Journal of Current Medical Research and Opinion
Received 09-11-2024 | Revised 11-11-2024 | Accepted 09-12-2024 | Published Online 13-12-2024

DOI: https://doi.org/10.52845/CMRO/2024/7-12-5 ISSN (O) 2589-8779 | (P) 2589-8760
CMRO 07 (12) 3817-3823 (2024) www.cmro.in

Case Reports

Uterine Angiolipoleiomyoma in a Premenopausal Woman: Clinical Development, Pathohistologic Findings, and Treatment - Case Report

Vefa ŞAKAR, MD[1, *] | Gülnur Güven, MD[2] | Özhan Özdemir, MD[3]

[1]University of Health Sciences, Gülhane Training and Research Hospital, Department of Obstetrics and Gynecology
[2]Ankara Pursaklar State Hospital, Department of Obstetrics and Gynecology
[3]University of Health Sciences, Gülhane Training and Research Hospital, Department of Obstetrics and Gynecology

Abstract:

Introduction:

Angiolipoleiomyomas (ALLMs) are benign overgrowths of smooth muscle, adipose tissue and blood vessels. These neoplasm belong to a particular group of tumors known as mesenchymal tumors whose growth can occur in any anatomical site. ALLMs usually occur in the kidneys, but are rare in other organs such as the uterus.

Case report:

A 45-year-old woman with 3 previous deliveries presented with abnormal uterine bleeding. She was being followed for hypertension. Initial ultrasonography revealed two fibroids in the uterus. She was implanted with a levonorgestrel-containing intrauterine device (RIA). She missed follow-up appointments due to the pandemic and her complaints increased. At her second presentation, ultrasonography showed an intramural fibroid measuring 50x20 mm and several subserosal fibroids. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were planned. The postoperative pathology specimen contained a 7 cm diameter angiolipoleiomyoma and an additional 4 leiomyomas.

Conclusion:

Uterine ALLM is a rare benign tumor. Definitive diagnosis is made by histopathologic examination. Surgical intervention takes care of the issue at a higher efficiency level, but patients should be followed up for a long-term.

Keywords: Angiolipoleiomyoma, Uterine Tumor, fibroid, hysterectomy

Introduction:

Angiolipoleiomyomas (ALLMs) are benign tumors composed of smooth muscle, fatty tissue, and abnormal arterial vessels.[1] These tumors are part of a broader family of mesenchymal neoplasms that can develop in different organs. Angiomyolipomas, which are closely related, are common in the kidneys. Renal tumors composed of smooth muscle, fat, and vessels are classified as classical or epithelioid variants of angiomyolipoma based on the presence or absence of HMB-45 immunopositive epithelioid cells. However, several differences between renal and extrarenal angiomyolipomas have been noted. Extrarenal ALLMs typically lack epithelioid components, are often HMB-45 negative, and are rarely associated with tuberous sclerosis.[2]

Uterine and skin lesions containing smooth muscle, fat, and vessels are often referred to as angiolipoleiomyomas, lipoleiomyomas, or angiomyolipomas in the literature. However, these terms are used interchangeably, causing some confusion. A consistent classification system is needed to distinguish these entities more clearly.

The concept of tumors containing both muscle and fat was first introduced by Lobstein in 1816, who described them as “pure” and “mixed” lipomas based on the presence or absence of muscle tissue.[3] In 1978, Willén et al. reported that the incidence of uterine lipoleiomyomas was approximately 0.03-0.2% among all uterine leiomyomas, emphasizing their rarity.[4] The incidence of symptomatic leiomyomas generally peaks during perimenopause and decreases after menopause.[5] However, some studies indicate that uterine lipoleiomyomas can continue to grow after menopause, which differs from the typical behavior of leiomyomas.[6] In fact, lipoleiomyoma has been noted as the most common variant in postmenopausal patients with uterine leiomyomas.[7]

In this case report, we present a growing angiolipoleiomyoma in a premenopausal patient, which contrasts with the more commonly observed postmenopausal presentations.

