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Case Report

Uterine angiosarcoma: A diagnostic challenge in an uncommon uterine tumor (A case report)

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Abstract

Uterine angiosarcoma is exceedingly rare, with few cases reported in literature. The prognosis is very poor, and no standardized treatment protocol has been established to date. We report here a 54-year-old postmenopausal woman with no significant medical history, including no prior uterine fibroids. She presented with severe fatigue and pallor, without other symptoms. Abdominal ultrasound revealed an abdominopelvic mass, and pelvic MRI suggested an atypical myoma. Total hysterectomy with bilateral salpingo-oophorectomy was performed. Grossly, we found in uterus a 19 cm heterogeneous, whitish-gray tumor with extensive necrosis and hemorrhage. Microscopically, the tumor was poorly differentiated, composed of epithelioid cells with focal vasoformative features. Immunohistochemical analysis showed positivity for CD31, ERG, and pancytokeratin. Clinical course was unfavorable, with multiple recurrences. She died one month after the initial diagnosis. Diagnosis of uterine angiosarcoma is challenging due to its rarity, nonspecific clinical and radiological features and broad histopathological differential diagnoses. A Correct diagnosis is critical to ensuring optimal management and care. Meticulous histopathological examination is crucial to raise suspicion of this uncommon entity and to incorporate endothelial markers into immunohistochemical panel.

Keywords: Angiosarcoma, Uterus, Sarcoma, Pathology, Diagnosis.

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1. Introduction

Angiosarcomas are a rare and heterogeneous group of malignant tumors of endothelial origin, characterized by highly aggressive behavior and a significant metastatic potential.[1]

Therefore, the prognosis is poor, with an overall 5-year survival rate of approximately 40%, dropping to 15% in the metastatic stage. Angiosarcoma predominantly affects the skin, soft tissues, and breast parenchyma. Less frequently, it can arise in visceral organs such as the liver, spleen, heart, and bones.[1]

In the female genital tract, angiosarcoma is an exceptionally rare entity.[2,3] To date, approximately 30 cases of uterine angiosarcoma have been reported in the English literature.[2] In contrast, other uterine sarcomas are more common, accounting for approximately 8% of all uterine malignancies.[4] Among these, leiomyosarcoma represents around 60% of cases, followed by endometrial stromal sarcoma, which accounts for 20%.[4]

Due to its rarity, clinicopathological characteristics and prognostic implications of uterine angiosarcoma remain poorly understood, and no standardized treatment protocol has yet been established.[3] Its histopathological diagnosis is particularly challenging, given the wide range of differential diagnoses.[1,4] Here, we report a case of uterine angiosarcoma diagnosed in a 54-year-old postmenopausal woman. We aim to discuss its clinicopathological features and the histopathological challenges associated with its diagnosis.

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2. Case Report

The patient was a 54-year-old nulliparous woman, postmenopausal for two years, with no significant personal or family medical history, including no history of uterine fibroids. She presented with a one-year history of severe fatigue and pallor, without any other associated symptoms, notably no uterine bleeding or pelvic pain. Clinical examination was normal, except for palpation of a pelvic mass. Following investigations were performed:

1. Complete blood count (CBC): anemia with hemoglobin at 7.5 g/dL.
2. Abdominal ultrasound: confirmed the presence of an abdominopelvic mass.
3. Pelvic MRI: suggested an atypical pedunculated myoma.

Following multidisciplinary consultation, uterine sarcoma was considered. Thoracoabdominal CT scan performed as part of metastatic workup revealed no secondary lesions. To establish the diagnosis, a total hysterectomy with bilateral salpingo-oophorectomy was performed.

Macroscopic examination revealed a 19 cm heterogeneous, firm, whitish-gray tumor located in the myometrium of the uterine fundus, with extensive areas of necrosis and hemorrhage (**Figure 1**).

Figure 1: Macroscopic findings: Large whitish-gray tumor with extensive necrosis and hemorrhage in the uterine fundus.

