Mucosal Small Bowel Metastasis from Uterine Leiomyosarcoma

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**U terine leiomyosarcoma** is a mesenchymal neoplasm composed of smooth muscle. It is the most common uterine pure mesenchymal tumor, although it represents only 5% of uterine malignancies [1]. It affects 0.4/100,000 women a year [2]. Owing to the aggressive nature of this tumor, women with uterine sarcomas have a poor prognosis with an overall survival of 50% at 2 years, even when diagnosed early [1]. Surgical resection is the treatment of choice and may be curative for lesions confined to the uterus. The role of radiotherapy and chemotherapy is well established, but there is no consensus regarding the optimal management of these patients. Metastases are common and recurrence rates are high, possibly due to the presence of micrometastases at the time of diagnosis.

We present here a patient who was diagnosed with leiomyosarcoma of the uterus presenting with distant metastatic spread in a rare location.

**PATIENT DESCRIPTION**

A 60 year old woman was admitted to hospital in March 2009 for exploratory laparotomy due to abnormal uptake on positron emission tomography with radiolabeled $^{[18}F\rangle$-2-fluoro-deoxy-D-glucose scan, revealing the presence of a small lesion suspected to be a metastatic leiomyosarcoma in the left lower abdominal quadrant.

Her medical history was remarkable for recurrent metastatic uterine leiomyosarcoma that was repeatedly treated with wide local excisions. In 1993 at the age of 44 and still premenopausal, the patient was diagnosed with symptomatic uterine myomas. Due to her morbid obesity and three prior cesarean sections, follow-up only was prescribed.

In 2005, at the age of 56, she was admitted for evaluation of abdominal pain. Diagnostic workup revealed a large pelvic mass causing partial small bowel obstruction. On surgical exploration a large (24 cm) pelvic mass originating from the uterus was revealed. A total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. Neither enlarged lymph nodes nor distant metastases were evident at that time. Histopathology examination showed spindle cell leiomyosarcoma with areas of myxoid and pleomorphic cells with a mitotic index of 10–15 mitotic figures per 10 high power fields. At the same time chest computed tomography scan revealed a lesion suspected to be a metastasis in the lower lobe of the left lung. This was confirmed by PET-CT and a segmental lobar metastasectomy was performed. Histopathology revealed a metastatic lesion of the primary uterine leiomyosarcoma. A local recurrence at the same site was found and resected at the end of the same year. In 2007, a right upper lobe metastasis was discovered by routine follow-up PET-CT scan. Consequently, another segmental lobar metastasectomy was performed.

In 2008, a routine PET-CT showed increased FDG uptake in the left lobe of the thyroid suspected to be a metastatic lesion. The patient underwent a partial thyroidectomy and again histopathology revealed a metastatic lesion of leiomyosarcoma.

In March 2009 a follow-up PET-CT scan showed increased FDG uptake in the left lower abdominal quadrant suspected to be a small metastatic lesion [Figure A]. At laparotomy no peritoneal, hepatic, retroperitoneal or intestinal serosal spread was found. Thorough manual examination of the small bowel revealed a small (3 cm) intraluminal polyloid mass at mid-jejunum. Segmental small bowel resection was performed and the

**PET-CT = positron emission tomography-computed tomography**

**FDG = $^{[18}F\rangle$-2-fluoro-deoxy-D-glucose**
for 25% of uterine mesenchymal tumors, endometrial stromal sarcomas for 15% and mixed mullerian tumors for 50% of the tumors, the latter being referred to as metaplastic carcinoma (carcinosarcoma) [4]. Sarcomas most commonly invade and spread locally, but may have an aggressive growth pattern with lymphatic and hematogenous spread. Micrometastases are often present at the time of diagnosis. The most common sites for metastatic spread are the peritoneal cavity and the omentum (30–50%), lung (30–40%) and liver (10%) [3]. Metastases to the heart, pericardium, skin, stomach and pancreas have also been described.

Metastases to the gastrointestinal tract from extra-abdominal sites are uncommon. Malignant melanoma and carcinoma of the breast and lung are the most common malignancies spreading to the gastrointestinal tract. Small bowel mucosal metastases from uterine leiomyosarcomas are extremely rare. To the best of our knowledge, only one prior case was reported in the English-language literature [5]. This rare occurrence should be suspected in patients who present with abnormal FDG uptake in the abdominal cavity and carefully searched for during exploration. Even though leiomyosarcoma is an aggressive and lethal tumor, it can be treated with routine follow-up and aggressive intervention for metastatic spread if and when it occurs.

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**References**

**COMMENT**
Uterine sarcomas are rare tumors that account for 5% of all uterine malignancies. Mean age at presentation is 55 years [3]. Leiomyosarcomas account

**Capsule**

**Enzymes as oncometabolites contribute to the biology of brain tumors and leukemia**

Identification of genes that are recurrently mutated in human cancers can potentially lead to new cancer treatments, but first we need to understand how the mutations alter the biochemical activity of the encoded protein and contribute to tumor development and progression. The recent discovery that a subset of human brain tumors harbor mutations in the gene encoding isocitrate dehydrogenase 1 (IDH1) has focused interest on this cytosolic metabolic enzyme and its mitochondrial homolog IDH2. Mutations in these genes have been detected in acute myeloid leukemia that always alter the same amino acid in the enzymes’ catalytic sites and are always present in heterozygous form, suggesting that tumor cells contain “normal,” as well as mutant, versions of the enzymes. Ward et al. (*Cancer Cell* 2010; 17: 1) and Dang et al. (*Nature* 2009; 462: 739) show how the tumor-associated mutations alter the biochemical activity of IDH1 and IDH2. The mutant enzymes not only lose their normal activity (the conversion of isocitrate to α-ketoglutarate) but also acquire a new activity: the reduction of α-ketoglutarate to 2-hydroxyglutarate. Indeed, elevated levels of 2-hydroxyglutarate were detected in human tumor samples that contained either IDH1 or IDH2 mutations. Determining how 2-hydroxyglutarate, a so-called oncometabolite, contributes to the biology of brain tumors and leukemia will be an important next step in moving from mutant gene to therapy.

Etan Israeli

“Nearly all men can stand adversity, but if you want to test a man’s character, give him power”
Abraham Lincoln (1809-1865), 16th President of the United States until his assassination in April 1865. He successfully led his country through its greatest internal crisis, the American Civil War, preserving the Union and ending slavery.