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Carcinoma Cervix With Brain Metastasis: Report Of Two Cases And Review Of Literature

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Abstract: ***Brain metastasis from carcinoma cervix is a rare clinical entity. Incidence of brain metastasis in carcinoma cervix ranges from 0.5-1.2 %. Cervical cancer usually spread by local extension and through the lymphatic to the retroperitoneal lymph node. Distant hematogenous spread to the brain is an uncommon and late event with poor prognosis. Herein we are reporting two cases of advanced carcinoma cervix that developed brain metastasis after two years of completion of treatment. Both cases were treated with whole brain radiotherapy. One of them responded well to treatment and was disease free at 11 months follow up and another patient died 3 months after completion of treatment. This case being reported due to rarity of brain metastasis in carcinoma cervix.***

Keyword: Brain, Cervical, Carcinoma, Metastasis

I. INTRODUCTION

Metastatic brain tumors are the most common type of cerebral neoplasm in adults which account for 40-50% of brain tumors. Advances in imaging including computed tomography and magnetic resonance imaging leads to early and more frequent detection of brain metastasis. Most of the brain metastases arise from lung cancer (40-50%), breast cancer (11-25%) and melanoma (5-20%),[1] .Other malignancies that also metastasize to brain arebladder, renal, thyroid and colon cancer. Gyaenacological malignancies rarely metastasize to brain except choriocarcinoma.[2] A review of literature of this uncommon metastasis shows that incidence of brain metastasis from cervical cancer is 0.5-1.2 %[3,4]. In present study we report two cases of advanced stage poorly differentiated squamous cell carcinoma of cervix who on follow up presented with brain metastasis two years after completion of treatment due to its rarity and also to review the current literature and management of the these metastasis, as the symptoms, treatment and its outcome are poorly characterized.

CASE REPORT-

Case-1

A 52 year old female clinically presented with headache, vomiting of four weeks duration followed by seizure of two weeks duration. She was a known case of poorly differentiated squamous cell carcinoma of cervix stage IIIB treated with concurrent chemoradiation i. e external beam radiation of 50 GY to whole pelvis in 25 fractions over 5 weeks with concurrent weekly cisplatinum of 40mg/m^2 followed by high dose rate brachytherapy of 7GY/fraction of three fraction two years back. Her systemic examination was unremarkable. Her gynecological evaluation did not show any locoregional disease. Computerized tomography scan of brain revealed a ring enhancing lesion with disproportionate perilesional oedema in the left fronto-parietal lobe with mass effect and minimal midline shift to right.Routine hematological and biological parameters were within normal limit. Ultra sound of abdomen and pelvis was non-contributory. Computed tomography of thorax however showed multiple pulmonary nodules. She was treated with external beam radiotherapy of 30 GY to whole brain in 10 fractions. After two weeks of completion of radiotherapy she was treated with six cycles of paclitaxel 175mg/m^2 and carboplatin dosed to an area under curve of 6. At present her disease is under control for last 11 months.

Case-2

A 65 year old female clinically presented with chief complains of shortness of breath for one month followed by severe headache and vomiting for three days. She was treated for carcinoma cervix stage IIB by Wertheim's hysterectomy two and half years back at peripheral hospital whose histopathological study showed poorly differentiated squamous cell carcinoma with involvement of left obturator and external illic group of lymph nodes. Based on this she received concurrent chemoradiation of 50Gy external beam radiotherapy in 25 fractions to whole pelvis over 5weeks followed by high dose rate brachytherapy of 7Gy/fraction x 3 fractions at weekly interval which was completed in October 2012. She had also received concurrent cisplatin 40mg/m^2per week for 5 weeks during external beam

radiotherapy. Her physical examination revealed no evidence of disease clinically and her primary was under control. Computed tomography of brain revealed a ring enhancing lesion in the right temporal lobe involving the gangliocapsular region with perilesional edema, mass effect and midline shift to left. Ultrasound of abdomen and pelvis showed absence of uterus & ovary with multiple hepatic metastases. X-ray chest revealed pulmonary nodules suggestive of pulmonary metastasis. She received external beam radiotherapy of 30 Gy to whole brain with palliative intent. Her neurological sequel improved. She refused chemotherapy and subsequently died after three months. .

DISCUSSION-

Carcinoma of cervix is the commonest female genital malignancy in developing countries. Early detection and improved treatment have resulted in better tumor control and improved survival. The occurrence of metastatic disease is still a rarity. Cervical cancer spread through direct, local and lymphatic pathway to retroperitoneal lymph nodes because of rich lymphatic network of. But hematogenous metastasis is relatively rare. The common sites of distant metastasis are lung, bone and liver.[5] Metastasis to brain from cervical cancer is extremely rare, usually seen late in the course of disease and have a poor prognosis.

Usual age of presentation is 6th decade. [4] In these study one of the patients was in 5th decade and another in 6th decade. Carlson et al reported that most metastasis appears within 5 years of completion of therapy,[6] which correlated with our report in which one case developed brain metastasis after two years and another after two and half years after completion of treatment. Various studies have shown that advanced disease, bulky tumor, endometrial extension and lymph node metastasis are associated with increased incidence of brain metastasis in cervical cancer .[7] Eifel et al reported that the incidence of distant metastasis was 9% when tumor burden was <3cm as opposed to 36% in patient of tumor size >3cm.[8] Our cases had tumor size >4cm presented with locally advanced disease with metastasis to lung in both cases and to liver& pelvic lymph nodes in one of the case.

