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Uterine Endometrial Stromal Sarcoma with Rhabdoid and Smooth Muscle Differentiation

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Uterine and extrauterine tumors composed of cells featuring endometrial stromal cells often show ovarian sex cord-like structures and smooth muscle differentiation. A few cases of endometrial stromal tumors showing rhabdoid differentiation have been reported. The present case is a 20-year-old woman with endometrial stromal sarcoma that had sex cord-like structures, smooth muscle components and rhabdoid differentiation.

Key Words: *Endometrial stromal sarcoma, Rhabdoid, Sex cord structure, Smooth muscle differentiation.*

INTRODUCTION

The first case of uterine tumor with rhabdoid features was described by Cho et al in a 46-year-old woman under the designation of malignant rhabdoid tumor(MRT) in 1989(Cho et al., 1989). One year later, Fitko et al reported a similar case under another designation of endometrial stromal sarcoma with rhabdoid differentiation, because they thought that the tumor arose from endometrial stroma(Fitko et al., 1990). In 1992, Lloreta and Prat described an unusual benign stromal nodule showing rhabdoid components, in addition to stromal, smooth and skeletal muscle and sex cord-like structures(Lloret and Prat, 1992). Recently, Mount et al.(1995) reported a case of uterine carcinosarcoma with rhabdoid tumor component. "Composite" extrarenal rhabdoid tumors(CERTs) which have reconizable "parent" neoplasm are considered as a heterogeneous group of lesions with a clonal overgrowth of rhabdoid cell population. The reason for retaining of the diagnosis of "rhabdoid tumor" in CERTs is their aggressive biologic behavior.

We report here a case of endometrial stromal tumor with rhabdoid and smooth muscle differentiation, which occurred in a 22-year-old unmarried woman, and review the possible origin of rhabdoid component.

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CASE REPORT

Clinical history

A 20-year-old unmarried woman presented with vaginal bleeding and low abdominal discomfort which she had had for 15 days. On hysteroscopic examination and pelvic CT, an ill-defined, walnut-sized mass was found in the endometrial cavity. Polypectomy specimen was diagnosed as endometrial stromal sarcoma and it was followed by a radical hysterectomy with preservation of the right ovary. She has been well after 3 cycles of VAC chemotherapy.

Pathology

Gross findings

The mass removed by polypectomy consisted of a gray-tan, soft mass, measuring 2.8 × 2.5 × 2.0 cm. On section, the cut surface showed a homogeneously

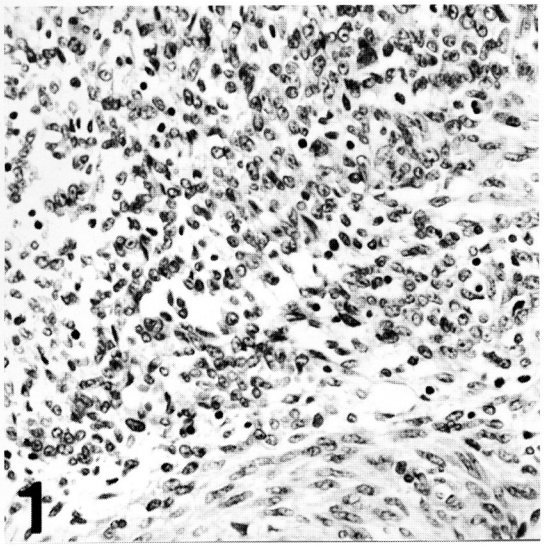

Fig. 1. The small uniform cells closely resemble the proliferative-phase endometrial stromal cells.

