

# Metastatic bone involvement in vulvar cancer: report of a rare case and review of the literature

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## Summary

**Purpose:** Bone metastasis secondary to vulvar carcinoma is an infrequent clinical entity. Only ten cases have been published in the literature. We describe a case of squamous vulvar carcinoma, that presented with cervical vertebral involvement, as a part of distant spread. **Case:** A 69-year-old woman presented with radicular pain and a painful cervical mass. MRI of the cervical spine was performed, showing an osteolytic lesion with spinal cord compression. **Conclusion:** This case was unique in presenting vertebral metastasis eight months after chemotherapy and radiotherapy.

**Key words:** Vulvar cancer; Bone metastasis; Radiotherapy.

## Introduction

The incidence of vulvar cancer in women is increasing, especially in younger women [1-4]. The incidence of invasive vulvar cancer is approximately 2.5 per 100,000 women per year in Germany [2]. For the UK similar age-adjusted incidence rates have been reported [5]. The main route of dissemination is by transcoelomic spread and through the lymphatics. Hematogenous spread is uncommon. Metastasis to bones from these tumors is rare and is reported in a few series [6, 7]. The prevalence of bony metastases secondary to vulvar carcinoma is reported to be far minor, 10% [6, 7]. In other gynecological squamous cell carcinomas such as cervical cancer, the prevalence is 15-29% [6, 8, 9]. Bone metastases from epithelial ovarian carcinoma are rare, usually discovered postmortem. The survival of these patients is poor. Since 1966 only three cases of endometrioid ovarian carcinoma with metastasis to the skeletal structures have been described in the literature [10-16]. Metastasis to bone from endometrial adenocarcinoma is rare but when metastasis occurs it usually locates in the axial skeleton [11]. Skeletal metastasis from carcinoma of the cervix occurs in 0.8-23% of cases. The majority of bone metastases are either in the long bones or in the vertebrae [12].

Spinal cord compression is an infrequent event in the natural course of metastatic vulvar carcinoma. A review of the literature showed only a few patients who developed radiculopathy or spinal cord compression secondary to bone metastases (Table 1). Malignant epidural spinal cord compression (MESCC) is a medical emergency that needs rapid diagnosis and treatment to prevent paraplegia. Patients with malignancy who present with a new onset of neurological signs and symptoms should undergo emergent evaluation including magnetic reso-

nance imaging (MRI) of the entire spine. Simultaneously, spine surgery and oncology teams should be consulted immediately. The initiation of early treatment can improve the quality of life and survival of the patients.

## Case Report

A 69-year-old woman presented to a local gynecologist with a vulvar mass, distention of the abdomen, loss of appetite and vague abdominal discomfort of three months duration. The patient had a medical history of hypertension and a negative family history for malignancies. Initial physical examination revealed a vulvar mass with associated palpable bilateral inguinal lymphadenopathy. Laboratory examinations were performed but did not lead to any remarkable finding. An ultrasound and an abdominal computed tomography (CT) scan were ordered, and showed a vulvar mass with anal, rectal invasion and inguinal, obturator, and external iliac lymphadenopathy. Radiograph of the chest was normal. A diagnosis of vulvar malignancy was made based on multiple biopsies. The histopathology report of the specimen showed a squamous cancer, grade 3. The patient was staged as having Stage IVB vulvar cancer (as per the FIGO 1986 staging system). Induction chemotherapy with paclitaxel and carboplatin was planned. The efficacy of this therapy has been analyzed by Noronha *et al.* [20]. The patient received chemotherapy at three weekly intervals under antiemetic cover. On imaging (abdominal CT scan) there was a partial response to induction chemotherapy. Extensive surgery was discussed, but the patient refused to undergo surgery. Because of this decision, she was started on concurrent chemotherapy (carboplatin) and external beam radiotherapy to the pelvis and inguinal nodes. She tolerated chemotherapy and radiotherapy well and was on regular follow-up thereafter. An abdominal CT-scan demonstrated partial response of the disease. According to the surgical standard of care of vulvar carcinoma, if cN+ is fixed or ulcerated, pre-op chemo-RT (45-50 Gy with cisplatin, 5-FU, and/or mitomycin C) provides about 50% complete response. Surgical salvage for persistent or recurrent disease includes bilateral lymph node dissection, while if there is extra nodal capsular extension, then a boost to

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Table 1. — Cases of metastatic bone lesions related to vulvar carcinoma.

Author/Group	No. of patient	Age	Dose to primary	Dose to metastatic	Localisation	Time to metastasis	Survival after primary diagnosis
Brufman <i>et al.</i> [16] (1978)	1	—	NA	—	Tibia	NA	—
Abdul-Karim <i>et al.</i> [18] (1990)	4	—	NA	—	Vertebrae Pelvic Bones	NA	9 months (range 3-21)
Fischer <i>et al.</i> [6] (2005)	1	68	59.4 Gy	—	Humeral Heads, Diaphysis Femur	4 months	—
Seltzer <i>et al.</i> [15] (1976)	1	59	NA	3990 cGy	Vertebrae Ulna Ribs Skull Humerus	12 months	—
Sharma <i>et al.</i> [12] (1985)	3	68 49 78	5000 cGy 5200 cGy NA	3000 cGy	Humerus Femur Tibia Fibula	4 months 2 months	9 months 9 months 9 months

NA: not applicable.

