Review Article

Brain metastases from cervical carcinoma: overview of pertinent literature

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Summary

Brain metastasis from cervical carcinoma is rare with only about 100 cases documented in the literature and an incidence among cervical carcinoma patients of 0.6%. The median interval between diagnosis of cervical carcinoma and brain metastases is 18 months. The brain can be the only site of distant metastasis of cervical carcinoma ("isolated brain metastases") (46.8%) or brain metastasis can be part of a disseminated cervical carcinoma involving also other sites of the body (53.2%). Brain metastasis of cervical carcinoma affects most often the cerebrum (73%) and can be either single (one metastasis) (50.6%) or multiple (≥ two metastases) (49.4%). Treatment of brain metastases has evolved over the years from whole brain radiotherapy (WBRT) alone to multimodal therapy including surgical resection (craniotomy) or stereotactic radiosurgery (SRS) followed by WBRT ± chemotherapy. The median overall survival after diagnosis of brain metastases is four months; however, a better survival is achieved with multimodal therapy (craniotomy followed by WBRT) compared to craniotomy alone or WBRT alone. The worst survival is observed in patients with no treatment. Although based on a very small number of patients, the best survival is noticed in patients having SRS either alone or in combination with other treatment modality.

Key words: Cervical carcinoma; Brain metastases; Craniotomy; Whole brain radiotherapy; Stereotactic radiosurgery.

Introduction

Cervical carcinoma is the second most common cancer in women worldwide, after breast carcinoma, with > 500,000 new cases diagnosed each year and an incidence of 15/100,000 women/year [1, 2]. Cervical carcinoma may spread by (1) direct extension to surrounding tissues and organs: parametria, vagina, urinary bladder, and rectum; (2) lymphatic drainage of the uterine cervix with the pelvic lymph nodes being first involved and then the para-aortic lymph nodes being the first extra-pelvic lymph nodes involved; (3) hematogenous route with the blood circulation carrying blood-born cervical tumor cells from the uterine cervix to distant sites [3]. The most common sites of distant metastasis of cervical carcinoma are the lung, bone, and liver and it has been estimated that 15% of cervical carcinoma patients develop distant metastasis during the course of their disease [4, 5]. It has been suggested that the evolution of therapy for cervical carcinoma over the years, especially the introduction of modern radiotherapy machines and techniques, has achieved better local control of the tumor in the pelvis and has allowed more patients to survive longer, which, in turn, has provided sufficient time for distant metastasis to develop and become clinically apparent [4].

The brain, along with the bone, liver and lung, is one of the most common sites of metastasis from various cancers with about 170,000 patients newly diagnosed with brain metastases each year in the USA [6-8]. Common sources of brain metastases are lung, breast, renal, and colorectal carcinoma and malignant melanoma; about 15% of patients with these cancers develop brain metastases during the course of their disease [6, 8-10]. Nevertheless, brain metastasis from female genital tract cancers, apart from choriocarcinoma, is rare, with only about 1% of patients with female genital tract malignancy developing brain metastasis during the course of their disease [11, 12]. The first report of brain metastasis of cervical carcinoma is attributed to Henriksen [13] who in 1949 reviewed 125 autopsies of cervical carcinoma patients and revealed one (0.8%) patient with brain metastases. Andrew [14] in 1953 was presumably the first to document brain metastasis in a living cervical carcinoma patient. Since then, 34 papers (single case reports and series of patients) on brain metastasis of cervical carcinoma in living patients have been published in the literature, totaling 96 patients [14-47]. This review summarizes these 34 papers and focuses on the following topics: pathway of metastatic spread from cervical carcinoma to the brain, incidence of brain metastases from cervical carcinoma, characteristics of the cervical carcinoma, interval between diagnosis of cervical carcinoma and brain metastases, characteristics of brain metastases from cervical carcinoma, treatment of brain metastases from cervical carcinoma, and survival after diagnosis of brain metastases from cervical carcinoma.

