Pathol. Oncol. Res. (2012) 18:529–533
DOI 10.1007/s12253-011-9391-x

CASE REPORT

Primary Synovial Sarcoma of the Uterus

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Received: 25 October 2010 / Accepted: 16 March 2011 / Published online: 14 April 2011

Abstract We report a case of a 52-year-old female with synovial sarcoma of the uterine corpus. Grossly, the partly polypoid tumor involved the endometrium with invasion into the inner half of the myometrium. Histologically, the tumor showed biphasic structure with the predominance of poorly differentiated small to medium sized round to oval cells. These cells showed high nuclear to cytoplasmic ratio and were arranged in diffuse sheets. Other component consisted of larger epitheloid cells with ample eosinophilic cytoplasm arranged in irregular nests. These cells were only present in a small amount. Immunohistochemically, the tumor cells in both components showed the expression of EMA, S-100 protein, CD99, and NSE. RT-PCR analysis showed the presence of SYT-SSX1 fusion transcript. At present, the patient shows no signs of tumor relapse 56 months after the diagnosis. To the best of our knowledge, this is the first report of synovial sarcoma arising in uterus.

Keywords Female genital tract · Immunohistochemistry · RT-PCR · Synovial sarcoma · Uterus

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Introduction

Synovial sarcoma is reported to be the fourth most common sarcoma, accounting for 5%–10% of soft tissue sarcomas [1]. This tumor typically occurs in adolescents and young adults; however, it can arise at any age including childhood. Most synovial sarcomas arise in paraarticural regions of extremities with the predilection for lower extremities, head and neck region, and trunk [1, 2]. However, it can occur in any site including various organs. We describe the first case of synovial sarcoma arising in uterus, including the clinicopathologic, immunohistochemical and molecular analysis of the tumor.

Case Report

A 52-year-old female was admitted to our Unit of Minimal Invasive Surgery for planned hysterectomy without bilateral salpingoophorectomy. Her medical history included serious episodes of metrorrhagia 3 years ago, which was conservatively treated. Currently, the surgical indication was uterus myomatosus and menometrorrhagia, which was resistant to hemostyptic therapy. The perioperative findings corresponded to a large uterus myomatosus. However, based on histological diagnosis of synovial sarcoma, she was referred to Oncogynecological Centre to finalize the appropriate surgical staging. The staging procedure consisted of a careful exploration of pelvic and abdominal cavity, bilateral salpingoophorectomy, total omentectomy, appendectomy, systemic pelvic and paraaortic lymphadenectomy and lavage. Then the patient underwent adjuvant radiotherapy in appropriate doses and time schedule (total dose 50 Gy, 25 fractions/5.5 weeks). To this date, the patient is in complete clinical remission, as confirmed by

recent PET/CT imaging. The disease-free interval reached 56 months after the first diagnosis of disease.

Materials and Methods

This study comprised the following specimens: hysterectomy, bilateral adnexectomy, omentectomy, appendectomy and lymphadenectomy. Sections from formalin-fixed, paraffin-embedded tissue blocks were stained with hematoxylin-eosin. Selected sections were analysed immunohistochemically using the avidin-biotin complex method with antibodies directed against the following antigens: vimentin (1:300, Bio-Genex, San Ramon, CA, USA), cytokeratin CAM 5.2 (1:10, Becton–Dickinson, Mountain View, CA, USA), cytokeratin AE1/AE3 (1:50, Dako, Glostrup, Denmark), EMA (1:100, Dako), desmin (1:200, Dako), S-100 protein (1:1600, Dako), neurofilament protein 2 F11 (1:100, Dako), chromogranin A (1:50, Dako), synaptophysin (1:25, Dako), NSE (1:400, Dako), CD99 (1:100, Dako), CD56 (1:50, Novocastra, Newcastle, UK), CD10 (1:100, NeoMarkers, Fremont), estrogen receptor (1:40, Novocastra), progesterone receptor (1:100, Novocastra), FLI-1 (1:50, NeoMarkers), and α-smooth muscle actin (1:100, Dako).

