

Case Series

Uterine carcinosarcomas case series of rare uterine malignancy

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ABSTRACT

Primary malignant mixed Müllerian tumor (MMMT) of the ovary is a rare and highly aggressive neoplasm predominantly affecting postmenopausal women. MMMT is a biphasic tumor comprising both epithelial and mesenchymal components and is associated with significantly higher mortality compared to epithelial ovarian neoplasms. Patients typically present with symptoms such as vaginal bleeding, abdominal pain, and a palpable mass. Surgery remains the primary treatment modality, while adjuvant therapies, including chemotherapy and radiotherapy, play a crucial role in improving locoregional control and managing distant metastasis. Due to the rarity of these tumors, there is limited literature on their optimal therapeutic management. This series aims to analyse the clinical presentations and treatment outcomes of patients diagnosed with this uncommon uterine cancer treated at our hospital.

Keywords: Carcinosarcoma, Biphasic, Treatment, Rare neoplasia

INTRODUCTION

Although uterine carcinosarcomas constitute less than 5% of all uterine malignancies, they account for over 15% of uterine cancer-related deaths.¹ These tumors are composed of a combination of malignant epithelial and stromal elements. Based on the sarcomatous component, uterine carcinosarcomas are classified into two types: homologous and heterologous. The homologous type consists of sarcomas derived from uterine tissues such as the endometrium or smooth muscle, whereas the heterologous type includes non-native tissues like cartilage, skeletal muscle, or bone.²

MMMTs have been reported in descending order of frequency in the vagina, cervix, ovary, and rarely in the fallopian tube. Risk factors for the development of these cancers include exogenous estrogen use, pelvic irradiation, nulliparity, obesity, and human papillomavirus (HPV) infection.³

Most patients present with symptoms such as abnormal uterine bleeding, an enlarged uterus, and pelvic pain. MRI

is a valuable preoperative diagnostic imaging tool. The primary treatment is total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO), while cytoreductive surgery is recommended for advanced-stage disease. Definitive diagnosis relies on histopathological examination and immunohistochemistry (IHC).

CASE SERIES

Case report 1

A 54 year old P₂L₂ female presented with four months history of vaginal bleeding and abdominal pain. On physical examination patient had enlargement of uterus with a palpable mass. Abdominal sonography showed an intrauterine mixed echoic lesion of size 4.0×3.1×3.4 cm with cystic areas within suggestive of endometrial soft tissue mass polyp.

Abdominopelvic CECT showed well defined cystic lesion with enhancing soft tissue within measuring 4.3×4.7×5.3 cm noted in endometrial cavity (Figure 1).

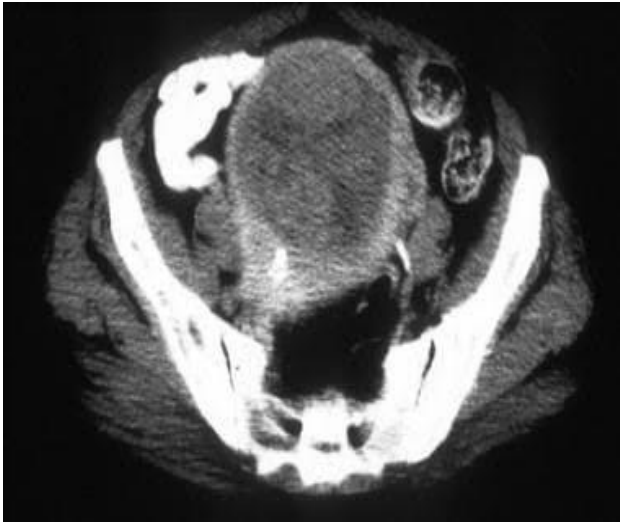


Figure 1: CECT pelvis-axial image showing large polypoidal mass in the uterus extending into the endometrial cavity.

Patient underwent total abdominal hysterectomy with bilateral salphingo-oophorectomy (TAH-BSO) and specimen was examined for histopathology. Gross examination of which revealed a friable polyp of size 4.5×4×3.5 cm which was superficially adherent to the myometrium. Microscopically on H and E staining infiltrating carcinosarcoma was seen. Also seen were stromal spindle shaped cells with atypical nuclei and small areas of cartilaginous tissue. Lympho-vascular space invasion (LVSI) was present. No pelvic lymph nodes showed metastatic deposits. Histological examination favoured MMT infiltrating myometrium (Figure 2).

