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UNIQUE METASTATIC PATTERNS OF UTERINE CARCINOSARCOMA: A RARE AUTOPSY CASE REPORT

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Abstract

Introduction: Uterine carcinosarcoma also called Malignant mixed Mullerian tumor (MMMT) is an extremely rare endometrial malignant tumor of biphasic character consisting of epithelial and mesenchymal components.
Case Description: This paper is a case of a 69-year-old obese woman been clinically evaluated for metastatic lung disease ?primary site for about a year. There was no history of postmenopausal bleeding per vagina, no offensive vaginal discharge and no family history of malignancy. She eventually died of metastatic disease and her body brought for post-mortem examination.
Findings: Autopsy reported findings of uterine carcinosarcoma (Figure 1) with rare metastases to previously reported sites such as the cervix, lungs, bladder, stomach and the chest. Also metastasis to atypical more rare sites such as the thyroid, pancreas, adrenals and the kidneys were found. Histology revealed a biphasic tumor with both epithelial and mesenchymal components (Figure 2). Immunohistochemistry showed positivity to pancytokeratin and desmin (Figure 3&4).
Conclusions: This is potentially the first documented case of uterine carcinosarcoma metastasizing to the thyroid gland, pancreas and kidneys. This is to raise the awareness of typical and atypical metastatic sites of endometrial carcinosarcoma, facilitating early diagnosis and treatment, and thus provides a learning point for clinicians.

Keywords: carcinosarcoma, uterine cancer, autopsy, case report, metastases

INTRODUCTION

Endometrial carcinosarcoma is a rare and aggressive high-grade endometrial carcinoma, accounting for about 5% of all uterine malignancies and nearly 20% of non-endometrioid endometrial cancer.[12] In particular, edometrial carcinosarcoma is responsible for 15% of deaths from uterine malignancies.[12]

Endometrial carcinosarcoma is an intriguing entity as it is a biphasic tumor characterized by coexisting carcinomatous (epithelial) and sarcomatous (mesenchymal) elements.[3] It is diagnosed at an advanced stage more often than other endometrial cancers. Up to 30–40% of patients present with lymph node metastases at diagnosis, and 10% have distant metastatic spread, especially in the lungs.[2-5]

CASE REPORT

A 69-year-old postmenopausal female patient presented to the medical emergency department with complaints of multiple bedsores of 2 months duration and loss of consciousness for one week duration with associated altered sensorium. No head trauma, no seizure, no vagina bleeding, no offensive vaginal discharge, however there is a positive history of significant weight loss. On her obstetrical history, was parity of eight (8), while her past medical history included cholecystectomy, and lumbar disk surgery three months prior (this resulted in the bed sores following prolonged immobility), and hypertension of over 20 years duration. She has no family history of malignancy.

She had several prior consultations where she was evaluated for metastatic lung disease and thromboembolic disease for about a year. Pleural biopsy showed chronic, nonspecific inflammation, no evidence of malignancy seen; Tuberculosis Quantiferon was negative; Chest HRCT scan showed 1. pulmonary and pleural metastasis ?primary, 2. bilateral hilar adenopathy, 3. a sclerotic lesion in the manubrium of the sternum possibly metastatic, 4. vertebral haemangiomas; Cytology

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report showed pleural effusion negative for malignant cells. Tumor markers checked a year prior to index presentation (CEA, CA19-9, CA125, CA15-3) were within the reference interval: Abdominopelvic ultrasound scan showed fatty liver grade I with hepatomegaly, right pleural effusion, status post cholecystectomy, uterine leiomyoma. CTPA: Impression: 1. No acute or chronic pulmonary embolism; 2. Massive right pleural effusion with loculations, CCTD in situ; 3. Pneumonic changes.

Patient died following rapid deterioration of her condition within twenty-four (24) hours of hospital admission, and her body was brought for postmortem examination.

Autopsy Findings: The uterus is bulky and measures 13x11x7cm, the cervix has a nodular appearance. There are multiple gray white serosal lesions ranging in size from 0.5cm to 1.0cm across respectively, some of which are coalescing into larger plaque-like lesions. The cut surface shows a solid gray to yellow appearance; these lesions are seen to extend into the myometrium. There are five intramural nodules ranging in size from 0.5cm to 2.0cm across respectively. The cut surface shows gray to yellow whorled appearance with gritty areas (Figure 1).

