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Synchronous Occurrence of Malignant Mixed Mulleriantumor In the Uterus And Ovary: A Case Report.

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ABSTRACT

Malignant Mixed MullerianTumor (MMMT) is a rare, aggressive and biphasic neoplasm of female genital tract. We report clinical, histopathological and immunohistochemicalfeatures of MMMT of uterus and unilateral ovary occurring synchronously in a 51 year old woman. MMMTs require high index of clinical suspicionand it should be considered as a differential diagnosis in cases of postmenopausal vaginal bleeding.

Keywords; Carcinosarcoma, Malignant mixed mulleriantumor, Ovary, Synchronous Uterus

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INTRODUCTION

Malignant Mixed MullerianTumor (MMMT) is a biphasic neoplasm of the female genital tract. It comprises of both malignant epithelial and mesenchymal elements, hence also called as carcinosarcoma. These tumors can occur in any of the female reproductive organs. Most common site is uterine corpus which is associated with the embryological development of the uterus.MMMT also occurs in ovary, cervix and fallopian tube. MMMT of the uterus accounts for 2-5% of all malignant neoplasms of the uterine corpus [1]. It isan uncommon, aggressive and extremely rare neoplasm with an incidence of lesser than 2 per 100,000 women per year These tumors have a poor prognosiswith a 5year survival rate of 33- 39% [2].Ovarian MMMT accounts for less than 1% of all ovarian malignancies [3].We report a rare case of synchronous occurrence of MMMT of uterus and unilateral ovary.

CASE REPORT

A 51 year old woman, menopausal since 3 years presented with irregular bleeding, white discharge per vagina for past 3 months, loss of weight and appetite along with abdominal distension since 1month.She had undergone cervical and endometrial biopsy with histopathology suggestive of moderately to poorly differentiated carcinoma, following which she was referred to our tertiary care centre. Computerized tomography showed bulky uterus with non-enhancing endometrial collection (4.3x4.3cm) with sub-acute haemorrhage. Right adnexa was bulky (6x6.5cm) with heterogeneous attenuation/ enhancement suggestive of ovarian malignancy.CA125wasincreased (714.5U/mL, Normal: 0-35U/mL), whereas CEA, CA19.9 and AFP were within normal limits. Staging laparotomywas planned and total abdominal hysterectomy with bilateral salphingo-oopherectomy, infracolicomentectomy, lymph node dissection and appendicectomy was done. Grossly, uterusshowed a grey white fleshy growth measuring 8x5x4.5cm, extending from the fundus upto 2.5cm from the external os. Right sided ovary was enlarged and cut section showed a tumor with grey white solid, papillary and necrotic areas. Other ovary, cervix and bilateral fallopian tubes were free of tumor. Omentum showed multiple tumordeposits(Fig 1).On microscopy,endomyometriumand right ovary showed tumor composed of malignant cells arranged in nests and sheets. Cells showed moderate cytoplasm, pleomorphic vesicular to hyperchromatic nuclei, anisonucleosis and prominent nucleoli, atypical mitosis, multinucleated tumor giant cells in a malignant spindle cell stroma with extensive areas of necrosis.Myometrium, isthmus, cervix,omentum, lymph nodes and periappendiceal surface showed tumorinvolvement.Other ovary,bilateral fallopian tubes andparametriumwere free of tumor. (Fig 2-5) Immunohistochemistry(IHC) performed on both uterine (Fig 6,7) and ovarian tumor (Fig 8,9) showed similar profile. Tumor cells were positive for Vimentin, focally for Epithelial membrane antigen (EMA); negative for Desmin. A diagnosis of MMMT of the uterus and unilateral ovary was given.She was advised chemotherapy with carboplatin and paclitaxel. Patient deferred the treatment, hence was discharged and later was lost on follow up

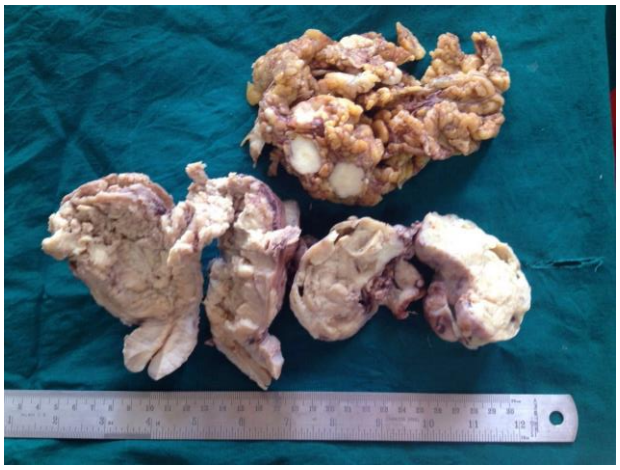

Fig 1: A fleshy grey white growth extending from the fundus of the uterus, ovarian solid growth, omental deposits