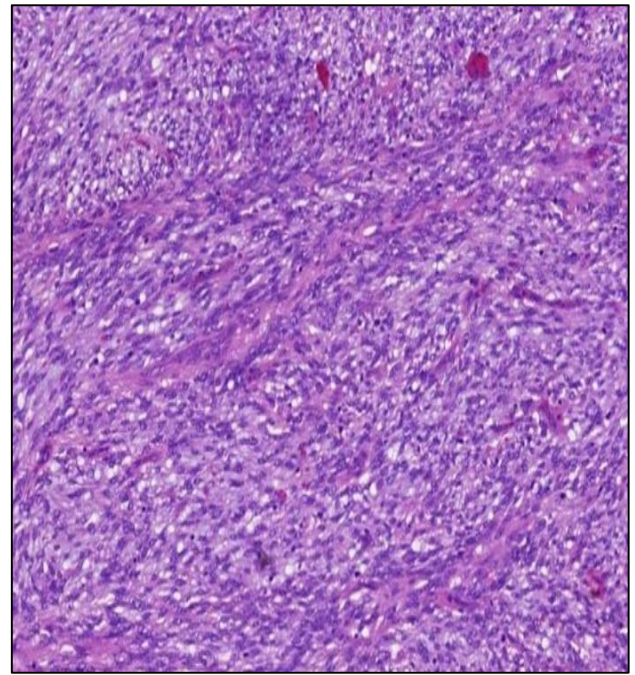


Figure 2: H and E stain-cells showing biphasic malignant epithelial and mesenchymal components.

Post-operative period was unremarkable. Patient was planned for adjuvant chemotherapy with Paclitaxel 175 mg/m² (d1) and Ifosfamide 1.5 mg/m² (d1-d4) three weekly six cycles and pelvic radiotherapy 50Gy/25#/5 weeks with concurrent cisplatin 40 mg/m² and intracavitary radiotherapy [ICRT] (Figure 3). Patient is now on follow up and long-term disease-free survival is under assessment.

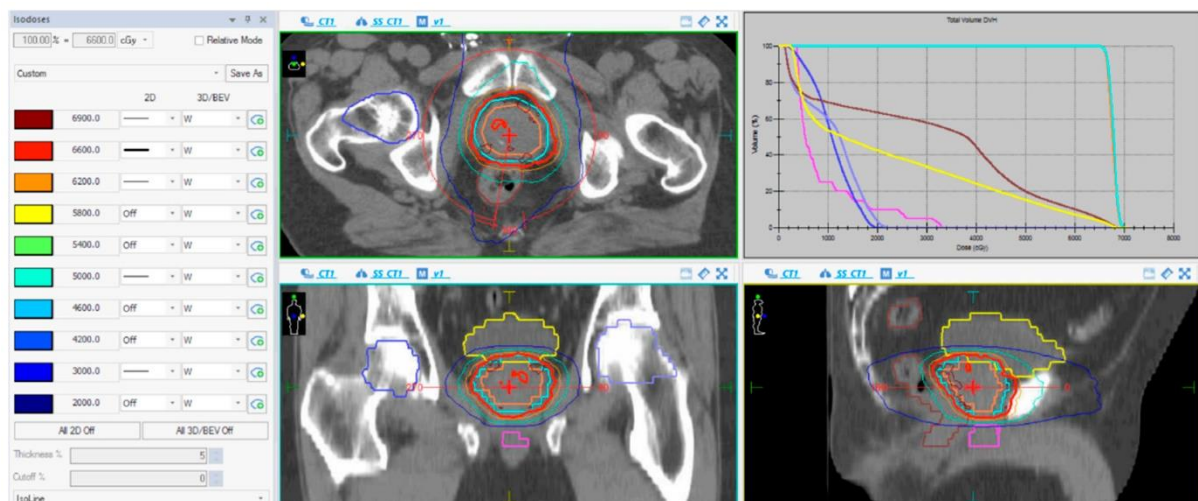


Figure 3: Contours and DVH for pelvic radiation.

