

Uterine Malignant Mixed Mullerian Tumour - Revisited In Newer Lights: A Case Report from a Tertiary Care Centre

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Abstract

Carcinosarcoma of the uterus, also known as malignant mixed mullerian tumour (MMMT) is a very rare and aggressive gynaecological neoplasm, having an overall poor prognosis. They can arise in any organ of the female genital tract but are most commonly found in uterus. They are histologically biphasic having malignant epithelial and mesenchymal components. We report a case of uterine MMMT, clinically presenting as uterine polyp, in a postmenopausal female.

Keywords: Carcinosarcoma, MMMT, Biphasic, Female genital tract.

1. Introduction

Malignant Mixed Mullerian tumour (MMMT) of the uterus is a rare aggressive tumour of the genital tract, most commonly found in the corpus. It is believed that uterine carcinosarcoma have a Mullerian duct origin and have the ability to differentiate into biphasic mesenchymal and epithelial components [1]. The overall incidence accounts for 1-4% of the cancers of the reproductive tract [2] with 5-year survival rates of approximately 30% [3-6]

2. Case report

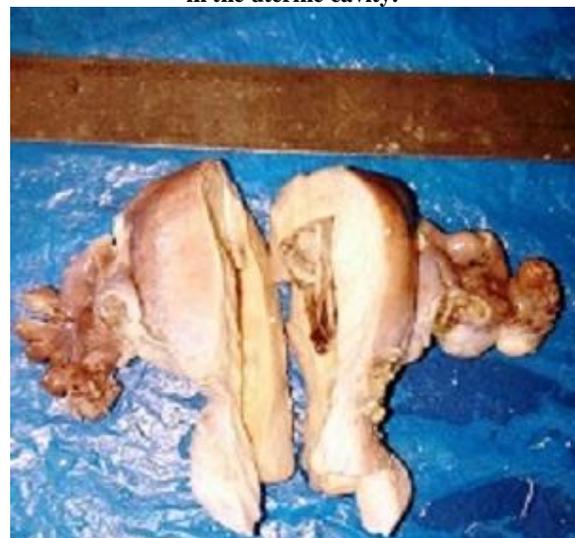
A 65 year old female with a menopause of 12 years presented with the complaint of post menopausal bleeding since six months. The patient was P3+0 and was hypertensive for the last 15 years taking anti-hypertensives since then. She had never undergone any surgery nor had been exposed to any radiation therapy.

Ultrasonography of pelvis showed a uterine mass attached to the posterior wall of the endometrial cavity presumably uterine fibroid measuring 62 x55x 40.2mm. The ovaries of both sides and the cervix appeared normal.

The patient underwent Total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH with BSO).

Gross examination showed specimen of uterus measuring 10.2x6x4.8 cm. Each ovary measured 3x1.5x1.0 cm. Endometrial cavity revealed an irregular mass of 5x4x3cm, brownish black in colour with haemorrhage, friable in consistency, attached to the posterior wall of the endometrial cavity. The rest of the endometrium, myometrium and adnexa were grossly normal. Serial sections from the endometrium, myometrium, cervix, both ovaries and fallopian tubes were embedded and whole of the mass was processed. (Figure 1)

Figure 1: Gross specimen of Uterus and cervix along with bilateral adnexa showing an irregular uterine mass in the uterine cavity.



Histopathological examination of mass revealed histology of a malignant lesion comprising of component of pleomorphic sarcoma (Figure 2) and squamous cell carcinoma (Figure 3) having plenty of tumour giant cells, atypical nuclei and areas of necrosis. Myometrial invasion was limited to inner half of myometrial thickness. Diagnosis of MMMT was given on histopathological examination.

Our patient is now on close follow-up.

Figure 2: Microscopic view of the sarcomatous component of the tumor having spindle shaped pleomorphic cells on histopathological examination

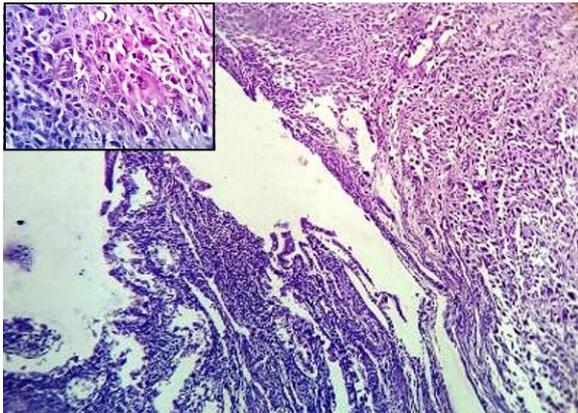
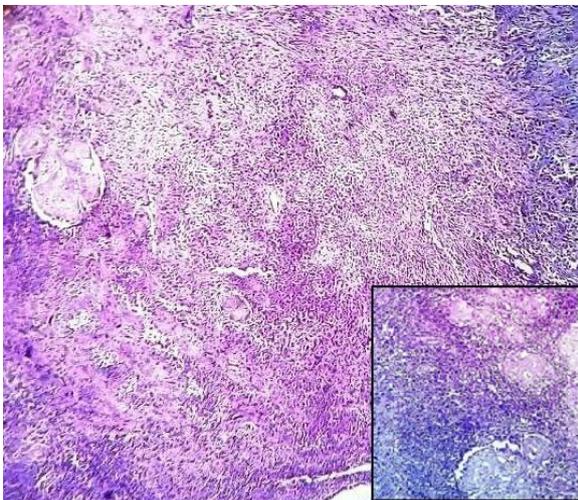


Figure 3: Microscopic view of the carcinomatous component of the tumour showing squamous cell carcinoma on histopathological examination



3. Discussion

MMMT of the uterus are uncommon highly aggressive neoplasms that are virtually always seen in postmenopausal patients. The mean age of patients with uterine carcinosarcoma is 62 years but the age spans in between 60-70 years [1].

