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Müllerian Adenosarcoma with Sarcomatous Overgrowth of the Cervix

Unusual Large Polypoid Mass

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Abstract

Müllerian adenosarcoma (MS) is a rare neoplasm of uterine cervix composed of benign epithelial and malignant stromal components. An aggressive variant of adenosarcoma, müllerian adenosarcoma with sarcomatous overgrowth (MASO) is extremely rare. The difference between MS and MASO is the pure high grade sarcoma features in MASO. In this report we present a MASO case, derived from uterine cervix of a 60 year-old-female patient presenting as a cervical polypoid mass, to our knowledge the second case of the English literature. In spite of sarcomatous overgrowth, high mitotic activity and huge tumor size of 12,5 cms, it displayed no myometrial invasion, vascular invasion and heterologous elements. The patient has been clinically free of disease for 14 months of follow up after total abdominal hysterectomy and bilateral salpingo-oopherectomy. The difficulties in diagnosis and treatment of this entity will be evaluated in this report.

Introduction

Müllerian adenosarcoma (MA) is a mixed epithelial/stromal neoplasm characterized by benign epithelial glands and malignant stromal components. It is a rare neoplasm typically arising in the endometrium, but has also been reported to occur in the ovary, cervix, and extra pelvic sites as well [1–4]. Müllerian adenosarcoma with sarcomatous overgrowth (MASO) is an uncommon aggressive variant of adenosarcoma. MASO is characterized by the pure sarcomatous portion constituting more than 25% of the neoplasm. It is frequently associated with postoperative recurrence or metastases and a fatal outcome [5]. In the cervix it is extremely rare. To the best of our knowledge, there is only one report in English literature [6]. Therefore the prognosis and optimal treatment options of cervical MASO are not well determined. In this report the second "primary cervical adenosarcoma with sarcomatous overgrowth" case of English literature is presented with the clinical and pathological findings.

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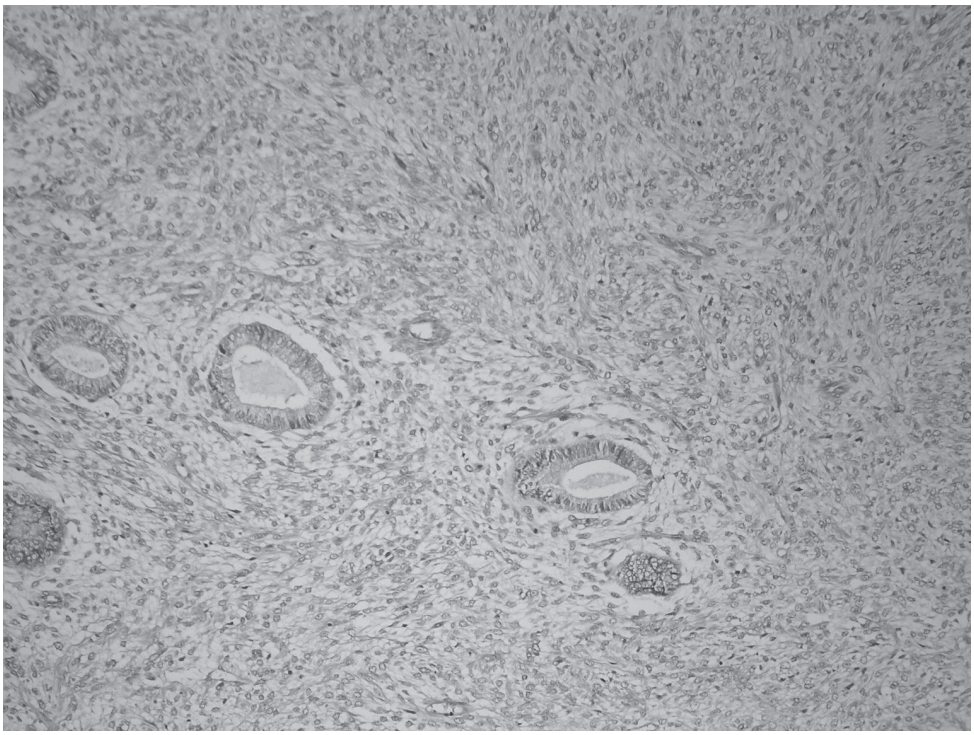

Figure 1. Benign glandular component and sarcomatous areas (H&E x100).

