Journal of Women's Health, Issues & Care

CASE REPORT A SCITECHNOL JOURNAL

An Asymptomatic Case of Mullerian Adenosarcoma following Tamoxifen Use

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Abstract

Mullerian adenosarcomas are rare: approximately 200 cases have been reported. This tumor usually occurs in peri/postmenopausal women and asymptomatic case is rarely reported. Use of tamoxifen has been considered to have some association with the occurrence of this tumor. We here report a woman after tamoxifen administration who suffered Mullerian adenosarcoma of the uterine body, but was asymptomatic. We wish to emphasize the importance of recognizing this tumor for both gynecologists and pathologists. A 62-year-old woman was incidentally diagnosed with a possibly malignant uterine mass on PET scan. She had a history of right breast cancer 9-year back, for which surgery+chemotherapy was done. Tamoxifen was administered for 5 years after the chemotherapy. PET scan for follow up revealed heterogeneously mass in uterine body with no lymph swelling. Ultrasound revealed a large heteroechoic mass in the uterine body. Total abdominal hysterectomy with bilateral salphingo-oophoectomy was done. Histological examination confirmed the diagnosis of mullerian adenosarcoma. Post-operative course was uneventful and radiotherapy is planned. Uterine adenosarcoma has variable survival rate depending on its sarcomatous component, lympho-invasion, and myoinvasion. This patient showed no lymph invasion and less myoinvasion, which may account for her good prognosis. Physicians should be aware that this tumor can occur in patients with history of tamoxifen use.

Keywords

Post menopausal; Mullerian adenosarcoma; Asymptomatic; Tamoxifen

Introduction

Mullerian adenosarcoma is a rare tumor which can occur in any part of the female genital tract [1]. The most common site is the uterine endometrium, and these account for 8% of all uterine sarcomas [2]. Till now only 200 cases has been reported since its 1st description by Clement and Sully in 1974 [3]. It is an uncommon variant of mullerian mixed tumor of the uterus characterized by a benign, but occasionally atypical epithelial component and a sarcomatous stromal component, which is usually low-grade [3]. It has been described as being midway along the spectrum between benign adenofibromas and carcinosarcomas [1]. Most commonly it is seen in perimenopausal women. Various presentations include irregular menstrual bleeding, painless mass in the introitus, postmenopausal bleeding, urinary retention, postcoital bleeding and vagina discharge [4]. The molecular pathogenesis of these tumors is still unclear. Some studies suggest that the use of tamoxifen may have a role in them pathogenesis of adenosarcoma [5,6].

Case Report

A 62 year old woman was accidently diagnosed with a possibly malignant uterine mass on PET scan, for which she was referred to our OPD. She was para3+3, all vaginal deliveries with last child birth 38 years back. She attained menopause 10 years back. She had a history of right sided breast cancer 9 years back, for which modified radical mastectomy was done and chemotherapy was given. She had taken Tamoxifen for 5 years. She was on follow up for initial 5 years during which there was no complaints. But she did not come for follow up after that. When she attended the Oncology hospital after 9 years, PET scan was done for follow up which showed a heterogeneously enhancing hypermetabolic mass of 5 × 5 × 6 cm in uterine body with no lymphadenopathy or any other suspected lesions. But the patient was asymptomatic. She was a known case of type 2 DM for 5 years on OHA. She had a history of cholecystectomy 5 years back.

Clinically a 16 weeks size uterus was present, with restricted mobility. Cervix and vagina appeared normal on per speculum and PV examination. She was diagnosed with atrial flutter and valvular dysfunction on evaluation, for which cardiology consultation was taken. Ultrasound showed a large, complex heteroechoic mass in fundobody region of uterus (Figure 1). Total abdominal hysterectomy with bilateral salpingoophoectomy was done. No pelvic lymph nodes were palpable. Cut section of uterus showed a 6 × 8 cm firm mass arising from fundal area, projecting into the endometrial cavity (Figure 2). HPE of the mass showed mullerian adenosarcoma with no myoinvasion (Figures 3 and 4). Post operative period was uneventful. The patient is now planned for radiotherapy.

