

## Endometrial stromal sarcoma metastasis to the lumbar spine and sphenoid bone

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### Abstract

Endometrial stromal sarcoma (ESS) is typically associated with metastasis to the abdomen, pelvis, and lung. We found three case reports of ESS metastasis to the bone (two to the thoracic spine, and one to the parietal bone). Our objective is to review the literature on ESS spinal and intracranial metastases and, report the first case of ESS metastatic to the lumbar paraspinal region and sphenoid bone. A 53-year-old female with ESS status-post radiation, chemotherapy, and pelvic exenteration surgery presented with right hip weakness, back pain, and radicular leg pain that were explained by chemotherapy-induced neuropathy, radiation-induced lumbosacral plexopathy, and femoral nerve and obturator nerve injury during pelvic exenteration surgery. During routine positron emission tomography, we found metastasis to the L3 lumbar spinal region. L3 laminectomy and subtotal resection of the mass was performed with tumor residual in the neuroforamina and pedicles. One month later, magnetic resonance imaging (MRI) performed for persistent headaches revealed a large lesion in the sphenoid bone that was biopsied transsphenoidally with the same diagnosis, but no further surgery was performed. She is intolerant of chemotherapy and currently undergoing whole brain radiation. Delay in the diagnosis and management of lumbar paraspinal and sphenoid bone metastasis of ESS likely occurred because of the uniqueness of the location and aggressiveness of ESS metastasis. Health care providers should be aware of potentially aggressive metastasis of ESS to bone, in particular the unusual locations of the lumbar paraspinal region and sphenoid bone.

### Introduction

Endometrial stromal sarcoma (ESS) is a rare form of uterine cancer, with fewer than 450 new cases diagnosed annually in the United States.<sup>1,2</sup> Most ESSs are clinically indolent, histologically classified as low-grade, with a 5-year survival rate of 65%.<sup>3</sup> In contrast, high-grade or undifferentiated ESS cases are more aggressive with less than a 25% 5-year survival.<sup>4</sup> Both low- and high-grade ESS are treated surgically with a hysterectomy, with some evidence from retrospective studies showing that adjuvant radiotherapy can reduce the recurrence of disease.<sup>4,5</sup> Recurrence of or advanced disease can also be treated with surgical resection and adjuvant hormone therapy in low-grade ESS and palliative chemotherapy in high-grade ESS.<sup>1</sup>

When metastasis occurs, ESS typically spreads to the abdomen, pelvis, and lung.<sup>5-8</sup> Rarely does ESS metastasize to bone. We found two reported cases of ESS with spinal metastasis – both in the thoracic spine.<sup>9,10</sup> One case appeared 18 years and the other 7 years, after initial ESS treatment.<sup>9,10</sup> We found one report of cranial ESS metastasis to the parietal bone, which occurred 1 year after initial ESS diagnosis.<sup>11</sup> We report here the first known case of metastasis to the lumbar paraspinal region and sphenoid bone, which occurred less than 2 years after initial ESS diagnosis, again demonstrating the ability of this tumor to metastasize to bone.

### Materials and Methods

This case report was developed from direct patient clinical encounters, events that took place in the operating room, review of medical records, review of radiographic studies, and pathology slides. An interdisciplinary group from neurosurgery, gynecologic oncology, and pathology reviewed, discussed, and developed this case report.

### Results

A 53-year-old Caucasian female with ESS was referred to our neurosurgery outpatient clinic in March 2010 after a routine positron emission tomography (PET) scan 2 months earlier revealed increased uptake in the L3 spinous process (Figure 1). Magnetic resonance imaging (MRI) of the lumbar spine in March 2010 revealed a 3-centimeter heterogeneously enhancing mass involving the lamina, spinous process, right pedicle, and right transverse process of L3, with expansion into the

