IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Uterine Malignant Mixed Mesodermal Tumor (MMMT) presented with DVT (as paraneoplastic syndrome), Case Report Series

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Abstract

Uterine carcinosarcoma (malignant mixed mesodermal tumor) are and aggressive tumors. Commonly presents with abnormal vaginal bleeding and rapidly enlarging uterus with polypoid mass that may protrude through the cervix. The absence of specific laboratory findings makes the diagnosis of this tumor difficult. Endometrial sampling should never be underestimate in any patient with abnormal vaginal bleeding and enlarged uterus after the age of 40 to diagnose and guide the management. However, negative histology does not exclude the disease as found in our case report series.

Key words: uterine carcinosarcoma (malignant mixed mesodermal tumor), endometrial carcinoma, deep vein thrombosis.

Introduction

Uterine carcinosarcomas (previously called malignant mixed Mullerian tumors) are rare and aggressive cancers that are dedifferentiated (metaplastic) carcinomas comprised of carcinomatous and sarcomatous elements arising from a single malignant epithelial clone. They may represent a stable disruption of the epithelial mesenchymal transition[1-3]. These tumors are rare that they account for less than 5 percent of all uterine malignancies[4]. Carcinosarcomas occur in older women; the median age at diagnosis ranges from 62 to 67 years, although rare cases occur in younger women and even children[5-7].

The diagnosis of carcinosarcomas is challenging due to its varied clinical presentation, which may include, but it is not limited to, abnormal vaginal bleeding, bloody or watery discharge, abnormal pelvic pain, and palpable pelvic masses[8]. The absence of any highly sensitive or specific clinical signs of this malignancy may inform why it's typically discovered relatively late on initial presentation[9].

The diagnosis of carcinosarcoma is based on histologic evidence of a dual population of carcinomatous and sarcomatous cells with invasion of stroma. The approach to treatment depends on whether the diagnosis was made preoperatively or following hysterectomy, but generally it's either surgical and/or chemotherapy.

Case scenario 1

A 64 years old lady, Para I, vaginal delivery, 37 years back, not diabetic or hypertensive presented to medical department with deep vein thrombosis, she was investigated and treated for almost a month. During the treatment course she had vague lower abdominal symptoms, she did ultrasonography which revealed enlarged uterus, so patient was evaluated by gynecologist and did endometrial biopsy, which was negative for malignancy. After three months she came with abnormal vaginal bleeding, vague pelvic discomfort and symptoms of anemia.

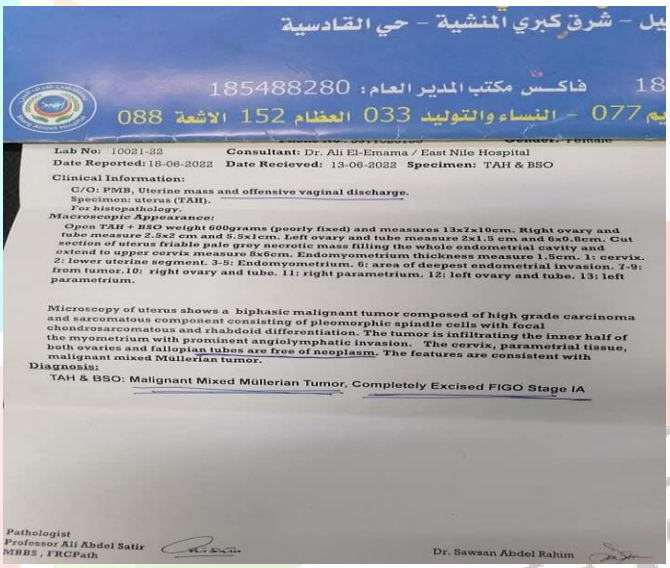
On physical examination: sick looking patient, pale conjunctive, non-icteric sclera. Vital signs, blood pressure 100/60mmHg, pulse rate 90beats/min, normal oxygen saturation and respiratory rate. No enlarged lymph nodes. Speculum examination: normal looking cervix with vaginal bleeding.

Investigation: complete blood count, hemoglobin:7.5g/Dl, otherwise other blood tests revealed normal. CT scan done showed enlarged uterus with no lymphadenopathy.

Patient stabilized and transfused with packed RBCs, received counseling therapy by multi-disciplinary team (MDT) and planned for surgery. She had uncomplicated total abdominal hysterectomy and bilateral salpingo-oopherectomy (TAH+BSO), peritoneal wash and omentectomy (picture 1 and 2). Histopathology result revealed malignant mixed mesodermal uterine tumor stage IA (picture 3). Patient followed till discharged and referred to medical oncology unit.

