Uterine tumor resembling ovarian sex cord tumor. Case report and review of literature

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Summary

A uterine tumor resembling an ovarian sex cord tumor (UTROSCT) shows a poly phenotypic immunophenotype with coexpression of epithelial, myoid, and sex cord markers, as well as hormone receptors. The authors present a case of a 59-year-old multiparous woman admitted to the Institute of Gynecology and Obstetrics Clinical Centre of Serbia in January 2010 due to prolonged vaginal bleeding and abdominal discomfort. The vaginal ultrasound showed an enlarged uterus size of 100 x 74 x 81 mm, with extended cavity with an unhomogenic content and myomas sized 54 x 69 mm located in fundus with secondary changes. She underwent abdominal hysterectomy with adnexectomy. Microscopic examination revealed submucosal uterine tumor with variabile histological organization that had anastomotic trabeculae with solid cellular grupations. Rare mitotic figures (2/10 HPF) were found. Additional imunohistochemistry showed immunophenotype: the sex cord areas were positive for vimentin(++), aSMA(++), AE1/AE3(+), PR(+), and ER(+). The poly phenotypic immunophenotype can be useful in differential diagnosis from other neoplasms but also suggests an origin of UTROSCT from uncommitted stem cell enabling for multidirectional differentiation.

Key words: Uterine tumors resembling ovarian sex-cord tumor; Immunophenotype.

Introduction

Uterine tumors resembling ovarian sex cord tumors (UTROSCT) belong to miscellaneous category of uterine tumors that consist of different amounts of sex cord-elements. Clement and Scully divided the ovarian sex cord tumors of the uterus into two groups: Group I of tumors are endometrial stromal tumors with sex cord like elements (ESTSCLE) whereas sex cord elements are minor components (40%) of tumors, characterized by increased risk of recurrence and metastasis. Group II tumors are UTROSCT consisting of more than half of sex cord tissue and characterized by low recurrence rate and metastasis [1, 2].

According to some authors, distinction of UTROSCT from endometrial stromal tumors can be subjective, but UTROSCT is reserved for tumors with predominant or exclusive sex cord differentiation. Classification of tumors of the female genital tract by World Health Organization (WHO) make a distinction between UTROSCT from endometrial stromal neoplasms, but there is still debate of its histogenesis [1, 2].

Uterine tumor resembling ovarian sex cord tumor shows a poly phenotypic immunophenotype with coexpression of markers of epithelial, myoid, and sex cord markers, as well as hormone receptors [1].

Case Report

A 59-year-old multiparous woman was admitted to the Institute of Gynecology and Obstetrics Clinical Centre of Serbia in January 2010 with prolonged vaginal bleeding and abdominal discomfort. Her last period was 15 years ago and two explorative curettages were performed because of abnormal vaginal bleeding during the last five months. Pathological findings of the procedure included phlogistic fibroglandular polyp in both samples. Patient was biochemically and clinical assessed and ultrasound-examined. The vaginal ultrasound showed an enlarged uterus sized 100 x 74 x 81 mm, with extended cavity filled with unhomogenic content and myomas sized 54 x 69 mm located in fundus with secondary changes. She underwent abdominal hysterectomy with bilateral salpingoophorectomy.

Macroscopic examination showed that the uterus weight was 310 g with polypoid prominence sized 50 x 60 x 105 mm that prominated in the endocervical canal, covered with atrophic endometrial layer, and with superficial myometrial infiltration. On the cut surface, the formation consisted of solid and cystic areas. Microscopic examination revealed submucosal uterine tumor with variabile histological organization that had anastomotic trabeculae with solid cellular grupations. In some part of grupations there were spindle-cellular forms, with cental ovoid round cells with eosinophils. There was a rare mitotic figure (2/10 HPF). There was neither tumor necrosis and pleomorphism nor evident signs of histological malignancies, but peripheral infiltrative growth was presented. The additional immunohistochemistry which was performed on parafin tissue block No 1821/10 technique LSAB/AEC visualization showed immunophenotype; the sex cord areas were positive for vimentin(++), aSMA(++), AE1/AE3(+), PR(+), and ER(+) (Figure 1). The patient continues to be without disease two years after the operation.