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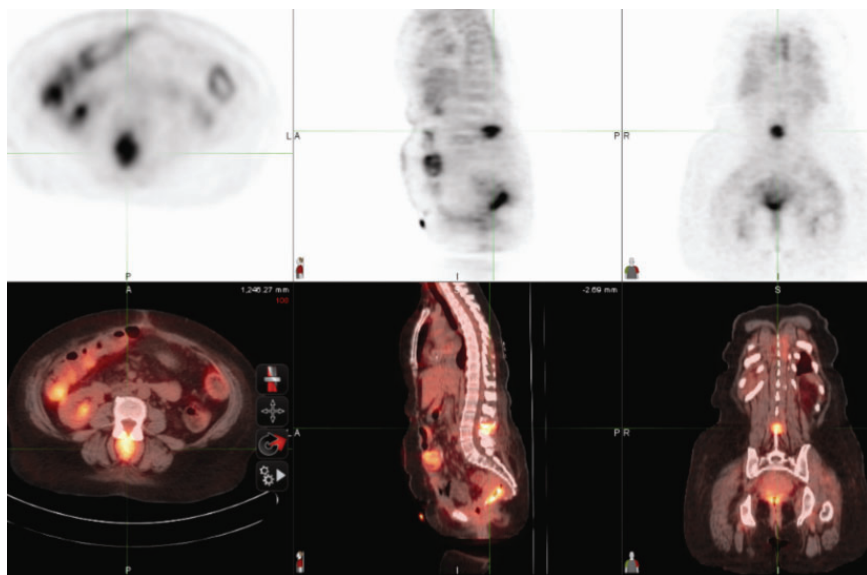
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paraspinal muscles and without involvement of the dorsal fascia or epidural space (Figure 2).

The patient initially presented to her primary care physician 3 years earlier with symptoms of urinary incontinence, and a workup revealed uterine fibroids. She underwent supracervical hysterectomy. The pathology report identified multiple leiomyomas within the myometrium, some with myxoid change. One year later, the patient developed worsening urinary incontinence. She was found to have a large pelvic mass. Core biopsy showed a myxoid spindle cell lesion with reactivity against desmin and weak reactivity against muscle-specific actin. Immunohistochemistry against CD10 was non reactive. The features were interpreted as suggestive of leiomyosarcoma. Biopsies of additional intra-abdominal lesions were morphologically similar, but these tumors failed to react against muscle-specific actin, smooth muscle actin and CD10. Therefore, a diagnosis of primary ESS was favored.

The patient underwent preoperative radiation therapy followed by extensive resection of



**Figure 1.** PET/computed tomography showing increased uptake and erosion of the spinous process in the dorsal L3 region.

the intraabdominal tumor. Discovery of metastatic disease led to an end colostomy and palliative chemotherapy with taxotere and ifos/Adria. Because of intolerable side effects (including leukocytosis, alopecia, skin changes, fatigue, and nausea) and local progression of disease, she was switched to hormonal therapy with megace, then an aromatase inhibitor. Her disease was stable for year on hormonal therapy, and then the patient underwent pelvic exenteration (hemicolectomy in October 2008; cystectomy, proctectomy, and partial vaginectomy in July 2009). Evaluation of the resected colon, urinary bladder and vagina again showed a spindle cell tumor morphologically similar to that seen in the patient's previous biopsies and resection, but also small areas of high-grade sarcoma. This specimen showed reactivity with anti-CD10 antibody and no reactivity against desmin, actin, myoD, or S100 protein. The findings were interpreted as consistent with ESS, predominately low-grade, with focal areas with high-grade features.

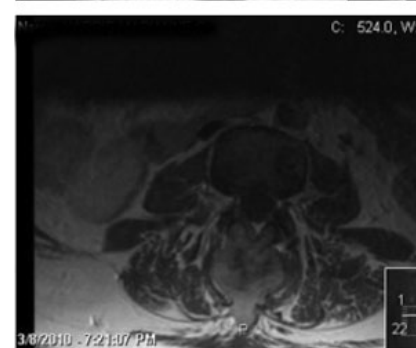
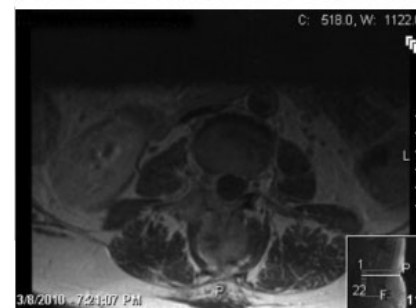
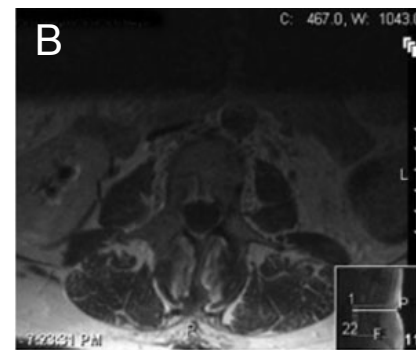
The patient's paraspinous mass was unusually aggressive. Two months after pelvic exenteration surgery, the patient reported hip flexion and abduction weakness. Diagnostic considerations included chemotherapy-induced neuropathy, radiation-induced lumbosacral plexopathy, and iatrogenic femoral nerve injury. Her obturator nerve was resected during the surgery. Electromyogram showed right obturator neuropathy, which was believed to explain her right hip flexion and abduction weakness.