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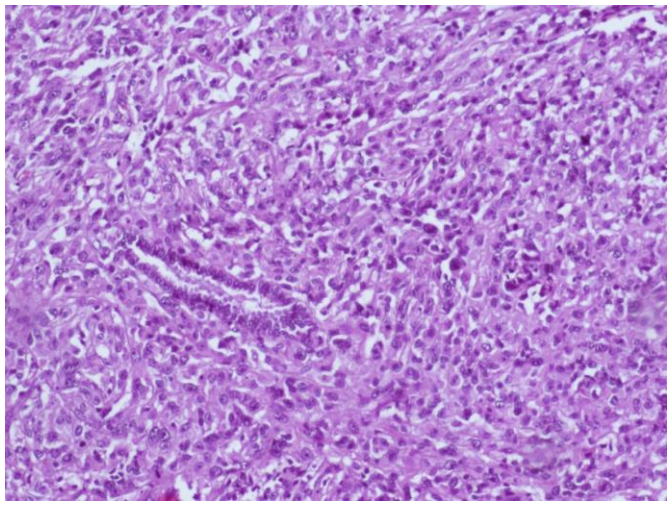

Fig 2: Endometrial growth- nests and clusters of malignant epithelial and mesenchymal component (H& E X100)

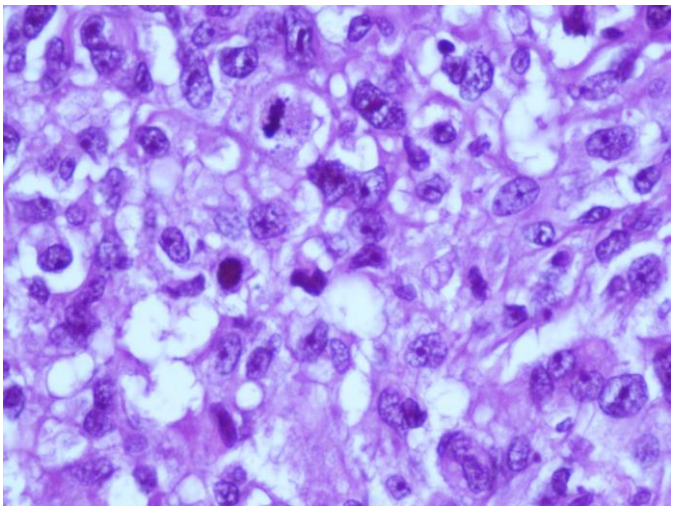

Fig 3: Endometrial growth, pleomorphic vesicular to hyperchromatic nuclei, prominent nucleoli, mitosis (H&E X400)

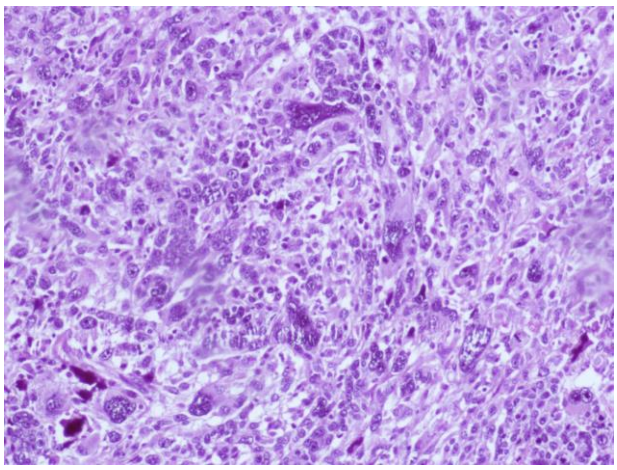

Fig 4: Ovarian tumor- sheets of tumor composed of malignant epithelial and spindle cell stroma H&E X 200