Picture 1. TAH+BSO, peritoneal wash and infra-colic omentectomy

Picture 2. TAH+BSO, peritoneal wash and infra-colic omentectomy (different view)



Lab No: 10021-22 Consultant: Dr. Ali El-Emama / East Nile Hospital
Date Reported: 18-06-2022 Date Recieved: 13-06-2022 Specimen: TAH & BSO

Clinical Information:
C/O: PMB, Uterine mass and offensive vaginal discharge.
Specimen: uterus (TAH).
For histopathology.

Macroscopic Appearance:
Open TAH + BSO weight 600grams (poorly fixed) and measures 13x2x10cm. Right ovary and tube measure 2.5x2 cm and 5.5x1cm. Left ovary and tube measure 2x1.5 cm and 6x0.8cm. Cut section of uterus friable pale grey necrotic mass filling the whole endometrial cavity and extend to upper cervix measure 8x6cm. Endomyometrium thickness measure 1.5cm. 1: cervix. 2: lower uterine segment. 3-5: Endomyometrium. 6: area of deepest endometrial invasion. 7-9: from tumor.10: right ovary and tube. 11: right parametrium. 12: left ovary and tube. 13: left parametrium.

Microscopy of uterus shows a biphasic malignant tumor composed of high grade carcinoma and sarcomatous component consisting of pleomorphic spindle cells with focal chondrosarcomatous and rhabdoid differentiation. The tumor is infiltrating the inner half of the myometrium with prominent angiolymphatic invasion. The cervix, parametrial tissue, both ovaries and fallopian tubes are free of neoplasm. The features are consistent with malignant mixed Müllerian tumor.

Diagnosis:
TAH & BSO: Malignant Mixed Müllerian Tumor, Completely Excised FIGO Stage IA

Pathologist
Professor Ali Abdel Satir
MBBS , FRCPath

Dr. Sawsan Abdel Rahim

Picture3. Histopathology report

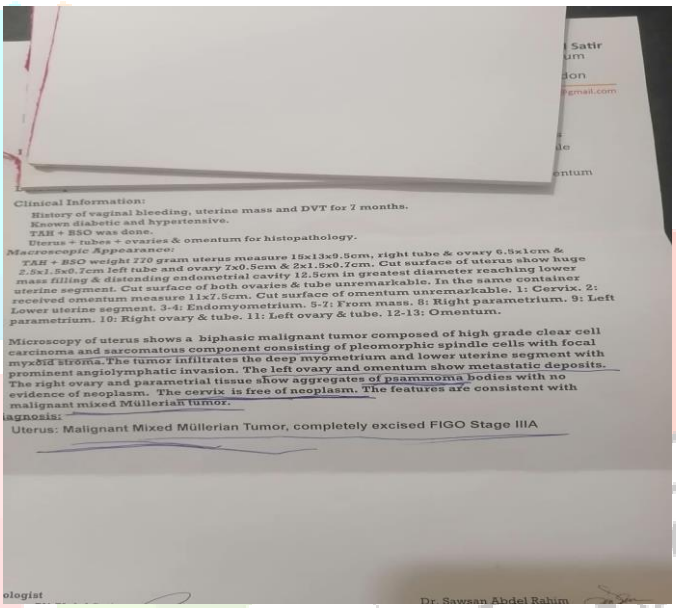
Case scenario 2

A 56 years old lady, Para II, vaginal delivery, diabetic and hypertensive on medication presented with abnormal vaginal bleeding of 3month duration associated with abnormal vaginal discharge.

Investigation: all of the blood investigation were normal. Ultrasonographic scan revealed enlarged uterus with no ascites. MRI showed also grossly enlarged uterus with no lymph node involvement.

Patient counseled with the finding and had endometrial biopsy which revealed malignant mixed mesodermal tumor of the uterus. Later, patient had uncomplicated TAH+BSO, peritoneal wash and omentectomy (picture 4). Histopathology again showed the above finding (picture 5). Patient followed till discharged and sent to medical oncology unit.

Picture 4. TAH+BSO, uterine carcinosarcoma with polypoid mass



Clinical Information:
History of vaginal bleeding, uterine mass and DVT for 7 months.
Known diabetic and hypertensive.
TAH + BSO was done.
Uterus + tubes + ovaries & omentum for histopathology.
Macroscopic Appearance:
TAH + BSO weight 270 gram uterus measure 15x13x9.5cm, right tube & ovary 6.5x1cm & 2.5x1.5x0.7cm left tube and ovary 7x0.5cm & 2x1.5x0.7cm. Cut surface of uterus show huge mass filling & distending endometrial cavity 12.5cm in greatest diameter reaching lower uterine segment. Cut surface of both ovaries & tube unremarkable. In the same container received omentum measure 11x7.5cm. Cut surface of omentum unremarkable. 1: Cervix, 2: Lower uterine segment, 3-4: Endomyometrium. 5-7: From mass. 8: Right parametrium. 9: Left parametrium. 10: Right ovary & tube. 11: Left ovary & tube. 12-13: Omentum.

