MALIGNANT MIXED MULLERIAN TUMOR OF UTERUS IN A DIABETIC PATIENT - A CASE REPORT

Gireesh V Achalkar[1]

HOW TO CITE THIS ARTICLE:
Gireesh V Achalkar. "Malignant mixed mullerian tumor of uterus in a diabetic patient - a case report". Journal of Evolution of Medical and Dental Sciences 2013; Vol. 2, Issue 46, November 18; Page: 8891-8894.

ABSTRACT: Uterine malignant mixed mullerian tumor (MMMT) is an uncommon carcinosarcomatous neoplasm with a highly malignant, biphasic pattern consisting of both epithelial and mesenchymal components. This paper reports the clinical, pathological and immunohistochemical features of MMMT of a diabetic patient. A 56 year-old woman presented with post- menopausal bleeding for eight months. The patient underwent Total Abdominal Hysterectomy with Bilateral Salpingo-oophorectomy (TAH&BSO) with pelvic lymph nodes dissection. In pathologic evaluation, a polypoid solid and grey white mass measuring 3.5 x 3 x 2 cm was identified. Light microscopy showed biphasic pattern of epithelial component with glandular change and sarcomatous elements of spindle cells with cartilage and bone differentiation. Immunohistochemistry was performed on formalin fixed and paraffin embedded tissue with a panel of immunohistochemical markers comprising of cytokeratin (CK), vimentin and $s_{100.}$ The epithelial component was reactive for CK. Vimentin, S_{100} positivity was seen in stromal and chondroid elements, so the diagnosis of MMMT was confirmed. CONCLUSION: There may be an association between diabetes mellitus and the development of malignant mixed mullerian tumor. Special attention should be paid when attempting to sample the endometrium of these patients.
KEYWORDS: post- menopausal bleeding, Malignant Mixed Mullerian Tumor, Diabetes mellitus.

INTRODUCTION: Uterine malignant mixed mullerian tumor(MMMT) is an uncommon carcinosarcomatous neoplasm with a highly malignant, biphasic pattern consisting of both epithelial and mesenchymal components[2]. The epithelial component may be any type of mullerian carcinoma, mucinous, squamous, endometroid, high-grade papillary, clear cell, undifferentiated, or mixtures of these types. It is traditional to divide the stromal components into homologous (leiomyosarcoma, stromal sarcoma, fibrosarcoma) and heterologous (chondrosarcoma, rhabdomyosarcoma, osteosarcoma, liposarcoma) types. Carcinosarcoma, with rare exceptions, is a disease of elderly menopausal women[3]. The clinical course of tumor is highly aggressive and it is usually diagnosed in advanced stage. This neoplasm has sometimes been associated with a history of radiation therapy[4]. Some patients have developed carcinosarcoma while taking tamoxifen[8] and raloxifene[6]. Diabetes mellitus and hypertension have been introduced as predisposing factors for uterine adenocarcinoma, but the relationship between these factors and MMMT is not clear.[10.11] This article reports the clinical, pathological and immunohistochemical features of MMMT in a diabetic and hypertensive patient.

CASE REPORT: A 56 year-old woman with chronic diabetes mellitus (type II) presented with post-menopausal bleeding for eight months. The patients diabetes mellitus (type II) was well controlled, using oral hypoglycemic drugs. Pelvic examination showed uterine enlargement. A mixed cystic and solid mass measuring 33mm x 31mm x 26mm was found using trans- abdominal ultrasonography.

In addition pap smear and dilation curettage were performed and the diagnosis of adenocarcinoma was suggested for the patient. Afterwards, the patient underwent surgery. The type of operation was total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH & BSO) with pelvic lymph node dissection. Adjuvant therapy was also included in treatment program following surgery.

In pathologic evaluation, grossly, the mass was polypoid, solid, grey white and with necrosis and hemorrhage, measuring 3.5 x 3 x 2cm (figure 1). Light microscopy showed a heterogenous malignant neoplasm with a biphasic pattern. The epithelial part of the tumor consisted of glandular component (figure 2). Furthermore, sarcomatous areas consisting of spindle cells with oval nuclei, focally arranged in bundles accompanied by foci of mature cartilage and bone were found (figure 3). Mitotic figures were moderate. Immunohistochemistry was performed on formalin fixed and paraffin embedded tissue with a panel of immunohistochemical markers comprising cytokeratin (CK), vimentin and S_{100}. The epithelial component was reactive for CK. Vimentin and S_{100} positivity was seen in stromal and chondroid elements. In post-operative follow up, the patient did not have any serious complaint up to one month after surgery.