Discussion

Till date a few asymptomatic cases have been reported. Typically it presents with a uterine mass or polyp with vaginal bleeding or discharge [3]. Correct histopathological diagnosis and characterization of mullerian adenosarcoma is the cornerstone of management and prognostication. Unfavourable prognostic factors are sarcomatous overgrowth, deep myometrial invasion, presence of heterologous elements and extrauterine spread [8]. Various reports have reported various management options as there no established protocols of treatment and no schema for staging the lesion (Figure 1). Treatments given have included hysterectomy, with or without bilateral salpingo-oophorectomy, with or without pelvic lymph node clearance and with or without adjuvant chemo- and/ or radiotherapy [1,8]. Most studies with total abdominal hysterectomy and bilateral salpingo-oophorectomy with/without pelvic lymphadenectomy have shown a 69% disease free survival for periods ranging between 3 months and 13 years [8]. Recurrence rate has been about 10% of cases and these have mostly presented with pelvic metastasis. The prognosis in our patient is considered to be better in view of no myoinvasion or lymphovascular invasion.

There is no optimal adjuvant or systemic treatment strategy. Tanner et al. recommend standard sarcoma regimens such as doxorubicin,

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Received: June 12, 2020 **Accepted:** July 22, 2020 **Published:** July 27, 2020

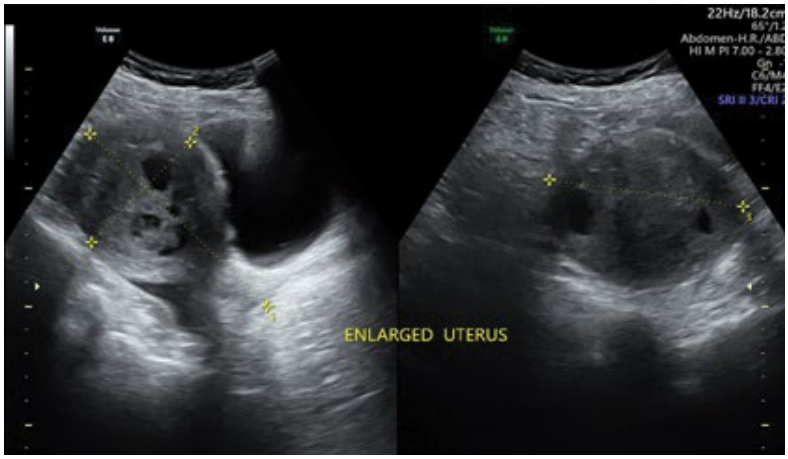

Figure 1: Ultrasound showing the heterogeneous lesion in uterus.

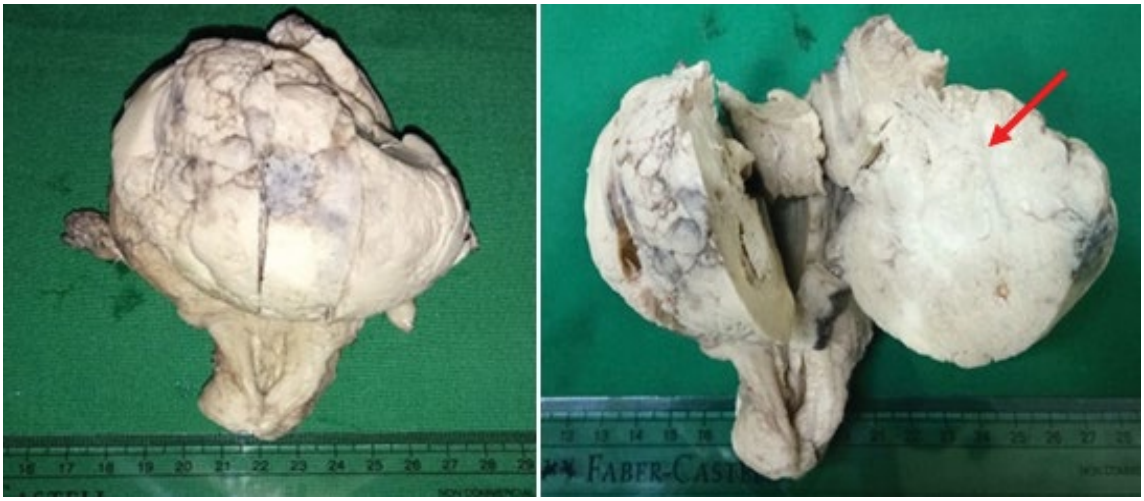

Figure 2: Intact uterus and cut section showing the mass projecting from fundal area (red arrow).

