

Isolated brain metastasis from uterine cervical cancer: a case report and review of literature

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Summary

The metastasis of cervical cancer to the brain is usually associated with systemic involvement such as lungs, liver and bones, and isolated brain metastasis is very rare because the primary mechanism of spread is by hematogenous dissemination of tumor cells. Although a few cases of isolated brain metastasis from cervical cancer have been reported, isolated brain metastasis from neuroendocrine cell carcinoma, which is characterized with aggressive and early metastatic features, has never been reported. A 44-year-old woman with cervical cancer composed of large neuroendocrine cell carcinoma was diagnosed with isolated brain metastasis at eight months after the definitive treatment with surgery followed by adjuvant chemotherapy. Careful evaluation would be needed during follow-up for the patients with cervical cancer with aggressive histologic type.

Key words: Cervical cancer; Neuroendocrine carcinoma; Isolated metastasis; Brain.

Introduction

Brain metastases from primary cervical cancer are rare. According to previous reports, brain metastasis from cervical cancer is usually associated with systemic metastases or accompanied by local disease with or without systemic involvement [1-7]. Although a few cases of isolated brain metastasis have been reported in squamous cell carcinoma or adenocarcinoma of the cervix [1, 8, 9], isolated brain metastasis from neuroendocrine carcinoma, which is a highly aggressive and early metastatic cell type, has not yet been reported until now. This report presents a case of isolated brain metastasis from neuroendocrine carcinoma of the uterine cervix.

Case Report

A 44-year-old woman presented with vaginal bleeding which had begun two months prior. Pelvic examination revealed a four-cm exophytic cervical mass. A punch biopsy was taken and pathologic diagnosis was squamous cell carcinoma. On thorough staging workup including pelvic magnetic resonance imaging (MRI) and positron emission tomography-computerized tomography (PET-CT), the clinical stage was determined to be IIA2 and there were no metastatic lesion in distant organs. The patient underwent a radical hysterectomy and pelvic and para-aortic lymphadenectomy. Histological examination revealed a mixed large-cell neuroendocrine cell carcinoma and poorly differentiated squamous cell carcinoma with lymphovascular space invasion (Figure 1). No metastases were found in the 82 resected lymph nodes. Three courses of adjuvant chemotherapy (5-FU 5,000 mg/m² + cisplatin 50 mg/m²) were given because of positive lymphovascular invasion and the aggressive histologic subtype. She was closely monitored with follow-up appointments every three months. Eight months after definitive

treatment, the patient came to the present emergency center with complaints of headache, dizziness, and fine motor incoordination. Multiple metastatic brain tumors were found on brain MRI (Figure 2). There were no metastatic sites on pelvic examination, chest, abdomen and pelvis CT, or PET-CT. She was diagnosed with an isolated brain metastasis from uterine cervical cancer. She was given whole brain radiation therapy of 3,000 cGy in 16 fractions. After treatment, her neurologic symptoms were resolved and she has survived with no evidence of disease for seven months.

Discussion

The mechanism of metastasis from the cervical cancer to the brain is by hematogenous spreading of tumor cells involving through liver, lung, and bones [4]. Therefore, isolated brain metastasis without other systemic disease is extremely rare. Table 1 shows review of published reports about brain metastases from cervical cancer. Of 42 cases, only four cases showed isolated brain metastasis. Histologic types of four cases were squamous cell carcinoma in two cases [1, 9] and adenocarcinoma in other two cases [1, 8]. Thus, to the authors' knowledge, the present case is the first report of isolated brain metastasis from neuroendocrine cell carcinoma which was mixed with squamous cell carcinoma of the cervix. Neuroendocrine carcinoma is an aggressive histologic type and usually showed concomitant systemic involvements at the time of brain metastasis [4, 5]. Once metastasis to the brain occurs, prognosis is very poor, with most patients surviving less than six months in spite of therapy [10]. However, early detection and treatment may improve the quality of life in these patients. Neuroimaging should be considered in patients with cervical

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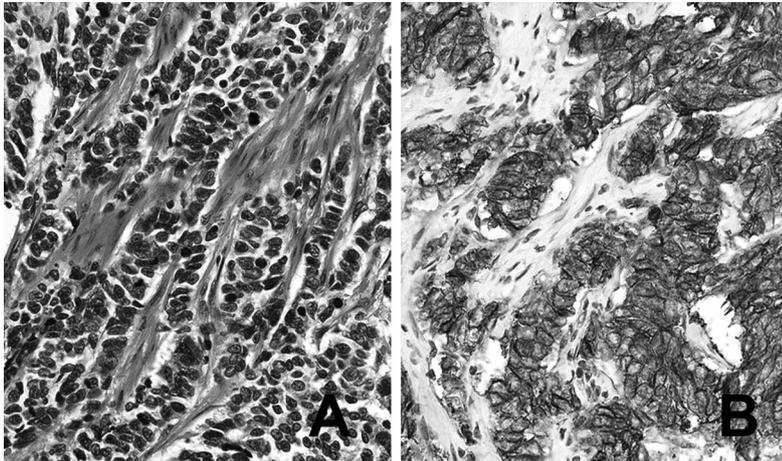


Figure 1. — (a) Microscopically, the tumor is composed of large cell neuroendocrine carcinoma with trabecular pattern (H-E stain, ×400). (b) CD 56 immunostaining reveals positive expression for large cell neuroendocrine carcinoma (×400).

