Heterologous type of malignant mixed Müllerian tumor of the uterus presenting as a vulvar mass

M. Grigore[1], C. Ilea[1], C. Terinte[2], A. Sava[3], R. Popovici[1]

[1]Department of Obstetrics and Gynecology, University of Medicine and Pharmacy "Gr. T. Popa", Iasi
[2]Department of Pathology, Oncological Institute, Iasi
[3]Department of Anatomy, University of Medicine and Pharmacy "Gr. T. Popa" Iasi (Romania)

Summary

Carcinosarcoma is a rare, extremely aggressive tumor of the uterus with a poor prognosis. The authors describe a case of a 78-year-old woman who presented with a giant mass protruding through the cervix, vagina, and vulva. A total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. The histopathological examination of the surgical specimen revealed a malignant mixed Müllerian tumor. The clinical and pathological features, molecular data, and prognosis of this aggressive neoplasm are discussed. Although uterine carcinosarcomas are extremely rare, when a postmenopausal woman with a vulvar mass is admitted to the gynecology clinic, the physician should consider that the mass may be a carcinosarcoma.

Key words: Carcinosarcoma; Malignant mixed Müllerian tumor; Vulvar mass.

Introduction

Carcinosarcoma of the uterus, also called malignant mixed Müllerian tumor, is a rare, extremely aggressive biphasic neoplasm. The term carcinosarcoma reflects the origin of these mixed tumors, characterized by a combination of epithelial and mesenchymal (stromal) elements, traditionally divided into homologous and heterologous subtypes. Carcinosarcoma is quite uncommon, with an incidence of fewer than two per 100,000 women per year. It has an extremely poor prognosis, with a five-year survival rate of 33% to 39% [1].

Case Report

The authors present the case of a 78-year-old woman diagnosed with carcinosarcoma of the uterus. She came to the hospital because of a large tumoral mass protruding through her vagina. She was not able to specify the time she first observed this mass. The patient (weight, 64 kg; body mass index, 25) had no pathological antecedents. Clinical examination revealed a large tumoral mass with areas of necrosis and hemorrhage; the origin of this mass was the uterus (Figure 1). An initial biopsy revealed only necrosis. The authors performed a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Because of the patient's critical condition and the high anesthesiologic risk, a bilateral pelvic lymphadenectomy and aortic lymphadenectomy were not performed.

The histopathological analysis showed a heterologous malignant mixed Müllerian tumor (Figure 2). The epithelial differentiation was endometrioid and poorly differentiated papillary serous carcinoma, and the mesenchymal component was rhabdomyosarcoma (Figure 3). After surgery, the patient was sent to the oncology unit.

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Discussion

Carcinosarcoma is a rare, extremely aggressive tumor of the uterus with a poor prognosis. It is predominantly identified in postmenopausal woman (median age 65 years), but it can also be found in young women or children [2, 3].

Carcinosarcomas and carcinomas of the uterus have similar risk factor profiles. Their incidence increases in association with marked obesity, which generates increased exposure to estrogen hormones, nulliparity, use of exogenous estrogen, treatment with tamoxifen (for breast cancer), and pelvic radiation. The incidence decreases in association with oral contraceptive use [4, 5]. None of the risk or protective factors was found in the present patient.

Uterine carcinosarcomas typically present with abnormal vaginal bleeding and also may present with bloody discharge, watery discharge, abdominal pain, or an abdominal mass [3]. Carcinosarcoma usually develops as a large, soft, polypoid mass, filling and distending the uterine cavity. In the present case, the tumor was very large (15 cm) and protruded outside the vagina through the cervical os. Histologic examination of standard hematoxylin and eosin-stained sections showed the two components of carcinosarcoma: malignant-appearing epithelial and stromal (mesenchymal). These two morphologies can be intimately admixed or may appear as distinct components. The epithelial malignant tissue can have the appearance of any of the malignant epithelial neoplasms encountered in the female genital tract: serous, endometrioid, clear cell, mucinous, and squamous patterns [3]. Of these patterns, the most frequent one encountered is serous [6]. The stromal component may resemble mesenchymal cell types normally present in the uterus (i.e., homologous differentiation) or

