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Cervical cancer with brain metastasis: Case report and review of literature

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ABSTRACT

Brain metastases arising from cervical cancer are exceedingly rare. We report the case of a 62-year-old woman with a history of cervical cancer who was admitted in our department and was diagnosed with a solitary symptomatic brain metastasis. Treatment included aggressive tumor resection, followed by radiotherapy, but overall, with a poor prognosis. Histopathologic examination confirmed the metastatic origin from a primary cervical squamous cell carcinoma.

Keywords: cervical cancer, metastasis, brain involvement

INTRODUCTION

Cervical cancer is the fourth most frequent cancer in women with an estimated 570.000 new cases in 2018, representing 6.6% of all female cancers. Romania has one of the highest mortality rates in Europe, with a world standardized rate of 13.7/100.000 women/year (1). Tumor cells can extend directly and involve the uterine corpus, vagina, parametrium, peritoneal cavity, bladder or rectum and can spread by lymphatic or hematogenous dissemination. The most common sites for hematogenous spread are lungs, liver and bone, with central nervous involvement being uncommon (2).

CASE PRESENTATION

A 62-year old female is brought to the Emergency Department in September 2018 for left hemiparesis, confusional state, personality changes with apathy and mild headache, symptoms that developed progressively during the last two weeks. She was a surgical nurse with a history of tobacco use and known with squamos cell cancer of the cervix, diagnosed 2.5 years ago, for which she had underwent surgical treatment and received radiotherapy, being asymptomatic for 2 years after completion of treatment. A cerebral CT (computer tomography) scan with contrast showed a solitary fronto-temporal heterogenous solid mass which had surrounding vasogenic edema, mass effect and early uncal hernation suggestive of either a high-grade primary lesion or a metastasis (Fig. 1A, Fig. 1B). A Magnetic Resonance Imaging (MRI) could not be performed because of important mood alteration and behavioral troubles.

Her laboratory workup showed elevated tumoral markers: cancer-antigen 125 (CA125), alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA). The patient received dexamethasone, which improved her symptoms, mainly her motor deficit, and underwent an emergency surgical resection of the tumor, the mass being removed en bloc. Histo-

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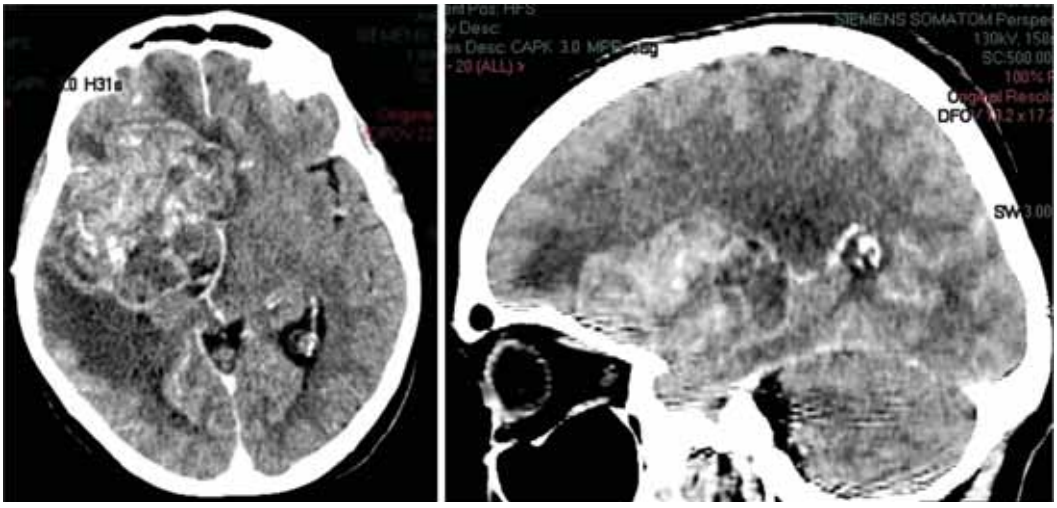