Case report

The patient was a 60 year-old woman with a cervical polypoid mass. She had noticed irregular vaginal spotting for 2 months. Pelvic examination revealed an elongated fleshy polyp, protruding through the cervical ostium, clinically considered as a suspicious endocervical mass. The uterus was normal in size and shape, and the adnexa were negative for palpable masses. The polypoid mass was removed for biopsy. Macroscopically, lesion was measured as 12,5x5x3cm. Microscopically, the mass was composed of a mixed proliferation of epithelial and stromal cells. The epithelial elements were glands of benign endocervical type. They were surrounded by a hypercellular spindle cell proliferation (Figure 1). There were markedly anaplastic focal areas composed of pleomorphic spindle cell proliferation, so-called sarcomatous overgrowth, at the submucosa (Figure 2). Pure sarcomatous component constituted approximately 40% of the tumor. Ten mitotic figures per 10 high power fields (HPF) have been counted in the spindle cell areas. The neoplasm exhibited no heterologous elements or myxomatous changes. Endometrial curettage material revealed endometrial polypoid fragments. The stromal component of these fragments was hypercellular but since no atypia and mitotic figures had been detected they were considered as endometrial polyp. With these find-

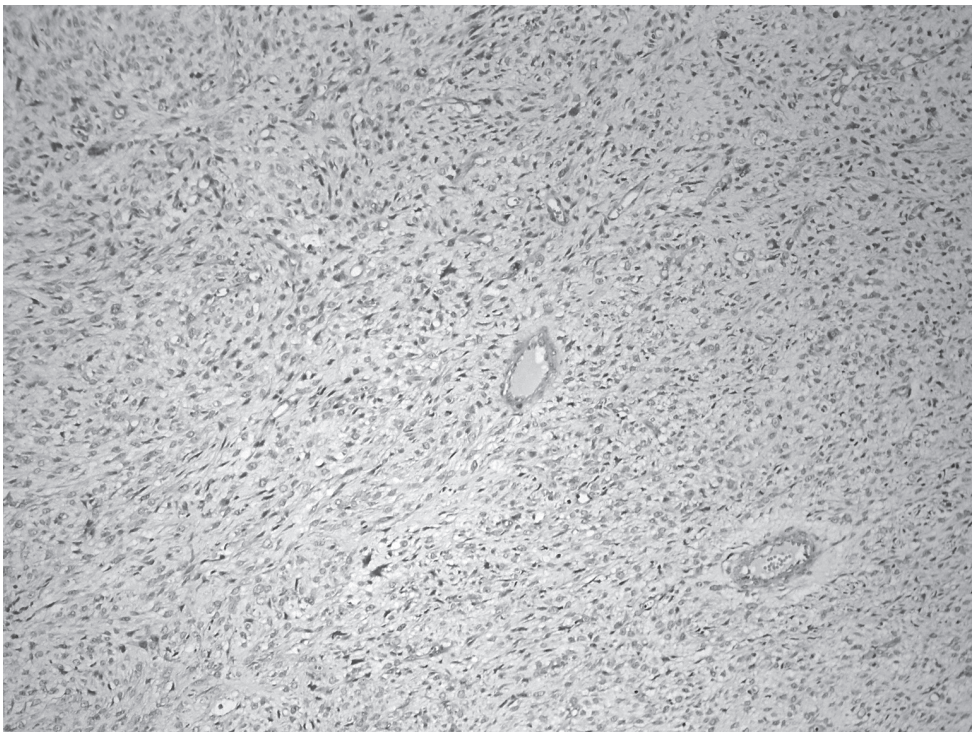

Figure 2. Sarcomatous overgrowth areas (H&E x100).

ings, a diagnosis of primary cervical adenosarcoma with sarcomatous overgrowth was rendered. Immunohistochemical studies were carried out by using a panel of commercially available antibodies on paraffin by the streptavidin-biotin method. Immunohistochemical results were summarized in Table 1. Total abdominal hysterectomy and bilateral salpingo-oophorectomy with pelvic lymph node dissection were performed. On gross examination, a normal sized uterus was revealed. Micro-

Table 1. Immunohistochemical features of MASO cases reported in English literature