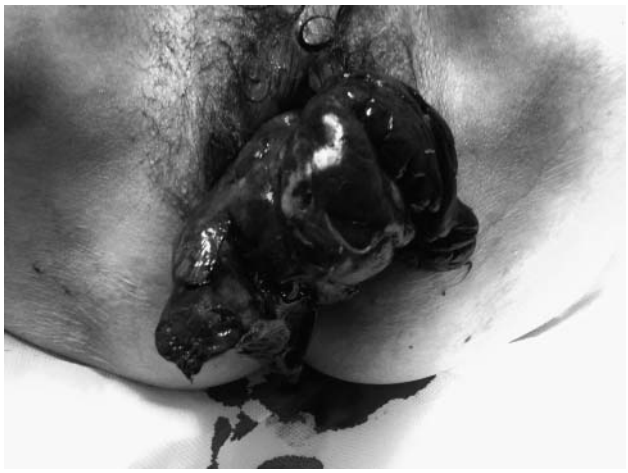

Figure 1. — A large (15x15 cm) mass protruding from the cervix and the vagina.

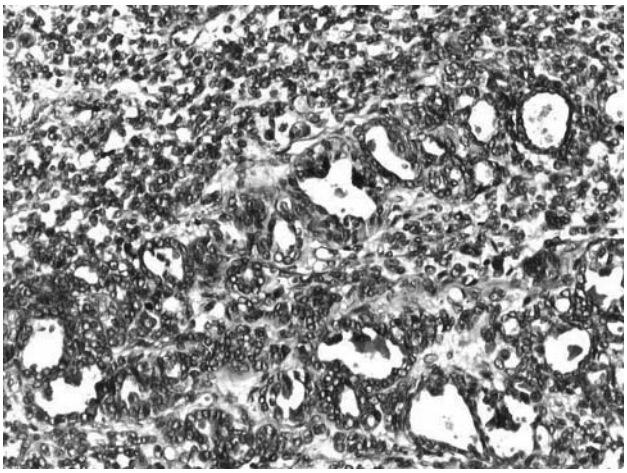

Figure 2. — Malignant mixed Müllerian tumor – the transition between epithelial and mesenchymal components is subtle.

may have heterologous elements that are not normally found in the uterus, such as rhabdomyosarcoma, chondrosarcoma, and osteosarcoma, listed in decreasing order of frequency [7]. Frequently, the histologic pattern is simply high-grade sarcoma, without appreciable specific differentiation.

Genetic and molecular data provides evidence of a monoclonal origin of most carcinosarcomas. The arguments for this monoclonal origin are the presence of similar chromosomal aberrations, concordant loss of heterozygosity, identical *p53* and *K-ras* mutations, and matching X inactivation patterns in both histologic components of most carcinomasarcoma cases studied [6-9].

Additionally, the specific patterns of genetic aberrations are more consistent with a high-grade carcinoma than a sarcoma, providing strong support for divergent differentiation within a primarily epithelial neoplasm (carcinoma) as the histogenesis. Although the theory of being monoclonal or biclonal is under investigation, the clinical implication of this fact is unknown. The carcinomatous component has been shown to have more aggressive behavior and be a better predictor of clinical outcome in carcinosarcomas. The carcinosarcoma evolution is unfavorable, even if it is identified and treated in the initial phases. The recurrence or survival do not correlate with the patient's age and the histological type of the tumor (homologous or heterologous) [10].

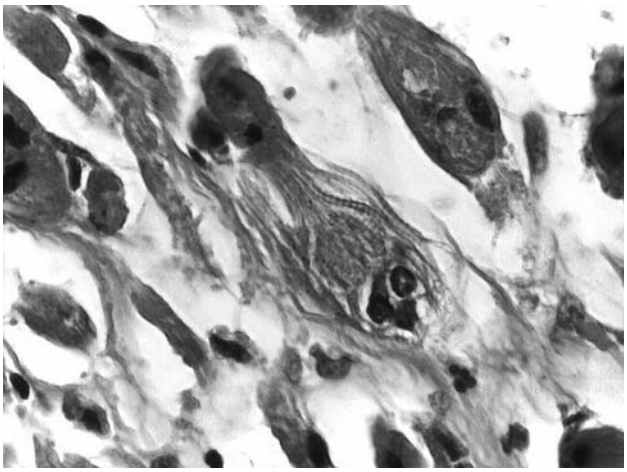

Figure 3. — The heterologous component of the malignant mixed Müllerian tumor: rhabdomyosarcoma.