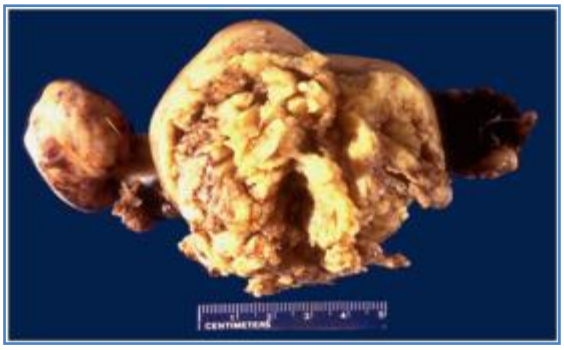

Fig. 1: Gross morphology of MMMT showing grey white tumor with areas of hemorrhage and necrosis.

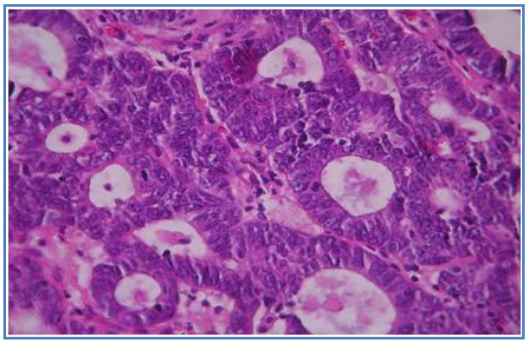

Fig. 2: Glandular component of malignant mixed mullerian tumor (H&E *400)

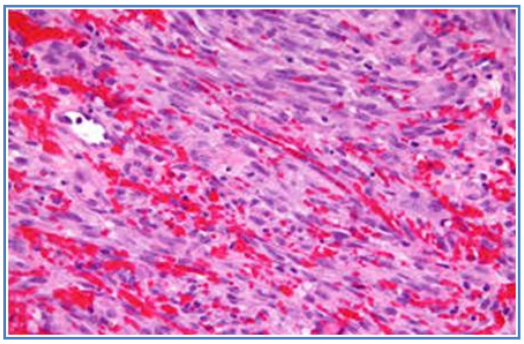

Fig. 3: Mesenchymal component of malignant mixed mullerian tumor (H&E *400)

DISCUSSION: Malignant mixed mullerian tumors of the uterus are uncommon neoplasms that are virtually always seen in postmenopausal patients. 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[8]. Infertility and obesity have

been reported in some patients[8]. The relationship between diabetes mellitus, hypertension and BMI with endometrial cancers was evaluated in a research in Sweden by Weiderpass et al[10].

Grossly, these tumors present as large, soft, broad based and polypoid masses involving the endometrium and myometrium with fleshy surfaces. Necrosis and hemorrhage are commonly found as well[1,2]. The characteristic microscopic features of MMMTs are the admixture of carcinomatous and sarcoma like elements resulting in a biphasic pattern. The carcinomatous component is usually a poorly differentiated adenocarcinoma. The appearance of the sarocomatous component is that of rhabdomyoblasts, mature appearing cartilage or chondrosarcoma, osteoid, bone or osteosarcoma and liposarcoma. The rest type of differentiation in MMMTs is neural.

Immunohistochemical studies revealed that cytokeratin was always detectable in the epithelial areas, but was also present in the sarcomatous component in over half of the cases. Vimentin is more diffuse and intense in the sarcomatous component. Various muscle markers, CD[10], and HER-2/ neu also have been encountered in MMMTs[8].