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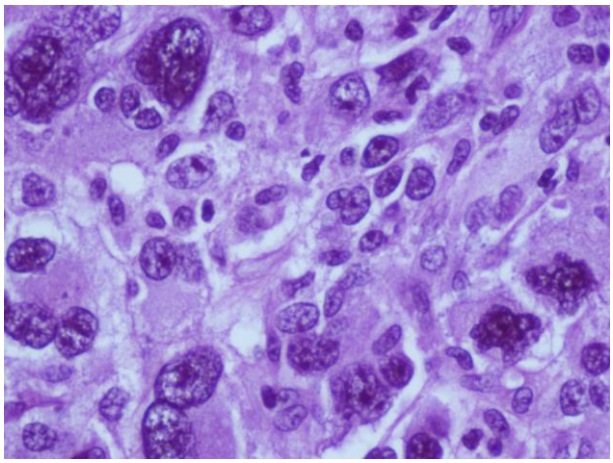

Fig 5: Ovarian tumor, pleomorphic vesicular to hyperchromatic nuclei, multinucleated tumor giant cells H& E X400

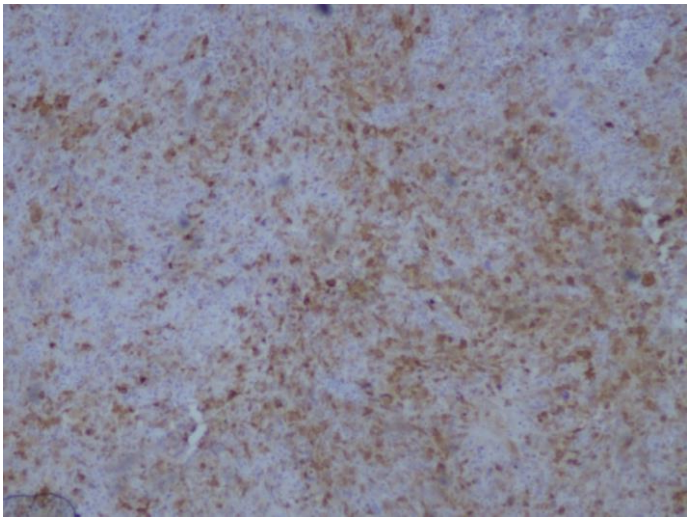

Fig 6: Endometrial tumorEMA- Positive in epithelial component (X100)

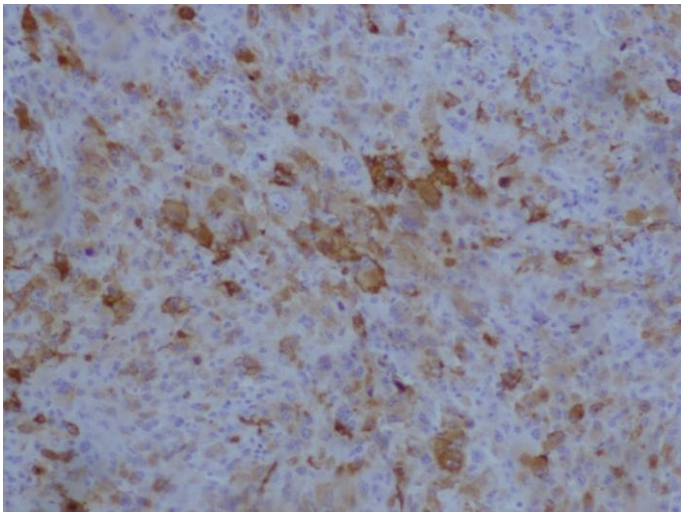

Fig 7: Endometrial tumorVimentin- Positive in mesenchymal component (X100)

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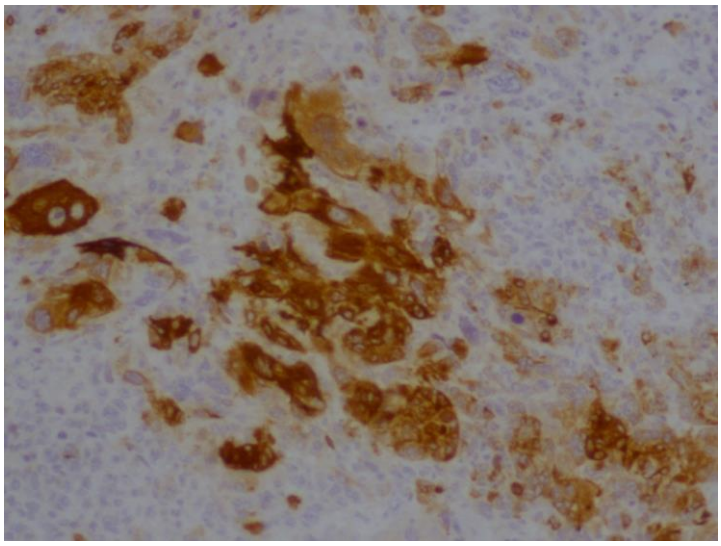

