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HYALINIZING SPINDLE CELL TUMOR WITH GIANT ROSETTES OF THE UTERUS – A CASE REPORT

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Summary

Hyalinizing spindle cell tumor with giant rosettes (HSCTGR) is unusual, recently recognized entity, histologically characterized by the presence of large rosette-like structures. Apart from these formations, histological features of HSCTGR are indistinguishable from low-grade fibromyxoid sarcoma (LGFMS), and available data suggest that these two tumors present different variants of the same entity.

Herein we report the case of HSTCGR found in the uterus. To our knowledge, the present case is the first description of HSTGR occurring at this location as well as the first HSCTGR described in the Croatian medical literature.

A 38-year-old woman presented to her gynecologist with symptoms of acute pain in the lower abdomen. Gynecological ultrasound examination showed an enlarged uterus with a tumor mass. Total hysterectomy and bilateral adnexectomy with selective pelvic and para-aortal lymphadenectomy were performed. Serial slicing of the enlarged uterus revealed a grayish white tumor mass with 15 cm in maximum length. The margins of the tumor merged with the uterine wall and the tumor infiltrated more than one half of the myometrium. Histologically, the tumor showed typical features of HSTGR.

Postoperatively, no complications occurred.

Twenty-two months after surgery, our patient is alive with no signs of recurrence. She needs to be followed up for a long period because HSTCGR belongs to a low-grade malignancy group with the potential to recur and produce late metastasis.

KEY WORDS: *giant rosettes, low-grade sarcoma, fibromyxoid sarcoma, uterus*

HIJALINIZIRAJUĆI TUMOR VRETENASTIH STANICA S GIGANTSKIM ROZETAMA NAĐEN U UTERUSU – PRIKAZ SLUČAJA

Sažetak

Hijalinizirajući tumor vretenastih stanica s gigantskim rozetama (HSCTGR) rijedak je, relativno nedavno opisan entitet, čija je histološka značajka stvaranje krupnih struktura koje nalikuju rozetama. Osim po prisutnosti ovih tvorbi, histološki ga se ne može razlikovati od fibromiksoidnog sarkoma niskoga gradusa i danas se vjeruje da su oni različite varijante istog entiteta.

Opisujemo hijalinizirajući tumor vretenastih stanica s gigantskim rozetama nađen u uterusu. Prema našim spoznajama radi se o prvom slučaju opisanom na toj lokalizaciji te također prvom slučaju HSCTGR u hrvatskoj medicinskoj literaturi.

Dotada zdrava 38-godišnja žena javila se ginekologu zbog akutne boli u donjem dijelu abdomena. Ginekološkim i ultrazvučnim pregledom nađena je veća tumorska tvorba u području uterusa. Učinjena je histerektomija s adneksektomijom i selektivnom limfadenektomijom. Serijskim rezovima kroz stijenku povećanog uterusa prikazao se sivkastobjelkasti

tumor najvećeg promjera 15 cm, koji je infiltrirao više od ½ debljine miometrija. Patohistološkom analizom postavljena je dijagnoza HSCTGR.

Postoperativni je tijek prošao bez komplikacija, a 22 mjeseca nakon operacije naša je pacijentica bez znakova recidiva bolesti. HSCTGR pripada skupini tumora s niskim malignim potencijalom te mogućnošću recidiviranja i metastaziranja nakon više godina, stoga se preporučuje dugoročno kliničko praćenje.

KLJUČNE RIJEČI: *gigantske rozete, sarkom niskoga gradusa, fibromiksoidni sarkom, uterus*

INTRODUCTION

Among highly heterogeneous groups of tumors and tumor-like conditions derived from soft tissue, tumors showing fibroblastic and myofibroblastic differentiation compose a large and important group of different entities with wide range of morphologic appearances (1). One of them is a hyalinizing spindle cell tumor with giant rosettes (HSCTGR). This unusual entity is presented in most cases as a grossly well-circumscribed, deep-seated soft tissue tumor of the extremities (2). Other sites of origin include prestyloid and parapharyngeal space (3), pararectal (4), presacral area (5) and broad ligament (6).

