

# Atypical Presentation of Cervical Carcinoma With Cerebral Metastasis

Shabnam Gupta, MD,<sup>1</sup> Sean Bandzar, MD,<sup>2,3,4</sup> Hany Atallah, MD, FACEP<sup>5</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Emory University School of Medicine, Atlanta, GA <sup>2</sup>Department of Emergency Medicine, New York–Presbyterian Hospital, New York, NY <sup>3</sup>Department of Emergency Medicine, Weill Cornell Medical College, New York, NY <sup>4</sup>Department of Emergency Medicine, Columbia University College of Physicians and Surgeons, New York, NY <sup>5</sup>Department of Emergency Medicine, Emory University School of Medicine, Atlanta, GA

**Background:** Cervical cancer is a leading cause of morbidity and mortality in women, but cerebral metastasis from cervical carcinoma is a rare event with a reported incidence of 0.57%.

**Case Report:** We describe a case of brain metastasis from primary cervical adenocarcinoma with several distinct features. This case illustrates uncommon presenting neurologic symptoms, a rare combination of histopathologic features, and atypical findings on radiographic evaluation.

**Conclusion:** Clinicians must maintain a high index of suspicion for cerebral metastasis to make an accurate diagnosis and initiate appropriate management of advanced cervical cancer.

**Keywords:** *Epilepsia partialis continua, neoplasm metastasis, uterine cervical neoplasms*

Address correspondence to Hany Atallah, MD, FACEP, Department of Emergency Medicine, Emory University School of Medicine, 49 Jesse Hill Jr. Dr., Atlanta, GA 30303. Tel: (404) 727-6123. Email: hatalla@emory.edu

## INTRODUCTION

Cervical cancer is a common cause of morbidity and mortality among women. Worldwide, it is the third most common cancer and the second most frequent cause of cancer-related death among women.<sup>1</sup> The incidence and mortality rates are related to the presence of screening programs and the availability of the human papilloma virus (HPV) vaccination.<sup>2</sup> Distant metastasis occurs late in disease progression via hematogenous dissemination after local spread and lymphatic invasion have occurred.<sup>3</sup> Common sites of distant metastasis include the liver, lungs, and bone. The development of cerebral metastasis from primary cervical cancer is rare, with only approximately 100 cases reported.<sup>4,5</sup> We describe a case of brain metastasis from a primary cervical adenocarcinoma and detail the atypical initial presenting symptoms, histopathologic features, and radiographic findings.

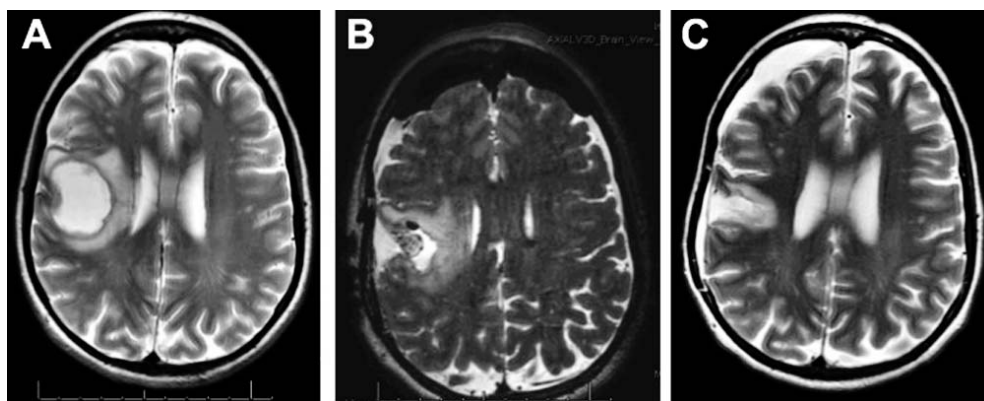
## CASE REPORT

A 52-year-old gravida 2 para 2 obese white female with no significant medical history presented with a 1-day history of sustained left-sided facial twitching and thumb paresthesia. She reported a 50-lb weight loss and increasing pelvic and back pain that improved with ibuprofen and tramadol during the previous 6 months. The patient reported no atypical genital bleeding. Review of systems was significant for fatigue, xerostomia, dysgeusia, nausea, constipation, and hematuria and negative for a history of tick bites, headache,

or vomiting. Social history was negative for tobacco and alcohol use. Family history was negative for any malignancies and neurologic disorders. The patient had not received Papanicolaou or HPV screening in 15 years because of poor access to medical care.

