CEREBRAL METASTASIS OF CERVICAL UTERINE CANCER

Report of three cases

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ABSTRACT - Cervical uterine cancer (CUC) spreads locally (pelvis and paraortic lymphnodes) or distantly (lungs, liver and bones). Metastasis to central nervous system (CNS) are rare. There are about 80 cases reported in the literature. Outcome is poor and survival varies from 3 to 6 months. Three cases of CNS metastasis from CUC are reported, one infratentorial and two supratentorials in location. In one patient, the initial manifestation was due to the cerebral lesion, a feature reported for the first time. All cases were treated by surgery, radiotherapy and/or chemotherapy. Clinical findings and treatment options of these rare lesions are reviewed.

KEY WORDS: cerebral metastasis, cervical uterine cancer.

Metástases cerebrais de câncer de colo de útero: relato de três casos


PALAVRAS-CHAVE: metástase cerebral, câncer de colo uterino.

Cervical uterine cancer (CUC) is responsible for 15% of deaths due to cancer in women older than 15 years of age in Brazil¹. It most often invades local structures, reaching pelvis and paraortic lymphnodes. Distant organs are reached by haematoogenous dissemination¹⁴. The frequency of distant organs metastasis varies from 38 to 85%⁵⁻⁷. Haematoogenous spread is responsible for a more aggressive behaviour. Most commonly affected distant organs are lungs, liver and bones⁶. Brain involvement is extremely rare¹⁻²⁴. There are reports of cervical cancer metastasis to pituitary gland, pancreas, urether, kidney, adrenal gland, ovaries, uterine tube, gallbladder, spine cord and to a convexity brain meningioma⁵,¹⁰,¹⁸,²¹,²⁴.

The objective of this article is to report three cases of cerebral metastasis from cervical uterine cancer and to discuss their clinical features and treatment options.

This study was performed with the approval of the Ethics Committee of the hospitals where these three patients were treated. Informed consent was obtained from either the patient or a relative in all cases.

CASES

Case 1 – A 60-year-old woman was admitted with a scalp lesion, history of local trauma and antibiotic therapy without improvement 30 days before admission. She had no other complaints. Physical examination revealed only an ulcerated left parietal-occipital scalp lesion. Skull X-ray demonstrated an ostepolytic pattern. CT scan revealed a hypodense right parietal-occipital cerebral lesion with ring enhancement and perilesional edema. The lesion was surgically removed and pathological diagnosis was that of a metastatic adenocarcinoma. Systemic screening revealed CUC II B clinical stage. She did not return for follow-up.

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Case 2 – A 31-year-old woman was admitted with headache and visual deficit since 2 weeks before admission. She had been submitted to lung metastasis resection from CUC 10 months before admission in another service. She received adjuvant chemotherapy and local radiotherapy. On physical examination she presented right homonymous hemianopsia. Cranial MRI revealed a 3 cm diameter left occipital lesion with ring enhancement, perilesional edema and central hypointensity in T1 and hyperintensity in T2-weighted images (Fig 1). The lesion was completely removed by craniotomy and pathological diagnosis was that of low differentiated carcinoma similar to her cervical uterine cancer. She received adjuvant whole brain radiotherapy. Postoperative period was unremarkable and she presented no other deficits. She had no recurrence of the lesion and no other neurological manifestation in 5 years of follow-up (Fig 2).

Case 3 – A 31-year-old woman was admitted with headache, drowsiness, vomiting, visual impairment and diplopia since 2 months before admission. Two years earlier she had been submitted to pan-hysterectomy for mucinous cervical uterine adenocarcinoma. She received adjuvant brachytherapy and teletherapy. On physical examination she presented with disorientation, right dysmetria ant gait ataxia. CT scan revealed a right hemispheric cerebellar heterogeneous lesion and supratentorial hydrocephalus. MRI showed a 5 cm diameter lesion iso-intense in T1-weighted images and irregular contrast enhancement. She was submitted to ventricular drainage and lesion removal through a subcortical craniectomy. Specimen was compatible with low differentiated adenocarcinoma similar to her cervical uterine cancer. She received adjuvant whole brain radiotherapy. Post-operatively she developed pneumonia and urinary tract infection. Abdominal ultrasound revealed local invasive recurrence. She died one month latter due to complications of urinary tract infection.