Histological features of HSCTGR are quite distinctive, characterized by bland-looking fibromyxoid stroma punctuated with large rosette-like structures. Despite its benign morphology, since the first description in 1997, a few cases of HSCTGR with pulmonary metastases have been reported (7-10) proving its malignant potential. Therefore, HSCTGR has been included in the latest WHO classification of soft tissue tumors as a variant of low-grade fibromyxoid sarcoma.

Herein, we report the case of HSTCGR found in the uterus. To our knowledge, the present case is the first description of HSTGR occurring in this location as well as the first HSCTGR described in the Croatian medical literature.

CASE REPORT

A 38-year-old woman, mother of four, presented to her gynecologist with symptoms of acute lower abdominal pain persisting for a few hours. Her past medical history was unremarkable. Ovarian torsion as a complication of an underlying ovarian lesion was suspected, and the patient was admitted for additional tests and surgical treatment. Gynecological ultrasound examination showed an enlarged uterus with a tumor mass, 16 cm in maximum length, consisting of solid and cystic areas (Figure 1). Preoperative chest radiogram, computed tomography and ultrasound examination of the pelvic and abdominal organs did not reveal enlarged lymph nodes or distant metastases.

Laboratory analysis revealed severe sideropenic anemia (red blood cell count $3.34x10^{12}$/L, Hemoglobin 60.5g/l, mean corpuscular volume 68.3 fL), while other parameters, including white blood cell count, were within normal limits (WBC $5.17x10^{9}$/L). The serum level of cancer antigen CA-125 was 16.8ng/ml (normal value ‹ 35 ng/ml).

The patient underwent total hysterectomy and bilateral adnexectomy with selective pelvic and para-aortal lymphadenectomy. Postoperatively, no complications occurred. No adjuvant treatment was performed.

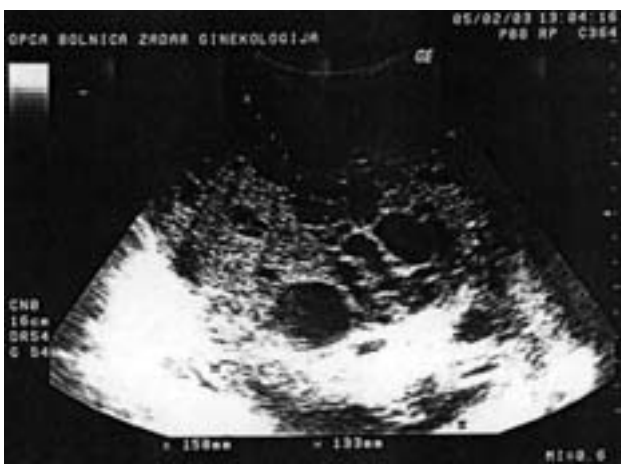

Figure 1. Preoperative ultrasound examination: enlarged uterus with tumor consisted of solid and cystic areas

MATERIALS AND METHODS

The surgical material was formalin-fixed, representative sections of the tumor were routinely processed, embedded in paraffin and 5 µm

sections were stained with hematoxilin and eosin. Additional sections from representative paraffin blocks were examined immunohistochemically using commercially available antibodies and the avidin-biotin-peroxidase method. Immunohistochemical stains used included vimentin (microwave pretreatment, 1:200 dilution, Dako), desmin (microwave pretreatment, 1:200 dilution, Dako), Cytokeratin AE1/AE3 (microwave pretreatment, 1:100 dilution, Dako), neuron specific enolase (NSE, microwave pretreatment, 1:50 dilution, Dako), S-100 (microwave pretreatment, 1:400, Dako), smooth muscle actin (SMA, microwave pretreatment, 1:500, Dako), sarcomeric actin (microwave pretreatment, 1:50, Dako) and CD34 (microwave pretreatment, 1:50, Dako).

RESULTS

The resected, diffusely enlarged, smooth surfaced uterus measured 20x18x12 cm. Serial slicing revealed a grayish white, myxoid, partially cystic tumor mass with 15 cm in maximum length. The margins of the tumor merged with the uterine wall and the tumor infiltrated more than one half of the myometrium.

