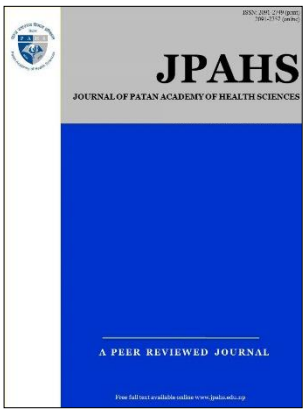

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Uterine carcinosarcoma: A rare cause for postmenopausal bleeding

Neebha Ojha[1], Eliza Shrestha[2], Jasma Mally[3], Rupam Pandey[4], Snigdha Rai[5]

[1]Assoc. Prof., Dept. of Obstetrics and Gynaecology, Institute of Medicine, Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu, Nepal; [2]Junior Consultant, [3]Registrar, [4]Medical Officer, Dept. of Gynecology, Bhaktapur Cancer Hospital, Bhaktapur, Kathmandu, Nepal; [5]Asst. Prof., Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu, Nepal

Abstract

Uterine carcinosarcoma is a rare aggressive tumor also known as Malignant Mixed Mullerian Tumor. Prognosis is poor with 30-40% having extrauterine involvement at the first presentation and over 10% with distant metastasis. The primary treatment is surgery, along with radio-chemotherapy. We report a case of uterine carcinosarcoma in a 65 y para four lady who presented with blood mixed discharge per vagina for 1 mo and polypoidal mass through the cervical os. Endometrial biopsy showed carcinosarcoma. She was managed with surgery. She received paclitaxel and carboplatin chemotherapy and with no recurrences at 6mo. Written consent was obtained for the case report.

Keywords: carcinosarcoma, postmenopausal bleeding, rare uterine tumors

Correspondence
Assoc. Prof. Dr. Neebha Ojha, Dept. of Obstetrics and Gynaecology, Institute of Medicine, Tribhuvan University Teaching Hospital, Maharajgunj Kathmandu, Nepal
Email: neebha.ojha@gmail.com

Peer Reviewers
Prof. Dr. Gehanath Baral, Nobel Medical College, Biratnagar, Nepal

Asst. Prof. Dr. Shiva Prasad Sharma Chalise, Patan Academy of Health Sciences, Nepal

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Introduction

Uterine carcinosarcoma is a biphasic malignant tumor with high-grade epithelial and sarcomatous components which is also known as malignant mixed Mullerian tumor (MMMT). It is mostly thought to be metaplastic carcinomas and not uterine sarcoma and behaves similarly to high-grade endometrioid adenocarcinoma.[1,2] It is a rare tumor and constitutes <5% of all uterine malignancies.[3,4] Prognosis is poor with 30-40% having extrauterine involvement at the first presentation and over 10% with distant metastasis.[5] Carcinosarcomas are staged the same as carcinomas. Most patients have an enlarged uterus, and the tumor protrudes through the cervical os as a polyp in half of the patients.[6] We present a case of uterine carcinosarcoma who initially presented as postmenopausal bleeding which is a rare cause for postmenopausal bleeding.

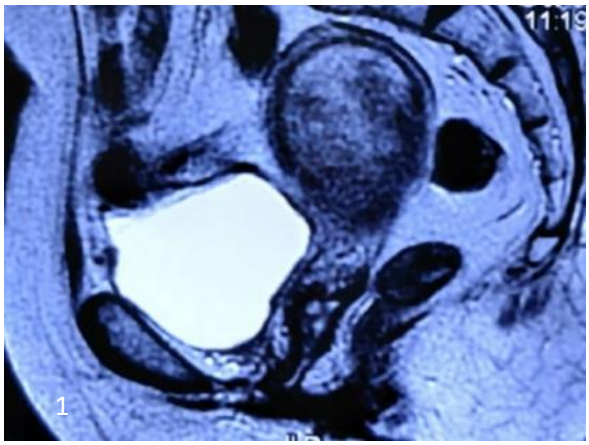
Case Report

A 65 y para-4 postmenopausal lady from Kathmandu came to the outpatient department with complaints of blood mixed discharge per vagina for 1 mo. There was no history of pain abdomen. Bowel and bladder habits were normal. She had menopause 11 y back. She was hypertensive for 11 y and was on medication. With this complaint, she had gone to the private clinic, where on examination, her uterus was 10 w size and there was a reddish polypoidal mass protruding from the cervical os. She underwent an endometrial biopsy with a cervical polyp biopsy. Histopathology report of the endometrial biopsy showed biphasic tumor comprising predominantly of sarcomatous component intimately admixed with carcinomatous elements. The carcinomatous component showed high-grade serous carcinoma and the sarcomatous component showed high-grade spindle and pleomorphic sarcoma features consistent with carcinosarcoma with heterologous rhabdomyoblastic differentiation. Cervical polyp biopsy showed a benign endocervical polyp. CA-125 sent was 16.2 U/ml. Magnetic resonance imaging (MRI) of the abdomen and pelvis showed uterus enlarged 9.8x6.5x6.2 cm with markedly thickened and distended endometrial canal (4.9 cm) and thin/stretched junctional zone, endocervical canal grossly widened, Figure 1. Mildly enlarged lymph node in the right external location measuring 1.1x1.6 cm, no significant retroperitoneal lymphadenopathy. Chest X-ray was normal.

