
A case report of Malignant Mixed Mullerian Tumor of the uterus with heterologous elements, in an elderly female**Dr Fakeha Firdous¹, Dr Madhavi Shrivastava², Dr Ch V Ramana Murthy³, Dr C. Dakshina Murthy⁴**¹Associate Professor, Pathology, Shadan Institute of Medical Sciences, Hyderabad, Telangana, India²Consultant Pathologist, Hyderabad, Telangana, India³Prof &HOD, Pathology, Shadan Institute of Medical Sciences, Hyderabad, Telangana, India⁴Professor of Pathology, Shadan Institute of Medical Sciences, Hyderabad, Telangana, India***Corresponding author**

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Abstract: Malignant Mixed Mullerian Tumor (MMMT) of the uterus is an uncommon (2% – 5%), extremely aggressive neoplasm histologically composed of malignant epithelial and mesenchymal elements. They are found predominantly in postmenopausal women, presenting with uterine bleeding and enlargement. The present case is of a 60 year old postmenopausal female who had per vaginal white discharge [sero sanguinous] since 2 months. Panhysterectomy was done, and the diagnosis of Malignant Mixed Mullerian Tumor of the uterus was confirmed. Histopathological examination showed Malignant Mixed Mullerian Tumor with heterologous elements.**Keywords:** Malignant Mixed Mullerian Tumor, Uterus, Postmenopausal.

INTRODUCTION:

Malignant Mixed Mullerian Tumors (MMMTs) of the uterus are rare, high grade neoplasms comprising only 2 to 5% of all tumors derived from the body of the uterus [1]. It is a biphasic neoplasm comprising of both carcinomatous (epithelial tissue) & sarcomatous (connective tissue) components. It is divided into 2 types, homologous (in which the sarcomatous component is made up of tissues found in the uterus such as endometrial, fibrous &/ or smooth muscle tissue) & a heterologous type (made up of tissues not found in uterus, such as cartilage, skeletal muscle &/ or bone) [1]. In the present case report, we describe a case of Malignant Mixed Mullerian Tumor of the Uterus with heterologous elements.

CASE REPORT:

A 60 Year old, multiparous woman, known diabetic, known hypertensive, known obese, with nil significant obstetric and gynaec history in the past, presented with post-menopausal per vaginal white discharge [sero sanguinous] and vague lower abdominal pain. Since 2 months.

P/S & P/V Examination: - bulky uterus. Chest X-ray - NAD. Ultrasonography revealed an ill-defined heterogenous soft tissue mass, suggesting possibility of neoplastic pathology of the uterus.

CT scan revealed heterogeneously enhancing mixed density lesions in the fundus/body of the uterus displacing the endometrial cavity. Total abdominal hysterectomy was done. Histopathological examination

showed a Malignant Mixed Mullerian Tumor with Heterologous Elements.

In pathologic evaluation:

Gross Morphology: TAH measured 12*8*5cm size, weight 125 Gms c/s revealed grey white slightly pinkish soft to very firm new growth occupying and obliterating the entire endometrial cavity, normal endometrial layer could not be made out. Infiltration of myometrium [more than 50% thickness] observed in most areas. Tumor showed areas of necrosis, hemorrhage, areas of fine nodularity and vague papillary configuration in some areas. Infiltration into the myometrium of fundus and body observed. Cervical canal and cervix proper not involved and appeared tumor free.

Light microscopy:

Cervix-chronic nonspecific cervicitis changes. No evidence of malignancy. Endometrial cavity new growth :revealed histology of moderate to poorly differentiated adenocarcinoma [endometroid type] with grade II nuclei and with squamoid changes and areas of infiltration into the myometrium, with areas of necrosis, haemorrhages and non-specific inflammation, mitotic figures seen [10/10 Hpf] also showed myxoid areas with cartilaginous differentiation, rhabdo myosarcomatous differentiation with pleomorphic tumor giant cells, alveolar pattern and few foci of bubbly cytoplasm [adipose differentiation] and vascular areas. The Final Diagnosis given was Imp: Carcinosarcoma [Malignant Mixed Mullerian Tumor with heterologous elements] of endometrium pathologic stage IC, nuclear grade II.