General physical examination was significant for left lower facial droop and intermittent twitching. The patient had normal motor function in the left digits. Pelvic examination revealed normal external genitalia. Speculum examination revealed a craterous lesion replacing the endocervix and ectocervix with necrotic tissue. Papanicolaou smear demonstrated atypical glandular cells suggestive of adenocarcinoma. The cervical biopsy specimen demonstrated moderately differentiated adenocarcinoma of the endocervix with positivity for cytokeratin (CK) 7, P16, carcinoembryonic antigen, vimentin, and mucin stain and negativity for estrogen receptor, progesterone receptor, CDX2, and CK20. Positron emission tomography scan demonstrated a 9 × 14 × 11.5-cm hypermetabolic necrotic cervical mass extending to the uterine fundus and involving the bladder and superior vagina bilaterally.

Magnetic resonance imaging (MRI) of the head with contrast demonstrated a single peripherally enhancing intra-axial lesion located within the posterior right frontal lobe abutting the postcentral gyrus at the gray-white junction, measuring 4.1 × 3.1 × 3.7 cm. The lesion included a small rim of vasogenic edema at the periphery, without midline shift. Microvascular white matter ischemic changes were also observed, as depicted in Figure 1A. Brain biopsy demon-

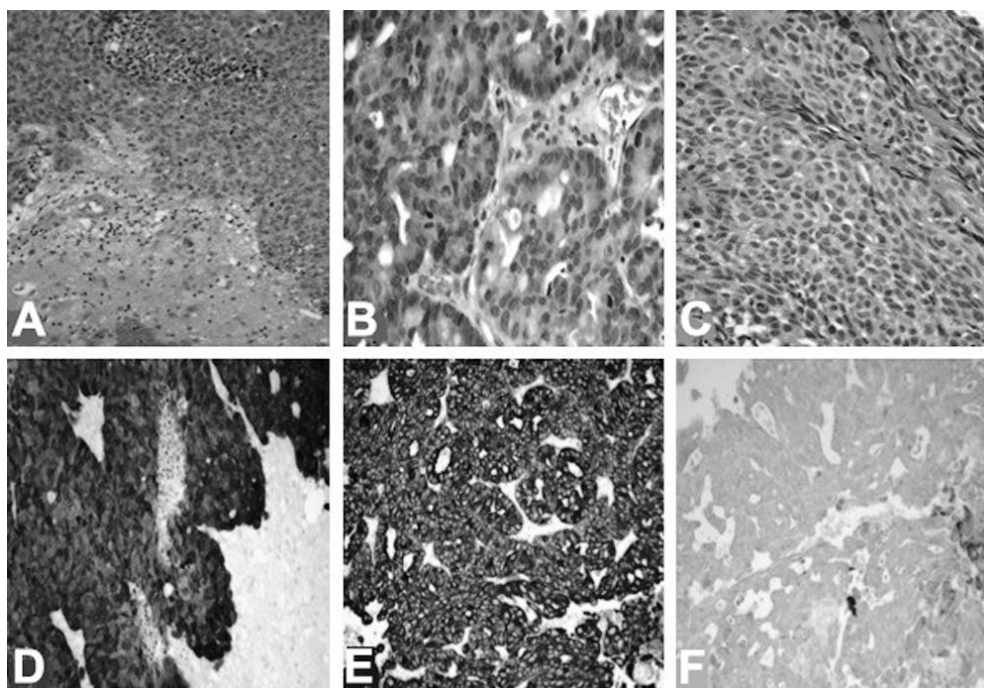


**Figure 1.** Axial T2/fluid attenuated inversion recovery magnetic resonance imaging of the brain shows (A) a tumor in the posterior right frontal lobe abutting the postcentral gyrus at the gray-white junction, measuring  $4.1 \times 3.1 \times 3.7$  cm; (B) status post tumor resection from the posterior right frontal lobe; and (C) expected postsurgical changes after 2 months of chemoradiation therapy status post tumor resection.

