

Case Report

Uterine adenosarcoma with ovarian sex cord-like differentiation: A case report and review of the literature

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Abstract

Objectives: To determine the prognosis of uterine adenosarcoma with ovarian sex cord like-differentiation after treatment and to review the literature.

Case Report: A 47-year-old premenopausal unmarried woman presented with irregular menstrual bleeding and uterine mass. Sonographic examination, suggested two uterine fibroids located in the uterine fundus and cervix measuring 4×3 cm and 3×3 cm, respectively. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed and the histopathology report confirmed the diagnosis of uterine adenosarcoma with ovarian sex cord like-differentiation. The patient received neither chemotherapy nor other adjuvant therapy because the tumor had low malignant potential, and the extent of myometrial invasion was less than half of the whole myometrium. The patient had an uneventful recovery, and no recurrence was detected for 2 years in the follow-up period.

Conclusion: Uterine adenosarcomas mostly have relatively low malignant potential. Surgery is the optimal standard treatment for patients. Although there is not enough data in the present literature, benign epithelial differentiations, such as sex cord-like elements may reflect the behaviour of the tumour and shows the tendency to have a benign course in most of cases.

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Keywords: Adenosarcoma; Sarcoma; Sex cord-like differentiation

Introduction

Uterine adenosarcomas are an uncommon group of stromal mullerian neoplasms characterized by admixture of benign, however occasionally atypical glandular epithelium and low grade sarcoma frequently of endometrial stromal type [1]. Adenosarcoma was first described by Clement and Scully in 1974. Following this, the same authors coined the term “mullerian adenosarcoma with sex cord-like elements” (MAS-CEs) to encompass all uterine adenosarcoma with sex cord-like

differentiation that are closer in histogenesis to ovarian sex cord stromal tumor [2]. Sex cord differentiation has been reported to be more common in endometrial stromal tumors [3–5], however, rarely reported in mullerian adenosarcomas [2,6,7]. Adenosarcomas mostly have relatively low malignant potential. Recurrences, which occur in approximately 20–30% of cases, may be associated with high grade sarcomatous overgrowth and deep myometrial invasion [1].

Because of the small number of tumors; optimal therapy, the prognostic factors indicating recurrence or survival of the patients are still unclear. To our knowledge, only 11 cases of adenosarcoma of the uterine corpus and cervix with ovarian sex cord-like differentiation are reported in English literature. We describe a case of uterine adenosarcoma with ovarian sex cord-like differentiation presenting as irregular menstrual bleeding

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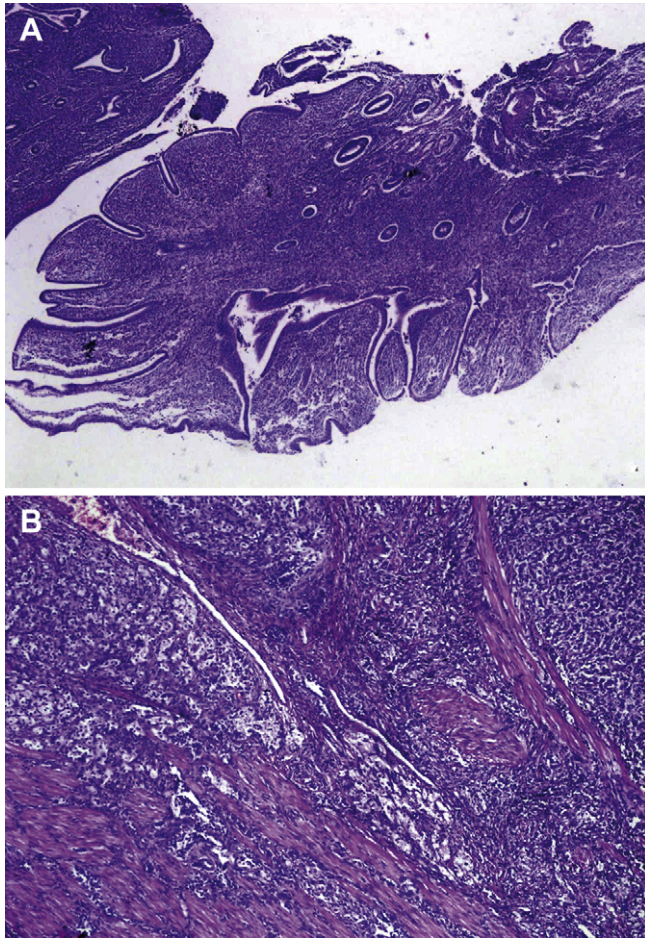


Fig. 1. (A) Benign appearing glands in the sarcomatous stroma. (B) SCEs appear as irregular nests and trabeculae and located especially in myometrial invasion areas (Hematoxylin and eosin staining).

in a premenopausal unmarried woman, and review its clinical, histopathologic and immunohistochemical features.

Case report

A 47-year-old unmarried woman presented with a 6-month history of irregular heavy menstrual bleeding. Her medical condition was unremarkable except antiepileptic drug use for nearly 40 years. Sonographic examination suggested two uterine fibroids located in the uterine fundus and cervix

measuring 4×3 cm and 3×3 cm, respectively. Fractional curettage was refused by the patient because of her virginity. A subsequent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH with BSO) was performed.

