Quiz

Correct answer to the quiz. Check your diagnosis

Case report

Primary epithelioid angiosarcoma of endometrium

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Angiosarcoma is a poor prognostic tumor observed less than 1% in soft tissue, while it is rarely detected in the endometrium and has been described in few case reports. In this report, we present a case of primary epithelioid angiosarcoma of endometrium to raise awareness and emphasize for pathologists and clinicians.

Key words: angiosarcoma, endometrium.

Introduction

Angiosarcoma is a malignant mesenchymal tumor of vascular origin, showing histological, immunohistochemical and molecular features in line with vascular endothelial cells [1]. Angiosarcoma constitutes about approximately 1% of all soft tissue sarcomas [2]. This tumor is frequently seen in the head and neck region and with a tendency to be higher in men [3], it rarely occurs in the genital tract [4]. Angiosarcomas originating from the vagina [5], ovary [6] and uterus [7] have been described in the female genital tract. To date, about 30 cases have been described in the literature, and in this report, it is aimed to investigate and highlight the clinical, histomorphological and immunohistochemical features of this rare entity.

Case report

A 55-year-old female patient with no known medical history was referred to our hospital because of postmenopausal bleeding in an external center. Pelvic computed tomography revealed a mass lesion originating from the uterine lodge and invading the left internal iliac area and ureter. Based on this, 18F-FDG uptake with an SUV_{max} value of 28.6 was detected in the midline of the pelvis in the positron emission tomography performed. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, bilateral pelvic

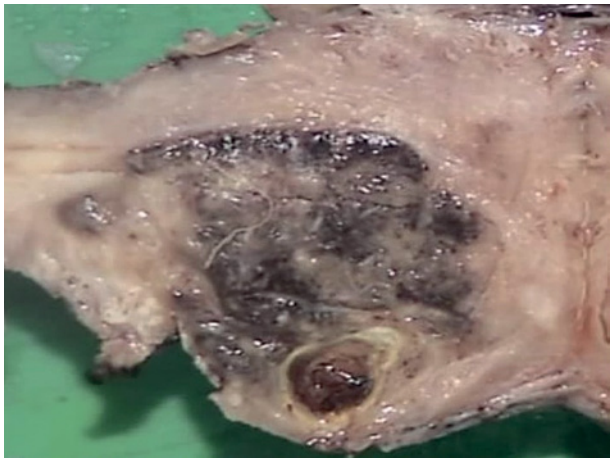

Fig. 1. Tumoral lesion located in the endometrium, with irregular borders, extending towards the lower uterine segment, containing cream-white and bleeding areas. Tumoral lesion is infiltrating the outer 1/2 of the myometrium

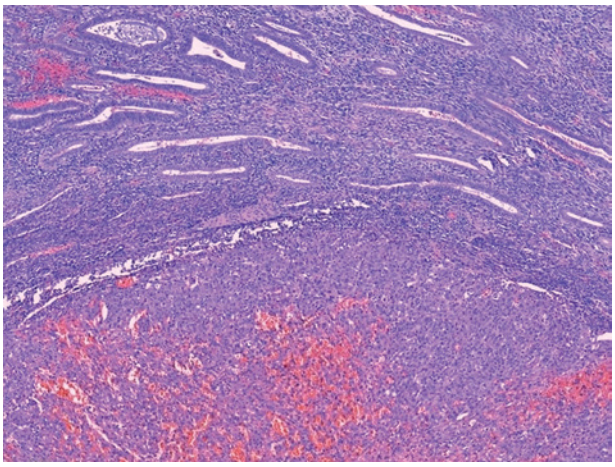

Fig. 2. Relationship of tumor and tumor-free endometrium. In this figure, benign endometrial glands are observed in the upper part, while a tumoral lesion that has infiltrated the endometrial stroma with pushing borders is observed in the lower part (HE, ×7.5)