Discussion

UTROSCT distinguish from ESTSCLE in clinicopathological features, although they seem at first sight very similar. Only 48 cases of UTROSCT have been reported in earlier international literature and usually the

Revised manuscript accepted for publication September 6, 2012

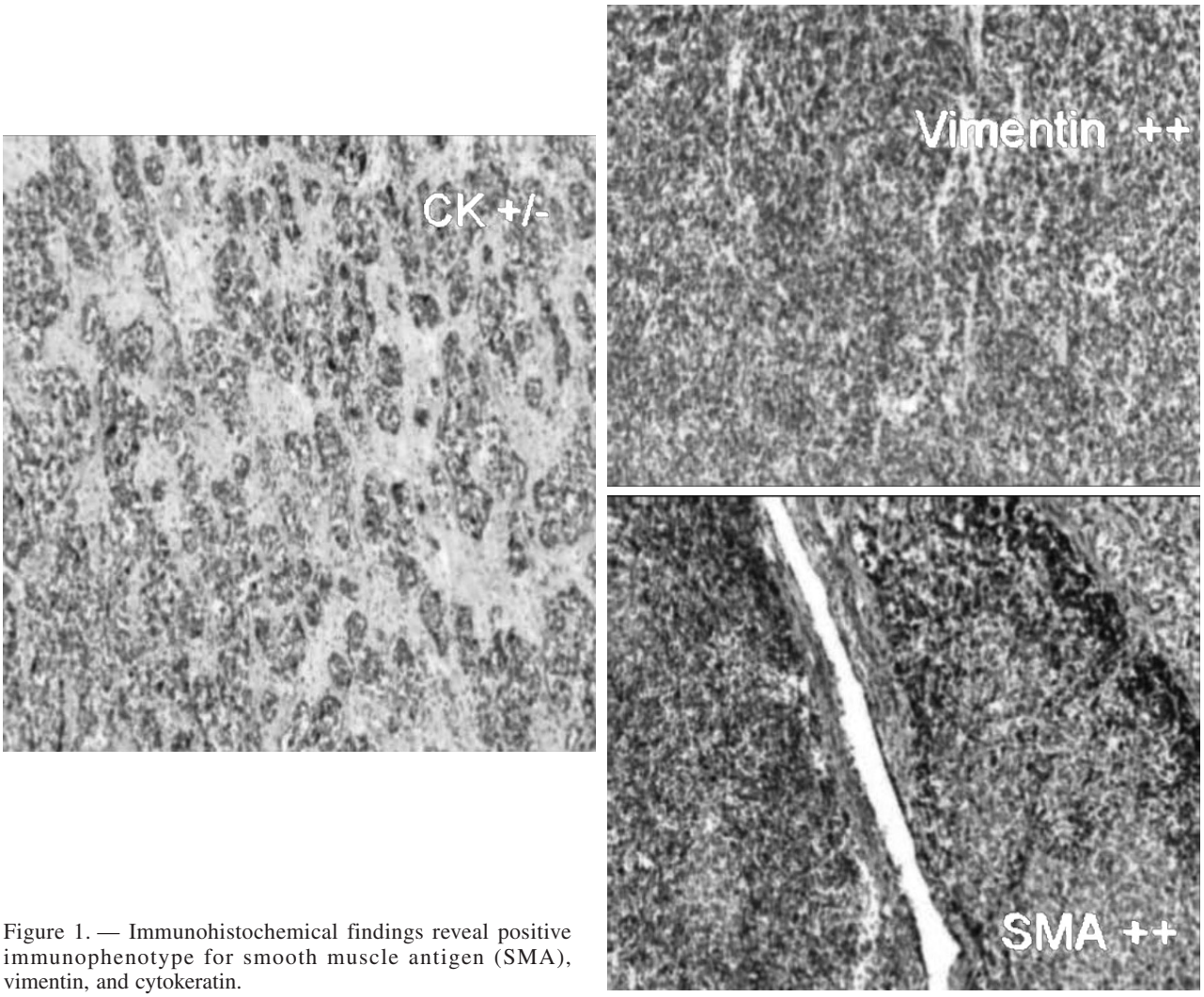

Figure 1. — Immunohistochemical findings reveal positive immunophenotype for smooth muscle antigen (SMA), vimentin, and cytokeratin.

diagnosis was made after hysterectomy or polypectomy [1, 2]. This rare tumor is mostly revealed incidentally, as it was in a new reported case of UTROSCT in patient with neoplasm which seemed to be the consequence of tamoxifen treatment for breast carcinoma. In latest citations, few new cases of these rare tumors have been published, but mortality from the UTROSCT has not yet been described [2, 3]. Recently the role of conservative therapeutic approach has become more acceptable in young patients, besides the standard procedure that considers hysterectomy.