At the time of the routine PET scan that revealed the lumbar mass (January 2010), she had no back pain. One month later, she devel-

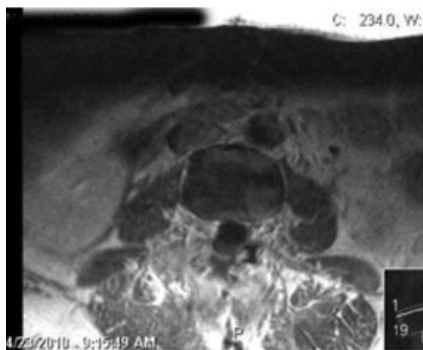
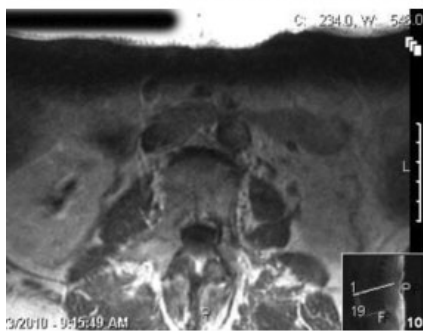
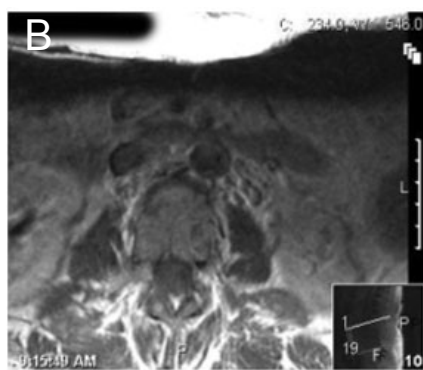
oped dull aching lower back pain, with occasional stabbing on the right, and paresthesias bilaterally to the feet. Physical examination revealed no neurologic deficits and no palpable mass in the lumbar region. An MRI of the cervical and thoracic spine showed a small, rounded, hypointensity of the C4 vertebral body but was otherwise normal. A bone scan showed suspected metastases in the bilateral femoral diaphyses, left humeral head, right seventh rib, and mid-lumbar spine. The original PET scan from January 2010 also showed mild enlargement of a right middle lobe lung mass and other bony metastases.

Despite the presence of other bony and soft-tissue metastases, we decided to decompress the lumbar mass because of the patient's good performance status, intolerance to chemotherapy, the large size of the lesion that correlated with the imaging and limited her daily activities, and the expectation of a minimally morbid surgery given the predominantly dorsal location of the lesion. The goals of surgery were to improve her hip and back pain and debulk the tumor to facilitate adjuvant treatment.

Intraoperatively, the tumor protruded through the lumbar fascia. A clear plane was evident between the tumor and paraspinous muscles in some areas, but roughly 60% of the tumor was blended with the surrounding muscle and the L3 spinous process was partially eroded. After L3 laminectomy, we found significant epidural tumor extension with adherence to the dura. Epidural tumor in the central canal was resected, but tumor remained in the lateral recess traveling out the neural foramen on the right at L2-3 and in the right L3 pedicle