RT-PCR analysis was performed from formalin-fixed, paraffin embedded tumor tissue by standard procedure described in our previous work [3]. The primer sequences (except SYT-SSX4) are described in the same publication. Primer sequences for SYT-SSX4 are: sense primer 5′-GTCAGCAGTATGGAGGATATAGAC-3; antisense primer 5′-TCTGGCACTTCCTTCAAACC-3′; annealing temperature T(A)=58°C and PCR product size is 120 bp.

Results

Grossly, the uterine corpus measured 65×60×45 mm. Intramurally, there were leiomyomas up to 35 mm in diameter. In cross section, the endometrium consisted of partly polypoid white friable tumor tissue 35×35×25 mm. The uterine cervix, adnexa, appendix and omentum showed no apparent changes.

Histologically, the tumor of the uterus showed biphasic structure with the predominance of poorly differentiated small to medium sized round to oval cells, some with dark nuclei with finely stippled chromatin, and others with vesicular nuclei and prominent nucleoli. These cells showed high nuclear to cytoplasmic ratio and were arranged in diffuse sheets. Multiple mitotic figures were present (up to 25 mitoses/10 HPF) (Fig. 1, 2). The other component consisted of larger epitheloid cells with ample eosinophilic cytoplasm arranged in irregular nests (Fig. 3).

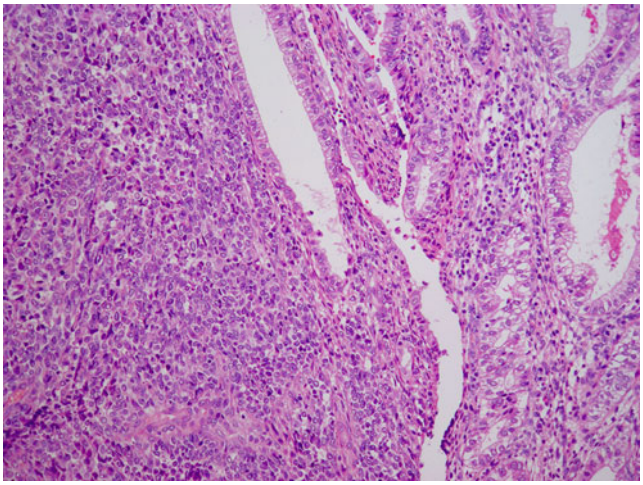

Fig. 1 Synovial sarcoma (left) infiltrating the endometrium with apparent secretory changes (H&E, 200×)

These cells were present in a small amount. The tumor showed invasion into the inner half of myometrium (maximum depth of invasion 3 mm). There was no evidence of tumor spreading into the uterine cervix. Focal areas of necroses were present. Angioinvasion was not found. Other tissue examined including bilateral salpingo-oophorectomy, omentectomy and appendectomy specimen showed no signs of tumor dissemination. The 63 lymph nodes examined were without metastases.

Immunohistochemically, the tumor cells in both components showed expression of EMA (Fig. 4), S-100 protein, CD99 and NSE. Expression of vimentin was found in poorly differentiated component only. Expression of cytokeratin CAM5.2 and AE1/3 was found in larger epitheloid cells as well as in scattered poorly differentiated cells (Fig. 5). Other markers examined including estrogen receptor, progesterone receptor, FLI-1, synaptophysin,

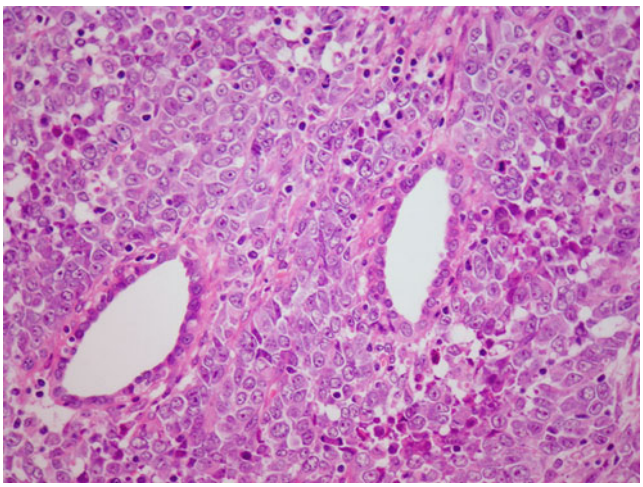

Fig. 2 Poorly differentiated synovial sarcoma with entrapped endometrial glands (H&E, 400×)