Case report 2

A 70 year old postmenopausal women presented with six months history of dull-aching, pain in lower abdomen. On examination an ill-defined mass of size 8×10 cm was

palpable in right iliac fossa. CECT abdomen revealed 8.7×5.2×13 cm solid cystic lobulated lesion in right paracolic gutter adherent to peritoneum, infiltrating ascending colon and caecum. Small peripheral nodules in subhepatic region measuring 1×1.2 cm of metastatic

deposit and omental caking. The alpha-feto protein, CEA and CA125 levels were all within normal limits.

Patient had a past history of carcinoma ovary about three years ago. Serum CA 125 level was 683.3U/ml at that time and she received neoadjuvant chemotherapy (NACT) with Paclitaxel 175 mg/m² and carboplatin AUC-5 (area under curve) three weekly four cycles then underwent TAH-BSO with omentectomy and bilateral pelvic lymph node dissection in private hospital. Post operative histopathology reports serous adenocarcinoma of ovary with no lympho-vascular and perineural invasion. (CRS3) noted CAP protocol. Post operative CA125 reduced to 113.35 u/mL Thereafter patient defaulted for treatment.



Figure 4: CECT abdomen-solid cystic lobulated lesion in right paracolic gutter adherent to underlying peritoneum.

We planned to give chemotherapy three weekly six cycles of gemcitabine 1 gm/m² (d1 and d8) and carboplatin AUC-5 (d1). Later patient underwent right hemicolectomy with ileo-transverse anastomosis. Intra-operative findings showed mass in caecum and adjacent ascending colon almost completely obstructing the lumen.

In the resulting surgical specimen a nodular growth of 8×9.5×5 cm size arising from muscularis propria of colon, infiltrating through muscularis propria into pericolic fat reaching serosal surface was found. Lympho-vascular invasion was seen. No lymph node invasion was observed. Findings suggestive of malignant spindle cell neoplasm. IHC panel showed CK-7, PAX 8, P16 positive while negative for WT, ER, Desmin, SAT-B2 and S-100 favouring metastatic carcinoma of mullerian origin.

Patient is currently planned for adjuvant chemotherapy with paclitaxel 175 mg/m² (d1) and ifosfamide 1.5 mg/m² (d1-d4) three weekly six cycles and is tolerating well.

Case report 3

A 65-year-old post-menopausal hypertensive woman presented with complaints of lower abdominal pain, dullness of two months duration. On examination her abdomen was soft and distended with ill-defined mass measuring 8×7 cm. CECT abdomen showed 8.7×8×6 cm well defined lobulated heterogeneously enhancing solid cystic mass in right adnexa adherent to fundus of uterus with gross ascites and pericardial effusion (Figure 5).

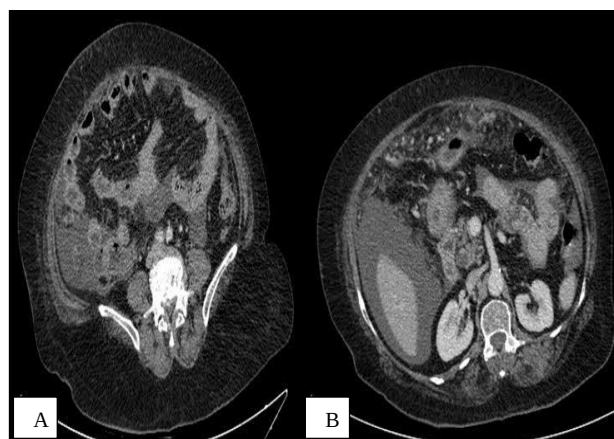


Figure 5 (A and B): CECT abdomen axial image shows solid cystic mass in right adnexa.

Laboratory examination revealed an elevated serum CA125 (312.5 U/ml). Peritoneal fluid cytology was positive for malignant cells. Biopsy from pelvic mass showed a poorly differentiated malignant neoplasm infiltrating endo-myometrium. IHC of the specimen revealed cells positive for CK7, PAX-8, P16 and negative for CK20, WT1, P53 and vimentin which confirmed the diagnosis of high grade adenocarcinoma of mullerian origin (Figure 6).