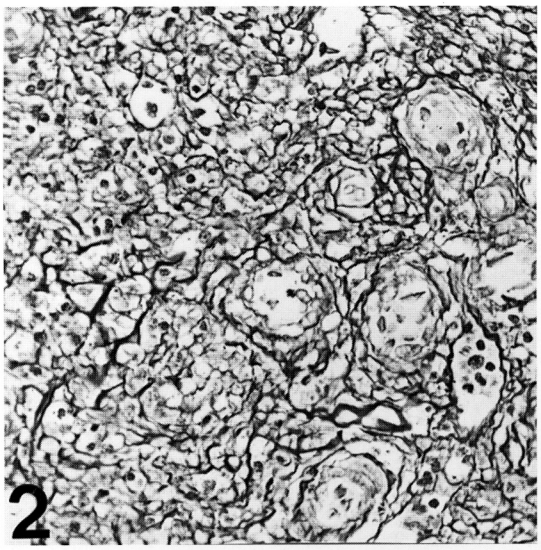

Fig. 2. Silver reticulum stain demonstrates reticulin fibers wrapping around individual tumor cells and prominent blood vessels.

yellowish gray solid appearance with multifocal hemorrhagic foci. On the hysterectomy specimen, a polypoid remnant of tumor, measuring 1.0 × 0.8 × 0.3 cm in size, was attached to the left cornus of the corpus. The nodule was yellow-tan, solid and appeared superficially infiltrative into the myometrium. Both adnexae were free of any pathologic findings.

Microscopic findings

The masses removed by polypectomy and hysterectomy were composed of diffuse proliferation of small, round tumor cells which had scanty amounts of cytoplasm with ill-defined borders and uniform round to oval nuclei with prominent nucleoli, resembling the stromal cells of proliferative endometrium (Fig. 1). Prominent vessels similar to the spiral arterioles of endometrium were found. These stromal cells were individually surrounded by reticulin fibers(Fig. 2). The bundles of spindle cells with long, acidophilic cytoplasmic processes, which were considered as smooth muscle fibers were intimately admixed with stromal cells(Fig. 3). In addition, the tumor cells were arranged in cords and trabeculae, mimicking the sex-cord like structures seen in the sex-cord stromal tumors of the ovary. In some areas, the tumor cells had a polygonal shape with abundant eosinophilic cytoplasm and eccentrically located round vesicular nucleus and a prominent nucleolus. Many of these

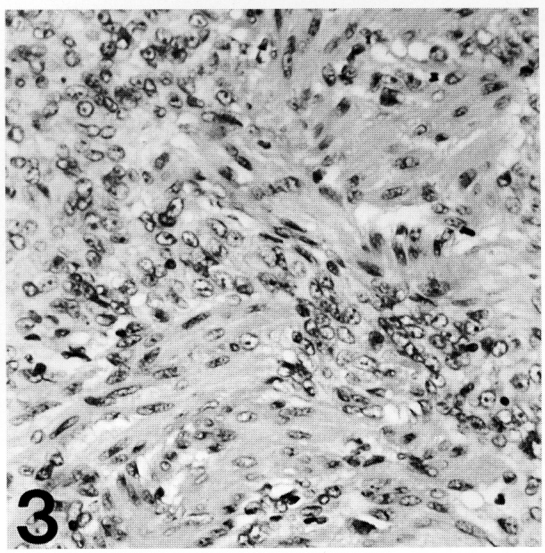

Fig. 3. The tumor with area of smooth muscle differentiation.

cells contained densely eosinophilic, hyaline globules in their cytoplasms(Fig. 5). These globules were negative for PAS stain. At the periphery, dilated endometrial glands were observed. The tumor infiltrated into the superficial myometrium.

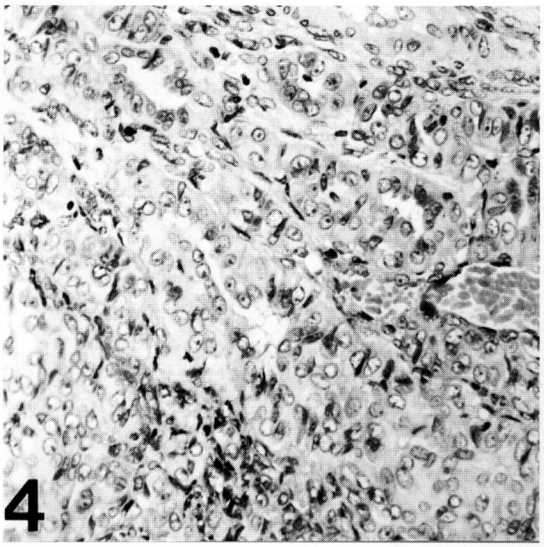

Fig. 4. Glands and cord-like arrangements of epithelioid cells.