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Pathway of metastatic spread from cervical carcinoma to the brain

The primary route of spread of blood-born tumor cells from cervical carcinoma to the brain is through the cervical veins, internal iliac veins, common iliac veins, inferior vena cava, right atrium, right ventricle, pulmonary artery, lungs, pulmonary veins, left atrium, left ventricle, aorta, carotid arteries, and brain arteries into the brain parenchyma [41]. The spread of cervical carcinoma to the brain via the arterial circulation of the brain is supported by the fact that about two-thirds of patients with brain metastases from cervical carcinoma have also lung metastases and nearly one-tenth of patients with lung metastases from cervical carcinoma have also brain metastases [21]. Another possible route is from the veins of the pelvis to the paravertebral venous plexus (Batson's plexus) into the venous sinuses of the brain and then to the brain parenchyma. It has been speculated that pressure increases in the thorax or abdomen due to coughing or straining and are presumed to induce a retrograde flow of venous blood from the pelvis into the paravertebral venous plexus [8, 14, 15, 48].

Incidence of brain metastases from cervical carcinoma

Incidence of brain metastases at autopsy of cervical carcinoma patients

Of 812 postmortem examinations performed in cervical carcinoma patients collected from reviews by Henriksen (1949) [13], de Alvarez (1953) [49], Holzaepfel and Ezell (1955) [50] and Badib *et al*. (1968) [51], 15 (1.85%) showed brain metastases. Interestingly, while Henriksen [13] in 1949 found one (0.8%) case of brain metastases among 125 necropsies of cervical carcinoma patients, Badib *et al*. [51] in 1968 found nine (3.2%) cases of brain metastases among 278 autopsies of cervical carcinoma patients. This increase in incidence of brain metastases in autopsies of cervical carcinoma patients has been postulated to be a result of better loco-regional control of the cervical carcinoma over the years resulting in prolongation of survival and thus enabling enough time for brain metastases to develop [24].

Incidence of cervical carcinoma as source of brain metastases at autopsy of patients with brain metastases

Kishi *et al*. [52] surveyed 101 autopsies of patients with brain metastases and found that cervical carcinoma was the source of brain metastases in four (3.9%) patients as opposed to lung carcinoma which was the source of brain metastases in 59 (58.4%) patients. In 80 autopsies of female patients with brain metastases reviewed by Graf *et al*. [53], cervical carcinoma was the source of the brain metastases in three (3.7%) patients as opposed to lung carcinoma, which was the source of brain metastases in 30 (37.5%) patients, breast carcinoma – 17 (21.2%), malignant melanoma – 13 (16.2%), renal or urinary bladder carcinoma – six (7.5%), thyroid carcinoma – five (6.2%), colorectal carcinoma – three (3.7%), choriocarcinoma – two (2.5%) and endometrial carcinoma – one (1.2%). Thus, cervical carcinoma represents only a small fraction of total metastatic deposits in the brain.

Table 1. — *Incidence of brain metastases in living cervical carcinoma patients*.

Authors	Study period	Number of cervical carcinoma patients	Number of patients with brain metastases	Percentage
Peeples *et al*. [17]	NR	644	2	0.31
van Nagell *et al*. [18]	1964-1976	526	4	0.76
Saphner *et al*. [21]	1972-1986	1,219	6	0.49
Kumar *et al*. [22]	1988-1989	481	2	0.41
Cormio *et al*. [23]	1982-1994	1,184	14	1.18
Ikeda *et al*. [25]	1974-1994	1,961	8	0.40
Mahmoud-Ahmed *et al*. [28]	1982-1999	1,279	6	0.46
Agrawal *et al*. [34]	2001-2003	674	4	0.59
Chura *et al*. [40]	1995-2006	1,565	12	0.76
Ogawa *et al*. [41]	1985-2006	1,716	7	0.40
Total		11,249	65	0.57

NR: not recorded.