Macroscopically, a large cervical polyp measuring $40 \times 30 \times 10$ mm was detected, and an intramural tumor, with irregular margins, yellow to tan in color in the cut surfaces, roughly 40×40 mm size was observed in the uterus. The tumor was invading the inner half of the myometrium and partially protruding into the uterine cavity. There was no necrosis or hemorrhagia within the tumor. Microscopic examination revealed a biphasic tumor composed of neoplastic glands which were lined by benign appearing endometrioid epithelium and low grade homologous mesenchymal component which was formed by endometrial stromal sarcoma. The polypoid part of the tumor, which was protruding into endometrial cavity, showed a leaf-like appearance at the surface (Fig. 1A). The stromal cells were spindle-shaped and slightly atypical, but periglandular stromal cuffing was not obvious. The mitotic count was 1 per 10 high power field (HPF). The sarcomatous stroma also showed a pattern reminiscent of an ovarian sex cord stromal tumor; the tumor cells were arranged in bundles, nests and tubules (Fig. 1B). Additionally there were numerous scattered sertoli-like foam cells with abundant clear to foamy cytoplasm. This pattern constituted 20% of the tumor volume and was located mainly in the myometrial invasion areas. The adjacent endometrium had a proliferative pattern as well, with focal simple hyperplasia and endometriosis externa was noted within the ovary.

Immunostaining techniques were performed for inhibin, calretinin, CD10, desmin, pancytokeratin (PCK) and epithelial membrane antigen (EMA). Endometrial stromal component was stained focally and was weak in intensity for CD10 and PCK. Desmin was typically positive in the myometrium while EMA and PCK stained glandular epithelium diffusely. Additionally, the sex cord cell and foam cell components showed focal immunoreactivity for inhibin, calretinin and CD10 (Fig. 2).

Based on the histopathological and immunohistochemical findings, the diagnosis was uterine adenosarcoma with ovarian sex cord-like differentiation, and the patient received neither chemotherapy nor other adjuvant therapy because the tumor had low malignant potential, and the extent of myometrial invasion was less than half of the whole myometrium. The patient had an uneventful recovery, and no recurrence was detected for 2 years in the follow-up period.

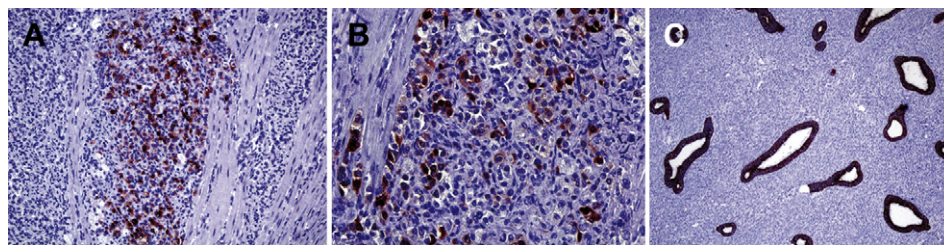


Fig. 2. Sex cord and foam cell components showed immunoreactivity for CD10 (A) and calretinin (B). Pancytokeratin was strongly positive for glandular structures (C).

Discussion

Uterine adenosarcomas represent for only 8% of all uterine sarcomas, which comprise 1–3% of all gynecological malignant tumors [1,8]. They mostly originate from the endometrium in 87% of patients, followed by the ovary, cervix, myometrium and pelvis. Two thirds of patients with this tumor are postmenopausal women, but young patients are seldom observed especially with cases of cervical adenosarcoma [8].

Adenosarcomas are composed exclusively of homologous mesenchymal elements such as fibroblasts and smooth muscle, but 10–15% of the tumors have heterologous elements like cartilage, bone and striated muscle [9]. However, unusual stromal differentiations such as sex-cord like elements (SCEs), identical to those seen in endometrial stromal neoplasms (UTROSCT) may rarely be present within the malignant stroma of adenosarcomas (MASCEs). The biologic behavior of MASCEs is likely to be predicted by the proportion and appearance of the stromal cell component. Therefore, the predominant pattern of SCEs shows the tendency to have a benign course. The sex cord-like differentiations have been reported in one cervical and 10 endometrial adenosarcoma cases (Table 1) [2,6,7]. Clinically, all of the reported cases presented with abnormal uterine bleeding. In the first series of eight cases, SCEs ranged from several microscopic foci (<5% of the tumor) to approximately 50% of the tumors [2]. In contrast, in another case report of two cases, uterine adenosarcoma was massively overgrown by SCEs that constituted more than 75% of the tumors [7]. In the present case SCEs were multifocal and accounted for 20% of the tumor volume.

In view of the similarity in tumor biology, treatment options are similar to endometrial stromal sarcoma [10], therefore standard treatment is TAH with BSO. In addition to this approach, the other step of the definitive staging surgery, which comprises pelvic and paraaortic lymph node dissection is deterministic in the new staging system that has been recently designed by the International Federation of Gynecology and

Obstetrics (2009). However, estrogen and/or progesterone receptors are frequently expressed in most low-grade stromal sarcomas [9], this may suggest a probable susceptibility of the mullarian adenosarcoma to estrogen, thus questioning the safety of ovarian preservation.