She was planned for a major operation under general anesthesia and underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy with bilateral pelvic lymph node dissection, infracolic lymphadenectomy, peritoneal fluid cytology. On per-operative findings, the uterus was uniformly enlarged to a 12 w size. Bilateral tubes and ovaries were normal, with no ascites. The liver, spleen, intestine, and peritoneum were grossly normal. On cut-section of the uterus, there was a polypoidal growth of 8x5 cm arising from the fundus covering the whole endometrial cavity and extending through the endocervix to the vaginal canal, Figure 2.

Histopathology came as carcinosarcoma, which showed fascicles of tumor cells with scanty cytoplasm and indistinct cytoplasmic border. The presence of frequent mitosis and malignant glands in between was seen. The tumor was infiltrating the upper half myometrium with a tumor dimension of 7 cm. Perineural and lymphovascular space invasion (LVSI) was not seen. Bilateral tubes and ovaries, omentum were all free of tumor. Both pelvic lymph nodes showed necrotizing granulomatous lymphadenitis suggestive of tuberculosis, Figure 1a, b, c. Peritoneal fluid cytology was negative for malignancy. Immunohistochemistry (IHC) showed p53 diffuse and strong positive, immunostain pan-cytokeratin and epithelial membrane antigen (EMA) highlight carcinoma component, Figures 3d-f. The American Joint Committee on Cancer (AJCC) stage was pT1aN0. Written consent was obtained for the case report.

The postoperative period was uneventful and she was discharged on the fourth postoperative day. The suture was removed on the 12th post-operative day. She received 3-cycles of adjuvant chemotherapy - paclitaxel and carboplatin (day 1, 8, 15) 4 weekly. On postoperative follow-up at 4 mo, MRI abdomen and pelvis done revealed normal findings. In the meantime, she has also received antitubercular therapy (ATT) as lymph nodes had shown granulomatous lymphadenitis suggestive of tuberculosis. At 6 mo follow-up, the patient was fine and no signs of recurrences.



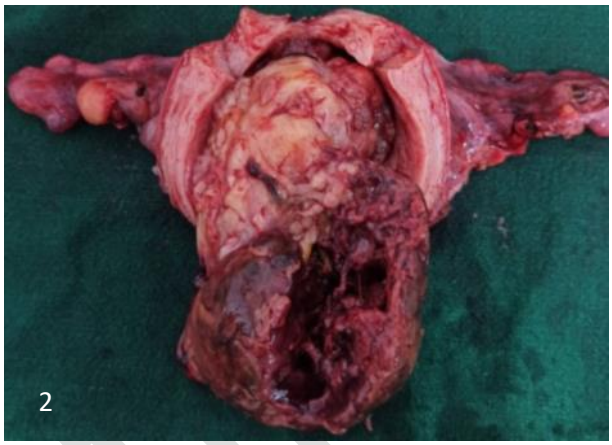


Figure 1. The MRI pelvis showing enlarged with distended endometrial cavity and widened endocervical canal

Figure 2. Cut-section of the uterus: A polypoidal growth 8x5 cm arising from the fundus covering the whole endometrial cavity and extending through the endocervix to the vaginal canal