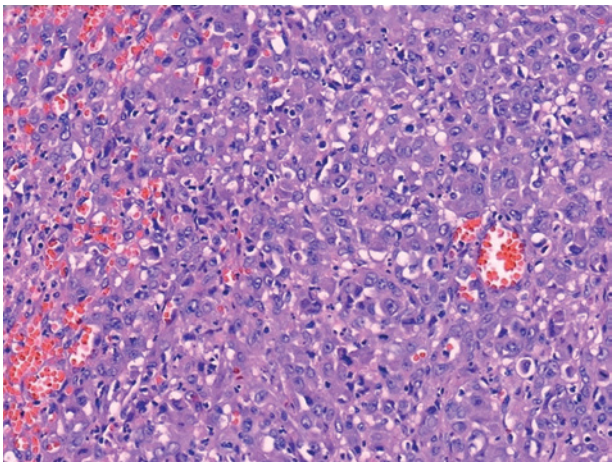

Fig. 3. Large and polygonal tumoral cells with solid architecture, prominent nucleoli, vesicular nuclei, prominent pleomorphism, frequent mitosis and eosinophilic cytoplasm are observed at the higher magnifications. Extravasated erythrocytes within dilated anastomosing vascular structures and scattered mononuclear inflammatory cells are detected intermingled with the tumoral lesion (HE, ×27.3)