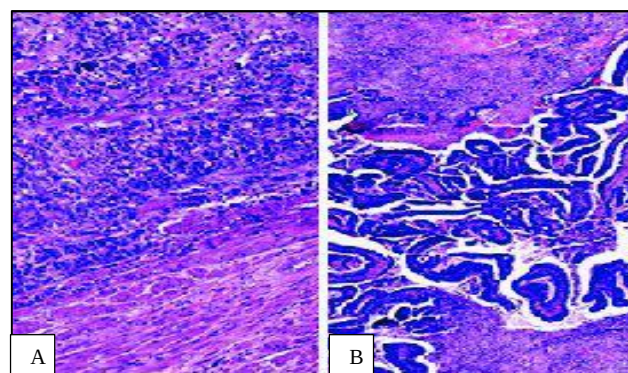


Figure 6 (A and B): HPE-poorly differentiated malignant neoplasm infiltrating endo-myometrium.

Evaluation by FDG-PET CECT showed 7.6×6.9 cm hypermetabolic solid cystic lesion in right adnexa, gross ascites with multiple omental deposits, nodule in the lower lobe of right lung and left supraclavicular lymph node (Figure 7).

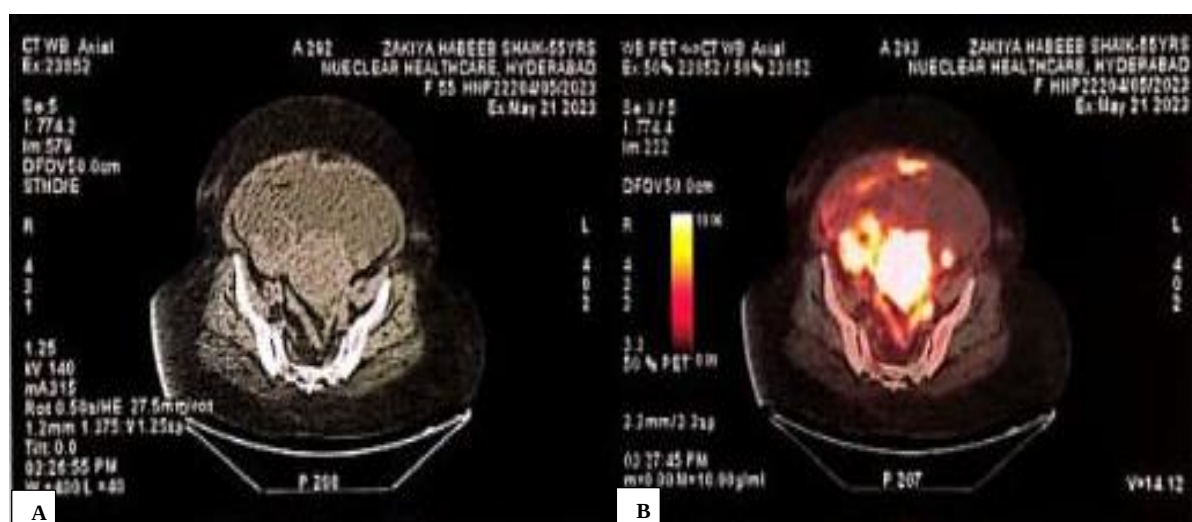


Figure 7 (A and B): PET CT showing solid cystic lesion in right adnexa.

Patient was planned for palliative chemotherapy with Paclitaxel 175 mg/m² (d1) and Ifosfamide 1.5 gm/m² (d1-d4) three weekly three cycles. The general condition of the patient deteriorated after the first cycle and even with best supportive care the patient expired.

Case report 4

A 70 year old P₂L₂ hypothyroid woman presented with complaints of postmenopausal bleeding and lower abdominal pain since three months. Per speculum and per vaginal examination showed a polypoid lesion arising through the os measuring 4×2 cm involving the right parametrium. Serum CA125 level was normal.

MRI pelvis revealed an ill-defined heterogenous lesion T1 isointense and T2 mild hyperintense mass lesion measuring 4.5×4.2×2.8 cm in endometrial cavity involving posterior uterine wall with mild post contrast enhancement more than 50% myometrial involvement along with posterior uterine wall (Figure 8).



Figure 8: MRI pelvis-sagittal section shows endometrial lesion involving posterior uterine wall.

D and C and cervical biopsy was done. Histopathology findings were suggestive of endometrial stromal sarcoma (ESS)/undifferentiated endometrial sarcoma (Figure 9).

