

Case Report

## Complete Response in Carcinoma Cervix with A Synchronous Solitary Bony Metastatic Lesion Treated with Concurrent Chemoradiation and SBRT: A Case Report

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### Abstract

**Back Ground:** Carcinoma cervix often fails locally and/or within the pelvis. Common sites of metastases are the liver, bone, and bowel. We report a rare case presentation of cervical squamous cell carcinoma where in a synchronous solitary bony metastasis occurred in the right ischial tuberosity adjacent to the primary disease.

**Case Presentation:** A 70-year-old, postmenopausal lady presented with a complaint of per vaginal bleed and backache of 2 months duration. She neither had any comorbid conditions nor any significant medical or surgical history in the past. On primary examination, she was in a good general condition, with no pallor, pedal edema, or icterus. There were no palpable neck or inguinal lymph nodes at presentation. Per speculum and vaginal examination revealed 3×3 cm ulceroproliferative growth involving both lips of the cervix with involvement of all fornices except the posterior fornix. B/L parametrium was involved medially (left > right), with 1 x 1cm nodule over anterior vaginal wall, 2 cm from the introitus. Rectal mucosa was free.



*There was no bony tenderness elicited anywhere in the body. Blood investigations were found out to be normal. Cervical biopsy revealed squamous cell carcinoma of the cervix, and PET CT done for metastatic workup revealed bony sclerotic lesion at right ischial tuberosity along with the primary disease and regional lymphadenopathy leading to being staged as FIGO stage IV B by virtue of a bony met. Considering the patient's good general and oligometastatic condition, she was planned for intent radical chemoradiation with nodal boost followed by intra-cavitary brachytherapy for 3 # followed by SBRT (35Gy/ 5#) to the solitary bony lesion. Accordingly, she received EBRT to a dose of 50 Gy/ 25 # to the whole pelvis over 5 weeks with concurrent weekly Cisplatin (40mg/m<sup>2</sup>) as per the medical oncologist followed by a nodal boost to a dose of 5.4 Gy/3 # over the next 3 days. Further ICA Brachytherapy was delivered to a dose of 7 Gy each for 3 # one week apart and the patient was simultaneously planned and treated with SBRT to the solitary ischial tuberosity lesion to a dose of 35 Gy/ 5# on alternate days. Overall treatment time was 53 days. All the doses were calculated and summed up to remain within the tolerance limits of adjoining organs at risk with EQD2 to point A, rectum, bladder and sigmoid being 79.8 Gy, 67.5 Gy, 65.3 Gy, and 62.6 Gy respectively. The entire treatment was uneventful and well tolerated by the patient with maximum RTOG toxicity of skin –II, GI/GU – II. On first follow-up, the patient was asymptomatic with the follow-up PET CT scan being suggestive of complete response at the primary as well the oligometastatic site. As on date after 27 months of follow up patient is completely asymptomatic with no clinical or radiological evidence of the disease.*

**Conclusion:** *This is a rare synchronous metastatic presentation of cervical cancer with a solitary bony met in proximity to the primary lesion raising a treatment challenge in achieving a desirable clinical outcome with minimal side effects. Such synchronous metastatic lesions can be treated safely with a curative intent using advanced radiation delivery techniques like SBRT and may be considered for an aggressive treatment protocol than a palliative approach.*

**Keywords:** *Carcinoma of the uterine cervix, solitary bony metastatic lesion, SBRT, toxicity*



## Abbreviation's:

FIGO - International Federation of Gynaecology and Obstetrics

EBRT – External Beam Radiotherapy

SBRT – Stereotactic Body Radiotherapy

PET CT – Positron Emission Tomography and Computed Tomography

Gy – Gray

EQD2 – Equivalent dose in 2Gy fractions

# - fractions

RTOG – Radiation Therapy Oncology Group

GI – Gastrointestinal

GU – Genitourinary

CBCT – Cone Beam Computed Tomography

QOL - Quality of life

## Background

As per GLOBOCAN 2020, carcinoma cervix is the second most common malignancy in Indian females after breast cancer and ranks third in the overall population. In 2020 about 1,23,907 new cases were registered while 77,348 females had succumbed to the disease. [1] Cancer of the cervix often fails locally and/ or within the pelvis.