Incidence of brain metastases in living cervical carcinoma patients

In ten clinical reports [17, 18, 21-23, 25, 28, 34, 40, 41] in which the number of cervical carcinoma patients is available, 11,249 cervical carcinoma patients were surveyed and 65 (0.57%) of them were found to have brain metastases (Table 1). The claim that the incidence of brain metastases among cervical carcinoma patients may be increasing over the years because of prolongation of life due to better loco-regional control of the primary disease is not supported by reports published in the literature over the last 40 years, showing that the incidence of brain metastasis among living cervical carcinoma patients has remained steady under 1%.

Characteristics of the cervical carcinoma

The stage of disease at initial diagnosis of the cervical carcinoma was available in 71/96 (73.9%) patients [14-47]. Of these 71 patients, 30 (42.2%) had Stage IB (17 – IB not sub-staged, seven – IB1, six – IB2), 26 (36.6%) – Stage II (two – II not sub-staged, seven – IIA, 17 – IIB), 13 (18.3%) – Stage III (one – IIIA, 12 – IIIB), and two (2.8%) – Stage IVB. Thus, most patients (56/71, 78.8%) with brain metastases from cervical carcinoma documented in the literature had Stage IB (42.2%) or Stage II (36.6%) disease at initial diagnosis of the cervical carcinoma.

Histologic grade of the cervical carcinoma was available in 56/96 (58.3%) patients [14-47]. Of these 56 patients, two (3.6%) had grade 1 (G1), nine (16.1%) – grade 2 (G2), and 45 (80.3%) – grade 3 (G3). Hence, the vast majority of patients (80%) with brain metastases from cervical carcinoma documented in the literature had poorly-differentiated (G3) tumor at initial diagnosis of the cervical carcinoma.

Histologic type of the cervical carcinoma was available in 83/96 (86.4%) patients [14-47]. Of these 83 patients, 54 (65.1%) had squamous cell carcinoma, 17 (20.5%) – adenocarcinoma, seven (8.4%) – adenosquamous carcinoma, three (3.6%) – neuroendocrine carcinoma, one (1.2%) – clear cell carcinoma, and one (1.2%) – undifferentiated carcinoma. Thus, the most common histologic type of the cervical carcinoma in patients with brain metastases from cervical carcinoma documented in the literature was squamous cell carcinoma.

Data regarding primary and adjuvant therapy of the cervical carcinoma was available in 74/96 (77.1%) patients [14-47]. Noteworthy is the accrual of these patients occurring over prolonged periods of time during which radiotherapy methods for cervical carcinoma evolved considerably and, in more recent years, radiotherapy for cervical carcinoma (either as primary therapy or as adjuvant therapy) has been given concomitantly with chemotherapy (chemoradiotherapy). Primary therapy in these 74 patients consisted in pelvic radiotherapy – 39 (52.7%) patients (radiotherapy – 23, chemoradiotherapy – 16), radical hysterectomy – 30 (40.5%), simple hysterectomy – one (1.4%), chemotherapy – one (1.4%), and no treatment – three (4%). Adjuvant therapy in these 74 patients consisted in pelvic radiotherapy – 19 (25.7%) patients (radiotherapy – 16, radical hysterectomy and radiotherapy – one, chemoradiotherapy – two), chemotherapy – eight (10.8%), simple hysterectomy – two (2.7%), radical hysterectomy – one (1.4%), and no adjuvant therapy – 44 (59.4%). Thus, in the vast majority of the patients (69/74, 93.2%), primary therapy for the cervical carcinoma consisted in either pelvic radiotherapy or radical hysterectomy. Adjuvant therapy was given to 30/74 (40.5%) patients; in most of the patients, it was pelvic radiotherapy. The surgical technique of radical hysterectomy was compatible generally with a Class III extended hysterectomy as described by Piver *et al*. [54]. Pelvic lymphadenectomy consisted generally in the removal of lymphatic tissue around the common, external, and internal iliac vessels and anterior to the obturator nerve. Pelvic radiotherapy consisted generally of external megavoltage photonic irradiation employing a high mega electron volt (e.g., 10 MeV) linear accelerator delivering generally 5,000 cGy to the whole pelvis in daily fractions of 200 cGy via an AP-PA opposed fields or four-field box technique. External pelvic radiotherapy was followed generally by brachytherapy using either a Fletcher-Suite applicator (comprised of a uterine tandem and vaginal ovoids) when pelvic radiotherapy was given as primary therapy, or a vaginal cylinder (Delclos) when pelvic radiotherapy was given as adjuvant therapy after radical hysterectomy. Brachytherapy was administered generally by two to three applications usually using Cesium-137 (each application usually 2,000 cGy). Since 1995, in many patients, external pelvic radiotherapy was given concomitantly with intravenous chemotherapy (chemoradiotherapy). The intravenous chemotherapy was composed generally of weekly cisplatin 40 mg/m^2.

