Acrometastases of the foot from vulvar squamous cell carcinoma: A case report

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Squamous cell carcinoma (SCC) of the vulva is a serious malignancy of the female genitalia, which in rare cases has the potential to metastasize to bone. Currently, there are only 12 known such cases of bone metastases reported that are directly linked from vulvar cancer. Acrometastasis, which is when a malignancy metastasizes to distal extremities beyond elbow or below the knee is a known rare phenomenon. It is even more uncommon when a tumor spreads to the bones of the foot. The literature is sparsely reported with only a few known articles of female genitalia metastasizing to the foot metatarsals with no known prior literature on specifically vulva SCC metastasizing to foot. In this case report, we present a case of a 68-year-old female with a complex history of vulva SCC treated with a prior radical vulvectomy and lymph node dissection about seven years before it was discovered that there was near complete osseous destruction of the third metatarsal. A pre-operative planning MRI distinguished the mass as actually a large soft tissue tumor rather than osteomyelitis. An incisional biopsy of the 4.7x3.6x5.8cm tumor was surgically performed with the goal of diagnosis. Surprisingly, the biopsy confirmed bone metastases to third metatarsal from vulvar SCC. The patient was referred for an extensive oncological work-up and multiple points of further metastases were identified. This case report briefly summarizes the limited literature on vulva cancer bone metastasis. The goal of this article is to establish that the potential exists for vulvar SCC to metastasize to the metatarsal. A well-trained physician should consider the possibility of acrometastases when encountering an unidentified soft tissue mass with the goal of identification. Surgical and oncological treatment of the lesion with early, aggressive intervention is important as suboptimal care may result in further metastatic spread.

**Keywords:** vulva cancer metastasis, squamous cell carcinoma, bone metastasis, metatarsal cancer

Each year in the United States there are roughly 4,000 new cases of vulva cancer, the fourth most common gynecologic cancer. Unfortunately, about 900 deaths each year will also be linked to vulvar cancer [1]. The most common form of vulva cancer is squamous cell carcinoma (SCC). This is most commonly found in postmenopausal women greater than 50 years old. Although the majority of vulvar SCC cases are found in situ and are able to be excised, SCC does have the capacity for metastatic spread. Clinical management of vulva cancer is complex and dependent on staging whether groin lymph nodes are involved and how many sites of metastatic spread are present. The 5-year survival rate of vulva cancer for negative lymph
nodes is 70-93% while it decreases to 25-41% once lymph nodes are involved [2]. If the cancer metastasizes, it will likely spread through the lymph system like other gynecological cancers. The vast majority of these metastases, however, do not metastasize to the distal extremities. This phenomenon when a tumor seeds distal to the knee or elbow is known as acrometastasis [3,4]. Acrometastases account for only about up to 0.3% of all metastatic tumor sites [3]. If it occurs, it paints an ominous clinical picture as there is likely widespread metastatic disease that is uncontrolled. The findings of Healey, et al., reviewed 41 sites of acrometastases in 29 patients to the hands or feet. Their study concluded there was no statistical difference on survival in the location of acrometastases, amount of acrometastases, or age [3]. By definition, acrometastases must be attributed to a primary site of origin. SCC in particular mostly occurs from the primary locations of lung, colon, and kidney [4]. Nearly half of acrometastases occurs from the lungs [3].

Vulva cancer rarely spreads to the bone and to our knowledge, there has not been an incident of vulva cancer metastasized to the foot reported in literature before. There have, however, been rare case reports of other types of genitalia cancer previously published to metastasizing to the foot, such as from the vagina and endometrium [6,7,8]. In a retrospective study performed by Prieske, et al., of 391 patients with primary vulva cancer, only 20 presented with distal metastasis and only 5 of these were known to be involved in bone [9,10]. Fischer, et al., specifically reported a case of distal humerus bone metastasis in a patient with a radical vulvectomy and lymph node dissection [10]. There has only been reported up to 12 cases of reported prior bone metastases from vulvar carcinoma [11]. These exceptionally rare instances of bone metastasis may travel to the upper or lower extremities, but have not been reported in the foot. One sign of this occurring has been suggested to be a pathologic fracture [3,12]. If discovered, the goal when treating squamous cell carcinoma in bone is most likely to remove the mass completely with clean margins to prevent further metastasis as quickly as possible. Unfortunately, this may result in partial or total amputation procedures depending on the location that it appears in the foot. In a case series of nine cases of SCC of the foot by Knackfuss, et al., treated with partial or total amputation, they had 7/9 cases with no recurrence or spread of the tumor the authors determined was due to inadequate excision [13]. Following excision, appropriate chemotherapy and/or radiation should then be administered based upon a full individual oncologic workup.

Squamous cell carcinoma in general is abnormal proliferation of keratinocytes that may manifest as either a de novo tumor or metastatic site [14,15]. Squamous cell carcinoma happens to be the most common primary cancer of the soft tissues in the foot, mostly appearing in the soft tissue rather than being involved in the bone when it is the primary site. Through hematologic spread, it may manifest in the bone rather than in the soft tissue. Of course, due to the overall rarity of SCC in the foot, it can lead to delays in diagnosis, especially if there is no apparent soft tissue changes. The longer SCC is left untreated, the greater chance it can grow and spread further throughout the body. It is, therefore, of the utmost importance to identify SCC early and be aggressive with excisional treatment. In a case series of 12 patients by Potter, et al., it was determined that 11/12 had no evidence of recurrence following amputations achieving desirable results [14]. With the presence of epidermoid SCC confined to the soft tissue, radiographically it will be benign, but when the bone is involved it can appear as osseous erosions. Biopsy via pathological examination of tissue is the gold standard for identification. It is important for the surgeon to be prepared for a variety of excisional approaches based upon the pathological results of the biopsy. A Mohs procedure depending on the extent of the tumor could be a good option to take thin slices of tissue for fresh frozen histology analysis to achieve complete intra-operative resection of the tissue.

