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Malignant biphasic tumor of the uterus: A case report and review

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Abstract We present a rare case of a 50-year old lady who presented with pain abdomen and bleeding per vaginum of 3 months duration. Per vaginal examination revealed an exophytic growth arising from vault. Histopathological examination of the vault biopsy showed malignant neoplasm with features suggestive of carcinosarcoma of vault with immunohistochemistry showing stromal cells positive for CD10 and negative for SMA. Ki67 index was 40%–50%. She received external beam radiotherapy to pelvis 50.4 Gy/25 fractions but did not respond to the same. The lesion was not surgically resectable and hence referred to the division of medical oncology for chemotherapy. She was started on ifosphamide with cisplatin with growth factor support. It was planned to do a reassessment after 3 cycles of chemotherapy, but patient succumbed to the illness.

Key words carcinosarcoma; uterus; vault

Case report

A 50-year old lady, a multiparous, obese woman with history of hysterectomy 17 months back presented with pain abdomen and bleeding per vaginum of 3 months duration. There was no history of bowel or bladder disturbances.

Her past history was significant for Type 2 diabetes mellitus and hypothyroidism for which she was on anti diabetic agents and thyroxine supplementation. On examination, there was no evidence of pallor or icterus or lymphadenopathy. Examination of the abdomen revealed a hysterectomy scar with no evidence of mass or organomegaly. Per vaginal examination revealed an exophytic growth arising from vault measuring 4 cm × 3 cm, bleeding on touch. Examination of the chest and heart were within normal limits. On evaluation, haemogram and metabolic profile including renal functions and liver function tests were unremarkable. Random blood sugar was 213 mg %. Serum for HIV and HBsAg were negative. Computed tomography of the abdomen and pelvis revealed a well defined heterogeneously enhancing soft tissue attenuating lesion in the region of cervical vault abutting the sigmoid colon, measuring 6.1 cm × 7 cm × 8 cm (Fig. 1). Vault lesion biopsy revealed a globular soft tissue lesion 5.5 cm × 4 cm × 3 cm on gross examination and histopathological examination showed malignant neoplasm with features suggestive of carcinosarcoma of vault with immunohistochemistry showing stromal cells positive for CD10 and negative for SMA. Ki67 index was 40%–50% (Fig. 2 and 3). ECG and echocardiogram were unremarkable.

Patient received external beam radiotherapy to pelvis 50.4 Gy/25 fractions but did not respond to the same. The lesion was not surgically resectable and hence referred to the division of medical oncology for chemotherapy. She was started on ifosphamide 1.2 gm/m^2 days 1–3 with cisplatin 20 mg/m^2 on days 1–3 with growth factor support. It was planned to do a reassessment after 3 cycles of chemotherapy, but patient succumbed to the illness.

Discussion

Uterine carcinosarcomas or malignant mixed Mullerian tumors (MMMT) are rare but highly aggressive, biphasic tumors composed of epithelial and mesenchymal components and represents 1.5% of all malignant uterine cancers [1]. Various theories regarding histogenesis of this tumour, namely the collision, combination and conversion theory are proposed [2]. Depending on the sarcomatous component, carcinosarcomas are divided into two histological

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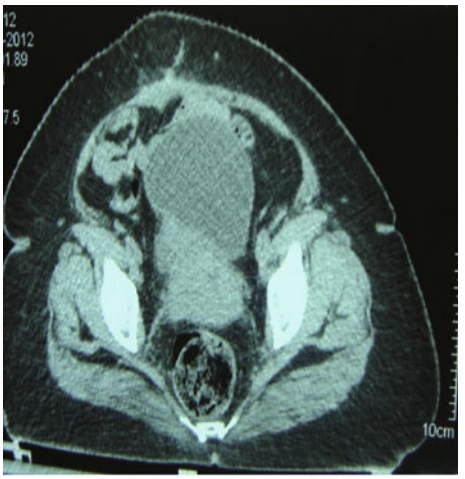

