RUTGERS
New Jersey Medical School

Rare Small Cell Neuroendocrine Cervical Cancer - Hiding in Plain Sight

Vincent Wong MD, Monica Abreu Diaz MD, Maninderpal Kaur MD, Sherif Elhosseiny MD

Department of Medicine, Rutgers New Jersey Medical School, Newark NJ 07103

UNIVERSITY HOSPITAL
Newark, New Jersey

Learning Objectives

1. Recognize the symptoms of Small Cell Neuroendocrine Cervical Cancer (SCNECC)
2. Understand the difficulty in diagnosing SCNECC

Presentation

- 38-year-old G6P3 female with fibroid uterus presented with six days of intermittent achy, crampy mid-back pain.
- Symptoms began 3 months prior with right shoulder, then left shoulder pain, and upper back pain which were diagnosed as muscle spasms/arthritis, treated with NSAIDs and muscle relaxers, and resolved
- Unfortunately, mid-back pain returned with episodic bilateral leg weakness causing multiple falls, without recent trauma or injury
- One month duration of vaginal bleeding prior to presentation as well
- Her menstrual cycles have been regular ranging from light spotting to heavy bleeding, while having a copper intrauterine device for 14 years
- History of Chlamydia that was treated but her last Pap smear is unknown
- Denies alcohol or tobacco use, last marijuana use 6 months ago
- Family history of ovarian cancer in maternal aunt
- T 98.3^{0} F (oral), HR 85 bpm, BP 140/91 mmHg, RR 18 bpm, SpO_2 98% on ambient air, BMI 25.5 kg/m^2
- Alert, oriented, and in no acute distress
- Cardiovascular, respiratory and abdominal exams were unremarkable
- Strength: R hip 4/5, R knee 4/5, R foot 4/5, others 5/5
- Sensation: decreased at umbilicus to genitalia; urinary incontinence; but rectal tone preserved
- Initial laboratory evaluation showed:

WBC	16 x10^3/uL
Hgb	11.2 g/dL
Plt	241 x10^3/uL
Procal	Negative

ESR	**30 mm/hr**
CRP	**28 mg/L**
COVID	Negative

- Computed tomography (CT) scans of the chest/abdomen/pelvis showed an osteolytic process of the T6 vertebrae with burst fracture, multiple enlarged pelvic- and para-aortic lymph nodes, as well as an enlarged fibroid uterus with calcification (shown in Figure 1)
- Magnetic resonance imaging (MRI) showed cervical spondylosis with posterior ridging at the C3-C7 vertebrae abutting the cervical cord, loss of height at T6 vertebrae with cord compression, and demineralization of T12 vertebrae (shown in Figure 2 and 3)

HPI

- 38 y/o F with several ED visits for MSK pain, returned for mid-back pain, vaginal bleeding, LE weakness
- Found to have metastatic lesions in the spinal cord causing vertebral fracture and cord compression

Course

- After emergent neurosurgical intervention, biopsy showed metastatic neuroendocrine cancer
- Cervical biopsy confirms small cell cervical cancer
- Tx with radiation and chemotherapy – in hospice care

Conc.

- SCNECC is rare and aggressive, with poor prognosis
- Limited treatment based on small cell lung cancer
- Difficult to diagnose, can be mistaken for fibroids, so need a thorough history, physical, and chart review