In the sixth week of embryogenesis, the paramesonephric (mullerian) ducts arising from intermediate mesoderm of coelomic epithelium invaginate lateral to the mesonephric duct. Epithelial

and mesenchymal structures originate from this duct.[7]

They present with uterine bleeding and pain abdomen. The usual location is the uterine body, particularly the posterior wall of the fundus but a few cases with MMMT of the uterine cervix have been reported as well. Apart from these two sites it can also occur in ovaries, fallopian tube, vagina, peritoneum and extragenital sites [8].

Risk factors for development of carcinosarcomas are nulliparity, advanced age, obesity, radiation exposure, exposure to exogenous estrogens, hypertension and diabetes. Oral contraceptive pills are reported to offer protective effect against these tumors [1].

The disease tends to present, most commonly, with vaginal bleeding. Another typical presentation of carcinosarcoma is a polypoid mass that protrudes through the cervical os. The triad which points towards carcinosarcoma includes pain, severe vaginal bleeding, and necrotic material coming out of the vagina [9]

Grossly uterine carcinosarcomas appears as a solitary polypoid mass with regions of haemorrhage and necrosis projecting into the uterine cavity. Gritty or hardened areas may suggest osseous or cartilaginous differentiation [1]. MMMT most commonly arise on posterior wall of uterine body near the fundus and grows to obliterate the uterine cavity.[1]

Microscopically, these two elements may be mixed or be seen as two distinct components. It is currently believed that carcinosarcomas have a monoclonal origin from a common multidirectional progenitor stem cell. Recent studies have shown that neoplasms are derived from Mullerian epithelium's single stem cell with dedifferentiation resulting in the sarcomatous elements [7].

Previously MMMTs were thought to be sarcomatous in origin, and consequently treatment protocols followed this guideline. But recently the carcinomatous component is being favoured as the primary determinant of tumour aggressiveness resulting in a change in the management styles [1].

The epithelial component is often a high-grade carcinoma such as papillary serous (66%) or endometrioid (42%)[10] though it may be composed of a variety of histological subtypes . The mesenchymal element may be homologous, containing cells native to the uterus including fibrosarcoma or leiomyosarcoma or heterologous with mixed components including rhabdomyosarcoma (18%), chondrosarcoma. There may be more than one sarcomatous component present with stromal sarcoma component being the most common [10].

The pathological staging and histological features of the carcinomatous component of carcinosarcoma are responsible for the tumour's biological potential and aggressiveness [1]. The carcinomatous component is usually a poorly differentiated adenocarcinoma[2]. In most carcinosarcomas, the metastatic deposits are epithelial in origin only [1]. Neuroendocrine or melanocytic differentiations are associated with bad prognosis [11]

Histopathology remains the gold standard for diagnosis [1] but ancillary techniques like immunohistochemistry can be tried. Immunohistochemically carcinosarcomas express epithelial markers like Epithelial Membrane Antigen (EMA), pancytokeratin and stromal lineage markers like desmin or S100 are also expressed.[1]

Radiological techniques like CT ultrasonography are not of much help in confirming the diagnosis though MRI has proved helpful in commenting on the invasiveness of the tumour into the adjacent areas[1].

It is believed that uterine carcinosarcoma is similar to metaplastic endometrial carcinoma so generally management is based on treatment protocols for high-risk endometrial carcinoma [12]

Most commonly followed treatment modality is TAH with BSO, pelvic lymphadenectomy, and para-aortic lymph-node sampling with peritoneal washings [1]. It has been seen that patients having predominant epithelial element show a better response rate to chemotherapy (87.5%) than with patients with predominant sarcomatous component [13]. Studies have shown that patients undergoing chemo-radiotherapy have decreased mortality as compared to patients taking irradiation or chemotherapy alone [14]. But the role of neo adjuvant and adjuvant chemo-radiotherapy is debatable and its effect on survival is controversial. Even after all these modified treatment protocols the recurrence rates, local and metastases were found to be high and the survival rates of the advanced diseases was found to be declining.

Prognostic factors include extent of tumour, lymphovascular space involvement, histology of carcinomatous component and extent of sarcomatous component [1]. Serous or clear cell carcinoma as the epithelial element is associated with poor outcome [1] so is advanced stage and myometrial invasion.

4. Conclusion

MMMTs are highly aggressive neoplasms. Generally, at the time of presentation the patient presents with evidently alarming symptoms and angry looking masses in the uterine corpus. Even

appropriate radical excision based on clinical suspicion is not enough to predict an outcome. Keeping this scenario in mind, our case presented with a benign innocuous looking mass in the corpus which grossly did not even show any necrosis let alone any other feature to raise any doubt. We report this case to raise the awareness about this fatal tumour and the innocent ways in which it can mislead the surgeon into not suspecting a malignancy. The aim of this case report is to emphasize the massive role of histopathological examination in the accurate diagnosis of MMMT and determination of the presence carcinomatous element which ultimately decides the tumour aggressiveness and chances of metastasis. This further reinforces the importance of early diagnosis and treatment as metastasis leads to lesser and lesser response to adjuvant therapy and poorer disease outcome and survival rate.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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