IHC was performed which reported CK positive in epithelial as well as stromal component, vimentin variably positive in stromal component, Ki-67 very high index, CD10 positive in stromal component, WT1 variably positive, p53 overexpressed, EMA positive in glandular component. Cells negative for ER, cyclin D1 and SMA confirming the diagnosis of HG-MMMT.

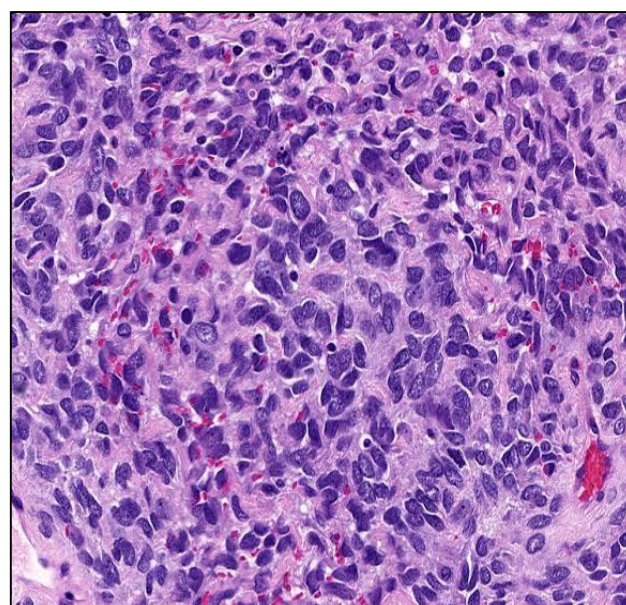


Figure 9: H and E-high grade endometrial stromal sarcoma.

Patient was planned for chemotherapy with Paclitaxel 175 mg/m² (d1) and Ifosfamide 1.5 gm/m² (d1-d4) three weekly three cycles. The patient however rapidly deteriorated after the first cycle of chemotherapy. Extensive nutritive and

supplementary support is advised in view of advanced age and now patient is on close follow up.

Case report 5

A 50 year old postmenopausal hypertensive patient presented with two months history abnormal vaginal bleeding. USG abdomen pelvis revealed bilateral ovarian solid and cystic mass lesion suggestive of malignant potential. MRI pelvis showed lesion filling endometrial cavity measuring 4.9×4.4×4.2 cm with fluid collection.

Post operative histopathology reported a polypoidal growth in endometrium of size 4.2×4.1×3.5 cm, tumor invading full myometrial thickness and focally into

parametrium. Squamous morules and lymphovascular invasion seen. Stroma shows sheets of pleomorphic large spindle to oblong cells with pleomorphic nuclei and foci of chondroid elements. Abnormal mitosis and areas of necrosis were seen. The final diagnosis of MMTT-heterogenous type was made after pathological examination.

Patient received adjuvant chemotherapy with Paclitaxel 175 mg/m² (d1) and Ifosfamide 1.5 gm/m² (d1-d4) three weekly six cycles followed by radiotherapy to pelvis 50Gy/25#/5 weeks using IMRT technique (Figure 10). Now patient is on follow up and long-term disease-free survival is under assessment.

