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**Case Report**

# CARCINOMA OF UTERINE CERVIX WITH MULTIPLE SKULL METASTASES AS THE FIRST PRESENTATION OF RECURRENCE: A CASE REPORT

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**Abstract**

Carcinoma of cervix recurring as multiple skull metastasis is a very rare presentation. A 49-year-old woman, a diagnosed case of carcinoma cervix [International Federation of Gynecology and Obstetrics (FIGO) stage IB1] treated with radical hysterectomy presented with generalized seizures to us after 40 months of initial diagnosis. Contrast-enhanced computed tomography showed metastasis to left temporoparietal bone and left frontal bone. Biopsy from the left temporal lesion showed non-keratinizing squamous cell carcinoma. She was thus diagnosed as recurrent carcinoma cervix with multiple calvarial metastases with the controlled primary site. She received palliative radiotherapy to the entire skull. She further received 4 cycles of palliative chemotherapy with paclitaxel and carboplatin repeated every 3 weeks. However, she could not tolerate chemotherapy after 4 cycles owing to significant deterioration of performance status and expired after 12 months of diagnosis of metastasis.

**Keywords: Carcinoma cervix, calvarial metastasis, recurrent**

## Introduction

Carcinoma of uterine cervix mostly recurs locally in the pelvis or in para-aortic lymph nodes after definitive treatment. Lungs, liver, bones (in that order) are frequented sites of distant metastasis [1]. The incidence of bone metastasis has been reported in around 10-20% of cases in recent series [2]. The lumbar spine is the most common site of bone metastasis followed by pelvis and long bones and usually, it occurs after a median time of 16 months [3]. Metastasis to calvarium is very rare and only a few cases have been reported so far. While 6 cases of solitary skull metastasis from carcinoma cervix have been reported so far [4-7], only 2 cases of multiple calvarial metastases has been reported [5-6].

We hereby report multiple calvarial metastases as the first symptom of recurrence in a patient of carcinoma cervix.

**Case report**

A 49-year-old post-menopausal lady presented to our gynecology oncology clinic with complaints of seizures for 2 days and low back pain for 1 month in April 2015. Seizures were generalized and she had suffered two such episodes before presenting to us. There was no history of fever, weakness of limbs, urinary or bowel complaints or seizures in the past. Pain in the back was insidious in onset since 1 month, progressive, moderate to severe in intensity, localized to lower lumbar and sacral region without any radiation and relieved by pain killer medicines.

Earlier she had been diagnosed with carcinoma of uterine cervix stage IB1 (FIGO 2009) in December 2011. She underwent Wertheim's hysterectomy for the same at a different institute and histopathology reported was: 2.5x2x1.5cm growth limited to the cervix; non-keratinising squamous cell carcinoma; rest of the uterus, bilateral fallopian tubes and ovaries were free of a tumor; margins were uninvolved and all 18 lymph nodes dissected were not involved. She was lost to follow up after that but was symptomatically doing well.

The present clinical examination did not reveal any sensory or motor deficit, cranial nerve palsy or spinal tenderness. She was conscious, alert and co-operative with apparently normal higher mental functions. Per speculum and vaginal examination showed a healthy vault without any evidence of disease and per rectal examination showed smooth and mobile rectal mucosa with normal parametrium. Eastern cooperative oncology group (ECOG) performance status was 1. Blood pressure in left arm was 130/86 mm of Hg under the resting condition and measured in the supine position. She was a febrile with a pulse rate of 80/ minute. There was no supraclavicular or inguinal lymphadenopathy and per abdominal examination was within normal limits. Systemic examination did not reveal any other abnormality.

Haemogram showed haemoglobin 11.7g/dL (12-15g/dL), platelet count 2.56 lacs/µL and total leukocyte count 7300/µL. Baseline blood urea nitrogen and creatinine was 20 mg/dL (7-22mg/dL) and 0.4mg/dL (0.56-1mg/dL) respectively. Baseline liver function test was within normal limits. Contrast-enhanced computed tomography (CECT) of the head showed multiple lytic deposits along with soft tissue component with contrast enhancement involving both inner as well as outer cortex of left temporoparietal bone (4x4 cm) and left frontal bone (2x2 cm). Underlying brain parenchyma was uninvolved [Figure 1 a-b]. Whole body bone scan ($^{99m}$Technetium methylene di-phosphate) did not show metastasis to extracranial skeletal sites. CECT chest, abdomen, and pelvis did not show any evidence of disease. Biopsy from the left temporal lesion showed sheets of tumor cells with abundant cytoplasm and central round nucleus with no keratinization suggestive of non-keratinizing squamous cell carcinoma, consistent with the primary diagnosis [Figure 3 a-b]. She was thus diagnosed as recurrent carcinoma cervix with multiple calvarial metastases.