DISCUSSION:

Malignant mixed mullerian tumors of the uterus are rare neoplasms that are practically always seen in postmenopausal patients [2]. The symptom triad indicative of MMMT includes pain, severe vaginal bleeding and passage of necrotic tissue per vaginum [3]. In our case the patient was 60yr old postmenopausal women presenting with abnormal vaginal discharge, with no known predisposing factor. Very little is known about the aetiopathogenesis of MMMTs. Exposure to radiation, excessive estrogen exposure, obesity, and nulliparity are believed to be associated with MMMT development [4].

Malignant uterine neoplasm's containing both carcinomatous and sarcomatous elements are designated in the World Health Organisation (WHO) classification of uterine neoplasm's as carcinosarcomas. Gebhardt in 1899 appears to have reported the first case, Meyer, after a personal examination of the slides, accepted it as authentic [7]. Carcinosarcomas representing less than 5% of all uterine tumors, account for 16.4% of all deaths caused by a uterine malignancy [8].

UC has been identified in decreasing order of frequency in the vagina, cervix, and ovary and most rarely in the fallopian tubes [9-12]. There are three main theories regarding the histogenesis of UC namely [13, 14].

- 1) The collision theory suggests that the carcinoma and sarcoma are two independent neoplasms.
- 2) The combination theory suggest that both components and derived from a single stem cell that undergoes divergent differentiation early in the evolution of the tumor.
- 3) The conversion theory suggests that the sarcomatous elements derive from the carcinoma during the evolution of the tumor. On exploring the literature we found that W G Mc Cluggage named one more theory: The composition theory suggest that the spindle cell component is a pseudosarcomatous stroma.

The usual location is the uterine body, particularly the posterior wall of the fundus but a few cases with MMMT of uterine cervix have been reported as well [5]. Traditionally diagnosis of MMMT is most often made postoperatively by histological examination. However, pre-operative diagnosis of uterine MMMT

will facilitate the planning of appropriate surgical management with adjuvant therapy [3]. Radiological investigations show MMMT to be a heterogenous, hypo dense, ill-defined mass filling the uterine cavity [3]. Grossly MMMTs are almost invariably fleshy, necrotic, haemorrhagic, polypoidal growths that often filled the uterine cavity [6]. In our case similar gross findings were noted. The characteristic microscopic features of MMMTs are a mixture of carcinomatous and sarcomatous elements resulting in a biphasic pattern. The epithelial component of a carcinosarcoma may be any type of mullerian carcinoma: mucinous, squamous, serous, endometrioid, high grade papillary, clear cells, undifferentiated, or a mixture of these types. The appearance of the sarcomatous component is the basis for division of these neoplasms into homologous (leiomyosarcoma, stromal sarcoma, fibrosarcoma) and heterologous varieties (chondrosarcoma, rhabdomyosarcoma, osteogenic sarcoma, liposarcoma) [6].

Diagnosis of UC is most often made postoperatively by histopathological examination and Immunohistochemical (IHC) Studies. Abdominal hysterectomy with bilateral salpingo oophorectomy and pelvic lymphadenectomy is the treatment of choice, usually followed by adjuvant therapy [2]. MMMTs are highly aggressive neoplasms. Recurrence occurs in over half of patients after primary surgical and adjuvant therapy. Specific factors that increase the risk of recurrence include patient's age, adnexal spread, and metastasis to the lymphnodes, tumor size, lymphovascular involvement, histologic grade, peritoneal cytologic findings, & the depth of invasion of the primary tumor [3].

Extension to the pelvis, lymphatic and vascular permeation, distant lymph-borne and blood – borne metastasis are all common [2]. The most common site of metastatic deposit include lung, peritoneum, pelvic or para-aortic, adrenal glands or bone, heart, & brain [3].

Although uterine MMMT account for less than 5% of uterine malignancies, they are responsible for over 15% of uterine cancer-related deaths. Over the past 30 years despite evolving and advancing therapeutic regimes, prognosis remain poor, with no significant improvement in survival or recurrence rate The most important prognostic features are the stage, the size of the tumor, and the depth of myometrial invasion [3].



Fig 1: Gross image of the TAH specimen with tumor.

