Annals of Diagnostic Pathology 18 (2014) 329–332

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

Uterine tumors resembling ovarian sex cord tumors, a clinicopathologic study of six cases

Elwira Bakula-Zalewska [a,*], Anna Danska-Bidzinska [b], Magdalena Kowalewska [c,d], Agata Piascik [a], Anna Nasierowska-Guttmejer [e], Mariusz Bidzinski [f]

[a] Department of Pathology, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, 02-781 Warsaw, Poland
[b] Department of Obstetrics and Gynecology, Medical University of Warsaw, 00-315 Warsaw, Poland
[c] Department of Molecular and Translational Oncology, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, 02-781 Warsaw, Poland
[d] Department of Immunology, Biochemistry and Nutrition, Medical University of Warsaw, 02-097 Warsaw, Poland
[e] Department of Pathology, Jan Kochanowski University, 25-517 Kielce, Poland
[f] Department of Health, Jan Kochanowski University, 25-517 Kielce, Poland

ARTICLE INFO

Keywords:
Uterine tumors resembling ovarian sex cord tumors
UTROSCT
Sex cord-like
Endometrial stromal tumor
Gestagen therapy

ABSTRACT

Uterine tumors resembling ovarian sex cord tumors (UTROSCTs) cause difficulties, both with respect to diagnosis as well as to the nomenclature. They belong to the group of low-grade malignant neoplasms, and their clinical course likely depends on the percentage of the sex cord–like component. Morphologically, they can be divided into type I and type II with less or more than 50% of sex cord–like areas, respectively. Six patients with an age range of 24 to 63 years underwent the treatment for primary UTROSCT at the Cancer Center and Institute of Oncology in Warsaw, Poland, between 2000 and 2011. In addition to the surgery, 4 patients were treated with gestagens. Biopsies or excisions from the tumors were examined microscopically and immunohistochemically. Two cases were classified as type I, and 4 cases, as type II tumors. The tumor size ranged from 3 to 24 cm. The sex cord component varied from 25% to 70%. By immunohistochemical examination, the sex cord–like component was calretinin positive, whereas the stromal component was positive for CD10 and negative for h-caldesmon in all the cases studied. In addition, progesterone receptor positivity was found in all the cases, and 4 tumors were positive for smooth muscle actin, cytokeratin AE1/3, and inhibin. No recurrences were noted in any of the 6 patients over 3 to 14.5 years of follow-up period. A correct subclassification of sarcomas of UTROSCT type is of crucial importance because most patients with this rare neoplasm respond well to gestagen therapy and have a good prognosis, compared with other uterine stromal sarcomas.

1. Introduction

Uterine tumors resembling ovarian sex cord tumors (UTROSCTs) are uncommon tumors described for the first time in 1975 by Clement and Scully [1]. Uterine tumors resembling ovarian sex cord tumors are included in the current 2014 World Health Organization classification of uterine tumors. These tumors are polyphenotypic neoplasms, and in the literature, they are termed as endometrial stromal tumors with sex cord–like differentiation, endolymphatic stromal myosis with sex cord–like differentiation, or low-grade endometrial stromal tumors with sex cord–like pattern [2]. To date, the number of UTROSCTs described in the literature has not reached 100 cases [3,4].

Depending on the sex cord–like histology, these tumors are divided into 2 groups: type I, where the differentiation in the direction of the sex cord elements occurs focally, and type II, showing predominant sex cord–like differentiation. The distinction between the 2 types of tumors is not accurate; it shall be considered as 40% to 50% of the sex cord–like histology [1,4,5]. Some authors use the UTROSCT term exclusively for the type II tumors, whereas those of the type I are referred to as endometrial stromal tumors with sex cord–like elements [6,7]. Type II tumors commonly follow a benign course, and their prognosis depends mostly on the percentage of the sex cord elements [2,6], whereas type I tumors (endometrial stromal tumors with sex cord–like elements) show a propensity to recur or metastasize, and their prognosis depends on the type, grade, and stage of the stromal component of the neoplasm [7].

When assessing specimens stained with hematoxylin and eosin, the diagnosis of UTROSCT may be challenging due to their heterogeneous histology. Microscopically, UTROSCTs show a pattern resembling ovarian Sertoli-Leydig cell tumor, that is, anastomosing cords, trabeculae, nests of cells, rosettes or tubular, pseudotubular and glomeruloid structures and epithelial-like elements. The stromal component of UTROSCT resembles stromal component of low-grade stromal sarcoma but rarely exhibits infiltration and vascular invasion. Moreover, occasional scattered foam cells and very rare smooth muscle

* Corresponding author. Tel.: +48 22 546 22 49; fax: +48 22 546 29 84.
E-mail addresses: elwirabz@onet.eu (E. Bakula-Zalewska), ad.bidzinska@gmail.com (A. Danska-Bidzinska), magdak@coi.waw.pl (M. Kowalewska), agata_piascik@o2.pl (A. Piascik), anna.nasierowska@cskmswia.pl (A. Nasierowska-Guttmejer), bidzinski.m@gmail.com (M. Bidzinski).

http://dx.doi.org/10.1016/j.anndiagpath.2014.08.009
1092-9134/

component may be seen. These tumors are characterized by a complex immunophenotype, often with a coexpression of epithelial, smooth muscle, and sex cord markers as well as hormone receptors [7–9].