Histological examination revealed a poorly differentiated tumor (**Figure 2**A) with extensive necrosis, composed of epithelioid cells exhibiting abundant eosinophilic cytoplasm and atypical nuclei with prominent nucleoli (**Figure 2**B). The mitotic index was 5.6 mitoses/mm². Focally, irregular, anastomosing vascular structures filled with red blood cells and lined by the same atypical cells were also observed.

Immunohistochemical analysis revealed that the neoplastic cells expressed CD31 (**Figure 3**A), ERG, and pancytokeratin (**Figure 3** B). In contrast, they were negative for CD34 (**Figure 3**C), podoplanin, CD10, estrogen receptor, progesterone receptor, S100, HMB-45, actin, desmin, and h-caldesmon.

The patient's clinical course was unfavorable, with rapid deterioration of her general condition and significant weight loss. CT scan revealed multiple tumor recurrences at the surgical site and within the peritoneum. She passed away one month after the initial diagnosis, without receiving chemotherapy or radiotherapy.

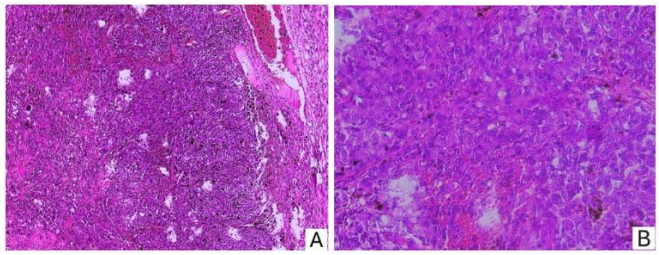

Figure 2: Histopathological findings: (**A**): Poorly differentiated tumor without evident vasoformative pattern (H&E stain, x100); (**B**): The tumor is composed of epithelioid cells with abundant eosinophilic cytoplasm and atypical nuclei with prominent nucleoli (H&E stain, x400)

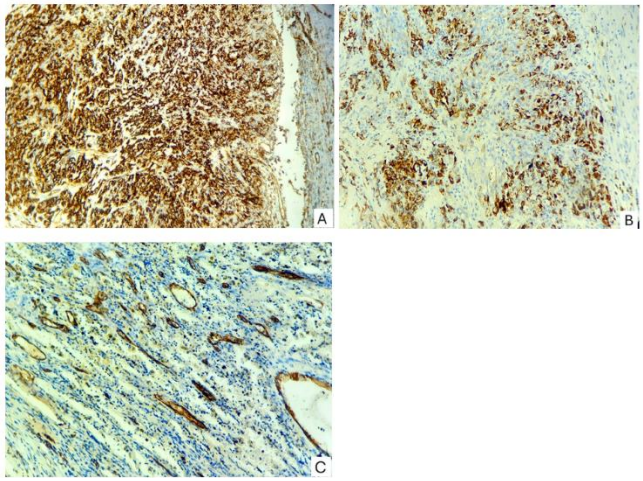

Figure 3: Immunohistochemical findings: (**A**) Positive CD31 expression; (**B**) Positive CK AE1/AE3 expression; (**C**) Negative CD34 expression.

3. Discussion

In this report, we describe a new case of uterine angiosarcoma. The exceptional rarity of this uterine mesenchymal tumor, combined with the broad spectrum of differential diagnoses, poses a significant diagnostic challenge. The clinical and radiological findings in our patient were non-specific, consistent with previously reported cases.[2,5] The most commonly described clinical manifestations of uterine angiosarcoma include abnormal uterine bleeding, the presence of a pelvic mass, pelvic pain, weight loss, and asthenia.[6,7] To date, no specific radiological features have been identified for the diagnosis of uterine angiosarcoma.[2,5]

Uterine angiosarcoma predominantly affects postmenopausal or perimenopausal women, with a reported mean age of 67 years (range: 17–81 years).[2,5] It may arise de novo or in association with a leiomyoma, suggesting a possible link between endothelial cell neoplastic transformation and the mechanical pressure exerted by the mass effect.[5,1]

