MALIGNANT MIXED MULLERIAN TUMOR: A ONE YEAR EXPERIENCE AT A TERTIARY CARE HOSPITAL

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ABSTRACT: AIM: To study the clinicopathological presentation of malignant mixed mullerian tumors of the uterus, their various treatment options and prognosis. MATERIAL AND METHODS: All diagnosed cases of malignant mixed mullerian tumor encountered in 1 year between October 2008 to October 2009 at the Dept. of Gynae and Obst, Medical College Kolkata were included and followed up. RESULTS: Only three such patients were obtained during the above duration. Vaginal bleeding and uterine enlargement were the most common symptoms. Young age and extrapelvic disease at presentation carried worst prognosis. Heterologous tumor was another poor prognostic indicator. Lymph node metastasis at presentation also carried poor prognosis. Combined surgery, chemotherapy and radiotherapy were advocated in management. CONCLUSION: MMMT is an uncommon but not rare tumor of uterine corpus with very poor prognosis. KEYWORDS: Malignant mixed mullerian tumor, cervical MMMT

INTRODUCTION: Malignant Mixed Mullerian Tumors (MMMTs) or carcinosarcomas are composed of malignant epithelial (carcinomatous) and mesodermal (sarcomatous) components. It was first reported by Ferriera in 1951.1 This unusual tumor has been mostly reported between age 60-69 although literature search has revealed occurrence from 12-93yrs.2,3 They can occur in any of the female reproductive organs but most commonly in the uterine corpus due to the embryological development of the uterus. MMMT of the cervix is extremely rare. They account for 2-5% of all malignant neoplasm of the uterine corpus.4-7 Five-year survival rates are about 30-40% in stage I disease8 and considerably less in advanced stages.4-6,9-11 MMMTs are sub-divided into homologous and heterologous tumors. In homologous tumors, both the carcinomatous and sarcomatous elements present are normal components of the Mullerian system.

In heterologous tumors, sarcomatous elements that have no benign counterpart in the uterus are present, such as skeletal muscle, bone and cartilage.12

MATERIAL: We here share our experience regarding three patients of MMMT encountered in 1yr between October 2008 to October 2009 at the Gynae and Obst Dept, Medical College Kolkata. Cases of other gynecological oncology were not included.

RESULTS: Our first patient, Mrs. DM, aged 56yrs, P3+0, with menopause attained 17 yrs. back came to us with complaints of mild bleeding PV in July 2009. There was no significant medical or surgical history. Ultrasonography on 7/8/09 revealed normal size uterus with thickened endometrium.

Other investigations were within normal limits. D/C endometrial biopsy revealed endometrial carcinoma with the involvement of cervix. Radical hysterectomy with pelvic lymph node dissection was done. Histopathology revealed malignant mixed mullerian tumor with carcinosarcomatous
component with involvement of more than half of myometrium with no lymphovascular or perineural involvement found. Adjuvant chemotherapy was given with cisplatin (100) + paclitaxel (230) + doxorubicin (70) 3 weekly x 6 such. She suffered from severe leucopenia which was managed with filgastrin.

She survived the disease for one and a half years but gradually debilitated and ultimately succumbed to pneumonia and severe sepsis.

Our second patient, Mrs M M, aged 75yrs, P4+0, menopause attained 25yrs back, presented with the chief complaints of postmenopausal bleeding for last 2 years. On examination, there was a polypoidal mass hanging through the cervical canal. Once again there was no significant medical or surgical history. Other investigations were within normal limits.

Extended hysterectomy was performed on 7/10/2009. Histopathology revealed malignant mixed mullerian tumor of the body of the uterus and cervix with invasion of full thickness of the myometrium. She was put on cisplatin 100mg, ifosfamide 2mg and doxorubicin 70mg three weekly x 6 such.
Mrs MM was initially lost to follow-up and returned back almost 2 yrs later with abdominal distension and multiorgan failure possibly owing to recurrence. Unfortunately before we could arrange for investigations, she expired inspite of symptomatic management.