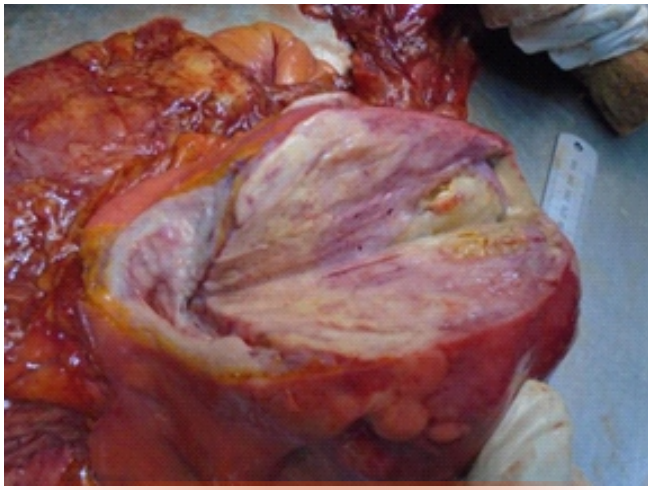

Figure 1 is gross section of the uterus showing the tumor

Metastatic tumor nodules ranging in size from 0.5cm to 3.0cm across were found in the cervix, lungs, chest wall, stomach, thyroid, pancreas, adrenals, kidneys and bladder. Other pathologies present were truncal obesity, chronic passive liver congestion, benign nephrosclerosis, chronic fibrosing pleuritis, patchy pulmonary consolidation amongst others.

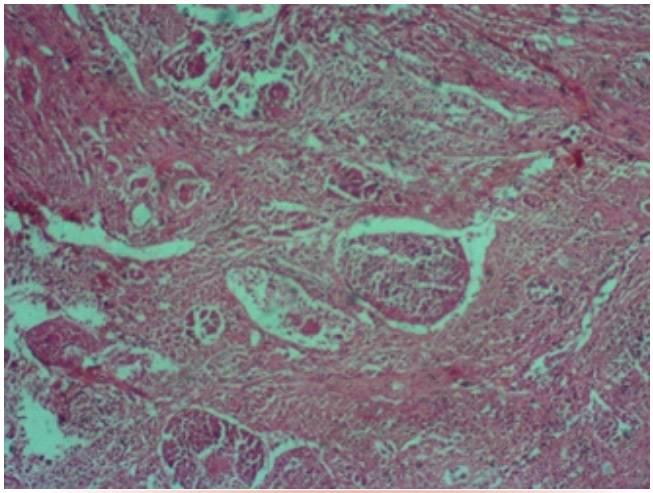

Figure 2. Photomicrograph from the uterus showing the biphasic tumour. H&Ex4

Histology sections from the intramural nodules of the uterus revealed a biphasic tumor with high grade admixed serous and endometrioid carcinomatous elements and high grade spindled (Figure 2) and pleomorphic sarcomatous elements. Morphology of metastatic sites were mostly of spindled sarcomatous elements lacking carcinomatous element.

Although immunohistochemistry is not required to diagnose carcinosarcoma, this tumor was positive to pancytokeratin and desmin (Figure 3&4).