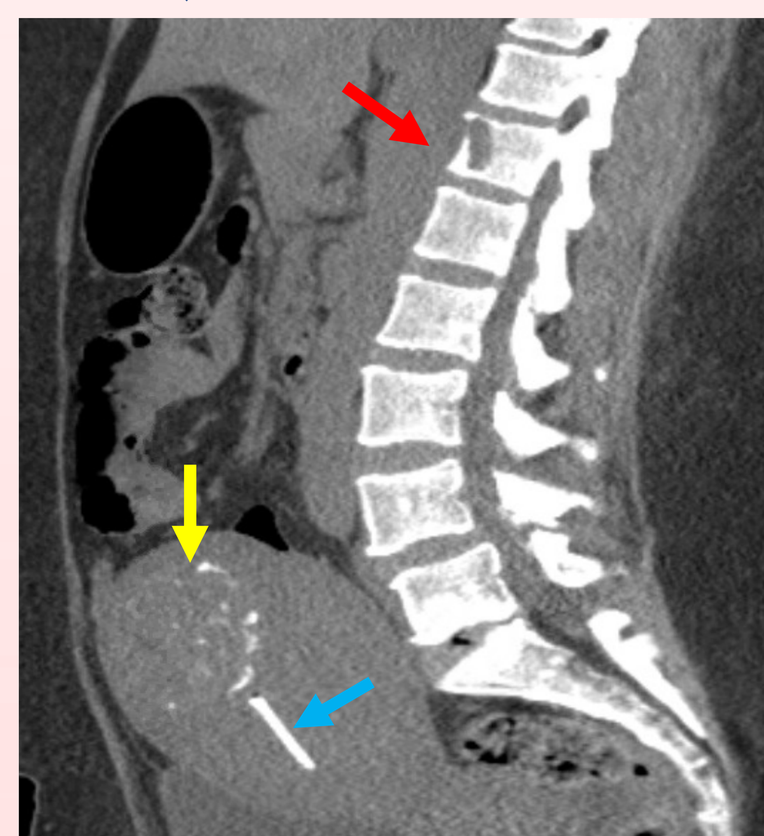

Figure 1. CT showing T6 osteolytic lesion (red arrow), calcified fibroid (yellow arrow), and IUD (blue arrow).

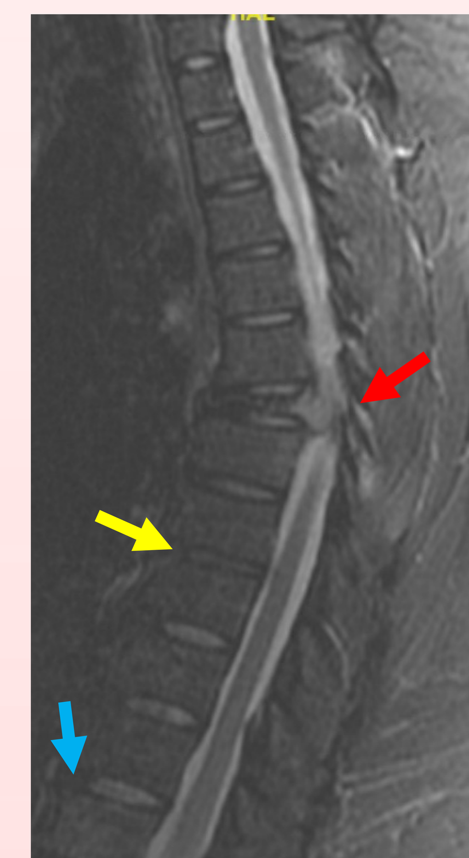

Figure 2. MRI showing loss of height at T6 vertebrae and cord compression (red arrow), diffuse spondylosis (yellow), and T12 demineralization (blue).

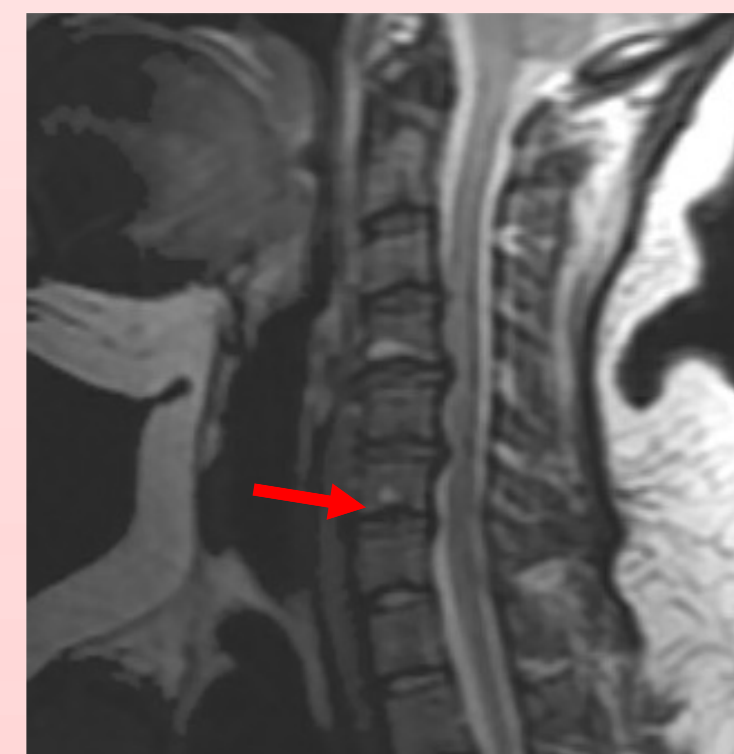

Figure 3. MRI showing cervical spondylosis at C3-C7 abutting the spinal cord and enhancing bony lesion (red arrow).