Optimal therapy and the role of adjuvant treatment are not clear and have not been fully evaluated in adenosarcomas. To perform TAH with BSO and pelvic lymph node sampling for stage I disease should be appropriate. Women with superficial myometrial invasion probably do not require adjuvant therapy. But those with deep invasion and a high degree of sarcomatous stromal overgrowth have a greater chance of recurrence and may benefit from pelvic radiation or chemotherapy [8]. Baker et al. [10] concluded on the basis of a series of six adenosarcoma cases that prevention of recurrence cannot be achieved by intra- or extracavity radiotherapy. In a recent study by Han et al. [11], there were nine patients with adenosarcoma, seven of these were stage I and two were stage III. Seven patients were treated by a single agent or combination chemotherapy (cisplatin, pharomubicin, ifosfamid) with or without hormone therapy after surgery. The remaining two patients were treated only by surgery. Radiotherapy in addition to chemotherapy was applied to only one of two stage III patients. Five of these seven patients who received chemotherapy were alive and well with no evidence of recurrence, while one stage I patient and one stage III patient developed a recurrent tumor and later died 1.2 years after surgery.

Interestingly, patients in this review had mostly noninvasive or superficial invasion and no deep invasion or sarcomatous overgrowth; hence, none of them received adjuvant chemo- or radiotherapy. Only one patient (Case 3), treated by curettage and radiation, had persistent intracavitary tumor at 7 months and died of an unrelated illness at 16 months. Another patient (Case 5) was initially treated by polypectomy. After 2 years the patient presented with similar symptoms and consequently was diagnosed with sarcoma botryoides and treated by

Table 1
Clinicopathological features of uterine adenosarcoma with sex cord-like elements reported in literature.

Case no.	Age (cm)	Size	SCEs (%)	Adenosarcoma		Treatment	Follow-up (years)
				MR	MI		
1	52	4 cm endocervical polyp	0.5 cm nodule area	5 MF/10 HPF	–	RH + BSO + partial vaginectomy + pelvic lymphadenectomy	NED (1.1 y)
2	22	2 cm endomet. mass	50%	7MF/10 HPF	+	TAH + BSO	LFU
3	85	NE	20%	8MF/10 HPF	NE	D&C + RT	DWD (1.3 y)
4	75	6 cm endomet. mass	25%	5MF/10 HPF	+	TAH + BSO	NED (3 y)
5	70	6 cm endomet. mass	25%	2MF/10 HPF	–	D&C/melphalan + RT/TAH + BSO	NED (5 y)
6	41	3 cm endomet. mass	40%	15MF/10 HPF	–	TAH + BSO	NED (8.5 y)
7	38	Bulky, endocerv. and endomet. mass	50%	1MF/10 HPF	+	TAH + BSO	NED (8.5 y)
8	40	1.5 cm endomet. mass	10%	3MF/10 HPF	–	TAH + LSO	NED (9 y)
9	70	3 cm endomet. mass	5%	2MF/10 HPF	+	TAH	NED (11 y)
10	71	2.5 cm endomet. mass	75%	1MF/10 HPF	–	TAH + BSO	NED (5 y)
11	64	8 cm endomet mass	75%	1MF/10 HPF	–	TAH + BSO	NED (3 y)
12 ^a	47	4 cm endomet. mass	20%	1MF/10 HPF	+	TAH + BSO	NED (3 y)

DWD = died with disease; LFU = lost to follow-up; LSO = left salpingo-oophorectomy; MR = mitotic rate; MI = myometrial invasion; NED = no evidence of disease; RH = radical hysterectomy; RT = radiotherapy; SCEs = sex cord elements.

^a present case.

melphalan followed by intracavitary radiation. Five years later, she again presented similar complaints and a TAH with BSO was performed.

Clement and colleagues evaluated 100 patients with uterine adenosarcoma [1]. Although adenosarcomas have less tendency to invade, four cases in this series were found to have metastases, and local recurrency was observed in 23 cases. In their report approximately one third recurred five or more years after hysterectomy. Analysis of literature from patients with MASCEs revealed extremely low recurrency rates compared with the typical adenosarcomas (23%). If one patient with recurrent tumor in different histological diagnosis (Case 5); who had been treated firstly with dilatation and curettage, later with melphalan and radiotherapy is excluded from analysis, the recurrence rate is 9% in MASCEs. Myometrial invasion and mitotic rates also were assessed in this review. Invasion was present in five cases; three superficially and two into the inner half of the myometrium. As well, sarcomatous stroma generally exhibited mild degrees of nuclear pleomorphism and had lower mitotic rates (mean 4) in MASCEs, than those of typical adenosarcomas (mean 9).

In conclusion, although there is not enough data in the present literature, benign epithelial differentiations, such as SCEs may reflect the behavior of the tumor. As in our case, a more innocent histopathologic architecture can be observed and may likely be responsible for low recurrences and the benign clinical course in most of cases, even if they have not received any postoperative adjuvant therapy.

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