Interval between diagnosis of cervical carcinoma and brain metastases

The interval between diagnosis of cervical carcinoma and brain metastases was available in 81/96 (84.4%) patients [14-47]. It ranged from – 0.25 months to 105 months with a median of 18 months. In 78/81 (96.3%) patients, brain metastasis was diagnosed after diagnosis of cervical carcinoma (range, one week – 8.75 years; median, 18 months). Brain metastasis was diagnosed one week before the diagnosis of cervical carcinoma in 1/81 (1.2%) patients [37] and simultaneously with the diagnosis of cervical carcinoma in 2/81 (2.5%) patients [16, 28]. The relatively wide interval (median, 1.5 years) between the diagnosis of cervical carcinoma and brain metastases strengthens the assumption that prolongation of life due to control of loco-regional disease by radical hysterectomy and/or pelvic radiotherapy (± chemotherapy) provides sufficient time for brain metastasis to develop and become apparent. Age at diagnosis of brain metastases was available in 77/96 (80.2%) patients and ranged from 26 to 73 years (median, 48 years; mean, 48.3 years) [14-47].

Characteristics of brain metastases from cervical carcinoma

Type of brain metastases from cervical carcinoma with respect to whether the metastasis is confined to the brain only ("isolated brain metastases") or is part of a disseminated disease affecting also other parts of the body was available in 79/96 (82.3%) patients [14-47]. Brain metastasis was an isolated disease confined to the brain in 37/79 (46.8%) patients, whereas brain metastasis was part of a disseminated disease in 42/79 (53.2%) patients.

The amount of brain metastases originating from cervical carcinoma with respect to whether the metastasis was single ("solitary") brain metastases or multiple brain metastases was available in 79/96 (82.3%) patients [14-47]. Brain metastasis was a single brain metastasis (one metastasis) in 40/79 (50.6%) patients, whereas brain metastasis was multiple brain metastases (two or more metastases) in 39/79 (49.4%) patients.

Site of metastasis in the brain with respect to whether the metastasis is supratentorial (cerebrum) or infratentorial (cerebellum) or both was available in 74/96 (77.1%) patients [14-47]. Brain metastasis was located in the cerebrum in 54/74 (73%) patients, cerebellum in 9/74 (12.2%) patients, and both cerebrum and cerebellum in 11/74 (14.8%) patients.

Thus, brain metastasis from cervical carcinoma is part of a disseminated disease in ~50% of the patients, single in ~50% of the patients, and supratentorial in ~70% of the patients.