60 Gy is employed, or in case of gross residual then irradiation up to 65-70 Gy [14]. Eight months later, the patient presented with a painful cervical mass, of one month's duration. The mass had gradually increased in size. On clinical examination, a firm and well circumscribed mass was palpable in the cervical spinal region, without ulceration or discharge. According to the sensory examination, radicular pain, weakness and sensory deficit were noted. She was investigated with a cervical spine MRI that showed an osteolytic lesion and presence of a paravertebral mass, suggestive of bone metastases in C1-C3 vertebrae. Epidural soft tissue collection was also present causing compression of the thecal sac, at the C1 vertebral level. The patient underwent MRI of the entire spine. There were no other bone metastases. Dexamethasone (10 mg IV bolus) followed by 16 mg per day in divided doses was administered. Fine needle aspiration cytology of the lesion was performed. A cytological diagnosis of a lesion favoring squamous carcinoma was rendered. She was diagnosed with progression of disease. Radiation therapy of the cervical spine was performed. She received palliative radiotherapy to the cervical spine (30 Gy in 10 fractions). After completion of radiotherapy (RT) there was symptomatic improvement in the pain intensity. When disseminated disease was diagnosed on the imaging control for the restaging, there were no other distant metastases present. The vulvar and lymphatic situation were stable at the time of recurrent disease. The patient was then treated by second-line chemotherapy with cisplatin and 5-FU. On second-line treatment there was a partial response on imaging after three cycles of chemotherapy. The patient presented five months after the diagnosis of cervical metastasis with lumbar pain. MRI of the lumbar spine showed an osteolytic lesion at the level of the fourth lumbar vertebra. The patient received radiotherapy to the lumbar spine (30 Gy in 10 fractions). At present, she is still alive 12 months after the diagnosis of the first metastatic bone involvement.

## Discussion

Vulvar cancer should not be considered a disease that remains confined to the pelvis and abdomen. This disease



Figure 1. — MRI image: spinal cord compression.

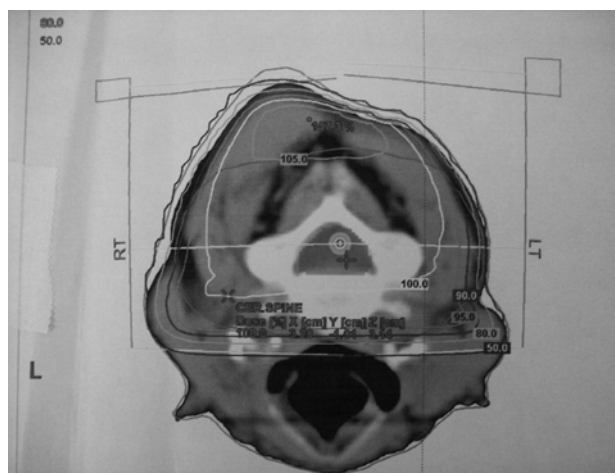


Figure 2. — RT plan (ECLIPSE Varian, TPS).

has significant potential for distant metastasis. Bony metastasis from vulvar malignancies is a rare pathologic entity, whose behavior is not completely understood. Reviewing the literature, only ten cases have been reported.

In 1976 Seltzer *et al.* [15] presented one case of multiple bone metastases. In 1978 Brufman *et al.* [16] reported a case of tibial involvement. As mentioned by Brufman *et al.*, different gynecological tumors tend to spread through the lymphatic system rather than by the hematogenous system. This might be a possible explanation for bone metastases being infrequent in gynecological malignancies [16]. Sharma *et al.* [17] in 1985 found three cases of clinically Stage III (FIGO classification). Postoperatively, these patients were found to have metastatic carcinoma of the bones. These findings suggest that patients undergoing surgery with advanced disease should have a bone scan or a bone survey as part of the preoperative workup [18]. Abdul-Karim *et al.* [18] in 1990 reported four cases of asymptomatic skeletal metastases during autopsies. It was supposed that osseous metastases might not be rare but significantly more common than clinically expected.

In 2005 Fischer *et al.* [6] described a case of multiple osseous involvement in a woman with a history of vulvar carcinoma who presented with pain confined to the bones. The epithelial origin of the lesion was confirmed by immunohistochemical examinations (overexpression of pan-cytokeratin MNF116) [5]. The atypical location should alert the physician to suspect distant metastases, rather than locoregional disease. The treatment modalities available for bone lesions are individualized with a definite role of corticosteroids, RT, chemotherapy, surgery and biphosphonates. The pretreatment degree of neurologic dysfunction and the radiosensitivity of the tumor are the strongest predictors of therapeutic outcome. Radiotherapy is an important part of the management of metastatic involvement and it helps in pain relief, cytoreduction of tumor, prevention of progressive neurological dysfunction and structural damage to the cord.

Malignant epidural spinal cord compression is a common neurologic complication of cancer. It represents a medical emergency that needs rapid diagnosis and treatment to prevent undergoing emergent evaluation including magnetic resonance imaging of the entire spine. The most common treatment offered is radiotherapy [19]. Available evidence suggests that the radiotherapy dose should be tailored to the individual patient, depending on the subtype of the tumor, the extent of metastatic disease and expected survival. Risk stratification for the optimum dose prescription for patients with spinal cord compression is recommended. If epidural spinal cord compression is diagnosed, corticosteroids should be administered. If indicated, patients should undergo maximal tumor resection and stabilization, followed by postoperative radiotherapy. Emerging treatment options such as stereotactic radiosurgery and vertebroplasty may be able to provide some symptomatic relief for patients who are not surgical candidates [15].

## Conclusion

Bone staging should be performed in advanced cancer stage in order not to overlook metastasis. The treatment of choice is always radiotherapy and should be administered as soon as possible. In case of a metastatic lesion in the spinal cord, an MRI study is the exam of choice.

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