Uterine tumors resembling ovarian sex cord tumors occur in women of different ages, but often in women of reproductive age. The prognosis for patients with UTROSCT is quite good, and a beneficial effect of gestagen treatment is observed [10]. It is possible to remove the tumor by hysteroscopy or laparoscopy, preserving uterus and maintaining fertility [11]. Therefore, the knowledge pertaining to these tumors and their diagnosis is of great importance. The differential diagnosis of UTROSCT, based on the microscopic and immunohistochemical findings, should include endometrial stromal sarcoma, epithelioid leiomyoma, epithelioid leiomyosarcoma, adenocarcinoma, low-grade mixed Müllerian tumor (adenosarcoma), and metastatic ovarian sex cord tumor.

2. Materials and methods

The material was obtained from 6 patients aged between 24 and 63 years (mean age, 41.5 years), which underwent surgical treatment for primary UTROSCT at the Cancer Centre and Institute of Oncology in Warsaw, Poland, between 2000 and 2011. In 4 cases, simple hysterectomies were performed. Two younger patients (aged 24 and 25 years) were treated conservatively using operative hysteroscopy techniques because of their requests. Sections for histologic examination were routinely processed in paraffin. Immunohistochemical staining was performed using DAKO EnVision + System, Peroxidase (AEC) kit (DakoCytomation, Glostrup, Denmark). The following antibodies were used: CD10, smooth muscle actin (SMA), h-caldesmon, desmin (DES), sarcomeric actin (SrMA), cytokeratin (CK) AE1/3, CD117, calretinin, inhibin, progesterone receptor (PGR), and MIB1 (anti–Ki-67) (DakoCytomation).

3. Results

All 6 patients underwent surgical treatment for primary UTROSCT, and 4 patients received additional adjuvant treatment with gestagens. No recurrences were noted in any of the 6 patients over 3 to 14.5 years of follow-up period. The clinicopathologic data and follow-up results are presented in brief in the Table.

Tumors were ranged from 3 to 24 cm in size. The cut surfaces were creamy and white in 4 cases and, in the 2 cases, yellowish. In 3 of the 6 patients (case nos. 1, 2, and 5), the tumors were presented as endometrial mass in the uterine fundus showing broad tumor protrusions in to myometrium of less than 3 mm depth. In 1 patient (case no. 6), the tumor was presented as polypoid mass projecting into the uterine cavity. The mass was seated in the endometrium showing less than 4 mm of myometrial infiltration by some broad protrusions. In 1 patient (case no. 3), the tumor was limited to the endometrium with well-circumscribed pushing borders. In 1 patient (case no. 4), the tumor was presented as 24-cm mass in the uterine fundus involving endometrium, myometrium, and subserosa. Two of tumors were of type I, and 4, of type II. Sex cord–like patterns comprised from 25% to 70% of the tumor volume and exhibited different level of maturity: from cords, trabeculae, nests, and rosette-like structures to well-defined rings and pseudotubular structures (Figs. 1 and 2). In addition, 3 tumors contained focal aggregates of cells with foamy cytoplasm (Fig. 3), and cells with abundant eosinophilic cytoplasm were found in one tumor. The stromal component was similar to low-grade stromal sarcoma and was composed of small spindle cells and epithelioid cells showing low-grade nuclear atypia and mitotic index of 1 to 9 mitotic figures per 10 high-power fields. In 2 cases, tumor cells penetrated to the lymphatic vessels. Focal necrosis (<15%) was visible only in 1 tumor. The component corresponding to a low-grade stromal sarcoma was CD10 immunoreactive and negative for muscle markers (h-caldesmon, DES, and SrMA) in all the tumors examined. This component was SMA positive in 4 cases. In the sex cord–like elements, all the tumors showed calretinin expression (Fig. 4), whereas inhibin was present in 4 tumors (including 3 with only focal expression). Four tumors were also positive for cytokeratin (CKAE1/3). In addition, all 6 tumors showed a presence of PGRs. The results of immunohistochemical analysis are presented in the Table.

Sex cord–like patterns exhibited different level of maturity: from cords, trabeculae, nests, and rosette-like structures to well-defined rings and pseudotubular structures (Figs. 1 and 2). In addition, 3 tumors

Table
Clinicopathologic data and immunohistochemical results in 6 UTROSCT cases

Case no.	Patient age (y)	Tumor size (cm)	Surgery	Tumor type	Percentage of sex cord components	Disease-free survival period (y)	Immunohistochemical findings										
							CD10	SMA	CALD	DES	SrMA	CKAE1/3 in sex cord–like areas	CD117	Calretinin	Inhibin	PGR	MIB-1
1	50	5	Subtotal hysterectomy, bilateral salpingo-oophorectomy	II	65%	14.5	+	+/−	−	−	−	−	−	+	−	+ (100%)	15%
2	25	4	Tumorectomy	I	25%	7	+	+	−	+/−	−	+	−	+	+/−	+ (100%)	40%
3	51	3	Subtotal hysterectomy, bilateral salpingo-oophorectomy	II	70%	5.5	+	−	−	−	−	−	−	+/−	−	+ (99%)	8%
4	63	24	Subtotal hysterectomy, bilateral salpingo-oophorectomy	II	60%	5	+	+/−	−	−/+	−	+	−	+	+/−	+ (99%)	20%-35%
5	24	3	Tumorectomy	I	35%	4.5	+	+	−	−	−	+	−	+	+/−	+ (99%)	35%
6	62	4	Subtotal hysterectomy, bilateral salpingo-oophorectomy	II	70%	3	+	−	−	−	−	+	−	+	+	+ (100%)	10%

Abbreviations: +, positive; −, negative; +/−, partially positive reaction; *CALD*, h-caldesmon; *MIB-1*, antigen identified by Ki-67 antibody.