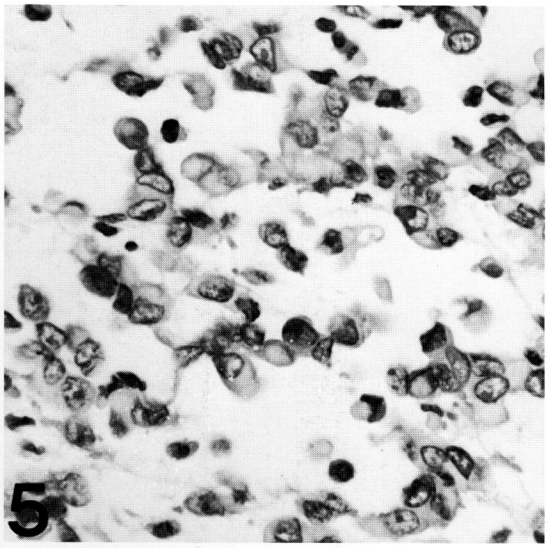

Fig. 5. The round tumor cells have deeply acidophilic hyaline globules in the cytoplasm.

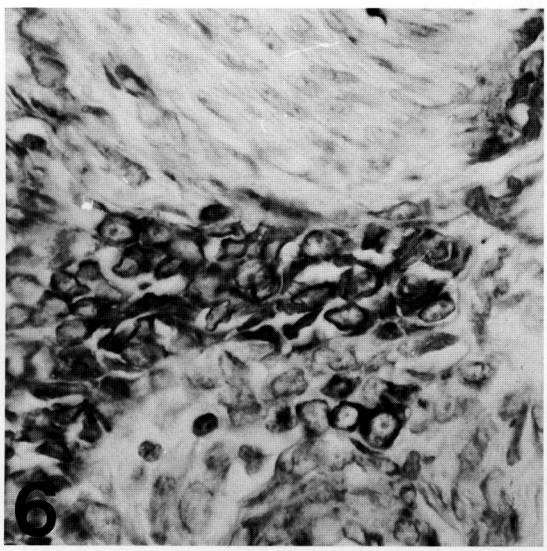

Fig. 6. Strong vimentin-positive tumor cells are found within the vimentin-negative smooth muscle fibers.

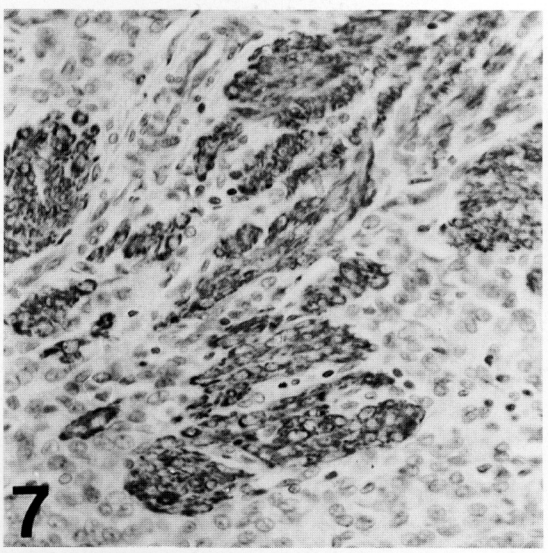

Fig. 7. Smooth muscle actin is negative in stromal cells, whereas smooth muscle fibers are positive.

