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CASE REPORT

Carcinoma Cervix with Synchronous Isolated Pelvic Bone Metastasis:A case report and review of literature

Short title: Bone metastasis in carcinoma cervix

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Abstract

Background. Bone metastasis in cervix cancer is uncommon. Its incidence ranges between 1.8%-6.6%. It indicates that the disease is advanced and carries a poor prognosis.

Case Presentation. We present a 47 years female case of non-keratinizing squamous cell carcinoma cervix with synchronous isolated pelvic bone metastasis. The bone scan was suggestive of metastasis to bilateral pubic bones, ischium, and a suspicious lesion in the right

iliac bone. There is no well described management of oligometastatic cervical cancer. Management of metastatic carcinoma cervix is individualized, but palliative chemotherapy is mainly included and has a median survival of about ten months. The presentation, diagnosis of a patient of carcinoma cervix with synchronous isolated pelvic bone metastasis has been discussed. Because of bone metastasis, she was started on palliative chemotherapy (Inj paclitaxel and Inj carboplatin) and zoledronic acid.She has received 4 cycles of palliative chemotherapy and 3 cycles of zoledronic acid so far and has good response.

Conclusions. Synchronous isolated bone metastasis in carcinoma cervix is very rare and is associated with poor prognosis.Appropriate investigations and palliative treatment should be offered.

Key words

Carcinoma Cervix; synchronous; oligometastasis; pelvic bone; bone scan.

Introduction

Bone metastasis in Carcinoma cervix indicates that the disease is advanced and carries a poor prognosis (1). The incidence ranges between 1.8% - 6.6%(1,2).Bone metastases in cervical carcinoma commonly occurs in the axial skeleton, chiefly spine, ribs, and pelvis (2) . Yoon et al (3), reported the prevalence of bone metastases in the lumbar spine to be approximately 30.7%, followed by the pelvis at 22.3% and the thoracic spine at 15.1%. Also isolated metastasis of the humerus, tibia, fibula, calcaneum, tarsal, and metatarsal bones have been reported (4-8). Management of metastatic cervical cancer is individualized but palliative chemotherapy is mainly included and has a median survival of about ten months (9). We report on a case of a 47-years female with carcinoma cervix and synchronous isolated pelvic bone metastasis.

Case Presentation

A 47-years female presented to the Radiation Oncology outpatient department with a complaint of abnormal vaginal bleeding for five months. She had had no primary cervical screening. On vaginal and rectal examination, 5×4 cm ulceroproliferative growth was visualized, replacing both the lips of the cervix, involving all the fornices and reaching up to the lower one-third of the vagina with the involvement of bilateral parametrial up to the pelvic wall. Blood parameters reported normocytic hypochromic anemia of 6 g/dl, for which she received two units of PRBC transfusion. She had normal renal and liver function tests. CECT Thorax and Abdomen scan showed heterogeneously enhancing mass measuring

5.2x6x4.2cm involving the uterine cervix extending to involve the lower third of the vagina inferiorly and superiorly involving the lower uterine segment along the anterior myometrium. Laterally, the disease infiltrated into the parametrium bilaterally; anteriorly, there was loss of fat planes with the urinary bladder and posteriorly focal loss of fat planes with the rectum. Also, mesorectal deposits with subcentrimetric bilateral external and common iliac lymph nodes were seen (Figure 1).

Figute 1-CECT Abdomen showing lytic lesion in right Ischium bone.

Lytic lesions were seen involving bilateral inferior pubic rami. Cystoscopy showed a bulge on the posterior wall of the urinary bladder with intact mucosa. The bone scan suggested metastasis to bilateral pubic bones, ischium, and a suspicious lesion in the right iliac bone (figure 2).

Figure 2- Bone scan showing metastasis to bilateral pubic bones, Ischium, and the right iliac bone

The cervix biopsy results were suggestive of non-keratinizing squamous cell carcinoma cervix. The patient was clinically staged as FIGO stage IVB. Because of bone metastasis, she was started on palliative chemotherapy (Inj paclitaxel and Inj carboplatin) and zoledronic acid.She has received 4 cycles of palliative chemotherapy and 3 cycles of zoledronic acid so far. Post 4 cycles palliative chemotherapy and 4 cycles of zoledronic acid CECT thorax and abdomen is suggestive of significant reduction the size of primary lesion and sclerotic change of previously existing lytic deposits in bilateral pubic rami and right ischeal tuberosity. She has good response and is doing well.