Common sites of metastases are the liver, bone, and bowel. [2–4] Bone metastasis in cancer of the cervix is relatively uncommon and indicates advanced disease with a poor prognosis. The incidence of bone metastases from cervical cancer ranges between 1.8% and 6.6% [5] Metastasis has been reported in all bones, with vertebra as the most common site and also in several unusual sites. [6-8] Fagundes et al report a higher incidence of 16% in a retrospective analysis of 1211 patients, mostly involving the thoracic and lumbar spine and ribs. [9] The incidence of bone metastases at various sites as reported by Yoon et al is lumbar spine 30.7%, followed by the pelvis 22.3% and the thoracic spine 15.1%. [10] Nevertheless, synchronous solitary pelvic bone metastasis is rare and might lead to a therapeutic challenge in delivering adequate curative doses of radiation without significant toxicities. Advanced radiation delivery techniques like SBRT have come to the rescue making it possible to achieve optimal and radical clinical outcomes without compromising on the normal tissue toxicity profile. We present one such case of oligometastatic carcinoma cervix treated radically using SBRT.



## Case Presentation:

A 70-year-old, postmenopausal lady presented with a complaint of per vaginal bleed and backache of 2 months duration. She neither had any comorbid conditions nor any significant medical or surgical history in the past. On primary examination, she was in a good general condition, with no pallor, pedal edema, or icterus. There were no palpable neck or inguinal lymph nodes at presentation. Per speculum and vaginal examination revealed 3×3 cm ulcero-proliferative growth involving both lips of the cervix with involvement of all fornices except the posterior fornix. B/L parametrium was involved medially (left > right), with 1 x 1cm nodule over anterior vaginal wall, 2 cm from the introitus. Rectal mucosa was free. There was no bony tenderness elicited anywhere in the body. Blood investigations were found out to be normal. Cervical biopsy revealed squamous cell carcinoma of the cervix, and PET CT done for metastatic workup revealed bony sclerotic lesion at right ischial tuberosity along with the primary disease and regional lymphadenopathy leading to being staged as FIGO stage IV B by virtue a bony met.

Considering the patient's good general and oligometastatic condition, she was planned for intent radical chemoradiation with nodal boost followed by intra-cavitary brachytherapy for 3 # followed by SBRT (35Gy/5#) to the solitary bony lesion. Accordingly, she received EBRT to a dose of 50 Gy/25 # to whole pelvis over 5 weeks with concurrent weekly Cisplatin (40mg/m<sup>2</sup>) as per the medical oncologist followed by a nodal boost to a dose of 5.4 Gy/3 # over the next 3 days.

Further ICA Brachytherapy was delivered to a dose of 7 Gy each for 3 # one week apart and the patient was simultaneously planned and treated with SBRT to the solitary ischial tuberosity lesion to a dose of 35 Gy/5# on alternate days. Overall treatment time was 53 days. All the doses were calculated and summed up to remain within the tolerance limits of adjoining organs at risk with EQD2 to point A, rectum, bladder and sigmoid being 79.8 Gy, 67.5 Gy, 65.3 Gy, and 62.6 Gy respectively. Plan parameters were divided into four different parts as depicted in Table 1 with respective dosimetric statistics.



Plan	DVH parameters
<b>Pelvic EBRT (50Gy/25#/5 weeks)</b>	<ul style="list-style-type: none"> <li>• <b>PTV_50/25 (Volume - 19.97cc): Maximum Dose: 54.28Gy, Mean Dose: 49.65Gy</b> <ul style="list-style-type: none"> <li>○ 95% dose was received by 96.91% volume of PTV</li> <li>○ 100% of PTV volume received 38.10 Gy dose</li> </ul> </li> <li>• <b>Bladder: Volume of 2cc bladder received 50.74Gy</b></li> <li>• <b>Rectum: Volume of 2cc bladder received 51.07Gy</b></li> </ul>
<b>Nodal Boost (5.4Gy/3#/3 days)</b>	<ul style="list-style-type: none"> <li>• <b>PTV Nodal Boost_5.4/3 (Volume - 61.18cc): Maximum Dose: 5.51Gy, Mean Dose: 5.28Gy</b> <ul style="list-style-type: none"> <li>○ 95% dose was received by 84.43% volume of PTV</li> <li>○ 100% of PTV volume received 4.05Gy dose</li> </ul> </li> <li>• <b>Bladder: Volume of 2cc bladder received 4.66Gy</b></li> <li>• <b>Rectum: Volume of 2cc bladder received 0.65Gy</b></li> </ul>
<b>Brachytherapy ICA (21Gy/3#, one week apart)</b>	<ul style="list-style-type: none"> <li>• <b>2CC Bladder dose: 11.3Gy</b></li> <li>• <b>2CC Rectum dose: 12.2Gy</b></li> <li>• <b>2CC Sigmoid dose: 9.6Gy</b></li> </ul>
<b>Bone Met SBRT (35Gy/5#)</b>	<ul style="list-style-type: none"> <li>• <b>PTV SBRT_35/5 (volume - 22.588cc): Maximum Dose: 40.44Gy, Mean Dose: 36.43Gy</b> <ul style="list-style-type: none"> <li>○ 100% dose was received by 95.86% volume of PTV</li> <li>○ 95% dose was received by 99.81% volume of PTV</li> <li>○ 100% of PTV volume received 31.41Gy</li> </ul> </li> <li>• <b>Bladder: Volume of 2cc bladder received 4.36Gy</b></li> <li>• <b>Rectum: Volume of 2cc bladder received 0.87Gy</b></li> </ul>
<b>Total cumulative OAR doses</b>	<ul style="list-style-type: none"> <li>• <b>2CC Bladder dose - 71.06Gy</b></li> <li>• <b>2CC Rectum dose - 64.79Gy</b></li> </ul>