Conclusions

Carcinosarcomas are rare, highly aggressive biphasic tumors composed of malignant epithelial and mesenchymal components. Although they can arise anywhere in the female genital tract, they are more common in the uterus. They usually appear to arise from the transformation of pluripotent stem cells capable of giving rise to cells with divergent differentiation. The authors present a rare case of a carcinosarcoma with an unusual clinical presentation as a giant tumor mass outside the vagina. Recent data have advanced understanding of the biology of this lesion, and clinical trials are underway to determine the most efficacious chemotherapeutic regimens.

References

[1] Vaidya A.P., Horowitz N.S., Oliva E., Halpern E.F., Duska L.R.: "Uterine malignant mixed mullerian tumors should not be included in studies of endometrial carcinoma". *Gynecol. Oncol.*, 2006, *103*, 68.

[2] Bansal N., Herzog T.J., Seshan V.E., Schiff P.B., Burke W.M., Cohen C.J. et al.: "Uterine carcinosarcomas and grade 3 endometrioid cancers: evidence for distinct tumor behavior". *Obstet. Gynecol.*, 2008, *112*, 64.

[3] Zaloudek C.J., Hendrickson M.R.: "Mesenchimal tumors of the uterus". In: Kurman R.J., (ed)., *Blaustein's pathology of the female genital tract*. New York: Springer–Verlag, 2002, 561.

[4] Zelmanowicz A., Hildesheim A., Sherman M.E., Sturgeon S.R., Kurman R.J., Barrett R.J., *et al.*: "Evidence for a common etiology for endometrial carcinomas and malignant mixed mullerian tumors". *Gynecol. Oncol.*, 1998, *69*, 253.

[5] McCluggage W.G.: "Uterine carcinosarcomas (malignant mixed Mullerian tumors) are metaplastic carcinomas". *Int. J. Gynecol. Cancer*, 2002, *12*, 687.

[6] Kernochan L.E., Garcia R.L.: "Carcinosarcomas (malignant mixed Müllerian tumor) of the uterus: advances in elucidation of biologic and clinical characteristics". *J. Natl. Compr. Canc. Netw.*, 2009, *7*, 550.

[7] Jin Z., Ogata S., Tamura G., Katayama Y., Fukase M., Yajima M., *et al.*: "Carcinosarcomas (malignant mullerian mixed tumors) of the uterus and ovary: a genetic study with special reference to histogenesis". *Int. J. Gynecol. Pathol.*, 2003, *22*, 368.

[8] Schulten H.J, Gunawan B., Enders C., Donhuijsen K., Emons G., Fuzesi L.: "Overrepresentation of 8q in carcinosarcomas and endometrial adenocarcinomas". *Am. J. Clin. Pathol.*, 2004, *122*, 546.

[9] Abeln E.C., Smit V.T., Wessels J.W., de Leeuw W.J., Cornelisse C.J., Fleuren G.J., *et al.*: "Molecular genetic evidence for the conversion hypothesis of the origin of malignant mixed müllerian tumours". *J. Pathol.*, 1997, *183*, 424.

[10] Temkin S.M., Hellmann M., Lee Y.C., Abulafia O.: "Early-stage carcinosarcoma of the uterus: the significance of lymph node count". *Int. J. Gynecol. Cancer,* 2007, *17*, 215.

Address reprint requests to:
M. GRIGORE, M.D., PhD
University of Medicine and Pharmacy "Gr. T. Popa"
Department of Obstetrics and Gynecology
Str.Universitatii 16,
700115 Iasi (Romania)
e-mail: mihaela.grigore@edr.ro