Case Report:

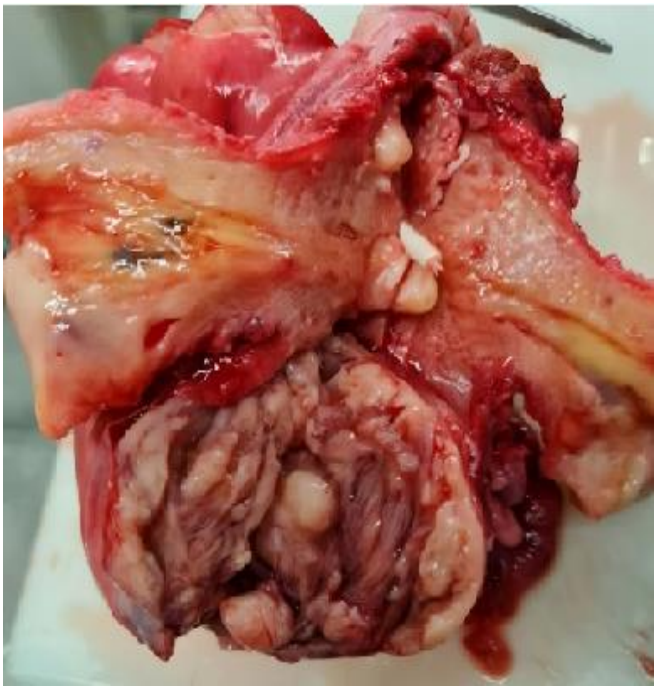
A 45-year-old woman presented to our clinic with abnormal uterine bleeding. The patient had a gravida of 3 and parity of 3. Her medical history revealed that she was being followed up for hypertension and was on dual antihypertensive medication. The patient had no other comorbidities and no history of smoking. Upon her first visit, a transvaginal ultrasound revealed two fibroid nodules: one measuring 3 cm on the posterior uterine wall and another 3.5 cm on the fundus. A biopsy performed at an external center showed a proliferative endometrium. The patient was advised for annual follow-up, and an intrauterine device (IUD) with levonorgestrel was applied to address her complaints.

However, due to the COVID-19 pandemic, the patient missed her scheduled follow-up visit. This delay in clinical monitoring likely contributed to the progression of her condition, as the patient's symptoms worsened over time. In 2022, she was admitted to our clinic again with complaints of intermittent bleeding, groin, and low back pain. At this second visit, a transvaginal ultrasound revealed a 50x20 mm hyperechogenic intramural fibroid on the posterior wall of the corpus. Several subserosal fibroids were also noted, the largest measuring 48 mm in diameter in the fundus. The endometrial thickness was 4 mm, and both ovaries appeared normal in size and echostructure. There was no fluid accumulation in the Douglas pouch, and no abdominal ascites or laparoscopy was performed. The Mirena IUD was not observed on ultrasound. The patient's hormonal profile was as follows: FSH 30, LH 7, E2 32, CA-125 34.6, CA19-9 18.65, and CA15-3 19.

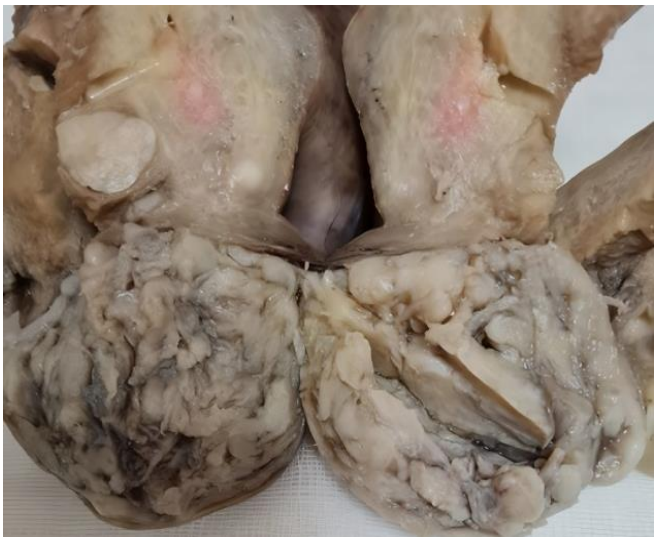
As the patient's symptoms of abnormal uterine bleeding and abdominal pain persisted and her fibroids continued to grow, a total abdominal hysterectomy and bilateral salpingo-oophorectomy were planned. Both the smear and the endometrial biopsy failed to show any malignancy or intraepithelial lesions. However, the endometrial biopsy showed an endometrial progestin-induced secretory pattern that correlated with the patient's previous hormonal treatment. She then underwent