**Figure 2.** Preoperative lumbar MRI images. (A) Sagittal T1 with gadolinium, (B) Axial T1 with gadolinium.



**Figure 3.** Postoperative lumbar MRI images. (A) Sagittal T1 with gadolinium. (B) Axial T1 with gadolinium.

(Figure 3). Based on preoperative imaging and the patient's known multiple metastases, we had not planned for gross total resection. We did not perform fusion and stabilization because the procedure is associated with a higher complication rate, and longer recovery time, and felt that it would not affect overall survival. Further, because of her planned radiation therapy, she had a higher risk of non union. Total volume of resected tumor submitted to pathology was 181.2 cm<sup>3</sup> compared with preoperative volume estimated by MRI to be 27 cm<sup>3</sup>. This change represented a 5.7-fold increase in total tumor volume over a 6-week period. The pathology report identified a malignant myxoid spindle cell lesion with predominately low-grade features and focal high-grade morphology which was consistent with origin from the patient's previously diagnosed sarcoma (Figure 3). The patient then received palliative radiation to the lumbar paraspinal region. She was offered systemic chemotherapy, but refused because of her previous experience with the chemotherapy-related side effects.

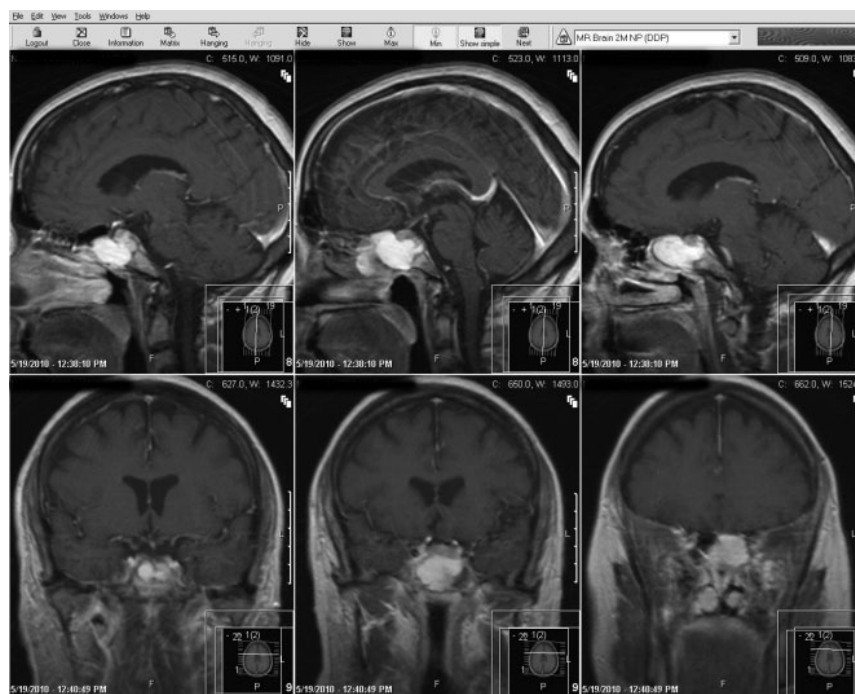
During workup for a persistent headache 1 month later, MRI of the head revealed an avidly enhancing expansile mass in the body of the sphenoid bone, with soft tissue extension into the sphenoid sinus and posterior ethmoid air cells. Abnormal marrow replacement surrounded the area in the lesser wing of the sphenoid bone and clivus (Figure 4). A stereotactic-assisted transsphenoidal biopsy was per-

formed without complication. The lesion was diagnosed as a myxoid sarcoma with histopathological features similar to those seen in the preceding biopsy and resection specimens (Figure 5). The tumor represented had features of a low histologic grade. The patient is currently receiving whole brain radiation. No chemotherapy was administered due to her history of intolerance.

## Discussion

This case represents a significant and unusual presentation for several reasons: i) ESS rarely metastasizes to bone; this is the first reported case of ESS metastasis to the lumbar spine and sphenoid bone; ii) contrary to most reported cases of ESS, this tumor grew very aggressively; iii) there was a delay in diagnosis due to the broad differential of hip weakness, back pain, radicular leg pain, and headache in patients receiving treatment for ESS; iv) these rare tumors pose significant challenges to pathologic diagnosis; v) limited clinical information about spinal ESS metastasis complicates treatment decision-making.