Antibodies (reaction in stromal cells)	Park HM et al's case	The present case
Vimentin	Strong positivity	Strong positivity
Pancytoceratin	Negative	Negative
CD34	Negative	Negative
S-100	Negative	Negative
HMB-45	Negative	Negative
Estrogen	unapplied	Slight positivity
Progesterone	unapplied	Moderate positivity
Desmin	Negative	Positive in sarcomatous stromal cells
Smooth muscle actin	Positive in focal area	Positive in sarcomatous stromal cells

scopically entire cervical wall, including the exocervix and endocervix were free of infiltration of the neoplasm and endometrium was uninvolved. There was no lymph node metastasis or vascular invasion. We did not observe any residual polypoid lesion in endometrium. Both ovaries were normal. No adjuvant chemotherapy was administered. The patient was well, without evidence of disease after 14 months of postoperative follow-up.

Discussion

Adenosarcomas arising from the cervix are very uncommon tumors. MASO cases originating from cervix are seen even more rarely. Only one such case has been reported previously (6). MASO variant contains obvious, high-grade sarcomatous areas in addition to a low grade form. A diagnosis of MASO is rendered when a pure sarcoma is present within more than 25% of the tumor, and when this sarcoma is in a grade similar to or higher than that of underlying adenosarcoma (5). Although adenosarcomas are generally of low grade malignancy, MASO in uterus is more aggressive and frequently associated with postoperative recurrence or metastases and fatal outcome [5]. However, the prognosis of MASO of cervix is uncertain because of the limited number of case reports in the literature [6]. Uterine MA consists of benign-appearing neoplastic glands and sarcomatous stroma. The tumor is stated to have a lower malignant potential than malignant mixed müllerian tumors (MMMT) [7]. However, uterine MASO is an aggressive variant of adenosarcoma and reported that the overall survival of this neoplasm was similar with that of MMMT [8]. Therefore the differential diagnosis of this entity should be made with caution. MA typically presents with polypoid mass extruding from cervical os. Differential diagnosis should also include endocervical polyp and adenofibroma. On histological examination, a pure sarcomatous component constituting approximately 40% of the tumor and obvious pleomorphism, multinuclear giant cells and 10 mitoses/10 HPF in this sarcomatous component were seen in our case, suggesting a MASO. Sarcomatous overgrowth, high mitotic rate, heterologous elements, deep myometrial invasion, necrosis, and extra-uterine spread are unfavourable prognostic factors [1,5,7]. Vascular invasion is stated to be a bad prognostic factor also [7,9]. In the present case sarcomatous overgrowth was prominent but heterologous elements, necrosis, vascular, endometrial and myometrial invasion were not detected. Park et al. reported a 37-year-old female presented with a cervical MASO measuring 2 cms [6]. Microscopically some areas of markedly anaplastic and pleomorphic spindle cell proliferation had been detected. The mitotic count had been measured focally up to 20/10 HPF. The entire cervical wall, endometrium and myometrium had been uninvolved [6]. The main difference between our case and the one Park et al. reported is that the largest diameter of the mass in our case was 12,5 cms. It may be speculated that in the view of these findings, in the absence of myometrial invasion and heterologous elements, a huge tumor size and a high mitotic index did not result in an adverse effect on the prognosis.

Immunohistochemically, sarcomatous spindle cells showed positive staining for vimentin, desmin, smooth muscle actin, progesterone (PR) and estrogen (ER). ER and PR expression status in sarcomatous component of uterine MA were shown in Amant and colleagues' study [10]. They have stated that although MA cases expressed ER [16/20, (80%)] and PR [12/20, (60%)], sarcomatous component of MASO cases rarely showed ER and PR immunopositivity [0/8, (0%) and 1/8, (12%) respectively]. Unfortunately Park et al. had not examined ER and PR status in their case. As Amant et al. suggested [10] we also think that hormone receptors might play role in prognosis and be of significant clinical importance. Furthermore, some researchers had taken notice of the MASO cases occurring after tamoxifen therapy, suggesting a hormonal relationship [11]. Interestingly, endometrial curettage material of our case disclosed endometrial polyp with a hypercellular stroma, supporting this statement. However, medical history did not reveal tamoxifen or hormonal replacement therapy.

Kerner et al. [7] separated MAs into two age groups: patients in their reproductive years (14–36 years) and peri-postmenopausal patients (51–63 years). They had stated that histologic picture was different in two groups. In the younger age group grade and mitotic activity of sarcomatous component had been higher [7]. Our patient was 60 years old, therefore it could be considered that age might play a role on prognosis of MASO, but more evidence is needed in order to support this statement.