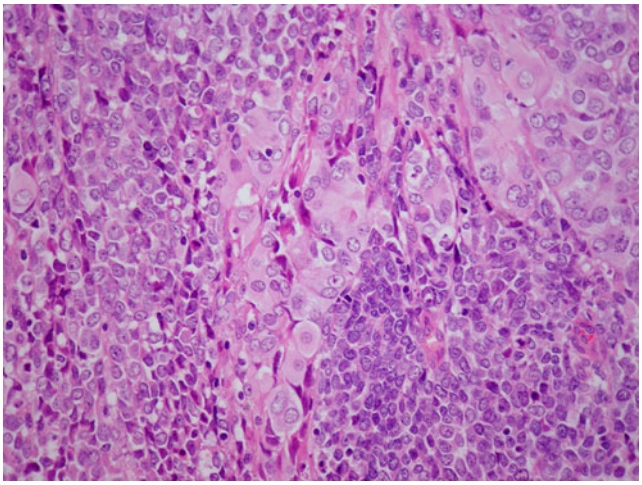

Fig. 3 Biphasic synovial sarcoma consisting of a poorly differentiated component with irregular groups of large epitheloid cells (H&E, 400×)

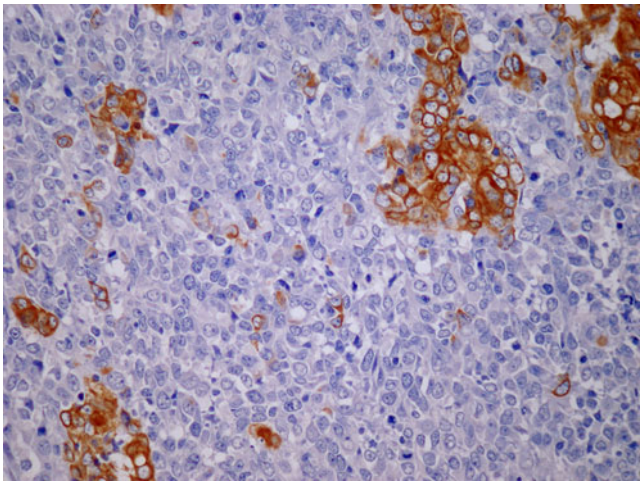

Fig. 5 Expression of cytokeratin CAM5.2 in larger epitheloid cells and scattered poorly differentiated cells (400×)

chromogranin A, neurofilament protein, α-smooth muscle actin, desmin, CD56, and CD10 were negative.

Molecular analysis of the tumor (SYT-SSX1, SYT-SSX2 and SYT-SSX4 fusion transcripts) showed the presence of the 331 bp PCR products corresponding to the SYT-SSX1 fusion transcript associated with the t(X;18) translocation typical of synovial sarcoma (Fig. 6).

Discussion

Synovial sarcoma is common soft tissue sarcoma, however, it can arise in almost any site including wide variety of visceral sites such as kidney, gastrointestinal tract, and lung [4–7]. In female genital organs, only few cases of synovial sarcoma were described including 4 cases arising in vulva, and one case each in vagina, fallopian tube, and ovary [8–13].

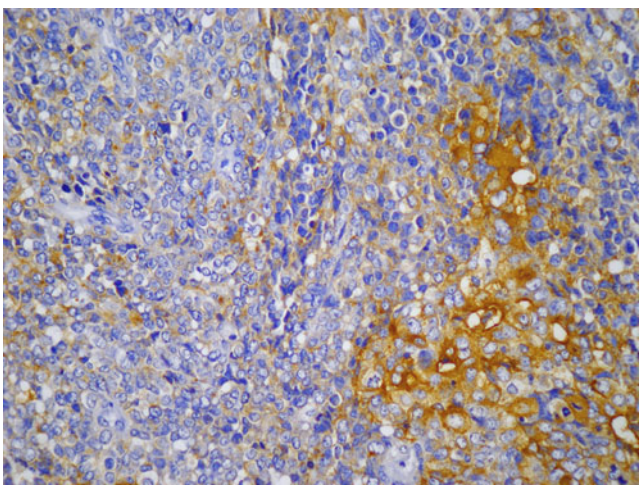

Fig. 4 Tumor cells positivity for EMA. Note the stronger positivity of larger epitheloid cells (400×)

In our case, the tumor arose in endometrium with apparent invasion into the myometrium.