She received palliative radiotherapy to the entire skull with bilateral opposed radiation portals to a dose of 30 Gray in 10 fractions over 2 weeks and started on anti-epileptics (levetiracetam) and other symptomatic medicines. She did not report any further episode of seizures after completion of radiotherapy. She was further planned for 6 cycles of palliative chemotherapy with paclitaxel (175 mg/m$^2$ intravenous day 1) and carboplatin (AUC 6 intravenous days 2) repeated every 3 weeks. However, she could not tolerate chemotherapy after 4 cycles owing to significant deterioration of performance

status. She expired in January 2016 (8 months after the diagnosis of metastasis).

**Discussion**

Carcinoma of the uterine cervix is the second most common malignancy among women in India with approximately 1 lakh cases diagnosed every year and 60-80% of them present in advanced stages. 20-30 % of patients either present up front or at the time of recurrence with distant metastasis. Apart from the common metastatic sites (lung, liver, bone), many unusual sites of metastasis have been reported in the literature. Skull metastasis is also one of them with limited reports in the literature.

Skull metastases in carcinoma cervix mostly present with local tenderness, headache or swelling [4-7]. Our case presented with seizures as the sole symptom. Abhishek et al also reported seizures as presenting symptom in their case; however, this was also associated with local tenderness. The median time of presentation is 2-20 months from initial diagnosis of disease [4-7]. In our case, this was 40 months after initial diagnosis and is longest of all reported cases in the literature. Initial clinical stage in presented cases till date was mostly advanced (FIGO IIIB), except by Abhishek et al [7]; the stage was IIA in this case report. Our patient`s stage was IB1, which is the earliest stage of initial presentation.

Skull metastasis reported so far are mostly solitary in occurrence [4, 7]. Only Niloofar et al [6] and Kapali et al [5] noted multiple calvarial metastases, like ours. Our case is unique in the way that the patient presented with multiple skull metastases with controlled primary after a gap of 40 months.

Prognosis of patients with solitary metastasis is usually better than those with multiple ones. All patients except 1 with such occurrence in reported literature were alive at the time of last follow up [4-7]. Patients with solitary skull bone metastasis may occasionally enjoy long-term survival. Zilberlicht et al [4] treated their patient of the solitary lesion with surgery and radiotherapy and reported a disease-free survival of 20 months. The outcome is fatal with multiple lesions or association with extra-calvarial skeletal metastasis. Patient-reported by Niloofar et al [6] having multiple skull metastases did not survive similar to our patient. Association with extra-calvarial skeletal metastasis usually carries a grim prognosis with median survival of fewer than 12 months [8]. Our case died after 12 months of diagnosis of recurrence.

Treatment should be tailored as per the performance status of the patient and number of metastasis. Solitary skull metastasis should be treated aggressively with surgery and postoperative radiotherapy [4] and in cases where this is not feasible, radical radiotherapy with or without chemotherapy should be used [5-7]. Long-term survival (3 years) has also been reported in a case of carcinoma cervix with isolated fibular metastasis treated with surgery and radiotherapy [9] and this may further justify aggressive treatment in selected suitable patients. In our case, the patient was treated with palliative intent in view of extensive primary recurrence.

Our case is unique in the way that seizure heralded the onset of recurrence of an early stage (IB1) carcinoma of uterine cervix after a long gap (40 months) of initial diagnosis. Clinicians should be aware of this unusual pattern of recurrence, so the diagnosis could be made earlier and the patient may be palliated of symptoms.

**Conflicts of interest**: None

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## Figure legends

**Figure 1(a-b):** Contrast-enhanced computed tomography of the head showing multiple lytic deposits involving left temporoparietal and left the frontal bone

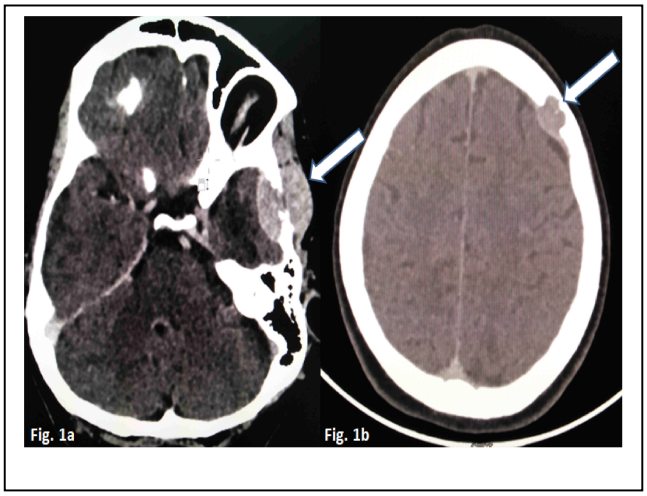

**Figure 2(a-b):** Biopsy from the left temporal lesion suggestive of non-keratinizing squamous cell carcinoma