FIGURE 1. *A (left) and 1B (right): Axial and sagittal CT with contrast showing a right fronto-temporal heterogenous mass, with necrotic areas, with surrounding edema, mass effect and early herniation.*

pathological examination of the resected tumor revealed keratinizing cells, with high mitotic activity, laminated keratin pearls, compatible with a squamous cell carcinoma, which also had large necrotic portions. Postoperative cerebral CT showed gross total resection of the tumor (Fig. 2A, Fig. 2B), and patient had a good outcome at the time of discharge. She was guided to the oncology department and started whole brain radiotherapy (WBRT).

Immunohistochemistry showed positivity for cytokeratin 34BE12 (Fig. 3A), p63 (Fig. 3B), and also immunopositivity for p16, reflecting an etiological relationship with human papilloma virus (HPV) (Fig. 3C), all of this being consistent with a metastatic origin from a primary cervical squamos cell carcinoma. Further, immunohistochemistry for human Ki67 protein, strictly associated with cell proliferation, used as a prognostic and predictive marker in tumors (3), revealed a high proliferation index, of approximatively 30%. (Fig. 3D).

DISCUSSIONS

Brain metastases originating from gynecological cancers are rare (2%), with the most common tumor that metastasizes to the brain being choriocarcinoma (35%) (4). The primary mechanism of metastatic spread from genital tract cancers to the brain is through the hematogenous route. Tumor cells are carried from the genital tract by the blood

FIGURE 2. *A (left) and 2B (right): Axial and sagittal CT showing total resection of the fronto-temporal tumor.*

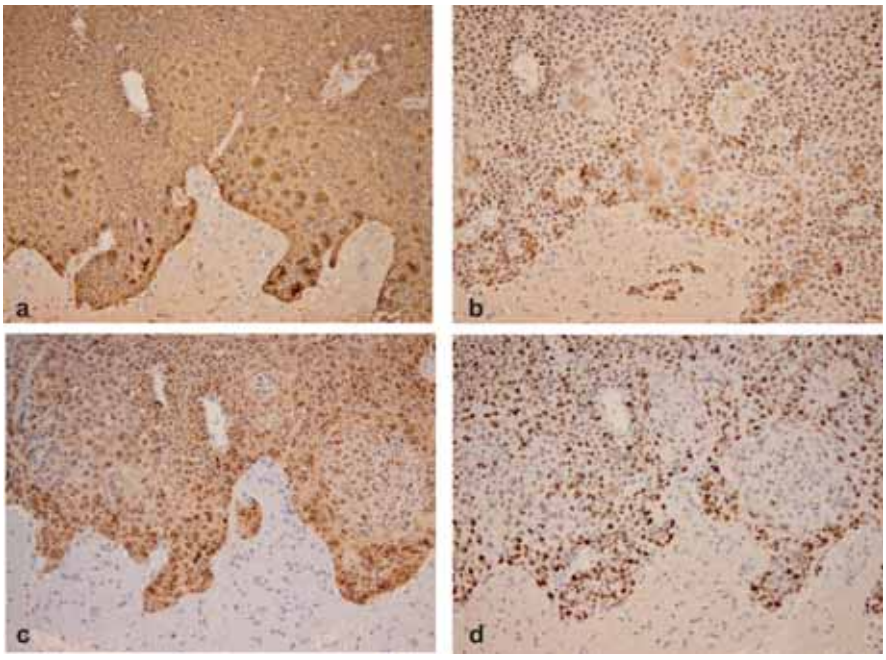

FIGURE 3. *Immunohistochemistry stains showing positivity for cytokeratin 34BE12 (a) and for p63 which is specific for squamocellular differentiation (b), compatible with squamous cell carcinoma of the cervix, metastatic to the brain. Tumor cells are also positive for p16, showing an association between squamocellular carcinoma with HPV infection (c). The proliferation index ki67 was high, approximatively 30%, important in determining the survival prognosis (d).*

