Primary uterine angiosarcoma: A case report in China with the literature review

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ABSTRACT

Primary uterine angiosarcoma is a very rare malignant tumor in the female genital tract and only 23 cases have been previously reported in the literature. It is often clinically misrecognized as another disease due to its low incidence. In this report, we present a new case of a 78-year-old woman diagnosed on histopathologic observation and immunohistochemical staining. Additionally, available studies are collected and reviewed to summarize the clinical and pathological characteristics of primary uterine angiosarcoma to remind gynecologists and pathologists of this rare disease when they encounter such cases.

KEY WORDS: Angiosarcoma, ERG, immunohistochemistry, uterine

INTRODUCTION

Angiosarcoma is a malignant vascular neoplasm that commonly involves the skin or soft tissues but rarely involves the female genital tract.[1] Only 23 cases of uterine angiosarcoma have been reported in the literature.[2-20] The most common symptoms such as irregular vaginal bleeding are not specific for differentiating angiosarcoma from other gynecological diseases. Sufficient clinicopathological data are not available because of its rarity, and the oncogenesis remains unclear. Here, we describe one new case of primary uterine angiosarcoma and perform a detailed literature review to raise awareness of such rare tumor in the female genital tract.

CASE HISTORY

A 78-year-old woman was evaluated in our gynecology department for irregular vaginal bleeding and previous curettage biopsies performed at a local hospital were negative within the past 2 years. The pelvic ultrasound and computed tomography scan revealed the thickened endometrium (0.7 cm) and a mass in the uterine corpus measuring 3.2 cm × 2.9 cm × 2.8 cm. The laboratory examination showed normal levels of tumor biomarkers including CA-125, CA19-9, and α-fetoprotein. The subsequent curettage biopsy indicated suspicion of malignancy, and a total hysterectomy with bilateral salpingo-oophorectomy was performed.

Grossly, the uterus measured 9 cm × 6 cm × 5 cm and the cavity was full of necrotic tumor tissue and hemorrhage, showing a spongy appearance [Figure 1a]. Histological examination revealed diffuse infiltration of malignant tumor cells in the endometrium, myometrium, and endocervical stroma. The bilateral ovaries and fallopian tubes were negative. Most of the tumor cells were spindle with marked atypia. In some areas, vascular differentiation and active mitotic figures could be seen [Figure 1b]. The tumor cells showed strong and diffuse positivity for CD31 and factor VIII-related antigen [Figure 2]; however, CD34 staining was negative. Moreover, positive staining was also detected for vimentin, Fli-1, erythroblast transformation-specific–related gene (ERG), and cyclin D1 [Figure 2]. Staining for the other markers including CD10, desmin, SMA, caldesmon, ER, PR, Pan-Ck and HMB45 was negative. Based on histology and immunohistochemistry, a diagnosis of uterine angiosarcoma was confirmed.

The patient received subsequent chemotherapy and is now alive 42 months after surgery. The CT scan revealed no evidence of recurrence.

DISCUSSION

Angiosarcoma is an aggressive malignant neoplasm of endothelial origin that is very rarely found in the uterus.[16] The clinical characteristics of 23 uterine...
angiosarcoma cases in the available literature are summarized in Table 1. The mean age of the patients was 67 years old (range, 17-81 years old), and the most common symptom was abnormal vaginal bleeding followed by a pelvic mass. Clinically, angiosarcoma might be misrecognized as many other kinds of gynecological diseases because of its uncommon location, low incidence and non-characteristic clinical manifestations. An ultrasound and CT scan may be helpful for revealing the uterine mass, but the final diagnosis depends on pathology. Even so, an accurate diagnosis was not obtained in some cases, such as the one we presented here, until several repeated biopsies or a hysterectomy was performed.

Microscopically, tumors are composed of spindle or epithelioid cells with prominent nuclear atypia. Tumor cells often show obscure vascular differentiation with cytoplasmic vacuolation containing erythrocytes, which should serve as a useful clue for pathologists. However, diagnosis can be truly challenging when such a clue is lacking. Immunohistochemical staining plays a significant supporting role in diagnosis and differential diagnosis. Several endothelial markers have been used for evaluating the diagnosis of uterine angiosarcoma in the past 20 years. Of all the markers, CD31 seems to be more sensitive than CD34,[16] and the lymphatic endothelial marker D2-40 is also sometimes used because lymphatic differentiation can be observed in angiosarcoma.[17] In the case presented here, immunohistochemical staining for CD31 and Factor VIII-related antigen was positive and that for CD34 and D2-40 was negative, which indicated that the tumor should be classified as vascular-type according to the cutaneous angiosarcoma subtyping criteria. The main differential diagnoses are leiomyosarcoma and endometrial stromal sarcoma, both of which are more common than angiosarcoma in the uterus, and the negative expression of some other markers including desmin, caldesmon, CD10, and HMB45 can be helpful to exclude the possibility of such kinds of tumors.