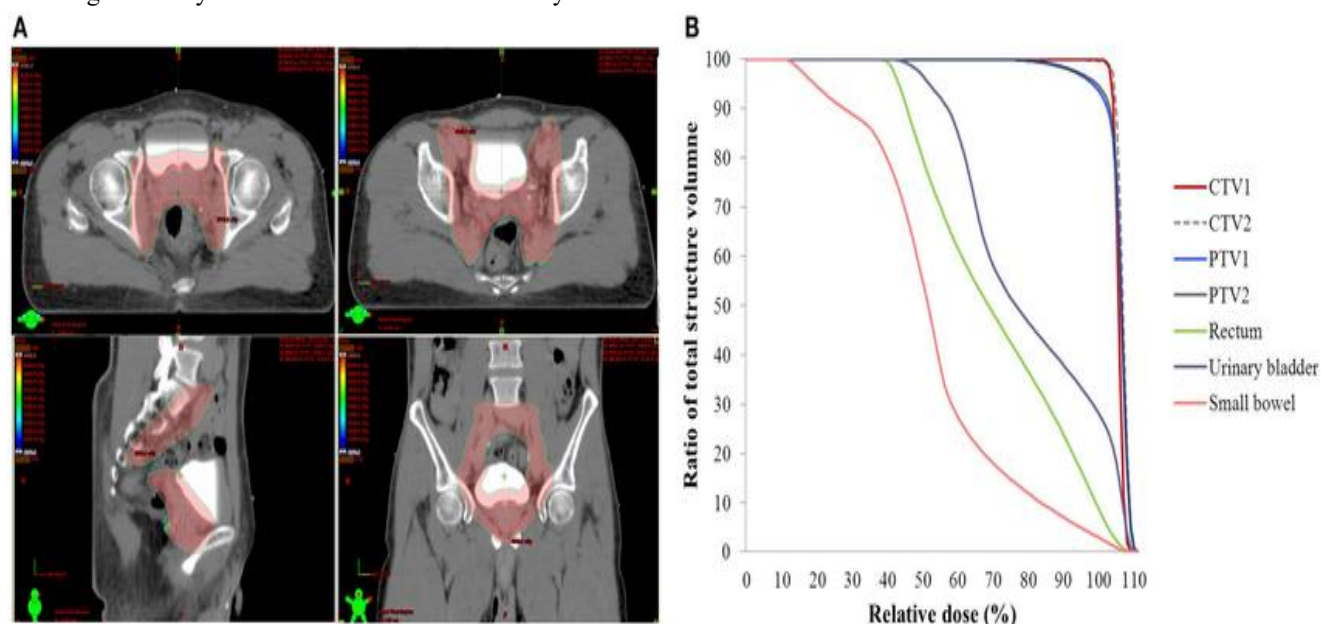


Figure 10 (A and B): Contours and DVH of radiotherapy to pelvis.

Case report 6

A 72-year-old post-menopausal woman presented with complaints of lower abdominal pain of two months duration. Abdominal examination revealed soft ill-defined mass in the uterus of 16-18 weeks. On pelvic examination the same mass was felt in the cervix. MRI pelvis showed an endophytic polypoidal lesion 6.8×5.8 cm in size arising from left lateral wall of the uterus showing heterogeneous high signal intensity on the T2 weighted images (Figure 11).

Laboratory examination revealed an elevated serum CA125 level (334.64 U/ml), CEA (27.76 ng/ml) and CA19.9 (154.10 U/ml). FNAC from pelvic mass suggested adenocarcinoma and patient planned for chemotherapy with paclitaxel 175 mg/m²(d1) and carboplatin AUC-5 (d1) three weekly three cycles followed by TAH-BSO with complete excision of the mass. Postop period was uneventful.

In the resulting surgical specimen, an irregular yellowish grey growth of 10×7×7 cm arising from uterine cavity. On cut surface, the studied sections of the growth showed biphasic tumour. Lympho-vascular invasion present.

Focal chondroid and rhabdomyoblastic differentiation seen. Tumour infiltrating more than half of myometrial thickness. Cervix and right fallopian tube were involved by the tumour.

No lymph node positive. Diagnosis of Malignant mixed mullerian tumour with focal chondroid and rhabdomyoblastic differentiation was confirmed (Figure 13 A-C).

Patient is currently planned for adjuvant chemotherapy with paclitaxel 175 mg/m² (d1) and Ifosfamide 1.5 gm/m² (d1-d4) three weekly three cycles followed by radiotherapy to pelvis 50Gy/25#/5 weeks.



Figure 11 (A and B): MRI pelvis-axial and sagittalT2-weighted MR image showing large mass with high signal intensity in the uterus.



Figure 12: Gross uterine specimen showing yellowish solid mass in the endo-myometrium.