Case Report

A 68-year-old female patient was first seen as a hospital consult following three months of worsening left foot pain. The patient had a well-documented extensive past medical history of Stage II N0M0 vulva cancer, which had been treated by radical vulvectomy, lymph node dissection about 7 years prior.
The patient's past medical history included atrial fibrillation on coumadin therapy, congestive heart failure, chronic obstructive pulmonary disorder, prior deep vein thrombosis, basal carcinoma of the skin, hyperlipidemia, and hypothyroidism. Prior to consultation by the podiatrist, the patient had incorrectly attributed the foot pain as peripheral neuropathy secondary to chemotherapy and thus, had not sought prior foot workup. This was significant for delaying appropriate treatment. Upon physical exam, she did not have any open ulcerations or obvious mass.

The foot did not have any epidermal changes that were concerning for cancer as visualized in Figure 1. She did not have appreciable fluctuance but did have tenderness to palpation overlying the third metatarsal with mild edematous changes. No erythema was noted to the foot. On initial imaging, there was nonspecific increased uptake in a ceretec bone scan along the midfoot of the left foot (Figure 2). Follow-up left foot radiographs in AP and lateral views showed near complete destruction of the third metatarsal as seen in Figure 3A and 3B. The bone scan and radiograph findings were immediately concerning for possible osteomyelitis. A preoperative MRI was ordered and showed a large enhancing lesion measuring 4.7x3.6x5.8cm in the space of the third metatarsal identifying a neoplasm rather than infectious process, seen in figures 4A and 4B. It was most important to identify the cause of the osseous destruction, so an incisional biopsy was scheduled. The biopsy was performed utilizing a dorsal incision and identifying a yellowish soft tissue mass (Figure 5) with very little identifiable remnants of the third metatarsal. Two pathology samples were taken, one of which sent to pathology for stat frozen section intraoperative biopsy that determined it was a clean margin. Pathological examination of the excised mass was positive as a site for metastatic squamous cell carcinoma and positive immunohistochemical staining for CK 5/6, P40, and weakly positive GATA3.
medication to the chemotherapy regimen. Following two more months of treatment, the patient was switched to three cycles of alimta. Follow-up CT showed a further increase in liver lobe mass along with 1cm bilateral pulmonary nodules and 3cm left renal mass were identified in the patient and a left anterior thigh lesion. She then failed navelbine chemotherapy due to excessive vaginal bleeding. Unfortunately, at this time the patient was deemed no longer a candidate for chemotherapy and became increasingly frail. The patient unfortunately passed away due to complications with metastatic cancer.

**Discussion**

There have been only 12 total reported cases of bone metastases from vulvar cancer [9]. There are no known cases of vulva SCC metastasizing to the bones of the foot as far as the authors can determine. Despite the rarity of this occurrence if left untreated it can be dangerous resulting in further metastatic spread, amputation, limb loss, and/or death. A higher index of suspicion should be present for any patient with a history of vulvar SCC cancer. Pain and pathologic fracture should not be taken lightly and radiographs should be the foremost method of determining whether osseous involvement is involved. If osseous erosion is suspected, an MRI should be the diagnostic modality of choice in determining how to proceed.

There are three possible explanations of how acrometastases actually occur from vulva cancer. One explanation is that metastasis can occur both proximally and distally and that the malignancy started in the foot rather than the vulva. This is however very unlikely in our case report as the vulva cancer was identified and treated nearly 6 years prior to any foot complaint. A second theory is via lymphatic spread, which as a gynecological cancer is of a much higher probability than hematogenous route [11]. Preventative measures were taken in the original treatment of the patient presented in our case report to prevent lymphatic spread by the original surgeon performing a lymph node dissection in addition to the radical vulvectomy. It is suggested that tumor cells can travel from the lymphatic system and could then enter the venous return and be carried along ultimately into the arterial systemic circulation [6,15]. Batson’s paravertebral valveless venous plexus is a third proposal to how acrometastases can occur.

**Follow-up**

The patient had no known recurrence or metastasis for about the first seven years following her initial vulva SCC diagnosis until the foot mass was indeed identified. This metastatic finding was a poor prognostic indicator. Following the surgery, CT chest and pelvis unfortunately revealed new 4.5cm right lobe liver mass and abnormal adnexal region. This was treated by oncology with two months of carboplatin and taxol chemotherapy regimen. Despite medication, the liver mass was shown to grow to 6.5cm, so avastin was added as a third
This theory suggests pelvic veins can quickly travel to distal sites circumventing more common veins [6,16].

In conclusion, we hope that physicians are aware of the potential for vulva SCC to metastasize to the foot as this was not previously published. If osseous involvement in a patient is observed on radiographs with a history of vulva SCC, then ancillary imaging and biopsy should be performed for definitive diagnosis. If possible, a well-trained physician should be prepared for possible aggressive excision or amputation which may be required with wide, clean margins. In the rare cases that a tumor seeds distally, it is important to be realistic about the survival outcomes once acrometastases has occurred and be upfront with the patient. Cancer is highly complex and unique to each patient so a careful review of the patient history and treatment plan should be considered on an individual basis. The correct sequence of appropriate chemotherapy and/or radiation determined by an oncologist to prevent further metastatic spread also varies. Our surgical goal in identification of this soft tissue mass via incisional biopsy was to help determine a diagnosis to aide in the oncological treatment plan to prolong this patient’s life. Further case studies on this topic of acrometastases of vulva SCC, especially in the foot, should be published to improve identification and management of this rare finding.

References