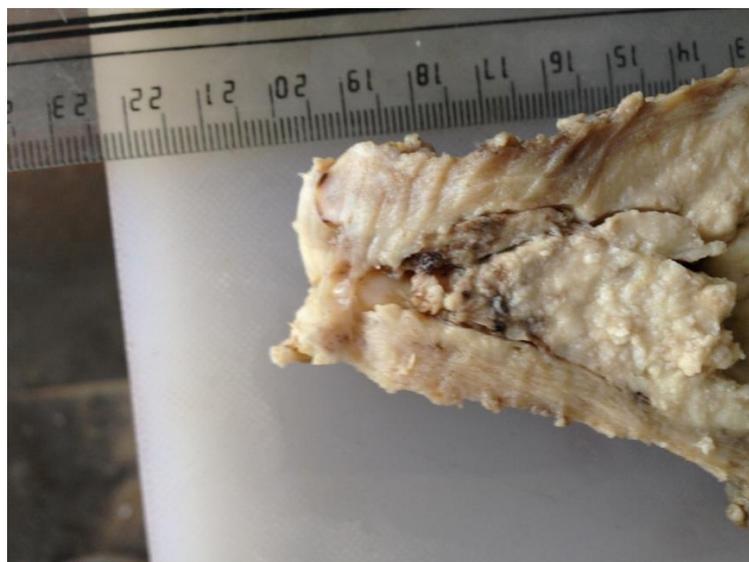


Fig 2: Gross image of the uninvolved cervix.