Symptoms and signs of brain metastases from cervical carcinoma

Symptoms and signs of brain metastases from cervical carcinoma are not different from symptoms and signs of other space-occupying lesions of the brain. In all 14

patients reported by Cormio *et al*. [23], the emergence of neurologic symptoms and signs i.e., motor weakness, headache, balance disturbance, seizures, visual disturbance, and confusion led to the diagnosis of brain metastases. In a series of eight patients reported by Ikeda *et al*. [25], nausea and vomiting due to increased intracranial pressure developed in four patients, headache was present in three patients, convulsion appeared in two patients, and hemiplegia emerged in two patients (evidently some patients had more than one symptom). All six patients reported by Mahmoud-Ahmed *et al*. [28] developed neurological symptoms that led to the diagnosis of brain metastases, with headache being the most common symptom. All 12 patients documented by Chura *et al*. [40] had apparent neurologic symptoms that prompted imaging studies of the brain (computed tomography CT and/or magnetic resonance imaging MRI) leading to the diagnosis of brain metastases. These symptoms included headache – six patients (50%), nausea and vomiting – three (25%), confusion – three (25%), paralysis – two (16.6%) and seizures – two (16.6%) (evidently, some patients had more than one symptom) [40]. In the vast majority of the cases of brain metastases originating from cervical carcinoma reported in the literature, it was the emergence of one or more neurological symptoms and signs that provoked a search for brain metastases with use of brain imaging studies, most often CT and less often MRI or both CT and MRI. In many cases, the lesion demonstrated in CT and MRI was associated with brain edema. Increased intracranial pressure caused by brain edema associated with the growth of the metastases in the brain parenchyma is the main reason for headache, nausea, vomiting, and development of papilledema in the fundus of the eye.

Treatment of brain metastases from cervical carcinoma

Because of the rarity of brain metastases from cervical carcinoma, the accrual of patients occurred over prolonged periods of time during which treatment approaches and modalities changed. Data with respect to treatment modality of brain metastases was available in 81/96 (84.4%) patients [14-47]. Of these 81 patients, 32 (39.5%) had whole brain radiotherapy (WBRT) alone, seven (8.6%) – WBRT and chemotherapy, one (1.2%) – WBRT and stereotactic radiosurgery (SRS), five (6.2%) – surgery (craniotomy) alone, 16 (19.8%) – surgery and WBRT, one (1.2%) – surgery and SRS, two (2.5%) – SRS alone, and 17 (21%) – no treatment (mostly, steroids only). Thus, overall, 56 (69.1%) patients had WBRT, 22 (27.2%) – surgery, seven (8.6%) – chemotherapy, four (4.9%) – SRS, and 17 (21%) – no treatment (evidently, some patients had more than one treatment modality). Thus, the most common unimodal therapy was WBRT alone and the most common multimodal therapy was surgery followed by WBRT.

Traditionally, patients with isolated (limited to the brain only) and single (solitary) brain metastases would generally undergo resection of the brain lesion by craniotomy followed by WBRT. Patients with multiple brain metastases (with or without extracranial disease) generally would be given WBRT alone (± chemotherapy). WBRT consisted generally in external megavoltage photonic irradiation employing a high mega electron volt (e.g., 10 MeV) linear accelerator delivering 3,000 cGy in ten fractions over two weeks or 4,000 cGy in 20 fractions over four weeks to the whole brain area [25]. Chemotherapy for brain metastases from cervical carcinoma included topotecan, etoposide, taxotere, cisplatin, and ifosfamide [40].

In case reports or series of patients published in literature before 2001, SRS or gamma-knife radiosurgery (GKRS) was not yet included in the treatment of brain metastases from cervical carcinoma. Mahmoud-Ahmed *et al*. [28] described in 2001 two patients with brain metastases from cervical carcinoma in which therapy for brain metastases included SRS. One patient was diagnosed with isolated multiple brain metastases one week after diagnosis of Stage IB cervical adenosquamous carcinoma. She had pelvic radiotherapy for the cervical carcinoma and SRS for the brain metastases and survived for 22.5 months. Another patient was diagnosed with isolated multiple brain metastases 18.5 months after pelvic radiotherapy for Stage IIB cervical squamous cell carcinoma. She had WBRT and SRS for the brain metastases and survived seven months after diagnosis of brain metastases [28]. Brown *et al*. [38] described in 2007 a patient that was diagnosed with isolated single cerebral metastases two weeks after diagnosis of Stage IB2 cervical adenosquamous carcinoma. She had radical hysterectomy for the cervical carcinoma and craniotomy + SRS for the brain metastases and remained alive with disease at the end of five-month follow-up [38]. Ulu *et al*. [42] described in 2009 a patient who developed isolated single cerebral metastases 24 months after pelvic radiotherapy and chemotherapy for Stage IIA cervical clear cell carcinoma. The cerebral metastatic lesion was operated with SRS and totally excised; nevertheless, there are no details of follow-up [42]. Although the experience of using SRS in the treatment of brain metastases from cervical carcinoma is very limited, it seems that there is an advantage for use of SRS in treating patients who are unable to tolerate craniotomy and for those with surgically inaccessible lesions.

