A Rare Case of Maliganan Mixed Mullerian Tumor (MMMT) of Uterus

**Case Report**

A Rare Case of Maliganan Mixed Mullerian Tumor (MMMT) of Uterus

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A 65 year old Non obese ,Non diabetic, Hypertensive Gravida 4 Para 4female presented to the outpatient department with complaint of Postmenopausal bleeding .She had undergone Endometrial biopsy for same at another medical college and Histopathology report showed Endometrial polyp. In perspeculum examination cervix was normal.In per vaginal examination uterus was bulky ,freely mobile ,fornices free.An ultrasonography was performed which showed a bulky uterus with thick endometrium with poor endo-myometrial differentiation and bilateral atrophic ovaries.USG whole abdomen was normal.She was counselled to undergo Endometrial biopsy again but she refused for same as she underwent the procedure 1 month back.

A preoperative evaluation was done .After taking her informed consent ,she was posted for surgery . Total abdominal hysterectomy with bilateral salpingo oopherectomy was done .Cut section showed a fragile growth occupying the uterus without disrupting the outer surface of uterus .Ovaries and tubes were normal.Post operative period was uneventful.

Histopathology report showed Poorly differentiated high grade malignancy(Adenocarcinoma).Tumor with Lymphatic and vascular invasion.Neural invasion not seen. Cervix and both tubes and ovaries were free of tumor.

IHC was advised to rule out Carcinosarcoma (MMT) and neuroendocrine differentiation. IHC results showed stroma to be strongly reactive for Vimentin while the glandular component showed reactivity for CK, thus confirming Malignant Mixed Mullerian Tumour.

**Figure 1** H&E (10x)-Both Malignant glandular as well as stromal component

**Figure 2** IHC- CK positive in glandular component and negative in malignant stroma

**Figure 3** IHC Vimentin positive in malignant stromal component,negative in glandular component

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invaded full thickness of myometrium
DISCUSSION
Carcinosarcoma of the uterus (malignant mixed Müllerian tumor [MMMT]), is a biphasic neoplasm composed of malignant epithelial and mesenchymal components. Although carcinosarcoma is the preferred term for this group of tumors, according to the International Society of Gynecological Pathologists (ISGyP)/World Health Organization (WHO) classification, it is also referred to as malignant müllerian mixed tumor. These tumors are currently thought to be monoclonal carcinomas with sarcomatous differentiation.

These are uncommon neoplasms, with an incidence of fewer than 2 per 100,000 women per year. They have an extremely poor prognosis, with a 5-year survival rate of 33% to 39%.

Carcinosarcoma comprises less than 5% of malignant neoplasms of the uterine corpus. It is typically seen in postmenopausal women, although rare cases occur in younger women and even children. The median age at presentation is 65 years. Although relatively rare, carcinosarcomas of the uterus, and of the gynecologic and urinary tracts in general, are more common than in other sites, such as lung, possibly because the epithelial stem cells are mesodermal in origin.

Clinicopathologic data support separation of carcinomas arising in the endometrium into 2 types. The more common type of neoplasm, type 1, is typically associated with hyperestrogenism, obesity (due to aromatization of androgens into estrogen), and hyperlipidemia, have well or moderately differentiated, typically endometrioid histology, and have a good prognosis (approximately 85%-90% 5-year survival rate). They are frequently associated with PTEN mutations. Type 2 endometrial carcinomas, which represent 10% to 15% of endometrial carcinomas, are typically seen in women without these clinical features. They typically have poorly differentiated endometrioid or serous histology and a worse prognosis (55%-60% 5-year survival rate) and are more often associated with p53 mutations.

Carcinosarcomas are part of the type 2 group, with an epithelial component that most often resembles high grade endometrioid, serous or clear cell carcinoma.

Uterine carcinosarcomas typically present with abnormal vaginal bleeding and may present with bloody discharge, watery discharge, abdominal pain, or an abdominal mass.

Risk factors for carcinosarcoma include excessive weight, exogenous estrogen use, and nulliparity, which are similar risk factors for (but not as strongly linked to) endometrial carcinoma. Oral contraceptives and smoking are thought to be protective. Some cases may result from prior pelvic radiation. In recent years, an association between long-term tamoxifen treatment and the development of carcinosarcoma has been suggested.

Surgical stage and, particularly, depth of myometrial invasion are the most important prognostic indicators. Myometrial invasion beyond the inner third is seen in 80% of tumors and 40% show deep myometrial invasion. However, confinement to an endometrial polyp in absence of myometrial invasion does not preclude extruterine spread.

Lymphatic and vascular space invasion is detected in many cases, with extruterine spread and metastases at the time of presentation. In general, most metastatic deposits and foci of lymphatic and vascular space invasion are composed of the carcinomatous element, with sarcomatous metastases being rare.

Carcinosarcomas should be staged as carcinomas of the endometrium. Management usually includes total abdominal hysterectomy and bilateral salpingo-oophorectomy with or without pelvic lymph node dissection. Adjuvant therapy with radiation therapy and/or chemotherapy is recommended depending on the clinical and pathological factors, including tumor stage, histological subtype, grade, lymphovascular invasion and distant metastasis. Adjuvant radiotherapy comprising a combination of external radiotherapy to whole pelvis followed by intravaginal brachytherapy.
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may be recommended to postoperative patients with early stages of carcinosarcoma. Postoperative radiation appears to improve local control.

A critical review of the literature on adjuvant chemotherapy in uterine carcinosarcoma has been described. Patients with higher stage of disease may be considered for ifosfamide plus paclitaxel combination chemotherapy. Although the effect of chemotherapy treatment varied among patients, adjunctive ifosfamide and cisplatin chemotherapy may also improve progression-free survival. Nevertheless, the incidence of tumor recurrence is high. According to immunohistochemistry (IHC) visualized tumor markers such as enzymes, oncogenes, tumor-specific antigens, tumor suppressor genes and tumor proliferation markers, doctors can efficiently predict oncogenesis and diagnose a cancer as benign or malignant, determine the stage and the grade of a cancer. Immunohistochemistry can be used to assess which tumors are likely to respond to therapy, by detecting the presence or elevated levels of the molecular target. Immunohistochemistry is typically not required to establish the diagnosis of this entity, although it may be required to distinguish it from a sarcomatoid carcinoma. The epithelial component is usually immunoreactive with cytokeratins, epithelial membrane antigen (EMA), and vimentin. The mesenchymal component usually stains for vimentin, smooth muscle actin, desmin, and focal cytokeratin. Both the sarcomatous and carcinomatous components often coexpress epithelial markers and vimentin to varying degrees.

CONCLUSION
Carcinosarcomas are very rare but highly aggressive tumors with poor prognosis. Immunohistochemistry can help in diagnosis and defining selection of chemotherapy targeted towards the more malignant component of tissue. Patients with Postmenopausal bleeding and large bulky uterus should be treated with high index of suspicion even if the reports of Endometrial biopsy shows a benign growth as in our case.

REFERENCES
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