ERG, a member of the erythroblast transformation specific factor family, is a new sensitive marker of endothelial differentiation. ERG has been reported to be used in the cytological diagnosis of angiosarcoma,[21] and it has also been regarded as a specific and sensitive histologically diagnostic marker in hepatic angiosarcoma.[22] However, previously, only Hara et al. had reported ERG positive staining in one case of uterine angiosarcoma arising from a leiomyoma,[19] and our study documented a new uterine case with ERG expression. Cyclin D1 was also found to be expressed in our case, and it suggested active proliferation and possible genetic alterations that had been demonstrated in high-grade endometrial stromal sarcoma. It was reported by Suzuki et al.[16] that the breakages at YWHAE, FAM22A, and FAM22B loci were detected in a case of uterine angiosarcoma, but no YWHAE-FAM22 fusion gene was observed. Neither breakage nor fusion of these genes was detected in another case by Liu et al.[17] These genetic abnormalities may indicate the oncogenesis; however, more cases are needed to evaluate the relationship between such alterations and oncogenesis of uterine angiosarcoma.

The clinical history of angiosarcoma is usually rapid and results in a poor outcome.[1] Extrafascial total hysterectomy and bilateral salpingo-oophorectomy are recommended for the first part of primary treatment in most cases. For the resection of adnexa, the patient’s age and reproductive desire should be comprehensively taken into consideration. Pelvic lymphadenectomy has not
been introduced into standard treatment because lymph node involvement is typically negative even in the case with the presence of extraterine spread. Adjuvant chemotherapy and radiotherapy may be of benefit to most patients; however, the effect seems limited. Individualized therapy is recommended. Our case had a good quality of life with no evidence of recurrence possibly due to the lack of extraterine spread and the negative surgical resection margins.

In summary, uterine angiosarcoma is a very rare malignant mesenchymal tumor in the female genital tract, and both gynecologists and pathologists should bear it in mind when they encounter these uncommon cases.

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Conflicts of interest
There are no conflicts of interest.

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Table 1: Summary of clinical data of uterine angiosarcoma in English literature

| Case no. | Author | Age (year) | Symptom | Tumor size (cm) | Therapy | Follow-up |
|---------|--------|-----------|---------|----------------|---------|-----------|
| 1 | Ehrmann and Griffiths | 17 | Vaginal bleeding | 9 | Surgery+CT+RT | DOD, 84 month |
| 2 | Mendez et al | 59 | Vaginal bleeding | No information | Surgery | DOD, 2.5 month |
| 3 | Ongkasuwana et al | 70 | Weight loss | 7×7 | Surgery+RT | NED, 5 month |
| 4 | Witkin et al | 71 | Vaginal bleeding | No information | Surgery+RT | Recurrence, 6 month |
| 5 | Milne et al | 62 | Vaginal bleeding | No information | Surgery | DOD, 6 month |
| 6 | Quinonez et al | 65 | Vaginal bleeding | 5×4 | Surgery+CT+RT | NED, 48 month |
| 7 | Lack et al | 71 | Vaginal bleeding | No information | Surgery+RT | DOD, 2 month |
| 8 | Tallini et al | 56 | Vaginal bleeding | 30×24 | Surgery+CT | DOD, 7 month |
| 9 | Drachenberg et al | 58 | Vaginal bleeding | No information | Surgery+CT+RT | DOD, 2 month |
| 10 | Schammel and Tavassoli | 49 | Vaginal mass | 29×29 | Surgery | DOD, 3 month |
| 11 | Schammel and Tavassoli | 58 | Vaginal bleeding | 12 | Surgery+CT+RT | DOD, 2 month |
| 12 | Schammel and Tavassoli | 70 | Vaginal bleeding | No information | Surgery | NED, 37 month |
| 13 | Schammel and Tavassoli | 75 | Vaginal bleeding | 6×6×5 | Surgery | DOD, 7 month |
| 14 | Konishi et al | 62 | Anemia | No information | Surgery+CT | NED, 2 month |
| 15 | Cardinale et al | 81 | Lower abdominal pain | No information | Surgery | DOD, 6 month |
| 16 | Cardinale et al | 35 | Shortness of breath | 25 | Surgery | No information |
| 17 | Owalaye et al | 54 | Enlarged uterus | 3 | Surgery+CT | NED, 12 month |
| 18 | Hwang et al | 61 | Vaginal bleeding/abdominal pain | 12×10×9 | Surgery+RT | No information |
| 19 | Suzuki et al | 62 | Vaginal bleeding | 7.5×5.5×3.5 | Surgery+CT | Recurrence, 50 month |
| 20 | Liu et al | 56 | Pelvic mass/anemia | 11×8×7 | Surgery | No information |
| 21 | Strickland et al | 67 | Fatigue/weight loss | 21×18×15 | Surgery | DOD, 2 month |
| 22 | Hara T et al | 48 | Abdominal fullness/weight loss | 28×23 | Surgery+CT | NED, 10 month |
| 23 | Gandhi et al | 41 | Uterine bleeding/back pain | 4.5 | Surgery+CT | DOD, 4 month |

CT: Chemotherapy. RT: Radiotherapy. DOD: Dead of disease. NED: No evidence of disease.
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