Majority of cases of brain metastasis are located in the supratentorial region of brain which may be related to the vascularity and spatial characteristic of this region.[4] Route of spread to the brain is hematogenous. However, the presence of intravascular tumor cells in cerebral circulation does not necessarily culminate in the development of brain metastasis. The development of brain metastasis depends on the immune response of host, tissue neovascularization, and the number of tumor emboli and the characteristic of tumor. [9] Churn and colleagues suggested vertebral venous system is the main route of brain metastasis.[10]

In our both cases tumor was located in the supratentorial region. Delattre et al on analyzing the distribution of brain metastases concluded that frontal and parietal lobes are more frequently involved than temporal and occipital lobe.[11] Similar to above presentation one of our reported case had metastasis at left fronto-parietal area.

Brain metastasis are more frequently seen with poorly differentiated squamous cell carcinoma.[12]Both of our patient had poorly differentiated squamous cell carcinoma. Although clinical manifestation depends on site of metastasis and surrounding vasogenic edema, headache and hemiparesis are the most commonly reported symptom and sign in these setting.According to Posner headache is the commonest clinical symptoms (53%) followed by focal weakness (40%), behavioral changes(31%), seizure (15%), ataxia(20%),aphasia(10%) in brain metastasis.[13]In the reported cases, both the patients had headache as the initial complain. There is no standard treatment guideline for brain metastasis from cervical cancer.[14] Treatment of brain metastasis involves surgery, radiation therapy or both depending on the clinical condition. Surgical excision is considered in cases with solitary lesion or adjacent multiple metastasis, cases with diagnostic uncertainty or with life threatening and critically located metastasis. Patients with non-adjacent, multiple or inoperable lesions are usually treated with palliative whole brain radiotherapy. Patchell et al reported that brain metastasis patients treated with surgery combined with adjuvant radiotherapy yields a longer survival, better neurological condition and lower recurrence of disease.[15]

Stereotactic radiosurgery such as cyberknife is as effective as conventional surgery and may be used in patients with surgically inaccessible lesions.[16] The decision between conventional surgery plus adjuvant radiotherapy and radiosurgery should be made on individual basis, considering size, number and location of lesion, clinical condition and available technology. Whole brain radiotherapy alone is the treatment of choice for multiple brain metastases than combination chemotherapy.[14]

Prognosis of brain metastasis from cervical cancer is very poor. Most studies have reported a median survival of only a few months, but there are few reports of long term, disease free survival.[17] One of our case is still surviving for last 11 months.

CONCLUSION-

Brain metastasis from cervical malignancy is a rare clinical entity, with the reported incidence of 0.4-1.2%. However, increased incidence of brain metastasis has been reported due to improved treatment of primary lesion and prolonged survival. Oncologist should keep high degree of suspicion about metastasis if patients develop symptoms, they should be thoroughly investigated without delay.

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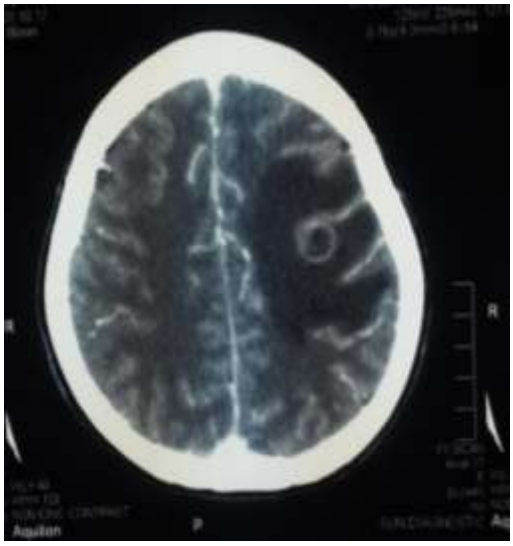
Figure-1-CT scan of brain showing a ring enhancing lesion with disproportionate perilesional oedema in the left fronto-parietal lobe with mass effect and mild midline shift to right.



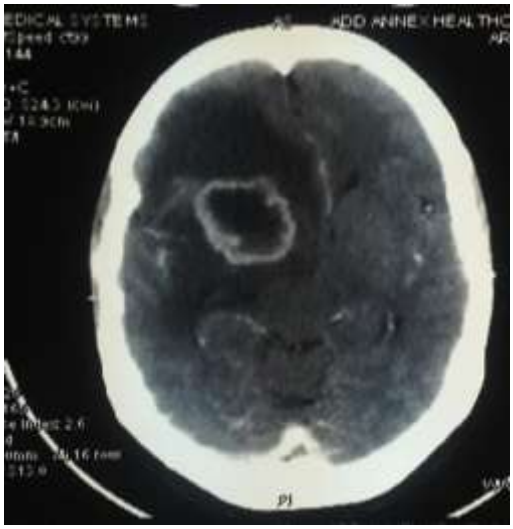


Figure-2- CT scan of brain showing a ring enhancing lesion in the right temporal lobe involving the gangliocapsular region with perilesional edema, mass effect and midline shift to left.