strated metastatic, poorly differentiated carcinoma with features of adenosquamous carcinoma (Figure 2A-2C) and diffuse positivity for P16 (Figure 2D) and CK7 (Figure 2E) consistent with adenocarcinoma. Squamous differentiation was supported by patchy positivity for CK5/6 (Figure 2F). Chest x-ray yielded negative findings. An electroencephalogram (EEG) demonstrated right centrotemporal focal polymorphic slowing with frequent sharp waves, occasionally occurring as sustained repetitive discharges.

A diagnosis of epilepsy partialis continua (EPC) and metastatic adenocarcinoma of the cervix was made, as evidenced by the patient's EEG and brain biopsy results,

respectively. The patient was administered Keppra (levetiracetam) 1,000 mg twice a day for seizure control with plans for a right craniotomy for tumor resection 3 days after initial presentation. After surgical removal of the tumor (Figure 1B), the patient's symptoms ceased, and she received external beam radiotherapy and cisplatin chemotherapy. Keppra was decreased to 500 mg twice a day for seizure prophylaxis after surgery. MRI follow-up at 2 months (Figure 1C) demonstrated expected postsurgical changes status post right frontotemporo-occipital craniotomy for subtotal resection of the posterior frontal intraaxial mass. The mass effect on the right lateral ventricle resolved with no evidence of tumor recurrence or



**Figure 2.** Brain mass biopsy specimen demonstrates (A) poorly differentiated carcinoma (hematoxylin and eosin stain [H&E],  $\times 50$ ); (B) glandular features (H&E,  $\times 100$ ); (C) squamous features (H&E,  $\times 100$ ); (D) P16 positivity (P16 immunostain,  $\times 50$ ); (E) cytokeratin (CK) 7 positivity (CK7 immunostain,  $\times 100$ ); and (F) CK 5/6 positivity (CK 5/6 immunostain,  $\times 100$ ).

new metastatic disease. The patient received palliative care and died 6 months after the diagnosis of brain metastasis.

## DISCUSSION

The most common intracranial tumor is a brain metastasis from a differing primary tumor. While brain metastasis is the most common intracranial tumor, brain metastasis from cervical cancer is extremely rare with an incidence of 0.57%.<sup>4</sup> This case of cervical carcinoma demonstrates many unusual characteristics, including a rare location for distant metastasis, an uncommon metastasizing cell line, and atypical presenting clinical symptoms and radiology imaging features. More common locations for distant metastasis of cervical cancer include the liver, lungs, and bone. Chura et al documented 12 cases of cervical cancer metastasizing to the brain, with three-fourths of cases identified as primary cervical carcinoma of squamous-cell origin.<sup>6</sup> Our patient presented with adenocarcinoma of the cervix with squamous features (Figure 2), a rare cell line to metastasize to the brain.<sup>4</sup>

The initial presentation of patients with symptomatic cervical cancer often includes abnormal vaginal bleeding, menorrhagia, dyspareunia, and unusual vaginal discharge.<sup>4</sup> Our patient never noted any genital bleeding or discharge, and sustained facial twitching, thumb paresthesia, and facial droop because of EPC were her predominant neurologic symptoms. Headaches, hemiparesis, and vomiting were absent. A literature search of case studies of primary cervical carcinoma with cerebral metastasis demonstrated that the most common neurologic symptoms include nausea, vomiting, and headaches, with hemiparesis and seizures being less likely presentations.<sup>7-9</sup> Most patients with cerebral metastasis present with headache, vomiting, and focal neurologic signs from mass effect of the tumor. Although patients with cerebral metastasis from primary cervical carcinoma most commonly present with these symptoms, our case illustrates the importance of maintaining suspicion in the presence of other neurologic signs such as EPC.<sup>10,11</sup>