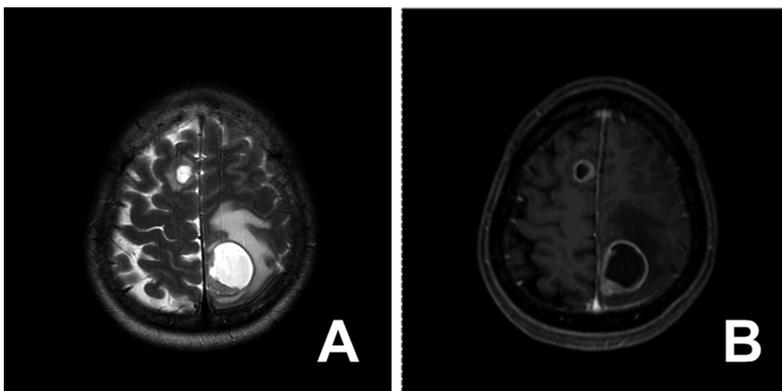


Figure 2. — Brain MRI. T2-weighted image (a) and contrast-enhanced T1-weighted image (b) shows multiple tumors with central necrosis and ring enhancement.

Table 1. — A review of literatures on brain metastases from uterine cervical cancer.

Reference	Isolated metastases (n=4)					Multiple metastases (n=38)				
	n	Stage (n)	Histology (n)	Initial treatment	Interval	n	Stage(n)	Histology (n)	PD or local recurrence [†]	Distant metastases sites (n)
Nagar <i>et al.</i> [3]	1	IIA	AC	S+RT	16					
Amita <i>et al.</i> [4]	1	IIA	SCC	CCRT	4					
Mahmoud-Ahmed <i>et al.</i> [2]	2	IIB(1) IIB(1)	AC(1) SCC(1)	RT RT	12 18.5	4	IB(1), IIB(2), IVB(1)	SCC(2), AC(2)	4	
Ikeda <i>et al.</i> [8]						8	IB(3), IIA(4), IIIA(1)	SCC(5), AC(2), Un(1)	2	L(3), B(2), O(4)
Chura <i>et al.</i> [1]						12	IB(6), IIB(3), IIIA(1), IIIB(1), IVB(1)	SCC(8), AC(3), AS(1)	10	L(9), B(4), O(1)
Hwang <i>et al.</i> [5]						11	IB(1), IIB(2), IIIA(1), IIIB(2), IVB(3), Unk(2)	SCC(5), AC(3), AS(2), NEC(1)	1	L(9), Li(4), B(2), O(6)
Komiyama <i>et al.</i> [6]						1	IB	NEC		L, O
Park <i>et al.</i> [9]						1	IB	SCC		O
Agrawal <i>et al.</i> [10]						1	IIB	SCC		Li

n, number of cases; Interval, interval from initial diagnosis of cervical cancer to diagnosis of brain metastasis(months); PD, persistent disease after initial treatment; AC, adenocarcinoma; SCC, squamous cell carcinoma; AS, adenosquamous cell carcinoma; NEC, neuroendocrine carcinoma; Un, undifferentiated type; Unk, unknown; S, surgery; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; L, lung; Li, liver; B, bone; O, other sites (including breast, skin, pancreas, and distant subclavian, cervical, mediastinal, and thoracic lymph nodes)
[†]cases of uncontrolled primary disease including peritoneal metastasis, pelvic cavity recurrence, and para-aortic lymph node metastasis.

cancer developing neurologic symptoms, even if PET-CT was negative because PET-CT would not be useful for detecting metastasis to brain. In summary, if the histologic type of primary cervical cancer is unusual and aggressive, as neuroendocrine carcinoma, more careful evaluation should be needed during follow up.

Conclusion

Isolated brain metastasis from cervical cancer is extremely rare because metastasis usually occurs by hematogenous spreading of tumor cells with other systemic involvement. Neuroendocrine carcinoma shows aggressive features associated with concomitant systemic involvements at the time of brain metastasis. However, clinicians should be aware of a possibility of isolated brain metastasis in case of complaining neurologic signs or symptoms by patients, although there would be no evidence of pelvic or systemic disease. Early detection and treatment may improve the quality of life in these patients.

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