Immunohistochemical staining

The staining for vimentin(Dako, Santa Barbara, USA) was positive in most of the tumor cells corresponding to typical endometrial stromal cells, sex cord-like structures and rhabdoid cells, but negative in the spindle cells which were considered as smooth muscle differentiation of the tumor(Fig. 6). In contrast, smooth muscle-specific actin and desmin(Dako, Santa Barbara, USA) were positive in the latter, but negative in the former(Fig. 7). There were no myoglo-

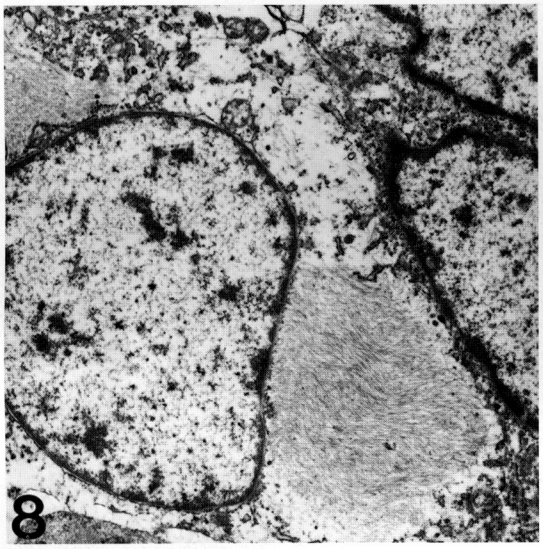

Fig. 8. The rhabdoid cells contain characteristic paranuclear whorls of intermediate filaments.

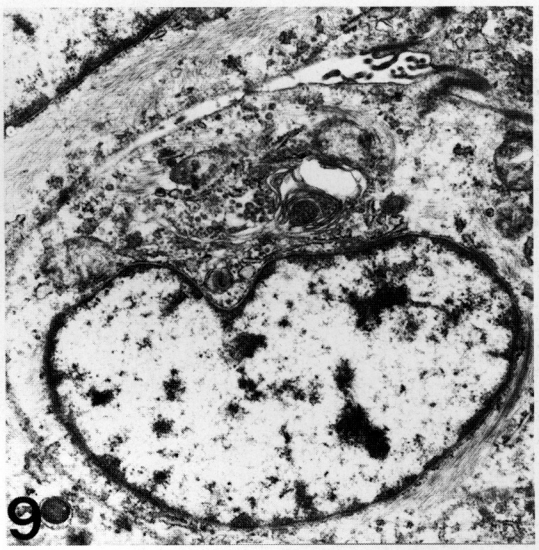

Fig. 9. Epithelioid cells are joined by poorly developed intercellular junctions, and the luminal surface has a few short microvilli.

bin-positive cells(Dako, Santa Barbara, USA). On staining for cytokeratin, some of the cells in the sex-cord like structures were positive for wide-spectrum cytokeratin(Dako, Santa Barbara, USA) and low molecular cytokeratin, CAM 5.2(Becton-Dickinson, San Jose, USA). Epithelial membrane antigen(Dako, Santa Barbara, USA) was negative in tumor cells. The immunostaining for estrogen and progesterone receptors(Immunotech, Marseille, France) showed numerous positive nuclei in the stromal cells.

DNA ploidy study

A Feulgen-stained touch imprint of the tumor was analyzed by CAS 200 Image Analyzer using Quantitative DNA Ploidy Software showed a diploid DNA pattern with DNA index 1.04 and proliferative index 16.7 %.

Ultrastructural findings

The cells featuring rhabdoid differentiation contained irregular indented nuclei and characteristic paranuclear whorls of intermediate filaments, corresponding to the vimentin-positive, hyaline globules(Fig. 8). Some of the cells were surrounded by basal lamina and joined by poorly developed intercellular junctions. Narrow luminal spaces with a few short microvillus projections were observed(Fig. 9).

DISCUSSION

Endometrial stromal sarcoma by definition is composed of cells resembling the stromal cell of the normal proliferative phase endometrium. Differing from stromal nodule, it has infiltrative margins and/or intravascular invasion. These tumors have been divided into low and high grade sarcoma on the basis of mitotic counts since Norris and Taylor's publication (Norris and Taylor, 1966). However, Evans classified this tumor into endometrial stromal sarcoma and undifferentiated sarcoma, depending on the degree of differentiation of stromal cells(Evans, 1982). The tumor described as uterine neoplasms with sex cord-like elements by Clement and Scully is generally included in the endometrial stromal group because of the resemblance of the stromal tumor cells to endometrial stromal cells(Clement and Scully, 1976).