Table 1

Entire treatment was uneventful and patient had tolerated well with maximum RTOG toxicity of Skin – II, GI/GU. On first follow up at 4 months patient had a complete clinical and radiological response as depicted in follow up PET CT shown in Figure 1 and Figure 2. Patient was kept on regular follow-up thereafter. As on date, after 25 months of follow-up, she is clinically asymptomatic with Grade I vaginal stenosis and no radiological evidence of any recurrence or distant metastases.

## Discussion

Carcinoma cervix is the second most common malignancy prevalent in Indian women, with an incidence of 19-44 per 100,000 women.[5] The risk of developing distant metastasis depends upon the presence of various poor prognostic features, such as advanced stage, endometrial extension, and local failure. Metastases from carcinoma cervix are predictable and well studied.[9] Apart from the local spread, the disease goes to the pelvic and para-aortic lymph nodes and then by hematogenous route to the supra

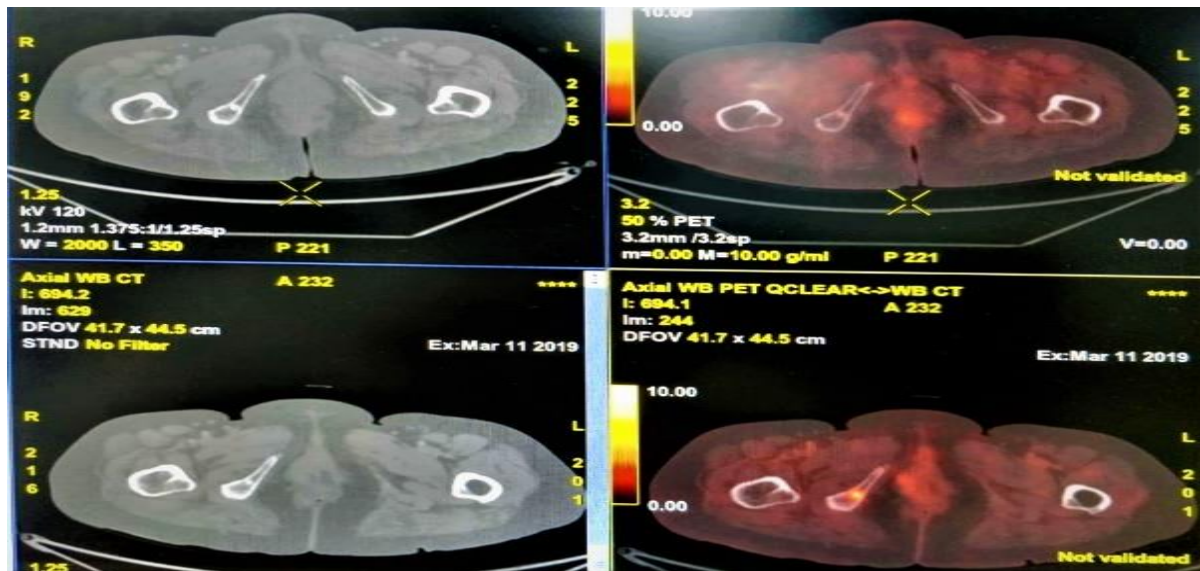


and infra-diaphragmatic viscera i.e. lungs and liver.