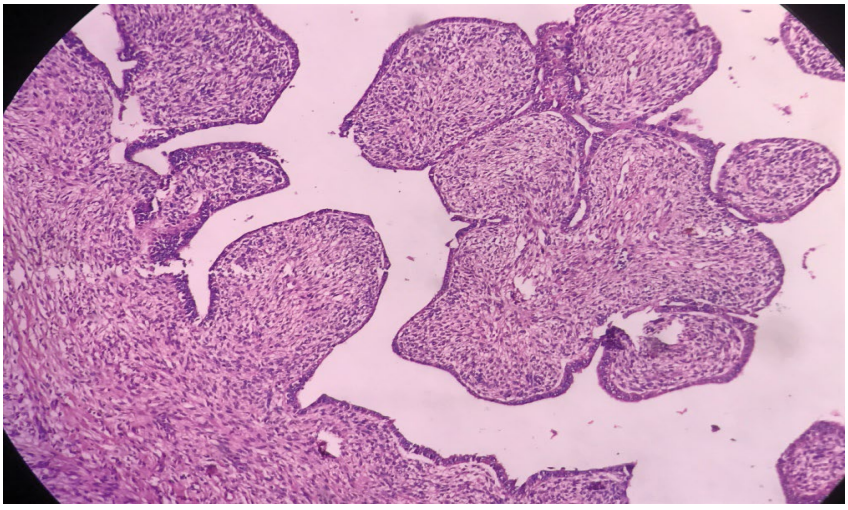

Figure 3: Low power view showing epithelial component and stromal hypercellularity (like phyllodes).

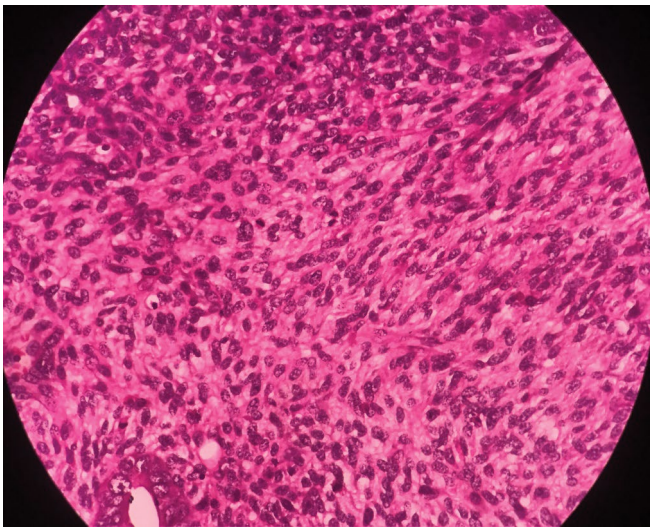

Figure 4: High power view showing stromal hypercellularity, nuclear atypia and 3 mitotic figures (red). Epithelium is non malignant (yellow).

ifosfamide, or gemcitabine/docetaxel to patients with measurable adenosarcoma with sarcomatous overgrowth [9]. Radiotherapy has also given by some. This patient is also planned for radiotherapy.

It is known that Tamoxifen is associated with endometrial hyperplasia and endometrial carcinoma. However till date around 17 cases of mullerian adenosarcoma has been described after tamoxifen use. In our case also, the patient had taken 5 years tamoxifen, but did not come for follow up in between. Clement et al. [10] described 6 cases of uterine adenosarcomas associated with tamoxifen therapy. Studies have shown that endometria of women receiving tamoxifen express the angiogenic growth factor adrenomedullin, postulating the mechanism by which tamoxifen results in endometrial hyperplasia [11] (Figure 2).