Pathohistological examination confirmed the diagnosis of HSTGR. The tumor consisted of paucicellular spindled stroma punctuated by large collagen rosettes which tend to cluster together (Figure 2-3). These structures were composed of a central, almost acellular core of collagen fibers surrounded by multiple layers of tumor cells. These cells were slightly plumper than the surrounding cells, but blend imperceptibly with the surrounding spindle-shaped tumor cells (Figure 4). The stroma of varied cellularity consisted of fibroblastic cells forming a storiform pattern in the hypocellular hyalinized and myxoid areas. The myxoid areas dominated in our material and highlighted the plexiform vascularity. Only mild cytologic atypia were present. Necrosis was absent and less than one mitosis per 50 high power fields was seen.

The results of immunohistochemical staining were consistent with diagnosis of HSTGR. All tumor cells showed strong positivity for vimentin. Some cells surrounding the rosettes showed mild positivity for NSE, smooth muscle actin and

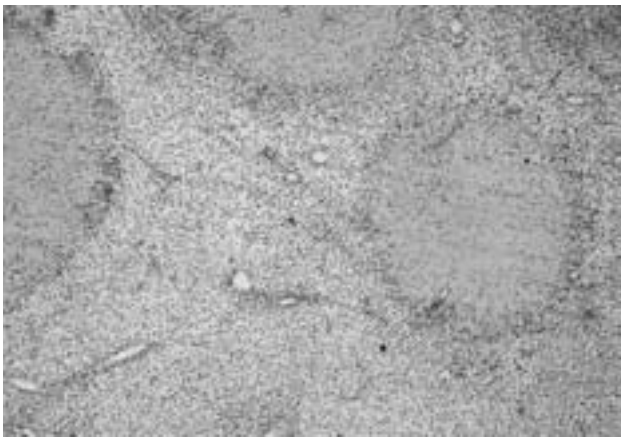

Figure 2. The typical feature of HSCTGR at low magnification, H&E x40

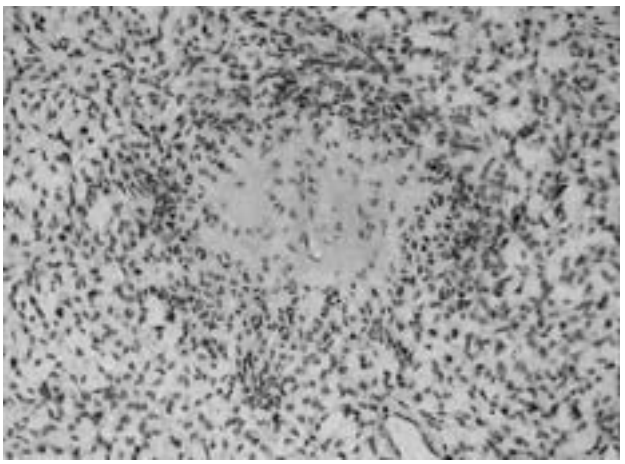

Figure 3. The central area of the rosette formed by collagen fibers, H&E x200

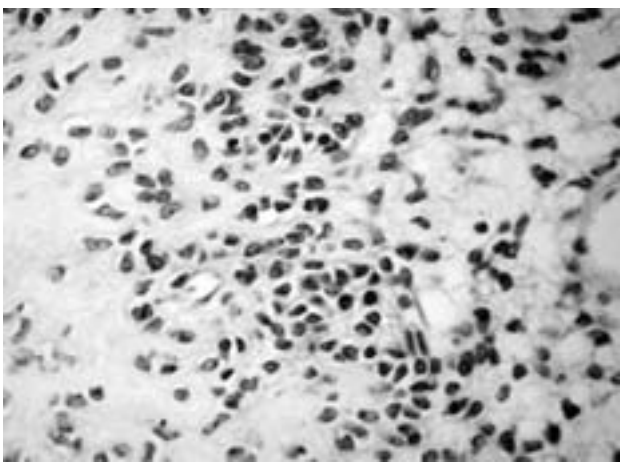

Figure 4. Palisaded rounded cells occupying the periphery of the rosette, H&E x400

desmin, and minimal for S-100. All tumor cells were negative for CD34, SA and cytokeratin.

DISCUSSION

HSCTGR was originally described by Lane, Shannon and Weiss in 1997 (2). They reported a series of 19 patients with a histologically distinct tumor characterized by fibromyxoid stroma punctuated with rosette-like structures in which neoplastic cells were arranged around a central collagenous core. In the initial series, the mean patient age was 38 years (age range 14-65), with male to female ratio of 7:3. A circumscribed, painless, deep soft tissue mass in the extremities was the most common clinical presentation. These tumors presented an oval or multilobated, well circumscribed masses, with mean diameter 6.3cm (2.3-20.3cm). Their cut surfaces were pale, whorled and predominantly solid. Some of them exhibited areas of cystic degeneration.