stream through the inferior vena cava, right heart cavities, pulmonary artery, lungs, pulmonary veins, left heart cavities and aorta to the brain (5). An alternative theory is that detached tumor cells from the genital tract may also travel to the brain via the Batson plexus (paravertebral venous plexus) (6). The incidence of cervical cancer to the brain has been reported as ranging from 0.4-2.3% (7). In recent years, an increase in the number of brain metastases from cervical cancer has been observed, this is thought to be due to better treatment of the primary cancer and therefore increased overall survival. Also the incidence of cerebral metastases at autopsy appears higher than that seen among living patients (7-9).

Patients who have brain metastases from cervical cancer are considered to have poor prognosis, particularly when it is detected late in the course of the disease (7,8). The median survival from the diagnosis of brain metastases to death was 2.3 months[7]. The majority of patients with cerebral involvement also had systemic metastases, with only a small fraction of patients having isolated brain metastases in the absence of any systemic disease (7-9). The median age of the patients was 48 years, ranging from 29 to 87. The median interval time from diagnosis of the primary tumor to diagnosis of brain metastases was 17.2 months (7,8).

The patient from our case was a 62-year-old female with a 2.5-year interval from primary diagnosis to brain metastases diagnosis. Clinical presentation depends on the site of the metastases, the most frequent symptoms are headache (31%), motor deficit (16%), seizures (11%), and altered mental status/confusion (9%). More than half of these patients (55%) have multiple lesions, while slightly less than half (45%) were found to have solitary metastases and most were supratentorial (75%) and were found in all the different lobes, which can be related to the vascularity and spatial characteristics of this regionbut there can also be infratentorial lesions with the most common involvement being the cerebellum (7,10). In our case, the patient presented in September 2018 with mild left side weakness, confusion, personality changes and mild headache, having a left solitary fronto-temporal lesion.

Treatment depends on the number and location of the metastases, the presence of metastases in other organs and the clinical status. The prognosis for metastatic spread to the brain appears to get

worse as the number of intracranial tumors increases. Factors related to a good prognosis are: age younger than 50, good performance status, single brain metastases and no extracranial metastases (7,11). Lung metastases appears to be related to brain metastases and can be regarded as a risk factor (11). Currently, there has been no therapeutic and standard effective treatment established for brain metastases. It has evolved over the years from WBRT alone to more complex therapy including surgery resection or SRS (stereotactic surgery) followed by WBRT and/or chemotherapy. This multimodal therapy produces a better survival rate (craniotomy followed by WBRT) compared to craniotomy alone or WBRT alone. The worst survival rate is achieved in patients with no treatment (12). The decision between conventional craniotomy plus adjuvant radiotherapy and radio-surgery must be made on an individual basis, considering the size, number and location of the lesions, clincal conditions and available technology (7). Craniotomy is usually performed in larger, symptomatic lesions, SRS is less invasive and is more suitable for inaccessible lesions or when patients are not eligible for surgery (8). Chemotherapy alone may be considered initially in patients with multiple brain metastases and other organ metastases because it may control both brain metastases and other metastatic organs, the most frequently used drug being cisplatin and also topotecan being an alternative option based on its it has the ability to cross the blood-brain barrier, but there is no specific study the best dose and regimen for patients with brain metastases. For multiple brain metastases, palliative brain radiotherapy is a more appropriate approach. For solitary brain metastases in the absence of systemic disease, the use of craniotomy is an optimal choice, combined with radiotherapy. In spite of all these treatments, the median survival from brain metastases to death is short, with a median survival around 2-8 months (7,12,13).

CONCLUSIONS

Intracranial metastases arising from cervical cancer are extremely rare, but may occur because survival from the primary tumor is prolonged by the availability of improved treatment facilities. Physicians should maintain a degree of suspicion about this condition in order to provide prompt and comprehensive treatment.

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