Optimal treatment options of MASO are still controversial. It has been stated that uterine MASO recurred and metastasized even with early stage disease [8] and recommended that total abdominal hysterectomy with bilateral salpingo-oophorectomy should be performed [1,8]. Since uterine MASO is associated with a poor prognosis, a thorough surgical evaluation is recommended. If disease was confined to pelvis, whole-pelvis radiation was offered. For distant metastatic disease, aggressive systemic chemotherapy was recommended [8]. Local excision has been curative in rare cases, and could be preferred especially in young patients (1). Even though uterine MASO is considered to have an aggressive malignant potential, the aggressiveness of cervical MASO is uncertain [6]. Park et al. reported that, for their cervical MASO case total abdominal hysterectomy and bilateral salpingo-ooferectomy with pelvic lymph node dissection had been performed [6]. The patient had been followed up and neither chemotherapy nor other adjuvant therapies had been administered. It was reported that she had been clinically free of disease after 9 months of surgery. The same procedure was followed for our patient and she is free of disease for 14 months since she received surgery.

In conclusion, we present an extremely rare case of MASO of cervix. In uterus, adenosarcomas with sarcomatous overgrowth are aggressive tumors frequently associated with postoperative recurrence or metastases, and poor prognosis, markedly contrasting with typical müllerian adenosarcoma of the uterus [5]. The presence of myometrial invasion and heterologous elements are proposed as the most important bad prognostic factors [5,6]. Aggressive behaviour of MASO of the uterine cervix is uncertain because they are extremely uncommon. However, it might be specu-

lated that if myometrial invasion and heterologous elements could not be found, high mitotic activity and huge tumor size would not result in an adverse effect on the prognosis. More case reports and prospective studies are needed for determining the treatment options of cervical MASO.

References

1. Clement PB, Scully RE (1990) Mullerian adenosarcoma of the uterus. A clinicopathologic analysis of 100 cases with a review of the literature. Hum Pathol 21: 363– 81.
2. Clement PB, Scully RE (1979) Extrauterine mesodermal (mullerian) adenosarcoma. Am J Clin Pathol 71:112–7.
3. Kao GF, Norris HJ (1978) Benign and low grade variants of mixed mesodermal tumor (adenosarcoma) of the ovary and adnexal region. Cancer 69: 276–83.
4. Kerner H, Lichting C, Beck D (1989) Extrauterine mullerian adenosarcoma of the peritoneal mesothelium: A clinicopathologic and electron microscopic study. Obstet Gynecol 73: 510–3.
5. Clement PB (1989) Mullerian adenosarcoma of the uterus with sarcomatous overgrowth. A clinicopathologic analysis of 10 cases. Am J Surg Pathol 13: 28–38.
6. Park HM, Park MH, Kim YJ, Chun SH, Ahn JJ, Kim CI, Sung SH, Han WS, Kim SC (2004) Mullerian adenosarcoma with sarcomatous overgrowth of the cervix presenting as cervical polyp: a case report and review of the literature. Int J Gynecol Cancer 14: 1024–9.
7. Kerner H, Lichtig C (1993) Mullerian adenosarcoma presenting as cervical polyps: A report of seven cases and review of the literature. Obstet Gynecol 8: 655–9.
8. Krivac TC, Seidman JD, McBroom JW, MacKoul PJ, Aye LM, Rose GS (2001) Uterine adenosarcoma with sarcomatous overgrowth versus uterine carcinosarcoma: Comparison of treatment and survival. Gynecol Oncol 83: 89–94.
9. Piura B, Rabinovich A, Meirovitz M (2000) Mullerian adenosarcoma of the uterus: case report and review of the literature. Eur J Gynaecol Oncol 21: 387–90.
10. Amant F, Schurmans K, Steenkiste E, Verbist L, Abeler VM, Tulunay G, De Jonge E, Massuger L, Moerman P, Vergote I (2004) Immunohistochemical determination of estrogen and progesterone receptor positivity in uterine adenosarcoma. Gynocol Oncol 93: 680–5.
11. Carvalho FM, Carvalho JP, da Motta EV, Souen J (2000) Müllerian adenosarcoma of the uterus with sarcomatous overgrowth following tamoxifen treatment for breast cancer. Rev Hosp Clin Fac Med S Paulo 55: 17–20.

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