Discussion

In females, carcinoma cervix is one of the most common malignancies.

Effective prevention strategies for cervical cancer include the use of screening tests for primary and secondary prevention, human papillomavirus (HPV) vaccination, and early detection and treatment of cervical intraepithelial neoplasia(10)

Artificial Intelligence interpretation of cervical smears or images could serve as an aid when combined with human evaluation. Further studies on prediction and detection are needed for making appropriate decisions about the treatment of cervical cancer(11). The incidence of bone metastasis varies from 1.1-8.2% (12-13). Incidence may be as high as 8.6-17.9%, as

per autopsy data reports (12-13). Case reports of Carcinoma Cervix with Isolated bone metastasis have been summarised in Table 1.

Yoon *et al (3)* included patients with bone metastasis with invasive uterine cervix carcinoma in their study and concluded that advanced stage , adenocarcinoma, and initial multiple metastasis of bone are account for earlier bone metastasis. Pattern of spread in carcinoma cervix is via direct involvement and predominantly through lymph nodes, haematogenous spread is somewhat uncommon. Bone metastasis is uncommon, and frequently involves the vertebral column, succeeded by pelvic bone while in appendicular bones, it is rather uncommon (17). Isolated metastasis to humerus, fibula and patella arising from carcinoma uterine cervix have been reported in many studies (6,7,18). Table 1 mentions few case reports with isolated bone metastases.

There are multiple possible mechanisms of bone metastasis. These are:
1. Direct spread to the bone from the pelvic soft tissue tumor in the parametrium.
2. Direct spread from soft tissue metastasis to bones outside the pelvis.
3. Batson's venous plexus as a route of spread to pelvic bones or the spine.
4. Spread to bones by hematogenous circulation of tumor cells.
There may be involvement of more than one mechanism in some patients (13).

Yun Han et al assessed the risk of metastasis to bone in patients wth cervical cancer by several models and found that risk factors are older age (more than 50 years), poor differentiation, non-squamous histology, advanced stage, along with other organ metastasis and no surgery at initial management. Carcinoma patients with advanced age, advanced disease, non squamous histology, and lymphatic metastasis are associated with high risk of bone metastasis and contribute to poor prognosis.
Nartthanarung A et al. described that patients of carcinoma cervix with bone metastasis younger than 45 years have poorer prognoses than elderly patients (15). Our case is of 47 years old, non-keratinizing squamous cell carcinoma, with advanced stage and involvement of pelvic lymph nodes.

The patient in our present case was asymptomatic for bone metastasis, an incidental diagnosis on imaging. Patients with bone metastases usually present with severe pain in metastatic sites which can lead to pathological fractures (16). Clinical symptoms along with imaging and histopathology, help in early diagnosis of bone metastasis rising from cervical cancer.

In this patient, a bone scan revealed increased radioactive uptake in bilateral pubic bone and Ischium. Standardized treatment are required for malignant tumors with bone metastases. Current treatment options focus on pain relief, improving overall survival and improving quality of life (20).

Pasricha *et al (6)* in the study included metastatic patients with good performance status and concluded that surgery and concurrent chemo radiotherapy might help in achieving good results. In their study, a patient of carcinoma cervix, FIGO stage IIB developed metastasis to fibula bone after nine months of treatment completion and underwent excision of the metastatic fibular lesion. The patient was disease free 4 years after presentation of primary symptoms.

Bisphosphonates are used in palliative setting and are effective in pain relief, lowers the chances of pathological fracture, and improve the quality of life but do not prolong survival (21)

Corrado *et al (20)* reported a stage IIB poorly differentiated cervical adenosquamous carcinoma cervix patient who underwent surgery of a metastatic lesion to femur but after 3 months, patient died. Bone metastasis carries a poor prognosis. It usually develops within two years of the primary tumour diagnosis and patients die within 18 months of diagnosing metastasis to bone.

Abdul-Karim *et al* (16) in their study included twenty cases of carcinoma cervix with metastases to bone and identified that 71% of bone metastases occurred within first two years of diagnosis.