The etiologic factors, involved in the development of MMMTs are not clear. Fotiou et al[11] reported two cases of MMMT secondary to tamoxifen treatment in patients with a previous diagnosis of carcinoma. Huang YT et al[7] reported a patient with stage IIIB cervical squamous cell carcinoma in whom MMMT developed 5 years after radiotherapy[4]. MMMTs have also been seen with chronic estrogenic stimulation (ovarian thecoma, polycystic ovarian disease, and prolonged estrogen therapy). In differential diagnosis, mullerian adenosarcoma should be considered. In adenosarcoma, the epithelial component is clearly benign. MMMTs may be misdiagnosed as pure carcinomas or sarcomas mainly in small biopsies and the lesion may be misinterpreted by inadequate sampling as occurs in our case.

MMMTs are highly aggressive neoplasm. Staging is the most important predictive factor in prognosis[3]. There are some evidences that the prognosis of MMMTs of the cervix is better than their corpus counterparts[8]. In our patient, light microscopy showed biphasic pattern of epithelial component with clear cell change and sarcomatous elements of spindle cells with cartilage and bone differentiation. Malignant features in epithelial component ruled out adenosarcoma, so the diagnosis of MMMT was confirmed.

CONCLUSION: There may be an association between diabetes mellitus and the development of malignant mixed mullerian tumor. Special attention should be paid when attempting to sample the endometrium of these patients.

REFERENCES:

1. Niculeseu M. simioneseu C, Novac L, Mogoanta L, Staneseu RM. The uterine carcinosarcoma – a case report. Rom J Morphol Embryol 2007: 48(4):431-435.
2. Semezuk A. Skomra D, Chyzynska M, Szewezuk W, Oleha P, Korobowicz E, Immunohistochemical analysis of carcinomatous and sarcomatous components in the uterine carcinosarcoma: a case report. Pathol Res Pract 2008; 204(3):203-207.
3. Rosai J. Uterus –corpus. In: Rosai J, editor, Rosai and Ackerman's surgical pathology. Philadelphia: Lippincott Williams & Wilkins, 2004: 1959-1602.
4. Huang YT. Huang KG, Ueng SH, Shaw SW, Irradiation-induced uterine malignant mixed mullerian tumor. Taiwan J Obstet Gynecol 2006: 45(4):353-355.

5. Saim M, Cote JF, Morel O, Malartic C, Akerman G, Gray Fetal,Malignant mixed mullerian tumor of the uterus following tamoxifen for breast cancer: case report Gynecol Obstet Fertil 2008: 36(2):166-168.
6. Goldman NA, Los Angeles MM, Jones JG, Goldberg GL, Malignant mixed mullerian tumor of the uterus in a patient taking raloxifene. Obstet Gynecol 2005: 105(5 Pt 2):1278-1280.
7. Huang ZH, Zuo YW, Wen AM, Luo HQ, Endometrial carcinoma in patients below 45 years of age: clinical analysis of 53 cases. Nan fang Yi Ke Da Xue Xue Bao 2007:27(12):1955-1957.
8. Ribeiro-Silva A, Novello-Vilar A, Cunha-Mercante AM, Angelo Andrade LA, Malignant mixed Mullerian tumor of the uterine cervix with neuroendocrine differentiation. Int J Gynecol Cancer 2002: 12(2):223-227.
9. Papanas N, Giatromanolaki A, Galazios G, Maltezos E, Sivridis E Endometrial carcinoma and Diabetes Revisited Eur J Gyenaecol Oncol 2006 27(5) 505-508.
10. Wiederpass E, Persson I, Adam HO, Magnusson C, Lindegren A, Baron JA: Body size in different periods of life: Diabetes Mellitus, Hypertension and risk of postmenopausal endometrial cancer (Sweden) cancer causes control 2000:11(2):185-192.
11. Fotiou S, Kyrousis G, kokka F, Apostolikas N: Long term tamoxifen treatment: a possible etiological factor in the development of uterine carcinosarcoma: Two case reports and review of literature : Anticancer Res 2000 20(3B) 2015-2020.

AUTHORS:

1. Gireesh V Achalkar

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Pathology, Raichur Institute of Medical Sciences, Raichur.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Gireesh V. Achalkar,
Associate Professor, Department of Pathology,
Raichur Institute of Medical Sciences,
Raichur – 584102.
Email – drgireesha@yahoo.com

Date of Submission: 16/10/2013.
Date of Peer Review: 17/10/2013.
Date of Acceptance: 06/11/2013.
Date of Publishing: 12/11/2013