Survival after diagnosis of brain metastases originating from cervical carcinoma

Follow-up after diagnosis of brain metastases of the 96 patients documented in the literature ranged from 0.1 to 72 months [14-47]. Data with respect to patient status (alive without disease or alive with disease or dead) at the end of follow-up was available for 87/96 (90.6%) patients. Of these 87 patients, seven (8%) were alive without disease at the end of follow-up ranging from two to 72 months, ten (11.5%) were alive with disease at the end of follow-up ranging from one to seven months, and 70 (80.5%) died of disease from 0.1 to 28.4 months (median,

Table 2. — *Survival after diagnosis of brain metastases according to mode of therapy of brain metastases*.

Mode of therapy	Survival	
	Range (months)	Median (months)
Craniotomy followed by WBRT (± chemotherapy)	1-72	7.1
WBRT (± chemotherapy) alone	0.1-22.6	3
Craniotomy alone	1-7	4
SRS (either alone or combined with other treatment modality)	5-22.5	13.7
No treatment	0.25-3.3	0.6
All modes of therapy	0.1-72	4

WBRT: whole brain radiotherapy, SRS: stereotactic radiosurgery.

four months) after diagnosis of brain metastases. Thus, the survival overall after diagnosis of brain metastases of patients with brain metastases from cervical carcinoma ranged from 0.1 to 72 months with a median of four months.

The survival of patients in relation to mode of therapy of brain metastases was assessed in series of more than four patients [21, 23, 25, 28, 40]. All six patients reported by Saphner *et al*. [21] had WBRT alone for brain metastases from cervical carcinoma and survived two to nine months (median, four months) after diagnosis of brain metastases. Of 14 patients with brain metastases from cervical carcinoma reported by Cormio *et al*. [23], 11 had steroid treatment only and succumbed within four months after diagnosis due to brain metastases, whereas three patients had WBRT for their brain metastases and survived two, six, and 21 months, respectively, after diagnosis of brain metastases. Of eight patients with brain metastases originating from cervical carcinoma reported by Ikeda *et al*. [25], three patients had multimodal therapy comprised of craniotomy followed by WBRT and survived 4.1, 7.5, and 10.3 months (median, 7.5 months), respectively, after diagnosis of brain metastases, whereas five patients had WBRT alone and survived 1.8, 1.9, 2, 12.3, and 22.6 months (median, two months), respectively, after diagnosis of brain metastases. Of six patients with brain metastases originating from cervical carcinoma reported by Mahmoud-Ahmed *et al*. [28], three had WBRT alone and survived 0.5, 7.25, and 8.25 months, one had craniotomy followed by WBRT and survived 10.5 months, one had SRS alone and survived 22.5 months, and one had WBRT + SRS and survived seven months. Although based on a small number of patients, the authors [28] concluded that extended survival may be achieved with more aggressive treatment such as surgery or SRS. Of 12 patients with brain metastases from cervical carcinoma reported by Chura *et al*. [40], four had WBRT alone and survived 0.3, 0.6, 1.1, and 1.5 months (median, 0.9 months), four had WBRT and chemotherapy and survived 3, 3.9, 4.4, and 7,9 months (median, 4.1 months), one had craniotomy followed by WBRT and chemotherapy and survived 6.2 months, and three had no treatment and survived 0.4, 0.5, and 3.3 months (median, 0.5 months). Since the median survival in patients who had WBRT followed by chemotherapy was significantly higher than in patients who had WBRT not followed by chemotherapy (4.4 months vs 0.9 months, $p = 0.016$), the authors [40] concluded that although the survival after diagnosis of brain metastasis is poor, the administration of chemotherapy after WBRT may improve the survival.