UTROSCT are myometrial tumors that consist of predominantly ovarian sex cord tissue that resembles granulosa cell or Sertoli cell neoplasms. They are usually located in the uterine fundus, but have also been seen in endometrial cavity and in the cervix as in the present case. Macroscopic appearance of these tumors often reveal lobulated and yellow structures. The microscopic image shows that the tumor is composed of anastomotic trabeculae, corded, nested, and glandular arrangements of tumor cells. Infiltrating borders of tumor can be seen but with rare lymphovascular invasion. Although 36% of UTROSCT have infiltrative margins, almost all of them behave as benign tumors. Nuclear atypia is mild to moderate and mitotic index is low in UTROSCT group [4, 5].

Diagnosis of UTROSCT is usually based on histologic pattern and immunohistochemical phenotype. These neoplasms have a variabile immunophenotype sometimes with coexpression of epithelial (AE1/3, epithelial membrane antigen), myoid (desmin, smooth muscle antigen), sex cord (inhibin, CD99, melan A, calretinin), neuroendocrine (chromogranin, CD56) markers, as well as hormone receptors, vimentin, and CD10 [6, 7].

Immunohistochemistry shows that the majority of UTROSCT express α inhibin, CD99, and vimentin. Some tumors are positive for smooth muscle antigen and myoglobin, and up to one-third are positive for desmine. Cytokeratin was expressed in 50% of cases and 10% patients with UTROSCT express epithelial membrane antigen [6, 7].

The poly phenotypic immunophenotype can be useful in differential diagnosis from other neoplasms, such as

endometrial stromal sarcoma or a low-grade mixed Müllerian tumor. The diverse immunohistochemical profile also suggests an origin of UTROSCT from uncommitted stem cell, enabling multidirectional differentation. Other studies suggests that UTROSCT are variants of endometrial stromal neoplasms [6, 7].

These rare uterine tumors occurred in women both in reproductive and postmenopausal ages and usually presented with abnormal vaginal bleeding. Preoperative assessment includes curettage that sometimes reveals endometrial hyperplasia that can be caused by hormonal production of this rare neoplasm. Sonographically, intramyometrial sex cord tumor is similar to leomyoma and its intracavitary form is difficult to distinguish from endometrial polyp or submucosal myoma. A pelvic magnetic resonance image (MRI) can demonstrate if the endomyometrial junctional area is disrupted and if there is a possible invasion of the uterine wall. Final diagnosis of UTROSCT is based on histologic pattern and immunohistochemical phenotype [8].

Although UTROSCT behave in benign manner, some of them might undergo malignant transformation and have a metastatic potency. First described metastasis was in a 86-year-old patient, detected on omentum during a hysterectomy with bilateral salpingoophorectomy, with no relapse at five-years follow-up. In one of the latest publications, a case of metastatic disease was discovered four years after hysterectomy. Patient developed obstructive ileus due to a large infiltrating tumor within the small bowel presenting same morphology and expression pattern as the previously diagnosed UTROSCT. Two benign gastrointestinal stromal tumors were also detected in the same patient [2, 9].

Recurrence of the disease was also published. Recent case of recurrence in literature was described in young patient with galactorrhea three years after hysterectomy because of UTROSCT. The extensive debulking surgery was performed because of relaps and it included partial bladder and colon resection, followed by chemotherapy. Galactorrhea and elevated prolactin level increased with tumor relapse, suggesting a hormonal imbalance due to the UTROSCT endocrine function [9].

Because of the occasional recurrence of these rare tumor, they should almost be considered as low-grade malignant potential. It has been suggested that the malignant potential of UTROSCT can be assessed by criteria for endometrial stromal sarcomas-like mitotic count, vascular invasion, infiltrative borders, and even serosal infiltration. However some authors suggest that the current histological features are still not sufficient for prediction of the behaviour of this tumor [3, 9].

On the basis of the uncertain malignant potential and low recurrence rate, these tumors are treated with hysterectomy. Conservative treatment has been proposed as an alternative to hysterectomy, in patients who want to preserve fertility [10, 11]. One of the first conservative treatments of UTROSCT was reported seven years ago, with local excision of the tumor performed in young nulliparous patient [12].

Recently, sparing procedures consist of tumor resection usually using resectoscopic surgery. There have been described four cases of UTROSCT that were managed by minimally-invasive hysteroscopic surgery [10, 11]. Up until now, three spontaneous pregnancies after conservative treatment of UTROSCT have been described. One pregnancy after hysteroscopic resection of tumor resulted in uneventful delivery [11, 13].

As the quality of life becomes even more important in medicine, fertility-sparing procedure should be reasonably considered in therapeutic approaches, without compromising patient survival. However, careful short- and long-term follow-ups are necessary in patients with UTROSCT.

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