Another study using in vitro model, found an increase in the proliferative activity due to tamoxifen in the endometrial stromal cells [12]. A study on tamoxifen-treated breast cancer patients and controls observed an antiproliferative effect of tamoxifen on the epithelium and a growth-promoting effect on the stroma, suggesting that the endometrial proliferation is mediated by the stromal component [13], thus leading to adenosarcoma (Figure 3).

Though a cause-effect relationship cannot be demonstrated between tamoxifen and these tumors and exact pathogenesis is not known, it has been seen in many reports that tamoxifen is related to these tumors. As these tumors are rare, further research and reports are needed to know the pathogenesis (Figure 4).

Conclusion

Uterine adenosarcoma is a histopathological diagnosis; thus it is important for gynaecologists to be aware of its entity and pathologists to be aware of its morphology. It has variable survival rate depending on its sarcomatous component and myoinvasion. Considering the rarity of these tumors, it seems that the association of tamoxifen therapy with mesenchymal neoplasm is higher than expected. So patients with tamoxifen use should be followed up well.

Conflict of Interest

There is no conflict of interest in this study.

References

1. McCluggage WG (2010) Mullerian adenosarcoma of the female genital tract. Adv Anat Pathol 17: 122-129.
2. Patrelli TS, Gizzo S, Di Gangi S, Guidi G, Rondinelli M, et al. (2011) Cervical Mullerian adenosarcoma with heterologous sarcomatous overgrowth: a fourth case and review of literature. BMC Cancer 11: 236.
3. Clement PB, Scully RE (1974) Mullerian adenosarcoma of the uterus. A clinicopathologic analysis of ten cases of a distinctive type ofmullerian mixed tumor. Cancer 34: 1138-1149.
4. Fleming NA, Hopkins L, de Nanassy J, Senterman M, Black AY (2009) Mullerian adenosarcoma of the cervix in a 10-year old girl: case report and review of the literature. J Pediatr Adolesc Gynecol 22: e45-e51.
5. Arici DS, Aker H, Yildiz E, Tasyurt A (2000) Mullerian adenosarcoma of the uterus associated with tamoxifen therapy. Arch Gynecol Obstet 264: 105-107.
6. Jessop FA, Roberts PF (2000) Mullerian adenosarcoma of the uterus in association with tamoxifen therapy. Histopathology 36: 91-92.
7. Sinha A, Phukan JP, Sengupta S, Guha P (2012) Mullerian adenosarcoma of uterus with sarcomatous overgrowth and heterologous component associated with stromal deposit in omentum: a case report and reviewof the literature. Case Rep Med 2012: 1-4.
8. Zaloudek CJ, Norris HJ (1981) Adenofibroma and adenosarcoma of the uterus: a clinicopathologic study of 35 cases. Cancer 48: 354-366.
9. Tanner EJ, Toussaint T, Leitao MM, Hensley ML, Soslow RA, et al. (2013) Management of uterine adenosarcomas with and without sarcomatous overgrowth. Gynecol Oncol 129: 140-144.
10. Clement PB, Oliva E, Young RH (1996) Mullerian adenosarcoma of the uterine corpus associated with tamoxifen therapy: a report of six cases and a review of tamoxifen-associated endometrial lesions. Int J Gynecol Pathol 15: 222-229.
11. Zhao Y, Hague S, Manek S, Zhang L, Bicknell R, et al. (1998) PCR display identifies tamoxifen induction of the novel angiogenic factor adrenomedullin by a non estrogenic mechanism in the human endometrium. Oncogene 16: 409-415.

12. Periwal SB, Farooq A, Bhargava VL, Bhatla N, Vij U, et al. (1995) Tamoxifen increases the proliferation of human endometrial stromal cells in vitro. A model for evaluation of endometrial hyperplasia. Indian J Exp Biol 33: 977-979.

13. Decensi A, Fontana V, Bruno S, Gustavino C, Gatteschi B, et al. (1996) Effect of tamoxifen on endometrial proliferation. J Clin Oncol 14: 434-440.

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