Metastasis of ESS typically occurs in the pelvic, abdominal, and lung regions. This case study demonstrates the ability to ESS to metastasize aggressively to bone. Adding to the paucity of case studies of ESS bone metastasis (two to the thoracic region, one to the parietal



**Figure 4.** MRI images of the head demonstrating large sellar/sphenoid sinus mass. Sagittal T1 with gadolinium (top) and coronal T1 with gadolinium (bottom).



bone), we see here for the first time that ESS can also spread to the lumbar spine and sphenoid bone. On bone scan, this patient also had lesions in the bilateral femoral diaphyses, left humeral head, and right seventh rib. MRI showed a lesion in the C4 vertebra. Although no biopsy was performed in these other regions, we have high clinical suspicion that these areas may also have ESS metastasis. This patient was unique because her mass was in the lumbar region without vertebral body involvement. The tumor extended into the surrounding soft tissues and epidural space, which has not been previously reported.

It is unclear how long the lesion had been growing and whether the dramatic expansion of the mass in the 6 weeks prior to surgery represented a transformation of a previously indolent lesion. Throughout 2009 while being treat-

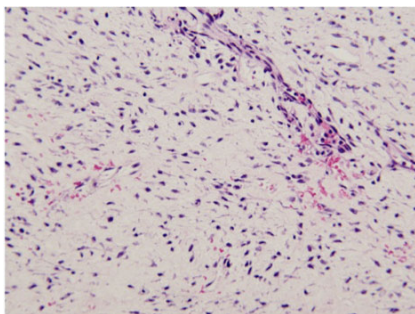


Figure 5. Pathology specimen from lumbar tumor resection, H&E stain, 200x magnification.

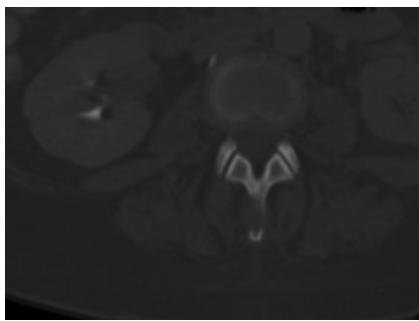


Figure 6. Abdominal axial CT scan images with bone windowing showing subtle, small mass lesion with erosion of the L3 spinous process.

ed for various abdominopelvic issues, including a suspected presacral abscess, the patient had multiple computed tomography (CT) scans of the abdomen and pelvis. At the time, no lumbar spine lesion was identified, though abdominal CT is not ideal for examining lumbar spine pathology. However, in retrospect we found erosion of the L3 spinous process and a 1.5-centimeter soft tissue mass that was missed in the original August 2009 report (Figure 6). In a minimally symptomatic to asymptomatic patient, it is doubtful that routine detailed imaging of the spine, such as screening MRI, would have been cost-effective. An appropriate workup, including electromyography testing, did not suggest a lumbar source for the patient's hip pain, so the suspicion of lumbar disease was not raised until the routine PET scan found her tumor. Although there was a delay in treatment, it is unclear if this affected her outcome given the aggressive nature of the ESS tumor.

This case also highlights the challenges of correctly diagnosing ESS, which is rare and difficult to characterize histopathologically.<sup>12</sup> These diagnostic challenges were evident in this patient's pathology reports, which showed an evolution in the diagnosis from leiomyoma with myxoid degeneration through a neoplasm with features favoring leiomyosarcoma, ultimately to ESS. The difficulty of accurately diagnosing ESS impacts the treatment decision-making. There is evidence that TAH-BSO and adjuvant radiotherapy can be effective for both low and high grade ESS. However, additional adjuvant treatments recommendations differ depending on the grade of ESS (hormonal and surgical treatment for low-grade, and chemotherapy for high-grade).<sup>1</sup> In our patient's case, the decision to operate despite the presence of other metastases was based on the low-grade of the ESS tumor, her good performance status, size of the lesion, and expectation of a minimally morbid surgery. We did not realize how aggressive this tumor was preoperatively.

In conclusion, delays in diagnosis and management in this case report likely occurred because of the uniqueness of the locations and aggressiveness of ESS metastasis. It is our hope that this report will increase awareness among health care providers of the potentially aggressive metastasis of ESS to the bone, in particular to the craniospinal axis.

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