The stromal cells showed fibroblastic differentiation and were arranged in a variety of patterns. In most areas, the cells were arranged in irregular fascicles separated by moderate amounts of collagen. There were areas with extensive hyalinization with paucity of neoplastic cells, but areas with myxoid stroma were also seen. The cellularity varied from case to case and in different areas of the same tumor. Stromal cells showed only a mild degree of nuclear atypia, and in most of the cases, mitoses were difficult to find. Characteristic rosette-like structures which tended to cluster together, were composed of the central core of eosinophyllic collagen arranged centrifugally from the center, surrounded by rounded to ovoid cells with clear to eosinophyllic cytoplasm and minimal nuclear atypia. Occasional cells showed intranuclear inclusions. In few cases, an osseous and chondroid metaplasia, areas of calcification, hemosiderin deposition and cystic degeneration were described.

Immunohistochemical studies in original, as in later reports have shown inconsistent results. The most consistent findings have been vimentin reactivity, in both stromal cells and the cells within rosettes. A small proportion of the latter also showed reactivity to S-100, NSE and CD57 (1-13).

In few cases examined with electron microscopy, both populations of tumor cells have demonstrated ultrastructural features of fibroblasts and myofibroblasts. These include discontinuous basal lamina, pinocytic vesicles, dilated rough endoplasmic reticulum, and microfilaments with focal dense bodies (3, 12, 13). Neurosecretory granules have been reported in one case (3).

Since the earliest report, Lane et al. pointed to the morphologic similarities between this lesion and low-grade fibromyxoid sarcoma (LGFMS). Originally described by Evans in 1987, this tumor is characterized by a bland fibromyxoid stroma which is in contradiction to high rate of local recurrence and pulmonary metastases discovered in a significant percentage of cases (14, 15). Lane et al. suggested that, despite the absence of evidence of its aggressive behavior at the time of reporting, with time HSCTGR may be proven to be a variant of LGFMS.

Subsequently, Woodruff et al. reported a case of HSCTGR in the arm of a 28-year-old woman with pulmonary metastases, detected 4 years after the original diagnosis (7). Farinha et al. provided a further case of multiple pulmonary metastases with long survival. They described multiple pulmonary nodules detected 5 and 8 years after diagnosis of HSCTGR involving the thigh of a 32-year-old woman (8).

Three years after the first reports of HSCTGR, the original authors of that series reassessed their experience by comparing 17 cases of HSCTGR (including some of those reported in the original series) with 44 cases of LGFMS (9). They concluded that LGFMS and HSCTGR are variants of the same entity and should be regarded as low-grade sarcomas. Their opinion was based on several facts. These two tumors can be histologically differentiated only by the presence of giant rosettes in HSCTGR cases. The revision of histological slides of tumors, originally classified as LGFMS, in a number of cases revealed miniature rosettes. In addition, one case of the classic histological appearance of HSCTGR showed features of LGFMS in metastasis.

In their final remarks, they recommended both HSCTGR and LGFMS should be referred as «fibrosarcoma, low-grade fibromyxoid type» noting either the presence or the absence of giant rosettes. According to this recommendation,

both tumors has been included in the latest WHO classification of soft tissue tumors as variants of fibrosarcoma.

In 2003, Reid et al. reported a common t(7,16)(q34; p11) translocation in two cases of HSCTGR and two cases of LGFMS (16). They provided the first cytogenetic proof that these tumors are variants of the same entity, and also suggested that cytogenetic analysis might help to diagnose doubtful cases with unusual histologic features.

CONCLUSION

HSCTGR is a rare low-grade malignancy, a variant of low-grade fibromyxoid sarcoma. Pathologists should be aware of its distinctive histological features and deceptively bland appearance. Accurate histological diagnosis followed by wide surgical excision and a close follow-up is essential.

Twenty-two months after the operation, our patient is feeling well with no signs of recurrence. We recommend a prolonged follow-up in order to rule out the development of local recurrence as well as metastatic disease.

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