The histogenesis of synovial sarcoma is uncertain; however, it is believed to arise from multipotent mesenchymal stem cell [14]. In the uterus, synovial sarcoma can represents the heterologous elements of a malignant müllerian mixed tumor (MMMT). In our case, however, we have found no other component suggesting this possibility despite the extensive sampling. Nevertheless, at least some pure heterologous sarcomas arising in the uterus are believed to represent complete heterologous stromal overgrowth in an adenosarcoma or MMMT, and we cannot exclude this possibility in our case as well.

Differential diagnosis of synovial sarcoma of the uterus is largely dependent on its histological type. Based on the composition and the degree of differentiation, synovial sarcoma can be classified as biphasic, monophasic fibrous type, monophasic epithelial type, and poorly differentiated type [1]. In cases of biphasic synovial sarcoma with well apparent epithelial structures, the most important differential diagnosis includes MMMT. In MMMT with a heterologous stromal component, such as malignant cartilage or skeletal muscle, the diagnosis is usually straightforward. To distinguish MMMT with homologous stromal component can be more difficult and the diagnosis should be based on

Fig. 6 RT-PCR amplification of SYT-SSX fusion transcripts

the type and degree of differentiation of epithelial and sarcomatous elements. Epithelial elements of MMMT are usually more atypical then those of synovial sarcoma, and usually represent serous adenocarcinomas or high grade carcinomas, not otherwise specified. However, epithelial elements in synovial sarcoma can be very similar to MMMT with endometrioid elements, including cases with focal squamous differentiation [15]. Monophasic fibrous type of synovial sarcoma can be confused with other mesenchymal tumors such as cellular leiomyoma, leiomyosarcoma, endometrial stromal sarcoma, malignant peripheral nerve sheath tumor, hemangiopericytoma, and fibrosarcoma. Differential diagnosis of poorly differentiated synovial sarcoma includes uterine tumors with neuroectodermal differentiation (including the Ewing sarcoma/PNET family of tumors), malignant lymphomas, alveolar rhabdomyosarcoma, mesenchymal chondrosarcoma, endometrial stromal sarcoma, undifferentiated uterine sarcoma, high grade leiomyosarcoma, and neuroendocrine carcinoma.

In most cases of synovial sarcoma, the correct diagnosis can be achieved by analysis of histologic and immunohistochemical features of the tumor. Synovial sarcoma in most cases expresses TLE1, EMA, cytokeratins, and bcl2 [1, 16]. In some cases expression of S-100 protein, CD99, calponin, and rarely muscle specific actin or α-smooth muscle actin can be found. Spindle cells are usually vimentin positive. However, the immunophenotype of synovial sarcoma is not specific and in poorly differentiated variants expression of epithelial markers may be absent. Therefore, panel of antibodies should be used in the differential diagnosis of these tumors. In all histological types of synovial sarcoma if the correct diagnosis cannot be achieved based on histological and immunohistochemical features, molecular analysis of t(X;18) (p11;q11), which is typical of synovial sarcoma, should be performed [17, 18].

Prognosis of synovial sarcoma is uncertain. Factors consistently associated with a poor prognosis are large tumor size, tumor location, histological grade, and age of the patient [19–23]. However, data regarding the significance of these factors remain controversial. Moreover, these prognostic factors are relevant of synovial sarcomas arising in their typical location. Regarding the therapy of synovial sarcoma, adequate surgical staging procedure is the mainstay of treatment. Adjuvant radiotherapy is commonly used and is most beneficial in patients with larger tumors and in the case of inadequate margins. Whether adjuvant chemotherapy provides a benefit for patients with localized disease is still debated [24]. Nevertheless, synovial sarcoma has been considered a chemoresponsive tumor in the metastatic or adjuvant setting. In our case, despite the high grade of the tumor with predominance of poorly differentiated component, the patient is with no sign of tumor relapse 56 months after the diagnosis.

In conclusion, we described the first case of synovial sarcoma of the uterus. Our case expands the spectrum of mesenchymal tumors occurring in the uterus and we should be aware of this possibility in the differential diagnosis of uterine tumors.

Acknowledgement This work was supported by Ministry of Education Research Project MSM0021620808.

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