Fig 8: Ovarian tumor- EMA Positive in epithelial component (X100)

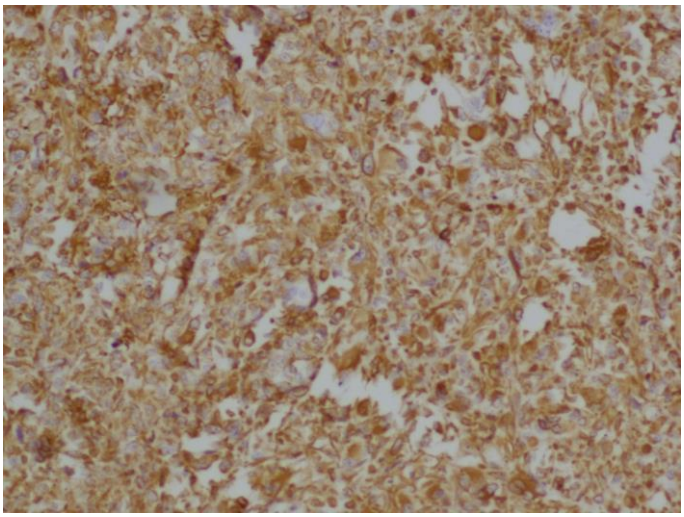

Fig 9: Ovarian tumor- Vimentin Positive in mesenchymal component (X100)

DISCUSSION

MMMT was first described by Ferriera and colleagues in 1951 [4]. It is a rare, aggressive tumor which arises from the female genital tract. Singh *et al*[5] reported that simultaneous occurrence of two or more malignancies in the female genital tract is rare and accounts for only 1-2%. However, the synchronized occurrence of endometrial and ovarian cancers are the most common among the simultaneous genital cancers as documented byEisner [6].Extra genital MMMT are also extremely rare, involves pelvic peritoneum, serosal surface of colon,retroperitoneum, abdominal peritoneum and omentum [7].

MMMTs develop mostly in postmenopausal women. However,few case reports describe their occurrence in reproductive females and even during teenage [3].Some studies have reported age of presentation ranging from 12-93 years [4].The most common presentation is abnormal uterine bleeding followed by abdominal pain and cervical mass.Peritoneal seeding is seen in ovarian MMMT. Nearly 67-100% of cases with peritoneal seeding has accompanying ascites as well [3].

MMMT represent a metaplastic carcinomas, where the carcinomatous component is responsible for the invasiveness of the tumor [8].Many hypothesis have been proposed to describe the its histogenesis. According toGorai*et al*, [9] stem cells were responsible to give rise to both the components of MMMT.These

tumors are found to be associated with certain medical conditions such as diabetes and hypertension. Nulliparity, obesity,exogenous estrogen, long term use of tamoxifen, previous radiation exposure and chemotherapy are considered to be the risk factors for MMMT[1].In a study nearly 7-37% of patients developing MMMT have been found to have a history of radiation exposure[10]

MMMTs can be sub-divided into homologous and heterologous tumors. The carcinomatous and sarcomatous elements in homologous MMMTs represent the normal components of the Mullerian system whereas in heterologous tumors, the sarcomatouscomponent have no corresponding benign counterpart in the uterus, for example skeletal muscle, bone and cartilage.Boucher *et al*[11]in their studyreported equal representation of epithelial and serous components, and the mesenchymal component was heterologous mostly, which included chondromatous and rhabdomyoblastic differentiation. Stage at presentation does notcorrelate with either epithelial or sarcoma predominanceaccording toMenon S *et al.*[12]

Preoperative diagnosis of uterine or ovarian MMMT is rarely made, as the clinical presentation and radiology mimics epithelial tumors as in our case.IHC shows cytokeratin and EMA reactivity in epithelial components; Vimentinand desminpositivity in mesenchymal elements as in our case.

Most authors recommend surgery combined with chemotherapy and or radiotherapy. In a small study by Kohorn*et al*,[13] 80% survival of patients with combined therapy was reported, although other larger studies have reported no beneficial effect on survival. Stage of the disease and the depth of myometrial invasion are the twoimportant prognostic parameters[14].5 year survival rates arevery low probably because majority of the cases present with advanced disease.

CONCLUSION

MMMT are rare biphasic neoplasms of the female genital tract. Synchronous occurrence of the primary MMMT in uterua and ovary is extremely rare and aggressive in nature with a poor survival rate.

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