size may indicate a more aggressive nature of the disease, leading to a higher likelihood of recurrence post-resection. Moreover, a high mitotic rate of 1/50 hpf, such as in our case with a 1.5 cm tumor, has been linked to an increased risk of metastasis. However, the exact timeline for recurrence or metastasis remains uncertain due to the rarity of such cases.

In our patient's case, the diagnosis of PEComa of the cervix was established through Hysteroscopic and MRI evaluations prompted by postmenopausal bleeding symptoms. Interestingly, there were no initial signs of CNS involvement until several weeks after the initial surgery, which involved a total abdominal hysterectomy and bilateral salpingectomy. This delay in CNS manifestation highlights the challenge in detecting brain lesions early, especially since many patients with brain metastasis may not exhibit symptoms initially. Detecting brain metastasis promptly is

Table 1. Showing worrisome features predictive of outcome in patient with PECOmas refference from Gadduci and Zannoni 2020.

Folpe *et al.*		Schoolmaster *et al.*		Bennet *et al.*	
Category	Histologic criteria	category	Histologic criteria	category	Histologic criteria
Benign	No worrisome features: less than 5 cm in diameter, non high nuclear grade and cellularity, mitotic rate <1/50 hpf, no necrosis, no vascular invasion	Bening/ uncertain malignant potential	Less than 4 worrisome features: size > 5 cm, high grade atypia(excluding degenerative atypia), mitosis > 1/50 hpf, necrosis, lymphovascular invasion	Uncertain malignant potential	Less than 3 worrisome features: size > 5 cm, high grade atypia(excluding degenerative atypia), mitosis > 1/50 hpf, necrosis, lymphovascular invasion
Uncertain malignant potential	One or both of the following features: nuclear pleomorphism,multinucleated giant cell only or size > 5 cm				
Malignant	Two or more worrisome features: Size > 5 cm in diameter, infiltrative, high nuclear grade and cellularity, mitotic rate> 1/50 hpf, necrosis, vascular invasion	Malignant	4 or more worrisome features: size > 5 cm, high grade atypia(excluding degenerative atypia), mitosis >1/50 hpf, necrosis, lymphovascular invasion	Malignant	3 or more worrisome features: Less than 3 worrisome features: size > 5 cm, high grade atypia(excluding degenerative atypia), mitosis> 1/50 hpf, necrosis, lymphovascular invasion
	Hpf:High power field				

crucial as it can significantly impact treatment outcomes, particularly in determining the need for adjuvant therapy post-resection.

The malignancy of PEComa is dependent on cellular characteristics irrespective of the site of origin. Prominent sites of metastasis include lung, bone, liver, intestine, and lymph nodes, with isolated CNS metastases documented in only three prior cases due to the protective nature of the blood-brain barrier [13]-[15].

Management strategies for PEComas are evolving with increasing focus on targeted therapies and risk-based stratification. Surgical resection remains the cornerstone for localized disease, and complete resection of metastases is pursued where feasible. Several case reports and small series have demonstrated efficacy of mTOR inhibitors such as sirolimus and everolimus, which act downstream of TSC1/TSC2 mutations, particularly in recurrent or metastatic disease [5] [10]. In our case, we did not give any chemotherapy since our patient declined genetic testing which could help to identify the TSC1/TSC2 mutations.

Surgical strategies for such tumors typically involve surgical resection of the brain lesions. A successful example can be seen in a study by Parfitt *et al.*, where a temporal craniotomy was performed, resulting in improved patient outcomes. Similarly, Jayapalan *et al.* conducted a dual lesion resection using intraoperative CT image guidance, showcasing the importance of precise surgical techniques. Additionally, Bharadwaj *et al.* opted for a right occipital craniotomy coupled with tu-

mor decompression and mTOR pathway inhibitor therapy, demonstrating the evolving landscape of treatment options in managing PEComa metastasis. Regular follow-ups, as seen in the 6-month monitoring plan, are crucial in monitoring the patient's response to therapy and detecting any recurrence early on. The reluctant use of neoadjuvant and adjuvant radio- and chemotherapy is attributed to the fact that PEComas are considered resistant to those treatments and, apart from several reports, there were no clear benefits of such an approach noted.

4. Conclusion

In conclusion, this case report sheds light on the very nature of including PEComas in differential diagnoses of post-menopausal bleeding, especially in the gynecological tract. The diagnosis of PEComa with brain metastasis in this patient challenges a more exigent discovery and relatively swifter intervention for such a rare tumor and the sustaining multidisciplinary approach in its management. The case further reiterates the importance of routine follow-ups assessing the patient's treatment response and the early detection of any recurrence. Finally, this case report adds to the literature regarding PEComas and shares the much-needed impetus for awakening awareness and recognition of this rare tumor in the gynecological tract.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Fitzpatrick, M., Pulver, T., Klein, M., Murugan, P., Khalifa, M. and Amin, K. (2016) Perivascular Epithelioid Cell Tumor of the Uterus with Ovarian Involvement: A Case Report and Review of the Literature. *American Journal of Case Reports*, **17**, 309-314. https://doi.org/10.12659/ajcr.896401

[2] Levin, G., Capella, M.P., Meyer, R., Brezinov, Y. and Gotlieb, W.H. (2024) Gynecologic Perivascular Epithelioid Cell Tumors (PEComas): A Review of Recent Evidence. *Archives of Gynecology and Obstetrics*, **309**, 2381-2386. https://doi.org/10.1007/s00404-024-07510-5