Radiographic workup was initiated after the abnormal pelvic examination and Papanicolaou smear. Cerebral metastases commonly present as multiple lesions in the cerebral gray-white junctions and are usually associated with systemic involvement.<sup>6,8</sup> Our patient presented with a solitary brain lesion on imaging without systemic involvement of the lungs, liver, or bones. In addition, other case studies of cervical carcinoma metastasizing to the brain report multiple intracranial metastases on radiology.<sup>7,12-14</sup> Single metastatic lesions to the brain are more commonly seen with breast, renal, and colorectal carcinomas.<sup>13</sup> Although this solitary lesion was located near the gray-white junction, the fact that it was a solitary lesion delayed the diagnosis by several days owing to uncertainty of the origin of the lesion. This case demonstrates an uncommon finding on radiology that clinicians should recognize.

## CONCLUSION

This case presents a rare set of clinical symptoms, histopathologic features, and radiologic findings attributed to a primary diagnosis of cervical adenocarcinoma with cerebral metastasis. The characteristics presented in this case should be considered when evaluating a patient with cervical cancer who is experiencing new neurologic symptoms to facilitate swift diagnosis and initiate appropriate management.

## ACKNOWLEDGMENTS

*The authors have no financial or proprietary interest in the subject matter of this article.*

## REFERENCES

1. NIH Research Portfolio Online Reporting Tools: Cervical Cancer. Bethesda, MD: National Institutes of Health; 2010 Oct. <http://report.nih.gov/nihfactsheets/viewfactsheet.aspx?csid=76>. Accessed June 15, 2015.
2. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin*. 2011 Jul-Aug;61(4): 212-236.
3. Brown JV III, Epstein HD, Kim R, et al. Rapid manifestation of CNS metastatic disease in a cervical carcinoma patient: a case report. *Oncology*. 2007 Sep;73(3-4):273-276.
4. Sato Y, Tanaka K, Kobayashi Y, et al. Uterine cervical cancer with brain metastasis as the initial site of presentation. *J Obstet Gynaecol Res*. 2015 Jul;41(7):1145-1148. doi:10.1111/jog.12668.
5. Piura E, Piura B. Brain metastasis from cervical carcinoma: overview of pertinent literature. *Eur J Gynaecol Oncol*. 2012; 33(6):567-573.
6. Chura JC, Shukla K, Argenta PA. Brain metastasis from cervical carcinoma. *Int J Gynecol Cancer*. 2007 Jan-Feb;17(1):141-146.
7. Hwang JH, Yoo HJ, Lim MC, et al. Brain metastasis in patients with uterine cervical cancer. *J Obstet Gynaecol Res*. 2013 Jan; 39(1):287-291.
8. Ikeda S, Yamada T, Katsumata N, et al. Cerebral metastasis in patients with uterine cervical cancer. *Jpn J Clin Oncol*. 1998 Jan; 28(1):27-29.
9. Robinson JB, Morris M. Cervical carcinoma metastatic to the brain. *Gynecol Oncol*. 1997 Aug;66(2):324-326.
10. Juul-Jensen P, Denny-Brown D. Epilepsia partialis continua. *Arch Neurol*. 1966 Dec;15(6):563-578.
11. Thomas JE, Reagan TJ, Klass DW. Epilepsia partialis continua: a review of 32 cases. *Arch Neurol*. 1977 May;34(5):266-275.
12. Chung SB, Jo KI, Seol HJ, Nam DH, Lee JI. Radiosurgery to palliate symptoms in brain metastases from uterine cervix cancer. *Acta Neurochir (Wien)*. 2013 Mar;155(3):399-405.
13. Setoodeh R, Hakam A, Shan Y. Cerebral metastasis of cervical cancer, report of two cases and review of the literature. *Int J Clin Exp Pathol*. 2012 Sep;5(7):710-714.
14. Branch BC, Henry J, Vecil GG. Brain metastasis from cervical cancer—a short review. *Tumori*. 2014 Sep-Oct;100(5): e171-e179. doi:10.1700/1660.18186.

*This article meets the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties Maintenance of Certification competencies for Patient Care and Medical Knowledge*