Zhao *et al (22)* analysed of eight patients of malignant uterine tumour with bone metastases. Their results were consistent to those reported by Abdul-Karim *et al.*

The prognosis of carcinoma cervix patients with metastasis to bone correlated with the number of bone metastatic site and disease burden (22). Standard treatment of primary malignant tumors or treatment options for bone metastases have been found to contribute to the prognosis.

Platinum based combination chemotherapy is the standard management for patients with metastatic carcinoma cervix with low response rates, and the median survival is less than 1 year (23). With the addition of Bevacizumab in addition to standard chemotherapy, the median overall survival is less than 18 months. In these two studies, chemotherapy was continued till

the progression of disease or in case of severe toxicity and in those patients who did not respond (9,23).

At present, immunotherapies have transformed the management of many solid tumors, including cervical cancer, and this approach is constantly evolving. For instance, in 2018, the American Food and Drug Administration (FDA) approved the programmed death 1 (PD-1) inhibitor pembrolizumab for patients with recurrent or metastatic cervical cancer whose tumors express PD-L1 (28).

Later,tisotumab was approved for second-line r/m cervical cancer,and pembrolizumab combined with chemotherapy ± bevacizumab was approved for first-line reccurent/metastatic disease based on the results of the KEYNOTE-826 study. In 2024, the results of different clinical trials are expected, considering that immunotherapy has the opportunity to establish new standards of care in the treatment of cervical cancer, and new biomarkers can be used to identify the ideal patient populations for these therapies (29).

In our case report, we started patient on palliative chemotherapy (Inj paclitaxel and Inj carboplatin) and zoledronic acid.She has received 4 cycles of palliative chemotherapy and 3 cycles of zoledronic acid so far.Post 4 cycles palliative chemotherapy and 4 cycles of zoledronic acid CECT thorax and abdomen is suggestive of significant reduction the size of primary lesion and sclerotic change of previously existing lytic deposits in bilateral pubic rami and right ischeal tuberosity. The strength of our study is that the patient has good response and is doing well. The limitation of our case report is that the patient is still on treatment. Treatment completion and follow up is required to know the outcome and prognosis of the disease in our patient.

Conclusion

Synchronous isolated bone metastasis in carcinoma cervix is very rare and is associated with poor prognosis. Bone scan in such patients is only indicated in case of patient being symptomatic or incidental finding on radiological imaging. Prognosis remains poor in presence of bone metastasis. Appropriate investigations and palliative treatment should be offered.

Authors contribution:

K.K. → Conceptulisation,Data curation, Formal Analysis, Investigation, Methodology, Project administration,Resources,Validation,Visualisation,Writing-original draft

S.R.N. →Investigation,Resources.

J.S. →Resources,Software.

R.R. →Investigation, Software.
N.R.S. →Software.Visualisation.
A.R. →Investigation,Visualisation.
S.G. →Project Administration, Writing-Review and editing, Methodology, Formal Analysis, Conceptualisation, Visualisation.
M.G. →Validation,Project Administration, Formal Analysis.

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Informed consent: yes.

EQUATOR network-Conform with CARE (Consensus based Clinical case Reporting) guidelines.
Data sharing: No.

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Figure 1. CECT Abdomen showing lytic lesion in right Ischium bone.