Fig. 1 Computed tomography of pelvis showing vault growth

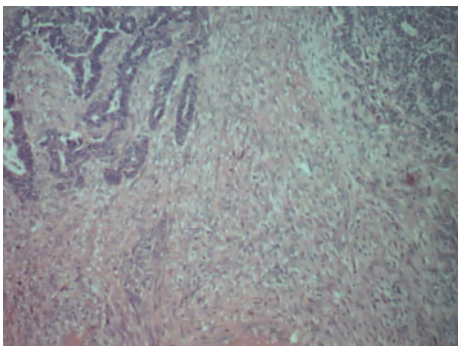

Fig. 2 H & E stained slide showing carcinosarcoma

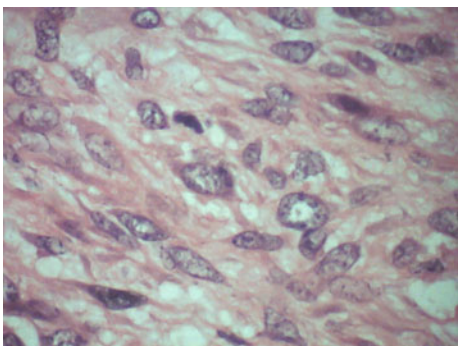

Fig. 3 Sarcoma showing mitosis

types – the heterologous type, where the sarcomatous component is either of rhabdomyosarcoma, chondrosarcoma, osteosarcoma, or liposarcoma and homologous type where the sarcomatous component is fibrosarcoma, endometrial stromal sarcoma, or leiomyosarcoma. The carcinomatous component may be endometrioid, serous, or clear cell type [2]. The aetiological factors in the development of carcinosarcoma include radiation to pelvis, obesity, nulliparity, human papilloma virus infection and exposure to exogenous estrogen [3]. Our patient was obese and this could have contributed to the pathogenesis. The pathological staging and histological features of the carcinomatous component of carcinosarcoma are responsible for the tumors biological potential and aggressiveness. Over half (53%) of carcinosarcoma patients present with advanced-stage disease [4]. Carcinosarcomas are positive for epithelial membrane antigen (EMA) and pancytokeratin and stromal lineage markers in relation to their histological appearances such as desmin in muscle differentiation or S100 in areas with chondroid or lipomatous differentiation. Our patient had stromal elements positive for CD10 and negative for SMA with a Ki67 of 50%.

Patients present with sign and symptoms of pyometra with vaginal bleeding, bloody or watery discharge, abdominal pain, or polypoidal mass protruding through the cervical os in an older, postmenopausal woman. On physical examination 50%–95% of patients have enlargement of the uterus with half of the patients having protrusion of a polypoid lesion through the endocervical canal [2]. These symptoms were also seen in our patient.

Outcome of carcinosarcoma of the uterus is very poor with 5-year survival rates between 33% and 39% [5].

Stage at the time of diagnosed is the important prognostic factor. The treatment of choice of carcinosarcoma of the uterus is surgery. After surgery local as well as distant recurrence is very high and requires adjuvant therapy in the form of chemotherapy or radiotherapy. Most of the recurrences develop within 12 months and at distant sites [6]. There is neither clear evidence that adjuvant radiotherapy, chemotherapy, or both improve the overall survival of these patients, nor there is clear consensus regarding therapeutic strategies for different stages of disease. The primary treatment option remains surgery (uterine carcinosarcoma is surgical staging with TAH with BSO, pelvic lymphadenectomy, and para-aortic lymph-node sampling with peritoneal washings) however with high rates of relapse that requires adjuvant therapies. A multimodality treatment plan has been suggested, with results of surgery followed by a combination of both chemotherapy and radiation therapy yields a longer median disease free survival (DFS) of 31 months versus surgery alone (DFS 3 months), radiation therapy alone (DFS 15 months), or chemotherapy alone (DFS 14 months) [7]. Callister *et al* reported that uterine carcinosarcoma patients undergoing sequential treatment of chemotherapy and irradiation not only have less toxic events, but also have a 50% and 80% decreased mortalities compared to patients taking irradiation and chemotherapy alone [8].

Adjuvant radiotherapy has role in decreasing the local recurrence; however, the role is controversy on overall survival. Even after complete resection of primary tumor, recurrence occurs in both local and distance sites. Chemotherapy has definitive role to minimize both local as

well as distal failure. There is no universal agreement on a postoperative chemotherapeutic regime for uterine carcinosarcomas. Response rate is better in the patients with predominate carcinomatous elements (87.5%) than those with dominant sarcoma. Most studies focus on the development of postoperative adjuvant treatment for stage I/II lesions and palliative treatment for advanced [9]. Active single chemotherapeutic agents include ifosfamide (RR = 29%–36%), cisplatin (RR = 28%–42%), doxorubicin (RR = 10%–25%), and paclitaxel (18%). Response rates (RR) to cisplatin are 19% as a first-line and 18% as a second-line agent against uterine carcinosarcomas. RR to paclitaxel is 18% with 4-month duration. Over half of the patients of carcinosarcoma have recurrence even after primary surgical and adjuvant therapy [6] in early-stage disease, rates of recurrence between 47%–64% and up to 80% of these associated with distant metastases. The most common sites of metastatic deposit include the lung (49%), peritoneum (44%), pelvic or para-aortic lymph nodes (35%), adrenal gland or bone (19%), heart or pericardium (9%), and/or brain (7%) [10].

Our patient was initially taken up for radiation therapy followed by chemotherapy (ifosphamide and cisplatin) as the tumour was inoperable.

The rarity of this neoplasm resulting in small sample size has precluded large trials for evaluation of various treatment protocols. Uterine carcinosarcoma though rare needs to be recognized as a distinct entity, as it is highly aggressive.

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