Though she was first encountered during the specified duration, our third patient was relatively young. Mrs BD, aged 36yrs, P3+0, presented in October 2008, with history of bleeding per vagina for past one month. She had already undergone hysterectomy owing to menorrhagia some 6 months back in some peripheral hospital, but unfortunately no relevant reports were available. She had pallor and abdominal examination revealed a 7x7cms mass in the left hypochondrium. On local examination we found friable finger like projections arising from the vault which were sent for histopathological examination. Meanwhile an abdominal CT scan done on 7th Nov 2008 revealed left sided para-aortic lymphadenopathy about 8.6cms x 6.8cms. HPE from the cervical protrusions revealed embryonal rhabdomyosarcoma. She was put on actinomycin D, vincristine, cyclophosphamide and adriamycin three weekly x 6 such. Concurrent radiotherapy was advocated too.
Her condition gradually worsened and a repeat CT two months later, revealed almost a similar lymphadenopathy. In her case due to high virulent nature of the disease, we lost her in another 2 months.

| Presentation and outcome of 3 MMMT cases diagnosed in 1 year |
|-----------------|-----------------|-----------------|
|                  | Premenopausal   | Postmenopausal  |
| Age              | 1               | 2               |
| Nature of tumor  | Homologous      | Heterologous    |
|                  | 2               | 1               |
| Lymphovascular and perineural involvement | Present | Absent |
|                  | 1               | 2               |
**DISCUSSION:** Vaginal bleeding and uterine enlargement as seen in our cases is the commonest symptom and sign as reported in literature. 2 of our patients were menopausal, at their 5th to 7th decade, 3rd was relatively young, 36 yrs of age. Relatively large proportions of cases (30-60%) present in advanced stages at the time of diagnosis reflecting the tumor’s aggressive nature. MMMT is a very aggressive disease with extremely poor prognosis. Literature reports survival of 8.5% in stages II and III, while there were no survivors in those with disease outside the pelvis (stage IV). Previous pelvic irradiation is a recognized predisposing factor for MMMT in about 15% (up to 29%).

However, in our cases, none had previous pelvic irradiation. MMMTs of the uterus arise in the endometrium and the epithelial component usually predominates. Endometroid adenocarcinoma is the most common epithelial component but other variations such as clear cell, mucinous and papillary-serous also occur. The mesodermal component is most commonly undifferentiated sarcoma in homologous tumors and rhabdomyosarcoma in heterologous tumors. Some authors have found that patients with tumors containing heterologous components do worse than those whose tumors contained homologous components.

Increasing depth of myometrial invasion was associated with poorer survival. Incidence of lymphatic metastases seem directly related to the depth of myometrial invasion. In our cases the first two discussed were homologous tumors, one being only carcinosarcoma, other having leiomyosarcoma components too. They did relatively better surviving longer than the third patient who despite being young, died early owing to the heterologous nature of the tumor, rhabdomyosarcoma. Uterine curettings can be misleading in that only one type of tissue may be obtained, i.e. either the epithelial or stromal component only, and the true biphasic nature of the tumor becomes apparent only when the entire specimen is available for study, a condition seen in our first patient. Piver & Lurain reviewed 19 studies including 610 patients; the average five-year survival for all stages was 21%. Seventy to 90% of tumor-related deaths occurred within 18 months of diagnosis.

The other important prognostic factor is the depth of myometrial invasion. The relatively large proportion of cases (30-60%) in advanced stages at time of diagnosis reflect the aggressive nature of the tumor. FIGO staging of MMMTs of the uterus is the same as for endometrial carcinoma. Tumor spread occurs by direct extension to the cervix and vagina followed by other pelvic organs including the bladder and rectum. Lymphatic spread to local and regional lymph nodes appears to occur at an early stage of the disease.
A third of patients have lymph node metastases at the time of diagnosis. Our third patient too had lymphatic involvement at initial diagnosis. Due to the aggressive nature of MMMTs and its poor prognosis, various therapeutic modalities have been employed in its treatment. Surgery in the form of abdominal hysterectomy and bilateral salpingo-oophorectomy remains the principal treatment. Adjuvant chemotherapy has been shown to be beneficial. Adjuvant radiotherapy was noted to improve disease controllability in the pelvis. The optimal mode of management for this aggressive tumor remains to be established.

CONCLUSION: Malignant mixed Mullerian tumors of the uterine corpus are uncommon but not rare. They present with vaginal bleeding and uterine enlargement like the majority of uterine cancers. They are highly aggressive tumors associated with poor prognosis.

REFERENCES:

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