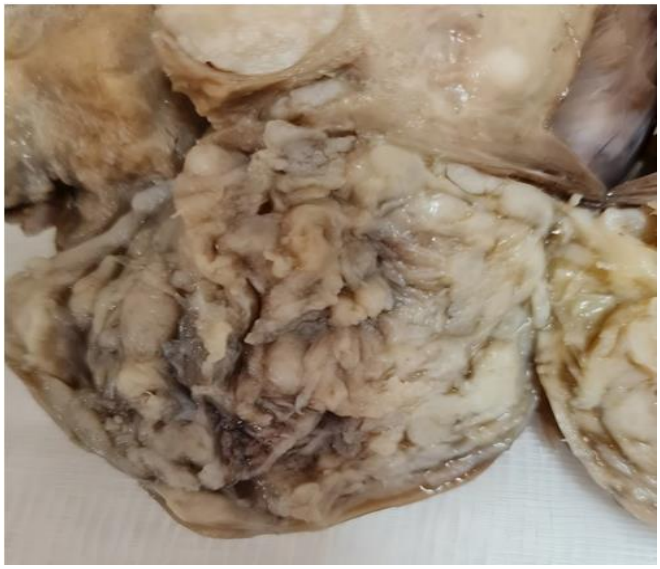
the scheduled total abdominal hysterectomy and bilateral salpingo-oophorectomy, and the surgical specimen, including the uterus, both adnexa, and omentum, was sent for pathological analysis.

Macroscopic Pathology Report:

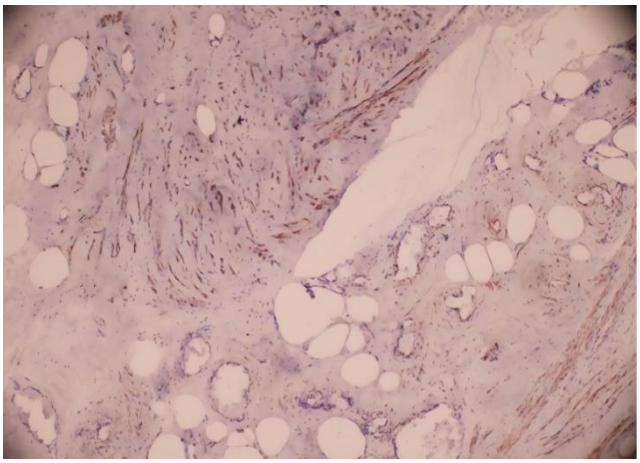


PICTURE 1: The cervix measured 4 cm in diameter, with a 4 cm long cervical canal. Naboth cysts were present on the cross-sectional surface of the cervix. Upon opening the uterus anteriorly, the uterine cavity was observed, and the IUD was noted in situ. The endometrial thickness was measured at 0.1 cm, while the myometrium was 1.7 cm thick. Upon slicing the uterus, five intramural fibroid nodules were noted, the largest measuring 7 cm and the smallest 1 cm in diameter.

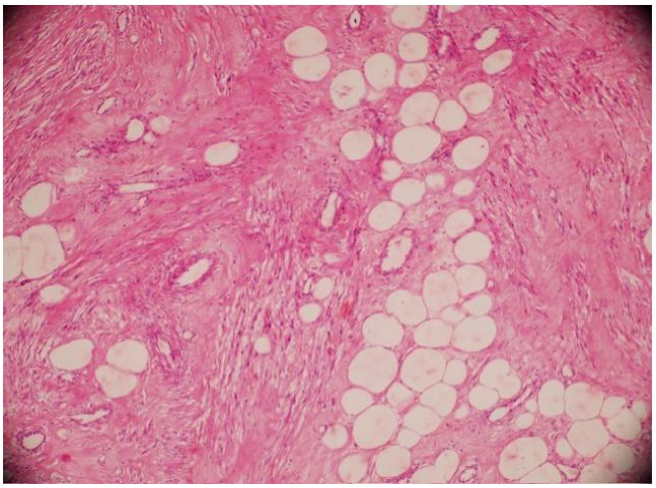




PICTURE 2: This image shows a section of the uterus removed by hysterectomy. There are several intramural fibroids (fibroids) in the uterus. Areas of yellowish and fatty tissue indicate angiolipoleiomyoma. This tumor is composed of fat cells, smooth muscle and blood vessels. The myometrium is thick and the endometrium is a thin layer. The different sizes of the tumors are clearly distinguished.