Microscopy of uterus shows a biphasic malignant tumor composed of high grade clear cell carcinoma and sarcomatous component consisting of pleomorphic spindle cells with focal myxoid stroma. The tumor infiltrates the deep myometrium and lower uterine segment with prominent angiolymphatic invasion. The left ovary and omentum show metastatic deposits. The right ovary and parametrial tissue show aggregates of psammoma bodies with no evidence of neoplasm. The cervix is free of neoplasm. The features are consistent with malignant mixed Müllerian tumor.

agnosis:
Uterus: Malignant Mixed Müllerian Tumor, completely excised FIGO Stage IIIA

Dr. Sawsan Abdel Rahim

Picture 5. Histopathology report

Discussion

Uterine carcinosarcomas are rare and aggressive tumors that arise in the genital tract of postmenopausal women. They comprise 5 percent of all uterine neoplasms and 16.4 percent of all uterine cancer-related deaths[10,11]. Despite increased research interest in the pathologic mechanisms of carcinosarcomas, risk factors, late diagnosis and variable access to treatment have further contributed to a poor prognosis. Uterine carcinosarcomas share similar risk factors with endometrial carcinomas. Both neoplasms are associated with obesity, nulliparity, and use of exogenous estrogen and tamoxifen, including history of exposure to pelvic radiation. Given that progestin-containing neoplasms are protective against the neoplasm[12-23].

Women with uterine carcinosarcoma may present with a classical triad of pain, bleeding and a rapidly enlarging uterus[24,25]. In the largest report involving 300 patients, presenting signs included postmenopausal bleeding (82 percent), pelvic pain (13 percent) and vaginal discharge (10 percent)[24]. Over 10 percent of patients with carcinosarcoma will present with metastatic disease, and 60 percent will have extrauterine disease on staging

scans[26,27]. Up to 15 percent of patients have involvement of the cervix identified through cervical biopsy, endocervical curettage or both[24].

Rarely patients may present with venous thrombosis in addition to the above symptoms or as a presenting manifestation. Approximately 20 percent of patients with symptomatic deep venous thrombosis have a known active malignancy[28,29]. However, thromboembolism can precede the diagnosis of malignancy[30,31]. In one report, for example, 250 consecutive patients with symptomatic DVT were evaluated. 42 percent of whom had an identified cause or risk factor for the thrombosis[30]. Malignancy was identified at the time of thrombotic event in 3.3 percent. During a two year follow up, there was an increased incidence of cancer in the patients with idiopathic thrombosis.

For women with suspected uterine cancer, pelvic sonography is often first line imaging study. For patients presenting with suspicion of a uterine malignancy magnetic resonance imaging (MRI) is occasionally performed to evaluate for local extent of disease. Computed tomography (CT) scan can also detect myometrial invasion, nodal involvement, and the presence of metastatic disease. This is important because up to 30 percent of patients have node involvement at presentation and over 17 percent present with metastatic disease[22,32,33]. There are no typical abnormalities associated with the diagnosis of carcinosarcoma, although anemia is present in up to 10 percent as a result of vaginal bleeding[25]. Cancer antigen (CA) 125 is one of the tumor markers that can be elevated in carcinosarcoma. If elevated it appears to correlate with metastases or tumor bulk.

Most patients are diagnosed by endometrial biopsy. A smaller number of patients are initially diagnosed after hysterectomy for treatment of presumed fibroids or pelvic pain. The approach to treatment depends on whether the diagnosis was made preoperatively or following a hysterectomy. For women with a biopsy proven diagnosis of carcinosarcoma, surgery and often adjuvant chemotherapy are implemented for those with no evidence of metastatic disease. For women with extrauterine disease limited to the peritoneum surgical cytoreduction is recommended and those with extra-abdominal metastatic disease, treatment goals are palliative. For those who are diagnosed post-hysterectomy; if there is no evidence of extra-abdominal metastatic disease, another exploratory laparotomy with or without lymphadenectomy. But for those with peritoneal carcinomatosis and those with visceral or extra-abdominal metastasis, again palliative treatment is the best option[34].

Conclusion

Uterine carcinosarcoma (MMMT) is one of the rare and aggressive uterine tumors, with non-specific clinical symptoms, laboratory or imaging finding, diagnosed by histology. Endometrial biopsy is standard before embarking on definitive staging surgery. The grade, histological subtype, lympho-vascular space invasion must be recorded and even molecular classification testing can be performed for prognostic value. Infra-colic omentectomy is needed to detect microscopic disease together with lymphadenectomy in high risk group.

Declaration

Ethical consideration: written consent was taken about personal details and accompanied images for publication.

Funding: no fund received for this case report series.

Data availability: all the data is included in the manuscript.

Conflict of interest: no conflict of interest.

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