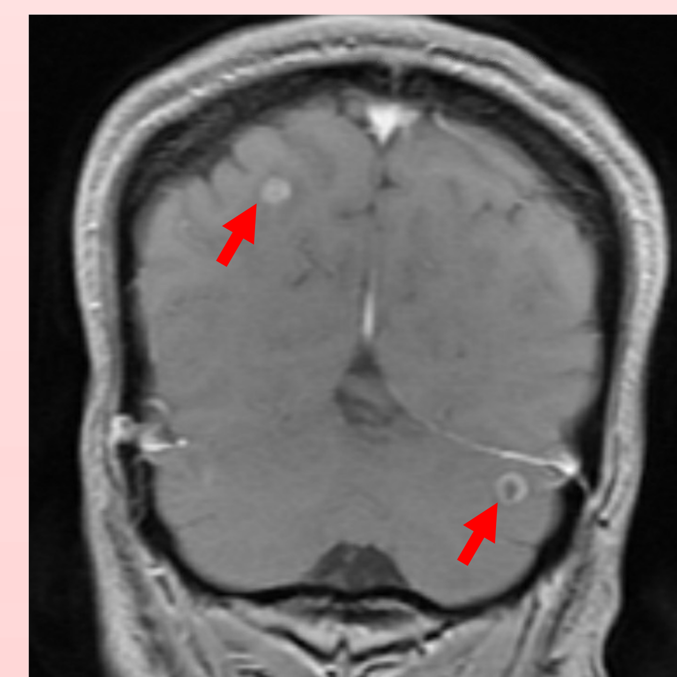

Figure 4. MRI showing metastatic lesions in the cerebrum and cerebellum (red arrows).

Hospital Course

- The patient was started on steroids and had emergent T5-T7 laminectomy, T4-T8 posterior thoracic fusion, and biopsy of T6 lesion that stained positive for synaptophysin, NSE, chromogranin and CD56, all suggestive of metastatic neuroendocrine cancer
- Pelvic Ultrasound showed a large uterus with multiple fibroids
- Pelvic exam was done in the operating room which showed a 20+ week sized globular uterus with irregular 3-4 cm mass on posterior cervix - Pap smear was negative for HPV and biopsy of the intrauterine lesion stained positive for NSE, p16, and vimentin which was identified as small cell neuroendocrine cervical cancer
- MRI of the Brain revealed metastatic lesions in the cerebrum and cerebellum (shown in Figure 4)
- She received 10 cycles of palliative radiation therapy and started on systemic chemotherapy with Carboplatin, Etoposide, and Atezolizumab
- The patient then had multiple hospitalizations for refractory musculoskeletal pain, bacteremia and neutropenic fever
- She was ultimately transitioned to hospice care given poor prognosis and worsening mental status

Discussion & Conclusions

- Final diagnosis: Small Cell Neuroendocrine Cervical Cancer with metastasis to lymph nodes, bone and brain
- SCNECC is rare and aggressive, making up <3% of all cervical cancers, affects 22-87 years old, and linked to HPV 16 and 18
- Symptoms include vaginal bleeding, pelvic pressure, low back pain, and metastasis to regional LNs early
- It is diagnosed by biopsy for specific markers: Synaptophysin, CD56, neuron specific enolase.
- However, it is commonly misdiagnosed as cervical myomas or polyps
- Treatment is limited because of lack of research – Cisplatin and Etoposide used for Small Cell Lung Cancer to treat SCNECC
- Poor prognosis ranging from 1 month in the late stage to 5 years in the early stage
- Our patient did not have routine follow-up, was diagnosed with fibroids and had an IUD, all of which confounded the clinical picture and might have delayed diagnosis
- A thorough history and physical exam, detailed chart review, and utilization of a multidisciplinary team from seven specialties were essential in diagnosing rare Small Cell Neuroendocrine Cervical Cancer

References

Tempfer, C. B., Tischoff, I., Dogan, A., Hilal, Z., Schultheis, B., Kern, P., & Rezniczek, G. A. (2018). Neuroendocrine carcinoma of The Cervix: A systematic review of the literature. *BMC Cancer, 18*(1). doi:10.1186/s12885-018-4447-x

V, P., Shalini, C. S., Priya, S., Rani, U., Rajendiran, S., & Joseph, L. D. (2014). Small cell neuroendocrine carcinoma of the cervix: A rare entity. *Journal of Clinical and Diagnostic Research*. doi:10.7860/jcdr/2014/6811.4036

Pan, L., Liu, R., Sheng, X., & Chen, D. (2019). Small cell Neuroendocrine carcinoma of the Cervix in Pregnancy: A case report and review. *Case Reports in Obstetrics and Gynecology, 2019*, 1-5. doi:10.1155/2019/8028459