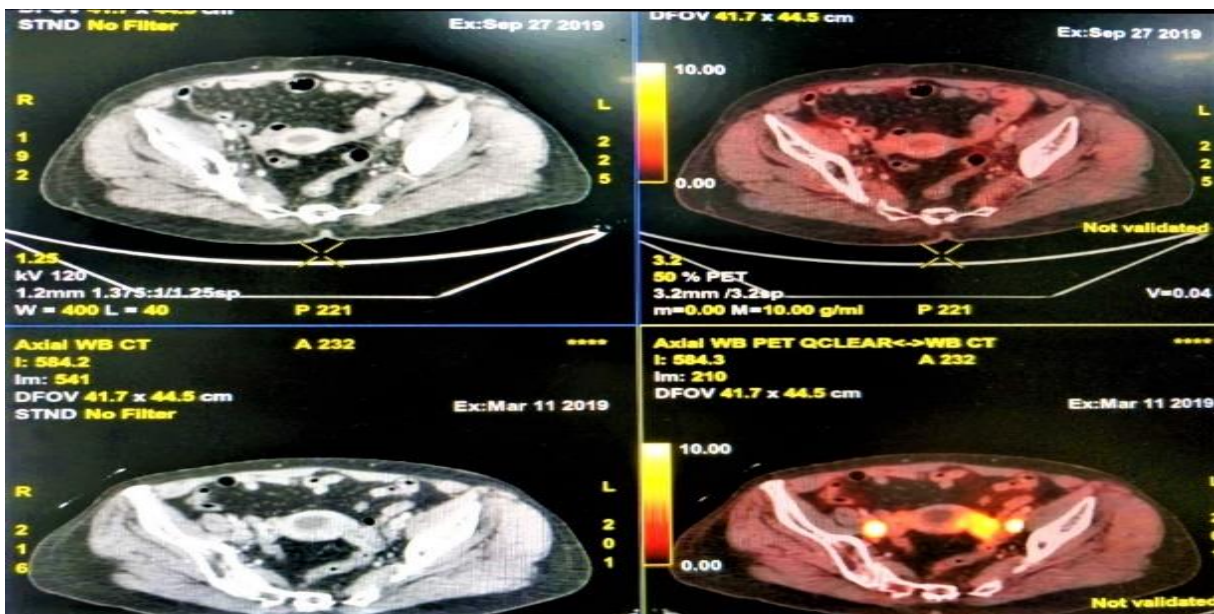
The frequency of bone metastasis is less. [7] Treatment of patients with such extensive metastasis is usually palliative. However, if the performance status is good with limited bone involvement (oligometastatic status), palliative treatment can be avoided, and instead, intent radical curative treatment may be offered, as in our patient. [11] FDG PET/CT is valuable in the assessment of distant metastatic disease. Liu et al studied patients with advanced-stage disease, lymph node metastases, and suspected recurrent disease, and found PET/CT to be superior to MRI and CT for evaluation of osseous disease. They also found an association between lymph node metastases and osseous metastatic disease. [12] Loft and colleagues found the metastatic disease in 10 of 119 patients and concluded PET/CT has a sensitivity of 100%, specificity 94%, positive predictive value (PPV) 63%, and negative predictive value (NPV) 100%. [13]

FDG PET/CT is a valuable tool to differentiate osteolytic lesions. The best cutoff value of SUVmax for differentiating MM from bone metastasis is 2.65. The significant correlation between the SUVmax of bone metastasis and that of primary tumors helps detect primary tumors [14] PET CT-based diagnosis was exclusively used in our case as fine needle cytology could not be attempted owing to the difficult anatomical site and smaller size of the lesion. Comparable SUV max to the primary also alleviated the need for the same. The prognosis of patients with bone metastasis is poor and most patients die within a year, after the appearance of a metastatic lesion. This poor prognosis is uniform and regardless of the duration of disease-free interval, or the presence of single or multiple organ metastases.[6] Modern advanced radiation delivery techniques like SBRT can result in better local control and pain management in non-spine bone metastases patients. [15] CBCT-guided SBRT is feasible and enhances setup accuracy using 3-D anatomical information. [16]

The same concept was utilized here along with the standard chemoradiation followed by brachytherapy protocol. The challenge of maintaining OAR doses below the threshold could be achieved using daily CBCTs, close patient follow-up, cumulative dose calculations, and adherence to strict immobilization and treatment protocols. Adjuvant chemotherapy was avoided in this case as per the patient's preference and to maintain a good QOL. Unlike the previous reports, this patient responded well to treatment and is free of disease, 27 months after detection of bone metastasis maintaining optimal QOL without significant side effects. She is on a routine 6 monthly follow-up as of now.



**Figure 1** – Comparative CT and PET CT images showing Complete Response at the solitary bony lesion in the first follow-up scan shown in the upper row vis-à-vis the index CT and PET CT depicted in the lower row.



**Figure 2** – Comparative CT and PET CT images showing Complete Response at the primary cervical lesion in the first follow-up scan shown in the upper row vis-à-vis the index CT and PET CT depicted in the lower row.



## Conclusion

The incidence of bone metastasis from carcinoma cervix is low and usually holds a poor prognosis. This is a rare synchronous metastatic presentation of cervical cancer with a solitary bony met in proximity to the primary lesion raising a treatment challenge in achieving a desirable clinical outcome with minimal side effects. Such synchronous metastatic lesions can be treated safely with a curative intent using advanced radiation delivery techniques like SBRT and may be considered for an aggressive treatment protocol than the traditional palliative approach.

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