[3] Nicolás, I., Fusté, P., Saco, A., Ordi, J. and Torné, A. (2019) Perivascular Epitheliod Cell Tumors: Study of Three Gynecological Cases. *Medicina Clínica*, **153**, 83-87. https://doi.org/10.1016/j.medcli.2019.01.009

[4] Conlon, N., Soslow, R.A. and Murali, R. (2015) Perivascular Epithelioid Tumours (PEComas) of the Gynaecological Tract. *Journal of Clinical Pathology*, **68**, 418-426. https://doi.org/10.1136/jclinpath-2015-202945

[5] Gadducci, A. and Zannoni, G.F. (2020) Perivascular Epithelioid Cell Tumors (PEComa) of the Female Genital Tract: A Challenging Question for Gynaecologic Oncologist and Pathologist. *Gynecologic Oncology Reports*, **33**, Article ID: 100603. https://doi.org/10.1016/j.gore.2020.100603

[6] Kovac, O., Babal, P., Kajo, K., Kobzova, D., Copakova, L. and Cermak, M. (2018) Perivascular Epithelioid Cell Tumor (PEComa) of the Uterine Cervix: A Case Report of a 43-Yr-Old Woman with Abnormal Uterine Bleeding Treated with Hysterectomy.

International Journal of Gynecological Pathology, **37**, 492-496.
https://doi.org/10.1097/pgp.0000000000000436

[7] Kudela, E., Biringer, K., Kasajova, P., Nachajova, M. and Adamkov, M. (2016) Perivascular Epithelioid Cell Tumors of the Uterine Cervix. *Pathology—Research and Practice*, **212**, 667-671. https://doi.org/10.1016/j.prp.2016.03.010

[8] Liu, C., Chao, W., Lin, S., Lau, H., Wu, H. and Wang, P. (2019) Malignant Perivascular Epithelioid Cell Tumor in the Female Genital Tract: Preferred Reporting Items for Systematic Reviews and Meta-Analyses. *Medicine*, **98**, e14072.
https://doi.org/10.1097/md.0000000000014072

[9] Mateva, S., Nikolova, M., Totev, T. and Gorchev, G. (2019) Malignant Cervical PEComa: A Case Report and Review of the Literature. *Journal of IMAB—Annual Proceeding* (*Scientific Papers*), **25**, 2759-2768. https://doi.org/10.5272/jimab.2019254.2759

[10] Starbuck, K.D., Drake, R.D., Budd, G.T. and Rose, P.G. (2016) Treatment of Advanced Malignant Uterine Perivascular Epithelioid Cell Tumor with mTOR Inhibitors: Single-Institution Experience and Review of the Literature. *Anticancer Research*, **36**, 6161-6164. https://doi.org/10.21873/anticanres.11208

[11] Thway, K. and Fisher, C. (2015) PEComa: Morphology and Genetics of a Complex Tumor Family. *Annals of Diagnostic Pathology*, **19**, 359-368.
https://doi.org/10.1016/j.anndiagpath.2015.06.003

[12] Shan, W., Shi, Y., Zhu, Q., Yang, B., Xie, L., Li, B., *et al.* (2018) Five Cases of Uterine Perivascular Epithelioid Cell Tumors (PEComas) and Review of Literature. *Archives of Gynecology and Obstetrics*, **299**, 185-190.
https://doi.org/10.1007/s00404-018-4920-4

[13] Bharadwaj, R., Singh Gahlot, G.P., Vashisth, R., Saxena, R., Shukla, S. and Singh, B. (2021) Metastatic Malignant PEComa of the Brain: An Unusual Entity with Rare Presentation. *Indian Journal of Case Reports*, **7**, 83-86.
https://doi.org/10.32677/ijcr.2021.v07.i03.003

[14] Jayapalan, R.R., Bahuri, N.F.A., Mun, K.S. and Narayanan, V. (2019) A Rare Case of Perivascular Epithelioid Cell Tumour Metastases to the Brain. *SAGE Open Medical Case Reports*, **7**. https://journals.sagepub.com/doi/10.1177/2050313X19828539
https://doi.org/10.1177/2050313x19828539

[15] Parfitt, J.R., Keith, J.L., Megyesi, J.F. and Ang, L.C. (2006) Metastatic PEComa to the Brain. *Acta Neuropathologica*, **112**, 349-351.
https://doi.org/10.1007/s00401-006-0105-5

[16] Bennett, J.A., Braga, A.C., Pinto, A., Van de Vijver, K., Cornejo, K., Pesci, A., *et al.* (2018) Uterine PEComas: A Morphologic, Immunohistochemical, and Molecular Analysis of 32 Tumors. *American Journal of Surgical Pathology*, **42**, 1370-1383.
https://doi.org/10.1097/pas.0000000000001119

[17] Folpe, A.L., Mentzel, T., Lehr, H., Fisher, C., Balzer, B.L. and Weiss, S.W. (2005) Perivascular Epithelioid Cell Neoplasms of Soft Tissue and Gynecologic Origin: A Clinicopathologic Study of 26 Cases and Review of the Literature. *American Journal of Surgical Pathology*, **29**, 1558-1575.
https://doi.org/10.1097/01.pas.0000173232.22117.37

[18] Schoolmeester, J.K., Howitt, B.E., Hirsch, M.S., Dal Cin, P., Quade, B.J. and Nucci, M.R. (2014) Perivascular Epithelioid Cell Neoplasm (PEComa) of the Gynecologic Tract: Clinico-pathologic and Immunohistochemical Characterization of 16 Cases. *American Journal of Surgical Pathology*, **38**, 176-188.
https://doi.org/10.1097/pas.0000000000000133