Smooth muscle cells present in about 10 % of the stromal lesions lead to misinterpretation as myometrial infiltration of endometrial stromal sarcoma in curettage specimen(Tavassoli and Norris, 1981). In the present case, the bundles of smooth muscle found in the polypectomy specimen were initially regarded as myometrial invasion. However, it was clearly evident that the smooth muscle cell was a component of the tumor, even though invasion to the superficial

myometrium was demonstrated in the hysterectomy specimen.

In our case, the differential diagnosis primarily included mullerian adenosarcoma and epithelioid leiomyosarcoma. In stromal sarcoma, the epithelial components are minor and take the form of poorly circumscribed small tubules, trabeculae or cords, whereas adenosarcomas are characterized by papillary growth, uniformly distributed glandular components and periglandular condensation of the stroma(Clement and Scully, 1974). Epithelioid leiomyosarcoma is defined as a smooth muscle tumor composed of round(epithelial-like) cells arranged in sheets and/or cords, often blending into more elongated cells. The cytoplasm may be clear or eosinophilic(Kurman and Norris, 1976). Generally, smooth muscle tumors have positive reaction for muscle-specific actin and desmin, but may be positive to cytokeratin and epithelial membrane antigen(EMA)(Brown et al., 1988 ; Miettinen, 1988). In contrast, the stromal cells are usually positive to vimentin, but negative for actin and desmin, although occasional reactivity for muscle-specific actin and desmin as well as focal cytokeratin positivity have been reported(Abrams et al., 1991 ; Binder et al., 1991 ; Lillemoe et al, 1991). The main tumor cells in the present case showed strong positive reaction for vimentin, whereas the epithelial-like structures were focally positive for keratin and EMA, and smooth muscle components were positive for smooth muscle-specific actin and desmin.

Malignant rhabdoid tumor(MRT) was initially described in 1978 by Beckwith and Palmer as a variant of Wilms' tumor(Bechwith and Palmer, 1978) and later, the term rhabdoid tumor was used by Hass et al.(Hass et al., 1981). Most commonly, malignant rhabdoid tumors arise in the kidneys of children and young adults, but approximately 100 examples of extrarenal neoplasms have been reported.(Lemos and Hamoudi, 1978, Ekfors et al., 1985, Frierson et al., 1985, Tsuneyoshi et al, 1985, Biggs et al., 1987, Parham et al., 1988). Malignant extrarenal rhabdoid tumors(MERTs) have been observed in pure form over a wider range of patient ages and anatomic locations, but they show morphologcal and biological homology with renal MRT. In "composite" extrarenal rhabdoid tumors(CERTs), rhabdoid elements are combined with another distinctive pathologic entity and show ultrastructural and immunohistochemical heterogeneous expression of epithelial, mesenchymal and neural defferentiations. Recently, it is generally accepted that the rhabdoid phenotype is not an entity but a final common pathway for the evolution of several varieties of neoplasms as they progress to a higher-grade, more aggressive biological form. However, the term of malignant rhabdoid tumor deserve the continuous use, because the rhabdoid phenotype is constantly associated with clinical aggressiveness.

Rhabdoid differentiation in uterine tumors has been rarely described.(Cho et al., 1989, Fitko et al., 1990). The case reported by Lloret and Prat as endometrial stromal nodule with smooth and skeletal muscle components showed very similar histologic, immunohistochemical and ultrastructural features to rhabdoid differentiation, even though the authors described them as stromal cells(Lloret and Prat, 1992).

Although the origin of malignant rhabdoid tumor is still uncertain in extrauterine location, the origin from endometrial stromal cells were speculated by Fitko et al.(Gonzalez-Crussi et al., 1982 ; Dervan et al., 1987). However, the origin of tumors composed of "parent" endometrial stromal sarcoma admixed with smooth muscle cells and rhabdoid components, like that of the present case, has been attributed to totipotential reserve cells or stem cells.

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