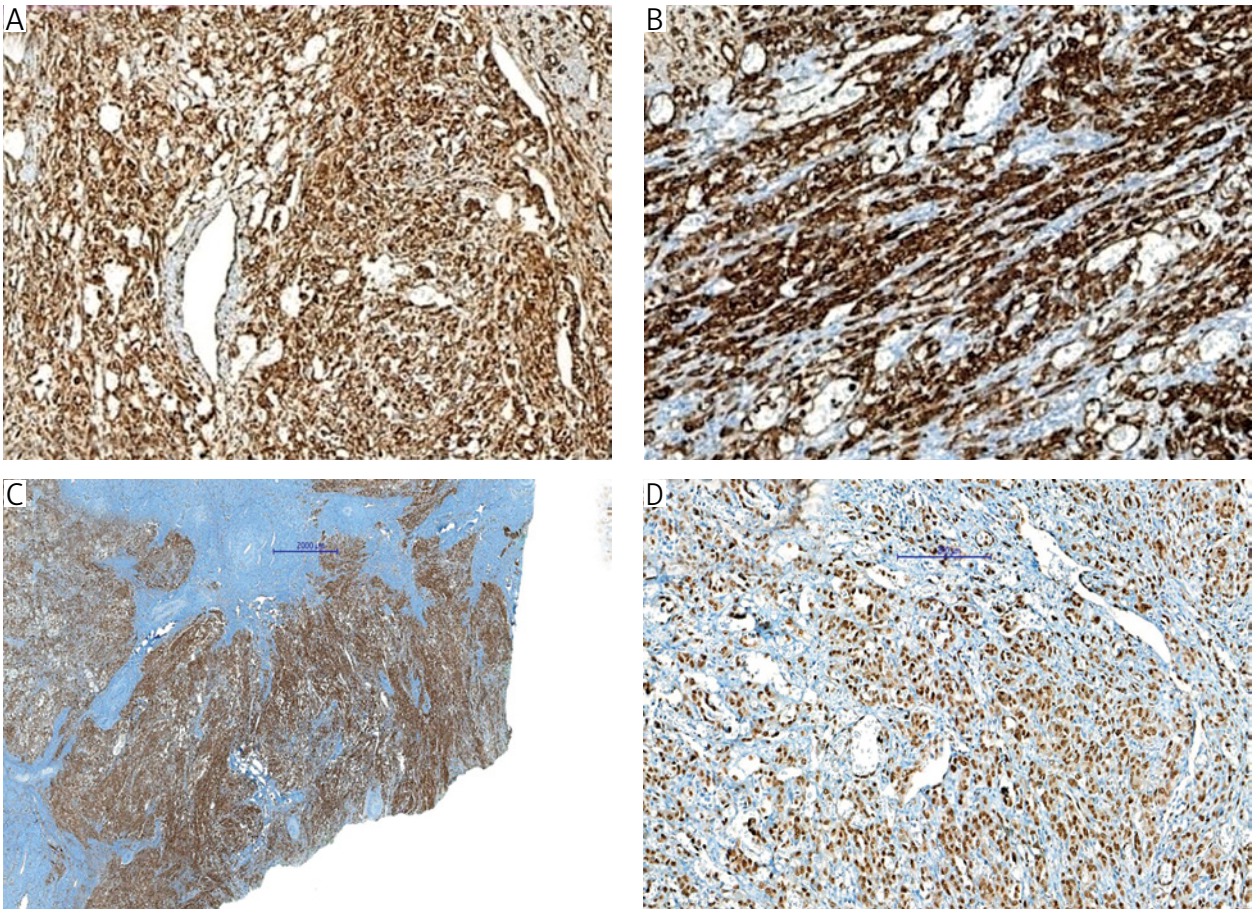

Fig. 4. A-D) Tumoral cells were diffuse positive with Vimentin (×12.3), HMW+LMW-CK (×12.2), CD31 (×0.8), and ERG (×10.8), respectively

lymphadenectomy, paraaortic lymphadenectomy and implant excision from serosa of the stomach.

In gross examinations, a tumoral lesion with a longest diameter of 35 mm, infiltrating the lower uterine segment and the outer 1/2 of the myometrium, with a cream-white cross-sectional surface and bleeding areas, was observed (Fig. 1). Tumoral implants are observed in bilateral ovaries; tubas and appendix were detected as tumor-free.

Histologically, a high grade tumoral lesion with epithelioid morphology was observed. Tumor was consisting of large epithelioid and polygonal cells forming solid structures. Hemorrhage, nuclear atypia, frequent mitosis, and occasional anastomosing vascular structures were observed (Figs. 2 and 3). Widespread lymphovascular invasion was detected in HE sections. Tumoral cells were diffuse positive with Vimentin (Fig. 4A), HMW+L-MW-CK (Fig. 4B), CD31 (Fig. 4C), and ERG (Fig. 4D). In addition, positive expression was observed in tumoral cells with FLI1 and CD34, while HHV-8, EMA, PAX8, Synaptophysin, Chromogranin A, CD56 were negative. No metastatic tumor was found in 32 dissected pelvic and paraaortic lymph nodes. In the light of these findings, the patient was diagnosed as primary epithelioid angiosarcoma of endometrium after excluding the body parts with detailed clinical and radiological examination that angiosarcomas can occur.

After 3 courses of adjuvant carboplatin and paclitaxel chemotherapy, the patient relapsed 4 months later. She received 3 more courses of the same chemotherapy protocol, and 6 months have passed since the last treatment and no recurrence was detected.

Discussion

Soft tissue sarcomas account for approximately 1% of all malignancies in adults, of which 1% are angiosarcomas [8, 9]. Although it can be detected in any part of the body; approximately 50% of all angiosarcomas are observed in the skin, breast and soft tissues [2]. Angiosarcomas may give symptoms in line with their anatomical localizations, endometrial angiosarcomas often present with vaginal bleeding in postmenopausal women, as in the current case. Radiology is helpful in identifying uterine tumors, but distinguishing angiosarcomas from other uterine tumors may not be feasible with imaging alone [10]. Thus, histopathological studies are needed to confirm the accurate diagnosis.

As observed in our case, anastomosing vascular structures, tumoral cells with rounded nuclei, prominent nucleoli and eosinophilic cytoplasm, nuclear pleomorphism, and frequent mitosis are frequently observed features in these tumors [2, 10]. However, the histopathological appearance of angiosarcomas can vary, and differential diagnosis might be difficult due to mimickers such as benign proliferative lesions or inflammatory pathologies. Therefore, further immunohistochemical and/or molecular examinations are very useful for the diagnosis. CD31 is the most specific marker for this tumor, ERG and cytokeratin positivity are also frequently observed [10, 11]. Since the expression pattern of CD34 in angiosarcomas is variable [11], this marker can be positive or negative, it should be kept in mind which its positivity does not make a definitive diagnosis, and negativity does not rule out this diagnosis. In our case, morphological findings and CD31, ERG, FLI1 and CD34 positivity supported the diagnosis. In addition, Suzuki et al. identified three specific breakpoints in uterine angiosarcoma, and it was argued that the presence of these molecular alterations would support the diagnosis in challenging cases [12].