The diagnosis of uterine angiosarcoma relies exclusively on histopathological examination, particularly on hysterectomy specimens.[2,9] In cases of intracorporeal uterine masses, endometrial and transvaginal biopsies have low sensitivity and carry a higher risk of iatrogenic uterine perforation.[9,10] Additionally, transabdominal biopsy and morcellation are contraindicated due to the risk of peritoneal tumor dissemination.[9]

Grossly, uterine angiosarcoma presents as a large, whitish-gray, heterogeneous mass with extensive areas of necrosis and hemorrhage. Due to the abundance of necrotic-hemorrhagic changes, thorough sampling is required to ensure the analysis of viable tumor areas.[5,10]

Histologically, uterine angiosarcoma can exhibit either a poorly differentiated solid form, composed of epithelioid[2,11] or spindle cells,[7,12] or a well-differentiated form with a vasoformative pattern.[5] The well-differentiated variant is distinguished by its irregular and complex vascular network, infiltrative growth, and layers of atypical neoplastic cells, all of which aid in establishing the diagnosis.[2,5,13]

The poorly differentiated variant is more challenging, particularly in the uterus, where it presents with a broad spectrum of differential diagnoses,[7,10,11] including carcinoma, melanoma, carcinosarcoma, leiomyosarcoma, endometrial stromal sarcoma, adenosarcoma, and alveolar rhabdomyosarcoma. Certain histological features,[7,13] such as focal vascular differentiation or vacuolated neoplastic cells containing red blood cells, may help orient the diagnosis toward angiosarcoma. Confirmation requires immunohistochemical analysis.

Uterine angiosarcoma typically expresses vascular differentiation markers such as CD31, CD34, factor VIII, podoplanin, Fli1, and ERG.[7,10] CD31 and ERG are the most specific and sensitive markers, whereas CD34 has lower sensitivity and specificity.[2,5,7] Podoplanin may be positive in some cases, suggesting lymphatic differentiation.[6,7] Additionally, pancytokeratin expression can be observed in poorly differentiated angiosarcomas, potentially leading to diagnostic confusion with poorly differentiated carcinoma, particularly in endometrial biopsies.[10] Uterine angiosarcoma does not express AML, h-caldesmone, hormone receptors, CD10, S100, or HMB45.[7,10]

Due to its extreme rarity, molecular profile of uterine angiosarcoma is difficult to characterize. Suzuki et al.[11] identified breakages at YWHAE (17p13), FAM22A (10q23), and FAM22B (10q22) loci in a single case of uterine angiosarcoma; however, these abnormalities have not been confirmed in other studies.[6,12] Roma et al. reported a case with an translocation.[12]

Uterine angiosarcoma is a highly aggressive tumor with a significant risk of recurrence and metastasis.[10] To date, no standardized therapeutic protocol has been established.[3,1,10] Management primarily relies on surgery, often followed by adjuvant treatment.[3,5] However, both chemotherapy and radiotherapy have yielded limited efficacy.[3,7,1] The prognosis remains poor, with a 5-year survival rate below 35%. In most cases, the disease progresses rapidly, leading to early mortality, as observed in our patient. Due to the swift and fatal progression of the disease in our case, the therapeutic contribution of our report remains limited.

4. Conclusion

Uterine angiosarcoma is a rare and aggressive tumor with no specific clinical or radiological features, making its diagnosis challenging. The presence of more common differential diagnoses, such as leiomyosarcoma, further complicates the diagnosis. A thorough histopathological examination, supplemented by an appropriate immunohistochemical panel, is essential to ensure accurate diagnosis. Macroscopically, its extensive necrotic component necessitates careful sampling of viable areas. A Correct diagnosis is critical to ensuring optimal management and care.

5. Source of Funding

None.

6. Conflict of Interest

The authors declare no conflicts of interest.

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