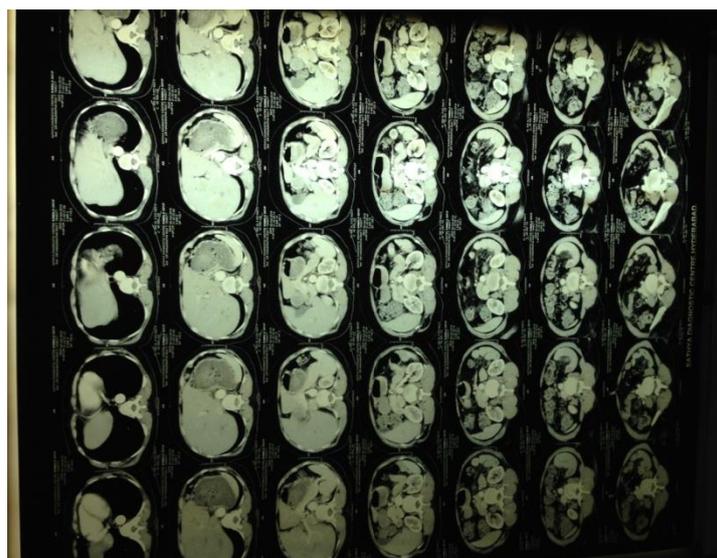


Fig 3: CT scan image of the Pelvis abdomen

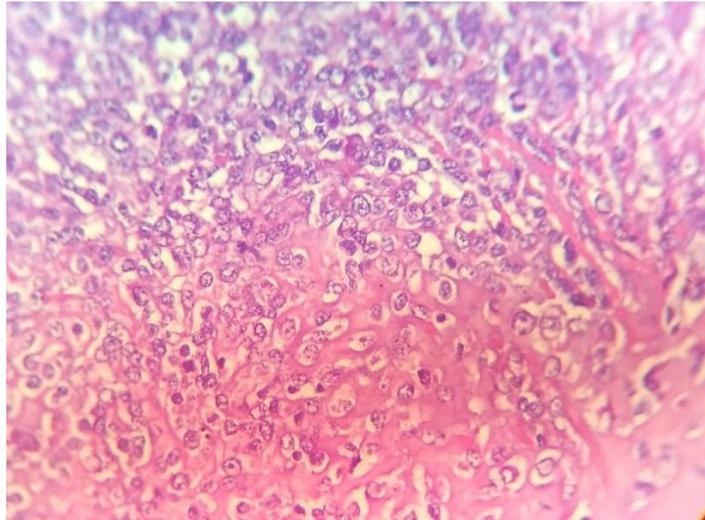


Fig 4: H&E section from tumor showing osteoid areas

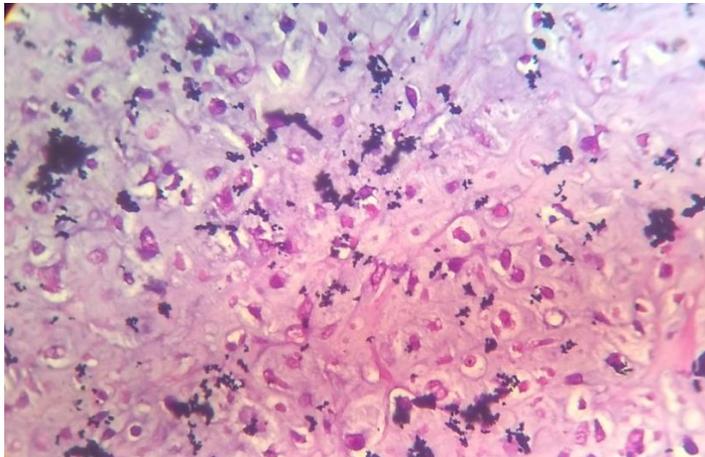


Fig 5: H&E section from tumor showing cartilaginous areas

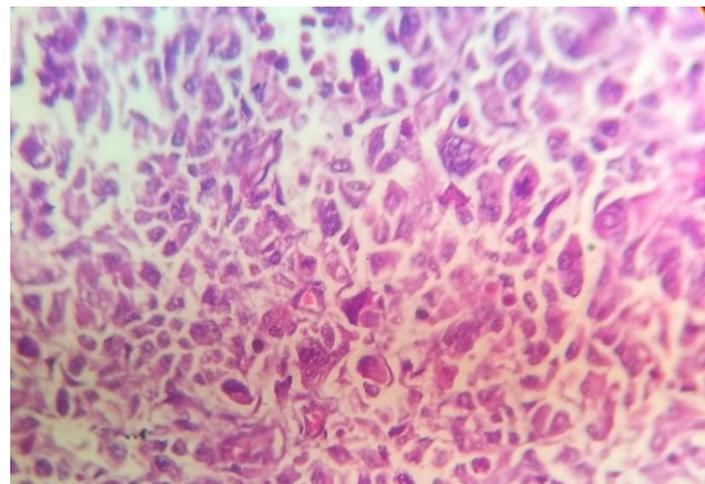


Fig 6: H&E section from tumor showing rhabdo myosarcomatous differentiation with pleomorphic tumor giant cells

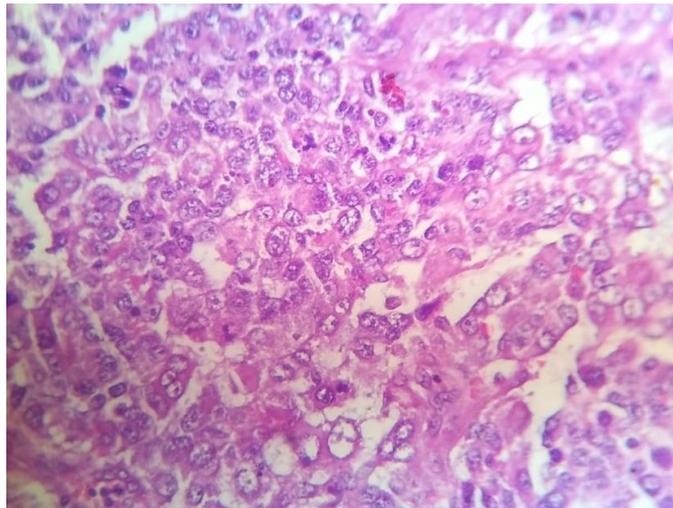


Fig 7: H&E section showing features of moderate to poorly differentiated adenocarcinoma [Endometrioid type]

CONCLUSION:

Malignant Mixed Mullerian Tumor (MMMT) of the uterus is an uncommon extremely aggressive neoplasm, histologically composed of malignant epithelial and mesenchymal elements. Traditionally diagnosis of MMMT is most often made postoperatively by histological examination and Immunohistochemical (IHC) Studies. Abdominal hysterectomy with bilateral salpingo oophorectomy and pelvic lymphadenectomy is the treatment of choice, usually followed by adjuvant therapy. Specific factors that increase the risk of recurrence include patient's age, adnexal spread, and metastasis to the lymphnodes, tumor size, lymphovascular involvement, histologic grade, peritoneal cytologic findings, & the depth of invasion of the primary tumor

CONSENT: Taken from the patient.

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