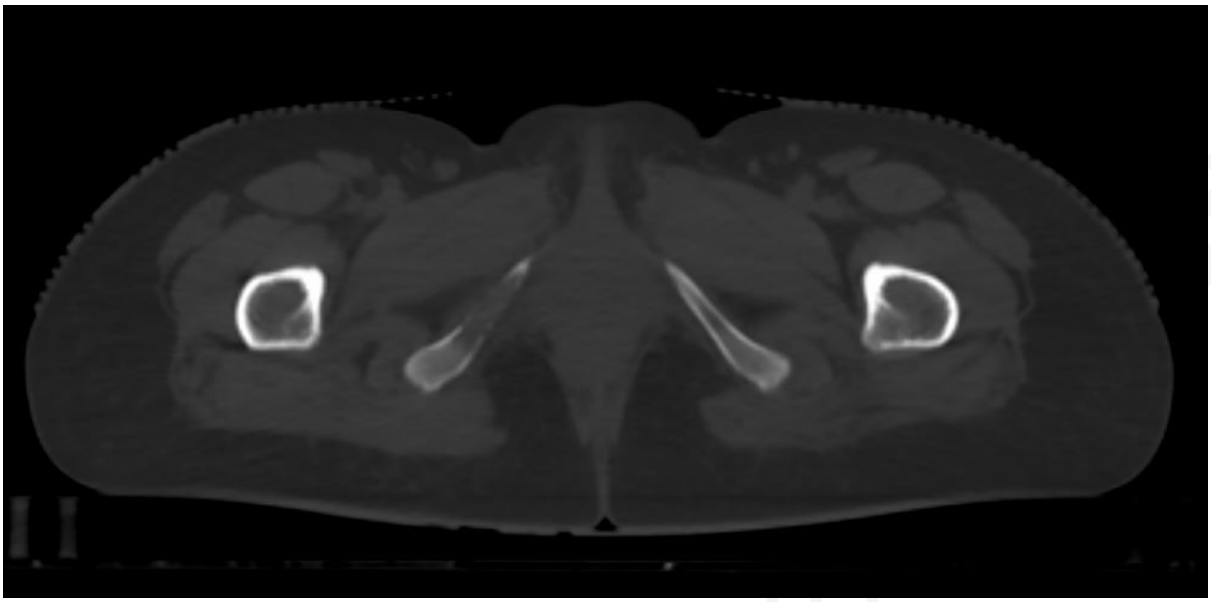
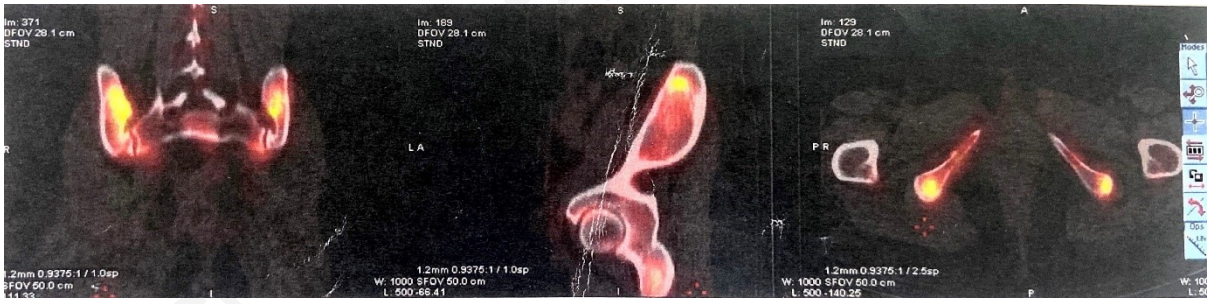


Figure 2. Bone scan showing metastasis to bilateral pubic bones, Ischium, and the right iliac bone.



Reference	Age	Histology	Stage	Site of metastasis at presentation	Site of bone metastasis	Synchronous/ Metachronous	Treatment	Follow up (after bone Mets diagnosis) and status at last f/u
Dewdney et al. [24]	70	SCC	IIIA	None	Right tibia, fibula and calcaneum	Metachronous	30Gy/10 # RT	NA

Crisci et al. [25]	41	Adenocarcinoma	IIIB	None	Left ischio-pubic branch	Metachronous	Chemotherapy	NA
Pasricha et al. [6]	36	SCC	IIB	None	Right fibula	Metachronous	Surgery	48 months (Alive)
Agrawal et al. [26]	60	SCC	IIIB	None	Scalp (calvaria)	Synchronous	20Gy/5# RT	NA
Yaun et al. [8]	43	SCC	IVB	Bone	Right tibia	Synchronous	Surgery/ Chemotherapy	41 months (Alive)
Corrado et al. [20]	40	Adenosquamous	IIB	None	Left femur	Synchronous	Surgery	3 MONTH (Death)
Robles et al. [27]	41	Epidermoid carcinoma	IIIB	None	Scalp (skull bone)	Metachronous	51Gy/17 # RT	18 months (Alive)

Table 1. Case reports of Carcinoma Cervix with Isolated bone metastasis.