An Unusual Site of Metastasis of Malignant Mixed Müllerian Tumor of the Uterus

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Abstract Malignant mixed Müllerian tumors (carcinosarcomas) are biphasic tumors of the uterus and uterine cervix with carcinomatous and sarcomatous components. Malignant mixed Müllerian tumors (MMMT) are rare tumors, accounting for <5% of uterine cancers. They most commonly metastasize to the vagina, pelvic wall, lungs, and ovaries. We report a unique case of MMMT, which developed in a 69-year-old woman after she presented with hip and knee pain. Ultimately, her pain was found to be caused by metastatic tumor deposits in her psoas muscle. The primary tumor was found to be a MMMT of the uterine corpus. We recommend practitioners be aware of this entity and include it and other metastatic lesions in their differential diagnosis in difficult cases of non-resolving pain.

Keywords: Malignant mixed müllerian tumor, metastasis, malignancy, uterus


1. Introduction

Malignant mixed Müllerian Tumors (MMMT) are biphasic tumors of the uterine corpus and cervix with carcinomatous and sarcomatous components. They make up less than 5% of uterine cancers [1,2,3] and commonly present between 62 and 67 years of age [4]. The most common sites of metastatic disease include the vagina, pelvic wall, lungs and ovaries. There have been case reports regarding unusual sites of metastasis including abdominal wall, skin, soft tissue, pancreas, thyroid gland, eye, brain, left atrium and left ventricle. They are highly aggressive tumors with a relatively poor prognosis compared to the other uterine cancers. Treatment typically consists of surgical resection, chemotherapy and radiation therapy. We present one of the first cases of MMMT with skeletal muscle metastases described in the English literature.

2. Case Presentation

A 69-year-old post-menopausal female with no significant past medical history presented to her primary care physician with complaints of right buttock and right knee pain. Her pain was initially thought to be due to arthritis for which she was prescribed acetaminophen and ibuprofen and recommended to lose weight. These recommendations did not provide symptomatic relief and she presented one month later with worsening pain which was affecting her activities of daily living including sitting, walking and sleeping. On physical examination she had decreased range of motion of the right hip joint with bony tenderness. The overlying skin was intact with no erythema or signs of infection. An x-ray of the right hip was obtained and showed mild degenerative joint disease with spur formation. Her vital signs and baseline laboratory investigations were normal. Her primary care provider gave her oxycodone for pain control and referred her to orthopedic surgery. The orthopedic surgeon diagnosed piriformis syndrome and recommended core and hip strengthening exercises. After a month, she returned to orthopedic surgery with continuing pain and discomfort. She underwent magnetic resonance imaging (MRI) of the lumbar spine and pelvis, which demonstrated changes of arthritis of the right sacroiliac joint, and inflammation and edema of the psoas muscle, which extended to the region of right iliocostal muscle. The MRI also revealed an enlarged uterus with a thickened endometrial stripe. On further evaluation, she noted a six-month history of occasional vaginal spotting.

The sacroiliac joint was aspirated and samples were sent for crystal analysis, gram stain, and cultures for bacterial, fungal, and acid-fast organisms. No crystals or microorganisms were identified. She underwent computed tomography (CT) guided biopsy of the psoas muscle. Hematoxylin and eosin stained slides of the psoas mass revealed a population of gland-forming malignant cells with focal areas of necrosis within a desmoplastic stroma (Figure 1A). Immuno-histochemical stains including a CK7, CK20, TTF-1, PAX-8, and CDX-2 were performed on the percutaneous needle biopsy specimen. The neoplastic cells were positive for CK-7 and PAX-8 suggesting the malignancy was of genitourinary origin.
A transvaginal ultrasound showed a significantly thickened and heterogeneous endometrium, which was highly suggestive of malignancy. She ultimately underwent endometrial biopsy. The biopsy specimen revealed a malignant population of back-to-back neoplastic glands composed of tall columnar cells consistent with an endometrioid adenocarcinoma, FIGO grade 1 of 3 (Figure 1C).

Because of the diagnosis of endometrioid adenocarcinoma, the patient underwent robotic total laparoscopic hysterectomy with bilateral salpingo-oophorectomy. Gross examination of the hysterectomy specimen revealed a 6.5 cm shaggy, papillary tumor, which invaded over one-half of the myometrium. Histologically, the large majority of the tumor resembled endometrioid adenocarcinoma. Sampling of softer more gelatinous polypoid fragments within the uterus revealed malignant epithelial nests and glands within a highly mitotic spindled stroma. The stromal cells showed areas of marked nuclear pleomorphism and atypical mitotic figures (Figure 1D).