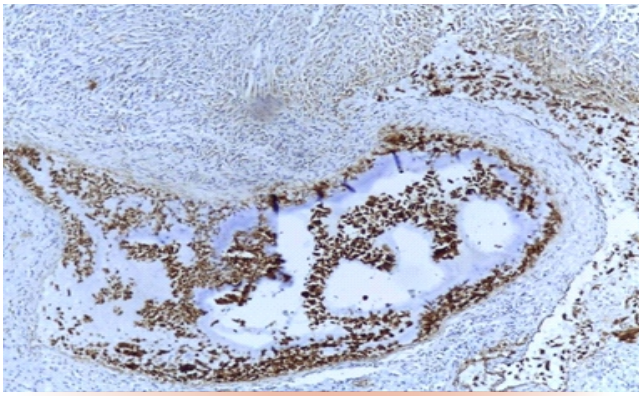

Figure 3. Photomicrograph from the uterus showing positivity for desmin x 4

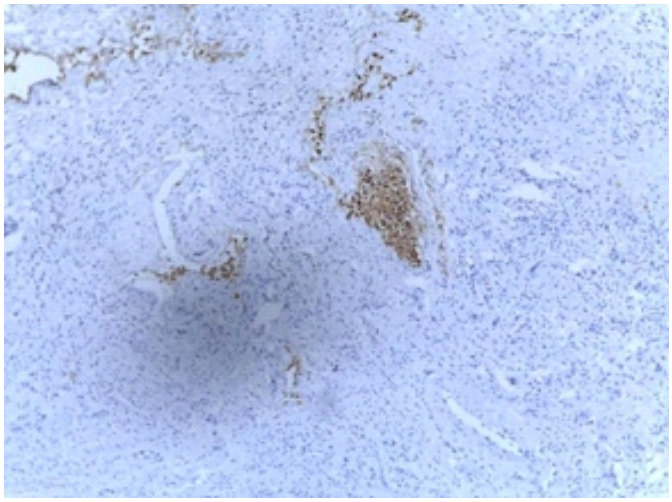

Figure 4. Photomicrograph from the uterus showing cytoplasmic positivity for pancytokeratin x 4

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DISCUSSION

UCS is a high-grade tumor including both epithelial and mesenchymal malignant components. The former is usually poorly differentiated and heterogeneous, potentially exhibiting endometrioid, clear-cell, or serous features along with organization of tumor cells in gland-like structures. The latter can be either "homologous", resembling endometrial stromal sarcoma or leiomyosarcoma, or "heterologous", with features typical of extra-uterine specialized connective tissues, such as muscles and cartilage[4].

Although some of the metastases of uterine carcinosarcoma such as lungs, cervix, bladder and stomach are well known, other atypical metastases involving sites such as the adrenals are less well known, and extremely rare sites such as the thyroid gland and pancreas are not reported.

The histologic features of the primary lesion in the cervix and uterus was that of both epithelial and mesenchymal origin while that of the metastatic sites was solely epithelial or mesenchymal with different features ranging from epithelioid to spindled morphology.

Many hypotheses have been formulated to explain the pathogenesis of this tumor, which is made up of both epithelial and mesenchymal cancer cells (Singh, 2014). Originally, it was classified among uterine sarcomas, but recent molecular acquisitions, based on the study of specific mutational patterns and gene expression profiles, have reasonably suggested its origin from a single endometrial tumor clone subsequently undergoing metaplastic differentiation (the so-called "conversion hypothesis") Therefore, uterine carcinosarcoma should be more appropriately considered as an epithelial dedifferentiated, rather than a simply "biphasic", tumor (de Jong et al., 2011).

Asfer et al (2024) reported a case of uterine carcinosarcoma with pulmonary metastasis in a postmenopausal woman with parity of eight and co-morbidities such as obesity and hypertension. She had a past medical history of cholecystectomy and lumbar surgery, these are similar to findings in this index case[5]. Uterine carcinosarcomas have high rates of lymphatic spread, peritoneal seeding, and pulmonary metastasis. Laguna et al (2023) reported a case with metastases to the intestine, omentum, presacral region and liver[5]. Although this index case didn't have any of the aforementioned metastases, it had a metastatic deposit in the stomach. Metastasis can occur in the lungs (49%), peritoneum (44%), bones (17%), liver (15%) and central nervous system[6].

The metastatic involvement of adrenal glands by endometrial carcinoma is rare, and there is some controversy over the most appropriate treatment due to the lack of specific guidelines[3].

CONCLUSION

Uterine carcinosarcoma is a rare biphasic gynaecological malignancy with a high rate of metastases and poor prognosis. A rare case of its metastases is reported in this study. Considering the highly invasive nature of uterine

carcinosarcoma, and its absence of vaginal bleeding in some patient, clinicians need a high index of suspicion to aid early diagnosis and intervention.

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