PICTURE 3: This image shows a closer section of the uterus that was removed along with the angiolipoleiomyoma described in the case. The masses in the intramural region of the uterus are shown in more detail. The large, irregular gray-white areas in the lower section reflect intramural leiomyomas, while the yellowish areas in the masses indicate fatty tissue. This fatty appearance is characteristic of angiolipoleiomyoma as it is composed of both fat cells and muscle and vascular structures. The masses are well circumscribed, but the dense and fibrous structure typical of fibroids is also noticeable. This macroscopic image clarifies the nature of both the angiolipoleiomyoma and the other fibroids in the patient's uterus.



PICTURE 4: The right ovary measured 3.5x2x0.8 cm, with corpus albicans observed on the cross-sectional surface. The right fallopian tube measured 8 cm in length and 0.7 cm in diameter. The left ovary measured 3x2x1.2 cm, with corpus albicans similarly observed on the cross-sectional surface. The left fallopian tube measured 6 cm in length and 0.5 cm in diameter. A paratubal cyst was also observed.

Microscopic Pathology Report:

Microscopically, the lesion was diagnosed as an angiolipoleiomyoma, a benign mesenchymal tumor composed of smooth muscle, mature adipocytes, and abnormal blood vessels. Immunohistochemical staining revealed diffuse, strong positivity for SMA and desmin, confirming the smooth muscle component of the tumor. S-100 staining was observed in the fat cells, but HMB-45 and CD117 staining were negative, ruling out the presence of an epithelioid component (picture 5).

Final Diagnosis: Angiolipoleiomyoma of the uterus, 7 cm in diameter, with four additional intramural leiomyomata.

Discussion:

Uterine ALLMs is a clinically rare benign gynecologic tumor and a member of the PEComas family. It is a mesenchymal neoplasm arising from perivascular epithelioid cells and is characterized by the presence of varying proportions of benign smooth muscle cells, adipocytes, and blood vessels. ALLM is more common in the kidneys and liver and less common in the female reproductive system. Unlike renal ALLMs, uterine ALLMs generally cannot be achieved with TSC (tuberous sclerosis).[2] Most renal ALLMs are associated with TSC, a group of autosomal dominant disorders that affect multiple organ systems and are caused by loss-of-function mutations in one of two genes: TSC1 or TSC2.[8] Because of the diverse and non-specific clinical manifestations of uterine ALLM and the presence of non-specific imaging features,[9] preoperative diagnosis is often difficult. ALLMs may appear homogeneous and resemble normal leiomyomas, or they may show heterogeneity and contour irregularity suggestive of degenerated leiomyoma or leiomyosarcoma.[10] To improve preoperative diagnosis, a combination of imaging modalities such as MRI and contrast-enhanced CT may be beneficial. These techniques can help differentiate ALLMs from other uterine tumors based on their characteristic fat components and vascular patterns.[11]

Since preoperative diagnosis of uterine ALLM is difficult, clinicians should be familiar with the characteristic signs of ALLM during surgery to increase the diagnosis rate. ALLMs are soft-hard and have a gray-pink surface.[12] Leiomyomas usually show a white, hard, firm, curved, trabeculated cut surface, while cases of leiomyomas with degenerative changes can also show soft to hard, dark red or yellow areas like ALLM. In our case, the specimen was yellow, yellow-white in color. If a soft-tissue uterine tumor with a yellow cut surface is seen during surgery, the

possibility of uterine ALLM should be considered. PEComa is diagnosed by a combination of histopathologic evaluation and immunohistochemical markers.[13] PEComas are characterized by positive results for myoid (such as desmin, SMA, muscle-specific actin, muscle myosin and calponin).[13] Other markers expressed less frequently include SMA (80%), caldesmon (77%), MiTF (66%), desmin (63%), Melan-A (46%) and S100 (10%). HMB45 and Cathepsin-K are the most sensitive markers and are positive in 99-100% of uterine PEComas.[13-14] However, previous studies have found that HMB-45 can be negatively expressed in uterine ALLM.[12'15] Based on immunohistochemistry, ALLMs are associated with antibodies against alpha-smooth muscle actin and desmin and show strong positivity, indicating a neoplastic muscle element in the tumor.