Immunohistochemical stains including pankeratin, OSCAR, CAM5.2, CK5/6, and PAX-8 were performed on the neoplasm. The epithelial elements, in addition to foci of the atypical spindled stromal cells, were positive for pankeratin and OSCAR. The spindled stromal cells were negative for CK5/6, CAM5.2 and PAX-8.Given these findings, a diagnosis of carcinosarcoma (Malignant mixed Müllerian tumor) was rendered. A morphologically similar tumor was removed from the right pelvic sidewall. The final pTNM stage was pT1b, pNX, and pM1. Given the presence of distant metastasis, the patient was classified as having stage IVB disease. The patient underwent palliative radiotherapy to the right iliopsoas. After completion of the radiotherapy she received 6 cycles of Paclitaxel and Carboplatin. She has been stable since then and getting regular follow up with no recurrence noted.

3. Discussion

MMMTs also known as carcinosarcomas are rare tumors involving the female genital tract. Initially, carcinosarcomas were thought to be a sub-type of sarcoma and were graded and treated similar to high-grade uterine sarcomas. However, there is now enough evidence to relate them more closely to high-grade endometrial carcinomas [5]. Most authors now agree that they are primary epithelial malignant tumors with areas of mesenchymal spindle cell differentiation [6]. Morphologically, MMMTs are heterogeneous biphasic tumors composed of an admixture of malignant (endometrioid and nonendometrioid) and epithelial (homologous and heterologous) mesenchymal elements in different proportions. Uterine carcinosarcomas predominantly
metastasize as carcinomas and are associated with a poor prognosis [5]. Most commonly they are thought of as a uterine cancer but can rarely arise from the ovaries, fallopian tubes and vagina. [7].

MMMTs occur predominantly in post-menopausal women [8] with vaginal bleeding and uterine enlargement being the most common clinical presentation [9]. Commonly, local metastasis to the vagina and pelvic cavity are identified, but hematogenous spread to the lung, liver, and bones is not uncommon [10]. Rare cases have been reported of MMMT metastasizing to the abdominal wall, skin and soft tissue, pancreas, thyroid gland, eye, brain, left atrium and left ventricle [11,12,13]. The strongest prognostic factor is tumor stage followed by lymph node metastases, deep myometrial infiltration, involvement of the cervix, and tumor size [14]. The prevalence of skeletal muscle metastasis in patients with MMMT is extremely low and is likely under recognized [15].

In patients with a known primary malignancy, malignant psoas syndrome and metastatic disease to the lumbar vertebrae should be considered when evaluating low back pain [16]. A recent case has been reported of a mass which was thought to be a psoas abscess and turned out to be a metastatic tumor deposit [17]. In fact, it has been reported that 40% of the lesions initially considered as psoas abscess were found later to be lymphomas, sarcomas, or metastasis [18]. Muscle metastasis can appear as focal or diffuse areas of muscle enlargement on non-contrast CT [19]. Contrast enhancement may provide further information on the extent of disease, but is nonspecific because more than 50% of inflammatory diseases show rim enhancement after contrast administration [20]. Some reports have shown that CT imaging gives poor accuracy and sensitivity in the differentiation of ilio-psoas neoplasm from abscess or hemorrhage [21].

Treatment of MMMT requires the combination of surgery, radiation therapy and chemotherapy. Surgical therapy includes removal of the gross disease along with hysterectomy, bilateral salpingo-oophorectomy, and lymph node dissection. Different options are available with regard to the use of radiation and the decision is made based on post-operation residual tumor, positive lymph node, and other factors. Among the chemotherapeutic agents, ifosfamide, paclitaxel, and cisplatin have been shown to be most effective and combination therapy is superior to a single agent [22]. 5 year survival is estimated to be around 33-39% despite the use of newer and aggressive therapies. [23]

4. Conclusion

We present this case of a MMMT with metastasis to an unusual location and the diagnostic challenge it posed. Back and hip pain are a very common cause of clinic visits and clinicians should keep metastatic disease in the back of their minds when working up resistant back pain, especially in elderly female patients.

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References