**DISCUSSION**

Cerebral metastasis from cervical uterine cancer were reported initially by Henriksen in 1949. They appear late in the clinical course of this disease. Their occurrence is very uncommon. There are about 80 cases reported in literature, with brain involvement usually occurring late in the course of the disease, usually preceeded by local pelvic invasion.

Haematogenous spread depends on histological type of the tumor. Cerebral metastases are more frequent in poorly differentiated tumors. Histological subtypes in decreasing frequency are squamous cells carcinoma, adenocarcinoma, carcinoid tumor and adenosquamous carcinoma. Cases in present report comprise one squamous cell carcinoma and two adenocarcinomas.

According to Kishi, most common clinical presentation include headache (34%), hemiparesis (25.8%), confusion (22.7%), monoparesis (14.4%) and nausea (9.2%)17. In Robinson's review, most common initial symptoms were hemiparesis, headache, facial palsy and seizures. Ikeda related a medium interval between initial diagnosis and brain metastasis of 28 months. Case 1 had no previous neurological or systemic manifestations and represents the only reported case in which diagnosis was initially made out of a metastatic brain and scalp lesion1-24. Case 2 is free from the disease 5 years after diagnosis and surgery. To our knowledge this is the first reported case with such a long survival in literature1-24.
CUC brain metastasis are solitary in one third of the patients and frontal lobe is the most common affected site. In Ikeda's review, 50% were solitary lesions and all of them were supratentorial. Cormio reported 6 single lesions, 8 multiple, 10 supratentorial, 2 cerebellar and 2 with infra and supratentorial involvement. As opposed to the literature, our 3 cases were solitary lesions and none in frontal lobe.

CUC brain metastasis are usually treated by surgery, chemotherapy and radiotherapy. Surgical removal is a consensus in the literature for solitary lesions. Surgery may also be considered in case of two or more lesions surgically removable in the same craniotomy. Other surgical indications are lack of diagnosis, life threatening situations (hemorrhage, hydrancephalus or infection), symptomatic relief after ineffective clinical treatment and insertion of intra- thecal chemotherapy devices.

Radiotherapy may play an adjuvant role to surgical resection or remains as the only local treatment, associated or not to chemotherapy. Patchell revealed that patients treated with surgery plus radiotherapy had longer survival, better neurological condition and lower recurrence of the disease in the nervous system, when compared to those who received radiotherapy alone. Most of the authors consider surgery followed by adjuvant radiotherapy the best option for solitary CUC brain metastasis.

Stereotaxic radiosurgery is as effective as conventional surgery for local brain metastasis control and may also be used in inaccessible lesions. There are no data in literature about radiosurgery effects in CUC brain metastasis. The decision between conventional craniotomy plus adjuvant radiotherapy and radiosurgery must be made on an individual basis, considering size, number and location of the lesion, clinical condition and available technology.

Chemotherapy plays an important role in clinical treatment of CUC and cisplatin is the most frequently used drug. Chemotherapy may determine regression of CUC brain metastasis and also has systemic effect. Its final influence in the outcome of CUC cerebral metastasis is still unknown. In cases with multiple lesions, chemotherapy may be the first choice of treatment. Cases 2 and 3 developed brain metastasis despite adjuvant chemotherapy for uterine disease.

Other therapeutic suggested strategies in study for clinical treatment of unresectable metastasis include selective intra-arterial chemotherapy, use of reversible haemato-encephalic barrier modifiers and hormonal therapy (melatonin) without, however, worthwhile effect. Outcome of patients with CUC brain metastasis depends on age, neurological status, length of clinical history, histological subtypes, number of lesions and clinical comorbidities. The prognosis is poor despite any treatment option, with survival of 3 to 6 months after diagnosis of brain metastasis.

REFERENCES