Carcinosarcoma of the uterus: a case report and review of the literature

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Summary

Carcinosarcoma is a rare tumor of the uterus with a poor prognosis. We present a case of uterine carcinosarcoma in an 82-year-old woman who suffered from pervaginal bleeding for ten months duration with progressive anemia. Abdominopelvic nuclear magnetic resonance (NMR) imaging showed the presence of an intrauterine mass, infiltrating the myometrium and reaching the cervix. The patient was submitted to total abdominal hysterectomy with bilateral salpingo-oophorectomy. The carcinosarcoma, arising from the lumen of the uterus, infiltrated the inner one-third of the myometrial layer (pT1b, pNx, pMx; FIGO Stage 1B). A CT of the total body performed six months after surgery showed no signs of recurrent and/or metastatic tumor.

The clinicopathological features, treatment options and prognosis of this aggressive neoplasm are reviewed.

Key words: Carcinosarcoma, Uterus.

Introduction

Carcinosarcoma, previously defined as malignant mixed Mullerian tumor, is a rare neoplasm, accounting for 2-5% of all malignant tumors of the uterus [1-4]. It is characteristically composed of malignant epithelial (carcinomatous) and mesodermal (sarcomatous) cells. Carinosarcoma is classified into homologous and heterologous types. In homologous tumors, both the carcinomatous and sarcomatous elements are normal components of the Mullerian system. In heterologous tumors, sarcomatous elements that have no benign counterpart in the uterus, such as skeletal muscle, bone and cartilage, are present [5]. Homologous and heterologous carcinosarcomas occur with approximately equal frequency [6].

We present a case of homologous carcinosarcoma and review the clinicopathological features, treatment options and prognosis of this aggressive neoplasm.

Case Report

A 82-year-old woman was admitted with the complaint of postmenopausal bleeding during the previous ten months.

The patient attained menarche at the age of 14 years and had a regular cycle with 6-day flow every 29 days until she was 50 years old when spontaneous menopause supervened. She was never submitted to Pap smear tests and she had never used any contraceptive device or pills. She was not sexually active. Obstetric history showed four full-term spontaneous vaginal deliveries.

At physical examination she was cachectic and pale. Her blood pressure was 130/80 mmHg. Abdominal examination did not reveal any abnormal mass or ascites. Per vaginal examination revealed ongoing bleeding with the presence of a cervical hematoma. The adnexa and the Douglas pouch were normal.

Blood cell count revealed signs of anemia (red blood count = 3,050,000/mm^3, hemoglobin = 8.8 g/dl, hematocrit = 28.5%). Anemia was treated with transfusion of two units of packed red cells (hemoglobin = 11.4 g/dl).

Transvaginal ultrasonographic (TVS) scan showed an enlarged uterus (8 x 7.5 x 4 cm) with an intrauterine mass measuring 5 x 5.5 cm. The adnexa were normal and no evidence of intraabdominal fluid collection was detected. Abdominopelvic nuclear magnetic resonance (NMR) imaging confirmed the presence of the intrauterine mass infiltrating the myometrium and reaching the cervix. The adnexa and other abdominal organs were normal (Figure 1).

The patient was submitted to total abdominal hysterectomy with bilateral salpingo-oophorectomy. There was no macroscopic evidence of intraabdominal dissemination and/or pelvic and paraaortic lymph node involvement. Her postoperative course was uneventful.

Gross examination of the surgical specimen showed a grayish exophitic mass, arising from the lumen of the uterus. Histological examination revealed the presence of mixed malignant epithelial and stromal cells, compatible with the diagnosis of carcinosarcoma (Figure 2). The neoplasm infiltrated the inner one-third of the myometrial layer (pT1b, pNx, pMx; FIGO Stage 1B).

A CT of the total body, performed six months after surgery showed no signs of recurrent and/or metastatic tumor.

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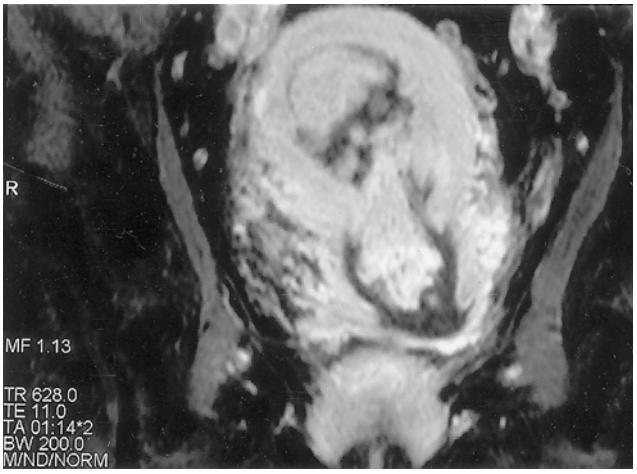
Fig. 1



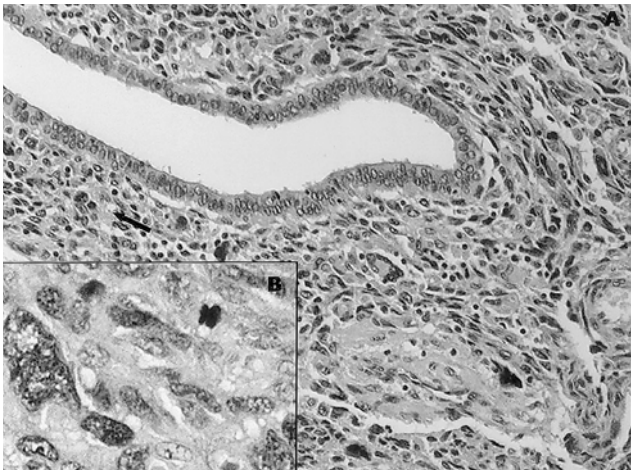


Fig. 2

Figure 1. — T2-weighted sagittal NMR of the pelvis, showing a pseudopolypoid mass (arrow) occupying the entire intrauterine lumen and infiltrating the myometrium.

