Rare Small Cell Neuroendocrine Cervical Cancer - Hiding in Plain Sight

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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. Symptons 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°F (oral), HR 85 bpm, BP 140/91 mmHg, RR 18 bpm, SpO2 98% on ambient air, BMI 25.5 kg/m²
- 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 x10³/ul
  - Hgb 11.2 g/dL
  - Plt 241 x10³/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 deminerlization of T12 vertebrae (shown in Figure 2 and 3)

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
- 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

Conc.

- 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

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 - PCR 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 Atazolizumab
- 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