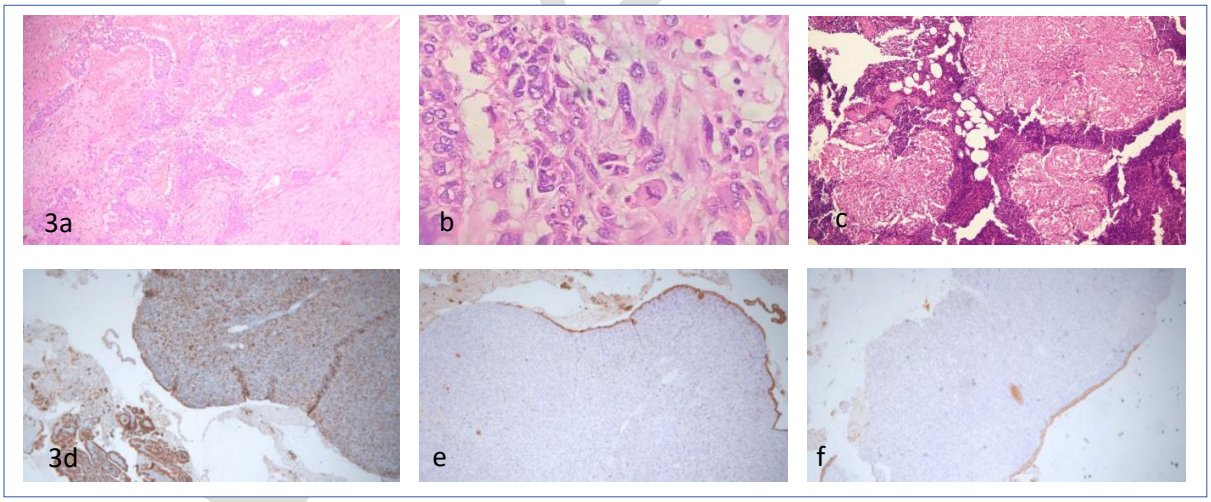


Figure 3a, b, c. Photomicrograph (40X); a. Uterine tumor shows malignant glands seen in between the stroma; b. Atypical mitosis-tripolar mitosis; c. The pelvic lymph node shows necrotizing granulomatous lymphadenitis and multinucleated giant cells along with the peripheral rim of lymphocytes in the topmost nodule; Immunohistochemistry of tumor shows- d. diffuse p53 positive, e. EMA positive, f. pan-cytokeratin positive

Discussion

Carcinosarcoma usually occurs in the older age group and presents as postmenopausal bleeding and polypoidal mass protruding through the cervical os. Clinical presentation is often the triad of abnormal uterine bleeding, pain, and rapid uterine enlargement.[5] Our case had a typical presentation with postmenopausal bleeding and polypoidal mass protruding through the cervical os. In about 37% of cases, there may be a history of prior pelvic radiation, which usually occurs in younger women.[6] Other risk factors include

obesity, nulliparity, tamoxifen therapy, and long-term unopposed estrogen usage.[4,7]

The histologic diagnosis of carcinosarcoma requires the presence of distinct biphasic neoplasm. The stromal component may be homologous (leiomyosarcoma, stromal sarcoma, fibrosarcoma) or heterologous (chondrosarcoma, rhabdomyosarcoma, osteosarcoma, liposarcoma). The presence of a heterologous component may have a worse prognosis than with a homologous component[8] and our patient had a heterologous component. The immunohistological analysis demonstrates both epithelial and stromal markers including p53, vimentin, smooth muscle actin, and desmin.[4]

Imaging is important for pre-operative surgical planning and postoperative evaluation for adjuvant therapy. The National Comprehensive Cancer Network (NCCN) guidelines recommend baseline imaging as well as follow-up imaging to detect metastatic disease, as it has a high recurrence rate.[9] In MRI uterine carcinosarcoma may be indistinguishable from endometrial carcinoma, however, their poor prognosis necessitates radiologists to consider it in the differential diagnosis of the strongly enhanced uterine lesion.[10] The positron emission tomography–computerized tomography (PET-CT) is generally superior for detecting distant metastasis, MRI can better demarcate pelvic organs' anatomy and extent of local involvement,[11] however it is not feasible in our setting due to its unavailability and expense. The CT scan is ineffective in distinguishing it from other uterine malignancies. However, it is useful for staging, follow-up, and evaluation of distant metastasis.[12] Ultrasonography of pelvis is an initial investigation, in early-stage shows hyperechoic mass relative to the endometrium.

The primary treatment option remains surgery along with radiotherapy and chemotherapy. Total hysterectomy and bilateral salpingo-oophorectomy along with surgical staging are the first-line treatment in patients without distant metastasis.[9] The role of lymphadenectomy is justified for staging and significant survival benefit (removal of micrometastasis, reduce recurrence).[13] Adjuvant therapy should be individualized. Results of a large randomized clinical trial comparing whole-abdominal radiation with three cycles of cisplatin, ifosfamide, and mesna (CIM) in stage I to IV carcinosarcoma concluded that the trial favored chemotherapy although the differences were small.[14] Our patient has received adjuvant chemotherapy for probable survival benefit. Postoperative radiotherapy should be tailored according to the operative findings and adjuvant chemotherapy may be beneficial. The local recurrences may be treated with radiotherapy or systemic chemotherapy.[9] Due to the aggressive nature of the disease, the women should be followed closely regardless of the disease state, because there is a high risk of local recurrence (60%) and distant metastasis.[4]

Clinical follow-up is usually performed with symptoms review, physical examination, vaginal cytology, and recommended every 3 mo for 2 y, then every 6 mo for 5 y.[5] On clinical concern for recurrence or metastasis abdominal-pelvic or chest CT is recommended. Whole-body PET-CT should be offered to patients who are being considered for locoregional therapy or surgery.[9] Prognosis depends on the stage, size of the tumor, and the depth of myometrial invasion. The overall survival of carcinosarcoma is poor even with the best of care thus our patient needs close follow-up to detect recurrence and manage accordingly.

Conclusion

Uterine carcinosarcoma is a rare aggressive tumor with a high risk for recurrence and metastasis. Surgery is the primary therapy, along with chemotherapy and radiotherapy. Patients need close follow-up postoperatively to detect recurrence and timely treatment.

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Conflict of Interest

None

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Author Contribution

Concept, design, planning: NO, ES, JM, RP, SR Literature review: NO, ES; Draft manuscript-NO, ES, JM, RP, SR; Revision of draft: NO, ES; Final manuscript: all authors; Accountability of the work: all authors.

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