Figure 2. A) Biphasic tumor with carcinomatous and sarcoma-like elements; neoplastic proliferation is formed by cells of different sizes - predominantly spindle cells, pleomorphic nuclei and ill defined cytoplasm. Moreover, the glandular component is composed of multilayered epithelium (hematoxylin/eosin 10 x). B) Neoplastic elements display marked nuclear anaplasia, variable pleomorphism, 20+ mitotic figures/10 HPF (hematoxylin/eosin 10 x).

Discussion

Carcinosarcoma generally occurs in postmenopausal women at a median interval from menopause ranging from 15 to 17 years [3, 7-10]. Recognized risk factors, similar to those reported for endometrial carcinoma, are obesity, nulliparity, exogenous estrogen use and tamoxifen therapy [11-18].

Our patient presented with postmenopausal bleeding for the previous ten months. Bleeding, combined with signs of uterine enlargement, is the commonest symptom [5]. In some cases abdominal pain is also present [19].

Endometrial curetting can be diagnostic in 50-70% of cases [20-22]. Recognized limiting factors are the small amount of tissue obtained, frequent necrosis, and inflammation of the tumor surface. Moreover, uterine curetting can be misleading in that only one type of tissue may be obtained, i.e. either the epithelial or stromal component only, so that the true biphasic nature of the neoplasm becomes apparent only when the entire specimen is available for study [6, 23].

Carcinosarcomas are characterized by an aggressive clinical course and an extremely poor prognosis. Seventy to 90% of tumor-related deaths occurred within 18 months after diagnosis [2, 24, 25]. Advanced stage at diagnosis has been postulated to account for much of the clinical aggressiveness of this tumor type, the prognosis being very poor when the neoplasm has extended beyond the uterus [2, 6, 7, 20, 26-31]. However, even patients with disease confined to the uterus have 5-year survival rates of less than 50% [21, 32-37]. An important prognostic factor is the depth of myometrial invasion [6, 23, 28, 29, 38-45]. However, given the high rate of microscopic metastases in patients with disease clinically confined to the uterus, this pathologic risk factor may simply be a surrogate marker for metastatic disease [46]. The homologous and heterologous subtypes do not seem to influence the prognosis [5].

Although the early literature is conflicting, recent studies have found that behavior and overall prognosis of carcinosarcoma is much more dependent on the characteristics of the epithelial than the stromal elements [43, 47]. Metastases invariably consist of the carcinomatous elements [43, 48, 49]. These characteristics, associated with evidence derived from immunohistochemical and molecular studies, suggested that carcinosarcoma is, in reality, derived from a single stem cell, in which the sarcomatous component is a metaplasic transformation of the epithelial component [50-56]. However, a small proportion of carcinosarcomas may originate from independent carcinomas and sarcomas [48].

NMR imaging has showed high accuracy in the local-regional staging of endometrial tumors, while the assessment of pelvic and lumbo-aortic lymph nodes seems more difficult [57].

Surgery in the form of abdominal hysterectomy and bilateral salpingo-oophorectomy including a visual inspection of the pelvic and paraaortic lymph nodes with removal of any and all suspicious lymph nodes, is the mainstay of treatment, according to the 1988 FIGO surgical staging system. About 20-60% of patients with disease confined to the uterus preoperatively will be upstaged after proper surgical staging [21, 33-37, 58]. Approximately, 20% of patients will be surgically upstaged because of metastases to regional lymph nodes [9, 34-37, 43, 58, 59]. The therapeutic importance of lymphoadenectomy still remains unclear, although an improved outcome may be expected to be similar to what was found in patients with endometrial carcinomas [46].

Due to its relative rarity, optimal adjuvant treatment of carcinosarcoma has remained poorly defined. Part of the difficulty with determining the “best therapy” stems from

the question of whether this entity should be treated as a "carcinoma" or a "sarcoma". While traditional treatment strategies have focused on both local and extended field radiation therapy and whole abdominal radiation techniques, a number of investigators have argued in favor of chemotherapy, because of the substantial activity observed with chemotherapy in endometrial adenocarcinomas. A randomized phase 3 trial reported by Wolfson and colleagues [60] has provided strong support for the superiority of chemotherapy compared with radiation in this difficult disease entity. This trial compared whole abdominal irradiation with a combination regimen of cisplatin plus ifosfamide in 224 women with optimally resected Stages I to IV carcinosarcoma. Adjusting for stage, the trial revealed a 28.5% reduction in the risk of recurrence associated with chemotherapy, and, most importantly, a 33% decrease in the death rate (hazard ratio 0.672; p = .042).

In conclusion, carcinosarcoma is a rare uterine neoplasm. Vaginal bleeding is the most common symptom. A correct diagnosis can often be achieved after histological examination of the entire surgical specimen. It is a highly aggressive tumor with poor prognosis. Surgery is the mainstay of treatment. The optimal adjuvant treatment remains to be established.

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