İn our patient, non-vascular smooth muscle cells were immunohistochemically positive for desmin, vimentin, progesterone receptor and a-SMA (smooth muscle actin) and negative for antihuman melanoma (HMB45), S-100, CD-34, cytokeratin and estrogen receptor. This further proves that it is the same as other cases of angiolipoleyiomyoma. Surgical resection is the main treatment for ALLM. All previously reported cases were treated with total abdominal hysterectomy alone or in combination with bilateral salpingo-oophorectomy, except for two cases in which myomectomy was performed.[12] For premenopausal patients desiring to preserve fertility, myomectomy may be considered as a fertility-sparing option. However, patients should be counseled about the potential risk of recurrence and the need for close follow-up.[16] Long-term follow-up is crucial for patients with uterine ALLM. While the tumor is generally considered benign, there is a lack of long-term data on recurrence rates. It is recommended that patients undergo regular imaging studies, such as ultrasound or MRI, every 6-12 months for at least 5 years post-surgery to monitor for potential recurrence.[17]

The effect of uterine ALLM on the subject's quality of life cannot be ignored. The patient may be worried about a diagnosis of a rare tumor and its impact on fertility, and may also suffer from physical complaints such as pelvic pain and abnormal menstrual bleeding. Providing comprehensive psychological support and patient education is an essential aspect of care.[18] In the differential diagnosis of uterine ALLM, it is important to consider other uterine tumors such as leiomyomas, leiomyosarcomas, and other types of PEComas. The presence of adipocytes and abnormal blood vessels in addition to smooth muscle cells is a key distinguishing feature of ALLM. Immunohistochemistry plays a crucial role in differentiating ALLM from other tumors, particularly the negative HMB-45 staining which distinguishes it from classic PEComas.[19] While surgical resection remains the primary treatment for uterine ALLM, future therapeutic approaches may include targeted therapies. For instance, mTOR inhibitors have shown promise in treating other types of PEComas and may potentially be effective in cases of ALLM that are not amenable to surgical resection or in recurrent cases.[20] Uterine angiolipoleiomyomas are usually benign tumors. Therefore, surgical options such as myomectomy may be preferred in premenopausal patients who wish to preserve fertility. However, it should be kept in mind that although rare, they may have malignant potential. Therefore, regular follow-up after surgery is essential. After patients have completed their fertile period, if there are symptoms such as recurrence of fibroids, abnormal uterine bleeding or pain, more radical treatments such as total hysterectomy may be considered.

Although the term angiolipoleiomyoma has been proposed for these benign tumors of the uterus, which lack epithelioid morphology and show negative immunostaining with HMB-45, the WHO is still silent on their inclusion in the classification of tumors of the genital tract.

Conclusion:

In conclusion, uterine ALLM is a rare benign tumor of the female reproductive system with a low incidence rate and most likely to occur in perimenopausal women. Clinical findings are similar to uterine leiomyomas. If the cut surface of the tumor is yellow and the tissue is soft like

adipose tissue during the operation, uterine ALLM should be suspected.

AML with more muscular components can be easily confused with uterine leiomyoma. The definitive diagnosis is made histopathologically. Current results suggest that uterine ALLM has a good prognosis and a low recurrence rate, but close follow-up is still recommended. Angiolipoleyiomyomas are non-malignant benign tumors that can be treated with appropriate surgery.

References:

1. Totev, T. P., Mateva, S. A., Nikolova, M. R., & Gorchev, G. A. (2014). Uterine angiomyolipoma: a case report, differential diagnosis with PECOMA and review of literature. *Journal of Biomedical and Clinical Research*, 7, 47–52. https://doi.org/10.1515/jbcr-2015-0125
2. Kim HJ, Chung CM, Park JY, Jung SG. Angiomyolipoma of the Glabellar Region. *Arch Craniofac Surg*. 2017;18(3):202-206. doi:10.7181/acfs.2017.18.3.202
3. Brandfass RT, Everts-Suarez EA. Lipomatous tumors of the uterus. *Am J Obstet Gynecol.* 1955; 70:359-367. doi:10.1016/s0002-9378(16)37680-3.
4. Willén R, Gad A, Willén H. Lipomatous lesions of the uterus. *Virchows Arch A Pathol Anat Histol.* 1978; 377:351-361. doi:10.1007/BF00507135.
5. erez-Lopez FR, Ornat L, Ceausu I, et al. EMAS position statement: management of uterine fibroids. *Maturitas.* 2014;79:106-116. doi:10.1016/j.maturitas.2014.06.002.
6. Kurman RJ, Carcangiu ML, Herrington CS, Young RH. *WHO Classification of Tumours of Female Reproductive Organs*. IARC Press; 2014.
7. Oi Y, Katayama K, Hirata G, et al. Significance of postmenopausal uterine leiomyomas: focus on variants. *J Obstet Gynaecol Res.* 2018;44:1445-1450. doi:10.1111/jog.13675.
8. Henske E, Jóźwiak S, Kingswood J, Sampson J, Thiele E. Tuberous sclerosis complex. *Nat Rev Dis Prim.* 2016;2:16035. doi:10.1038/nrdp.2016.35.
9. Giannella L, Delli Carpini G, Montik N, et al. Ultrasound features of a uterine perivascular epithelioid cell tumor (PEComa): case report and literature review. *Diagnostics.* 2020;10(8):553. doi:10.3390/diagnostics10080553.
10. Nguyen J, Ghandehari H, Parra-Herran C, Vicus D. Uterine rupture: an unusual presentation of a uterine perivascular epithelioid cell tumor (PEComa). *Int J Gynecol Cancer.* 2020. doi:10.1136/ijgc-2020-001837.
11. Tang Z, Yu D, Ni T, et al. Quantitative analysis of multiphase contrast-enhanced CT images: a pilot study of preoperative prediction of fat-poor angiomyolipoma and renal cell carcinoma. *AJR Am J Roentgenol.* 2019;1-13. doi:10.2214/ajr.19.21625.
12. Braun H, Wheelock J, Amaker B, Seeds J. Sonographic evaluation of a uterine angiolipoleiomyoma. *J Clin Ultrasound.* 2002;30(4):241-244. doi:10.1002/jcu.10057.
13. Conlon N, Soslow R, Murali R. Perivascular epithelioid tumours (PEComas) of the gynaecological tract. *J Clin Pathol.* 2015;68(6):418-426. doi:10.1136/jclinpath-2015-202945.
14. Kawauchi S, Nawata H, Yamagata Y, et al. Chromosomal imbalances detected by comparative genomic hybridization provide evidence that HMB-45-negative uterine angiomyolipomas belong to the PEComa family. *Histopathology.* 2010;56(7):974-977. doi:10.1111/j.1365-2559.2010.03567.x.
15. Yaegashi H, Moriya T, Soeda S, et al. Uterine angiomyolipoma: case report and review of the literature. *Pathol Int.* 2001;51(11):896-901. doi:10.1046/j.1440-1827.2001.01289.x.
16. Vidal-Mazo C, et al. Clinical recurrence of submucosal myoma after a mechanical hysteroscopic myomectomy: Review after

5 years follow up. *Eur J Obstet Gynecol Reprod Biol.* 2019; 243:41-45. doi: 10.1016/j.ejogrb.2019.10.014.

17. Seo G, et al. Uterine angiolipoleiomyoma with US, CT, and MRI findings: A case report. *Curr Med Imaging.* 2022. doi:10.2174/1573405618666220321123749.
18. Wang J, et al. Uterine angiomyolipoma: a clinical analysis of 8 cases and literature review. *Arch Gynecol Obstet.* 2021; 304:171-177. doi:10.1007/s00404-021-05992-1.
19. Garg N, et al. Angiolipoleiomyoma or HMB-45 negative angiomyolipoma of uterus: need for uniformity in terminology. *Indian J Surg Oncol.* 2021;12:239-240. doi:10.1007/s13193-021-01322-8.
20. Sanfilippo R, et al. Role of chemotherapy, VEGFR inhibitors, and mTOR inhibitors in advanced perivascular epithelioid cell tumors (PEComas). *Clin Cancer Res.* 2019;25:5295-5300. doi:10.1158/1078-0432.CCR-19-0288.