Paclitaxel is the most commonly used chemotherapeutic agent for angiosarcoma and there are studies indicating that patients benefit from this treatment [13, 14]. Chemotherapy regimen including paclitaxel was applied to the patient, but despite the recurrence, the patient is still alive after initial diagnosis. Additionally, in the review, which is the most detailed study on this subject, it was stated that when grouping according to the long diameter of the tumor, the survivals changed significantly and the best survival results were in tumors between 1-5 cm ($p = 0.016$) [1]. The patient's 14-month survival was thought to be related to the correct treatment scheme and relatively small tumor (35 mm) size.

In conclusion, primary epithelioid angiosarcoma of endometrium is an extremely rare entity performed in the literature with scattered case reports that should be aware of. For this reason, in the presence of histomorphological and immunohistochemical findings other than the more common tumors in the endometrium, this tumor and its differential diagnosis should be considered.

The authors declare no conflict of interest.

References

1. Deb PQ, Weiss RE, Heller DS. Angiosarcoma of the Uterus: A Systematic Review. Int J Gynecol Pathol 2022; 41: 496-502.
2. Hara T, Miyoshi A, Kamei Y, et al. Epithelioid Angiosarcoma Arising from a Huge Leiomyoma: A Case Report and a Literature Review. Case Rep Obstet Gynecol 2018; 2018: 7591769.
3. Antonescu C. Malignant vascular tumors – an update. Mod Pathol 2014; 27 Suppl 1: S30-S38.
4. Witkin GB, Askin FB, Geratz JD, Reddick RL. Angiosarcoma of the uterus: a light microscopic, immunohistochemical, and ultrastructural study. Int J Gynecol Pathol 1987; 6: 176-184.
5. Richer M, Barkati M, Meunier C, et al. Vaginal epithelioid angiosarcoma: a potential pitfall in gynecologic pathology. J Low Genit Tract Dis 2014; 18: E38-E42.

6. Yaqoob N, Nemenqani D, Khoja H, et al. Ovarian angiosarcoma: a case report and review of the literature. J Med Case Rep 2014; 8: 47.
7. Cardinale L, Mirra M, Galli C, et al. Angiosarcoma of the uterus: report of 2 new cases with deviant clinicopathologic features and review of the literature. Ann Diagn Pathol 2008; 12: 217-221.
8. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin 2017; 67: 7-30.
9. Goldblum JR, Folpe AL, Weiss SW. Enzinger and Weiss's soft tissue tumors. Seventh edition. ed. Elsevier, Amsterdam 2019.
10. Majeed NK, Adley B, Guzman G, Mehta V. Primary Epithelioid Angiosarcoma of the Uterus: A Rare Tumor with Very Aggressive Behavior. Case Rep Pathol 2020; 2020: 5461782.
11. Schammel DP, Tavassoli FA. Uterine angiosarcomas: a morphologic and immunohistochemical study of four cases. Am J Surg Pathol 1998; 22: 246-250.
12. Suzuki S, Tanioka F, Minato H, et al. Breakages at YWHAE, FAM22A, and FAM22B loci in uterine angiosarcoma: a case report with immunohistochemical and genetic analysis. Pathol Res Pract 2014; 210: 130-134.
13. Fata F, O'Reilly E, Ilson D, et al. Paclitaxel in the treatment of patients with angiosarcoma of the scalp or face. Cancer 1999; 86: 2034-2037.
14. Fury MG, Antonescu CR, Van Zee KJ, et al. A 14-year retrospective review of angiosarcoma: clinical characteristics, prognostic factors, and treatment outcomes with surgery and chemotherapy. Cancer J 2005; 11: 241-247.

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