The overall survival after diagnosis of brain metastases according to mode of therapy of brain metastases in the 96 patients with brain metastases from cervical carcinoma documented in the literature was as follows [14-47] (Table 2): craniotomy followed by WBRT (± chemotherapy) – one to 72 months (median, 7.1 months), WBRT (± chemotherapy) alone – 0.1 to 22.6 months (median, three months), craniotomy alone – one to seven months (median, four months), SRS (either alone or combined with other treatment modality) – five to 22.5 months (median, 13.7 months), and no treatment – 0.25 to 3.3 months (median, 0.6 months). To sum up, the survival of patients having multimodal therapy for their brain metastases (craniotomy followed by WBRT) was considerably better than that of patients having WBRT alone or craniotomy alone. The worst survival was observed in patients having no treatment for their brain metastases. Although based on a very small number of patients, the best survival was noticed in patients having SRS either alone or in combination with other treatment modality.

Conclusion

Brain metastases originating from cervical carcinoma are rare with approximately 100 cases documented in the literature and an incidence in living cervical carcinoma patients ranging from 0.31% to 1.18% (mean, 0.57%; median, 0.48%). The cervical carcinoma was most often Stage IB (42.2%) or Stage II (36.6%) at initial diagnosis, poorly differentiated (80.3%), and squamous cell carcinoma (65.1%). In most patients (93.2%), initial therapy for the cervical carcinoma was either pelvic radiotherapy or radical hysterectomy. Adjuvant therapy was given to 40.5% of the patients; mostly, pelvic radiotherapy. In the vast majority of the patients (96.3%), brain metastasis was detected after diagnosis of cervical carcinoma ("metachronous metastases") with an interval between diagnosis of cervical carcinoma and brain metastases ranging from one week to 8.75 years (median, 18 months). Brain metastasis was diagnosed simultaneously with cervical carcinoma ("synchronous metastases") in two (2.5%) patients and one week before diagnosis of cervical carcinoma in one (1.2%) patient. Thus, although brain metastasis originating from cervical carcinoma is usually considered a late event in the course of the primary disease, poorly differentiated cervical carcinomas with lymph-vascular space invasion may metastasize early in the course of the disease, even before clinical symptoms of the primary tumor become apparent. Brain metastasis originating from cervical carcinoma is either an isolated disease limited to the brain only (46.8%) or part of a disseminated disease (53.2%). Brain metastasis from cervical carcinoma is located most often in the cerebrum (73%) and is either single (50.6%) or multiple

(49.4%) metastases in the brain. Treatment of brain metastases has evolved over the years from WBRT alone to multimodal therapy including surgical resection or SRS followed by WBRT ± chemotherapy. The median survival of all patients after diagnosis of brain metastases from cervical carcinoma was four months; nevertheless, a considerably better survival was observed in patients having multimodal therapy including craniotomy followed by WBRT ± chemotherapy (median survival, 7.1 months) compared to craniotomy alone (median survival, four months) or WBRT alone (median survival, three months). The worst survival was observed in patients having no treatment (median survival, 0.6 months). Although based on a very small number of patients, the best survival was noticed in patients having SRS either alone or in combination with other treatment modality (median survival, 13.7 months). Early detection of brain metastases is indispensable since the metastases at their early stage of development in the brain are still of small volume and thus much more feasible for surgical resection or SRS with less complications and longer survival than metastases at advanced stage of their development. Thus, the emergence of one of more neurological symptoms and signs in cervical carcinoma patients should provoke an immediate search for brain metastases with use of brain imaging studies.

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