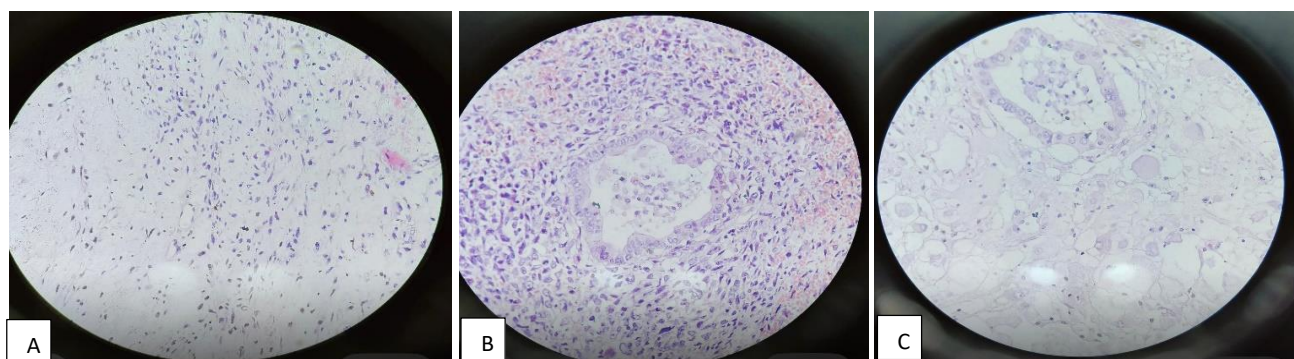


Figure 13 (A-C): A-sarcomatous element and gland and rhabdomyomatous component.

DISCUSSION

MMMTs are rare neoplasms of the female genital tract, occurring primarily in the uterus. They are the most common subtype of uterine sarcoma in postmenopausal women. Patients may be asymptomatic or present with non-specific symptoms such as abnormal vaginal bleeding and an enlarged uterus.

Carcinosarcomas exhibit a distinctive biphasic morphology, consisting of malignant epithelial and mesenchymal components. The carcinomatous element originates in the endometrium and may display serous, clear cell, or endometrioid features, alone or in combination. The sarcomatous component arises in the outer uterine muscle and can be homogeneous (non-specific malignant stroma) or heterologous (containing cartilage, skeletal muscle, or bone not native to the site).

IHC plays a vital role in distinguishing the tumor components. Expression of epithelial markers such as epithelial membrane antigen (EMA) and pancytokeratin, along with stromal markers like Desmin and S-100, is frequently observed. Overexpression of tyrosine kinase receptors such as HER-2, EGFR, and KIT has been studied to explore potential therapeutic targets.

MMMTs are staged similarly to endometrial carcinomas using the American joint committee on cancer (AJCC) system: Stage I: Tumor confined to the corpus uteri, stage II: Tumor involves the uterus and cervix, stage III: Tumor extends to the lesser pelvis and stage IV: Tumor exhibits extrapelvic extension

Standard treatment includes total abdominal hysterectomy with bilateral Salpingo-oophorectomy, though the role of lymphadenectomy remains under investigation. Histologically, the tumor exhibits a characteristic biphasic morphology, with epithelial and mesenchymal components appearing either distinct or intermixed.

The epithelial component often manifests as high-grade carcinoma, including serous, endometrioid, papillary, adenocarcinoma, squamous carcinoma, or undifferentiated forms.

Following cytoreductive surgery, chemotherapy has proven effective. While Ifosfamide alone was previously considered the most effective drug, the combination of Ifosfamide and Paclitaxel has become the standard of care, as supported by the GOG 161 study. Paclitaxel combined with carboplatin has also demonstrated efficacy as adjuvant chemotherapy. Advances in understanding the disease's biology have led to the investigation of combination chemotherapy (e.g., gemcitabine, docetaxel, topotecan) and targeted therapies such as sorafenib and imatinib. Concurrent chemoradiation can improve local control and delay recurrence, though it offers limited survival benefits.

Prognostic factors include myometrial invasion, large residual tumors (>2 cm), and advanced-stage disease. Notably, approximately 75% of patients present with stage III or IV disease. Despite advancements in treatment, the prognosis remains poor, with an average survival of less than two years for ovarian MMMTs and a five-year overall survival rate of 20-30%.

CONCLUSION

MMMTs are rare and aggressive tumors of the uterine corpus. Prognosis is closely linked to the stage of the disease and the depth of myometrial invasion. Most patients with advanced-stage disease experience recurrence or progression within one year.

Early diagnosis and a multimodal treatment approach, including surgery, chemotherapy, and radiotherapy, can lead to favorable outcomes. However, long-term disease-free survival remains under evaluation in our cases.

In this case series, we analysed the diverse clinical presentations and outcomes of MMMTs at our institute. The absence of established treatment guidelines for this rare malignancy highlights the need for further research to better understand patterns of disease progression and to explore potential therapeutic options to improve survival in these patients.

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