Eccrine Porocarcinoma: A Case Report of a Rare Soft Tissue Malignancy and Review of Treatment Recommendations

Allison McNamara, DPM
Tony Nguyen, DPM

INTRODUCTION

Eccrine porocarcinoma, also known as malignant eccrine poroma, is a rare, slow growing, locally aggressive tumor of the eccrine sweat gland (1). It often arises in the setting of a long-standing history of benign eccrine poroma (BEP), with a transformation rate of about 18%. It is potentially fatal (1,2). Although it is rare, representing only 0.005% of epithelial cutaneous neoplasms (2-5), when it does occur it demonstrates aggressive behavior compared with common nonmelanoma skin cancers (4). Eccrine porocarcinoma has been found to be chiefly a tumor of elderly adults, occurring most often in the 6th or 7th decade, and some suggest a male bias although this is questionable. Location of the lesions may vary, although they are most commonly found on the lower extremity (50%), head and scalp (20%), upper extremity (12%), and abdomen (10%) (2,3,5). There is an incidence of regional lymph node involvement of approximately 20% with distant metastases noted in about 10% (4). If distant metastases develop, they occur most often in lymph nodes, the lungs, the retroperitoneum, and the liver and they are felt to have a poor prognosis and high mortality (3). Here, we present a case of a single eccrine porocarcinoma of the great toe.

CASE STUDY

A 53-year-old man presented to the podiatric clinic in April 2016, with the complaint of a left great toe soft tissue mass, which he reported to have been present for 1.5 years prior to his initial presentation. He had previously been seen by another physician for the same mass, which was diagnosed initially as a wart, and then as a dermatofibroma. However, the mass was not responding to treatment and is now noted to be enlarging.

On physical examination the patient was noted to have a soft tissue mass of the left plantar-lateral hallux, clinically measuring approximately 1.5 cm x 1.5 cm x 0.8 cm depth. There were no breaks in the soft tissue and the mass was noted to be pedunculated without discoloration. A radiograph from 2 months prior was independently reviewed and showed cystic changes at the plantar lateral hallux distal phalanx, with possible bony involvement (Figure 1). Given this unusual presentation, a magnetic resonance image (MRI) was ordered to further evaluate the mass, with a tentative plan for excision of the soft tissue mass.

The MRI was obtained on May 21, 2016, and was read as showing a "nonspecific subcutaneous, exophytic, and somewhat preformed intermittent signal intensity lobulated soft tissue mass involving the plantar pattern at the distal first toe measuring approximately 9 mm in greatest dimension and almost extending to the plantar surface of the distal tuft without bony invasion or no abnormal signal within the adjacent bone possibly reflecting a fibrous lesion that is similar in appearance to plantar fibromatosis" (Figure 2).

In September 2016, the patient underwent a soft tissue mass excision of the left hallux, with ellipsed area measuring 3 cm x 1.5 cm x 1 cm, and this was sent to pathology. Surgical pathology showed a highly infiltrative neoplasm,

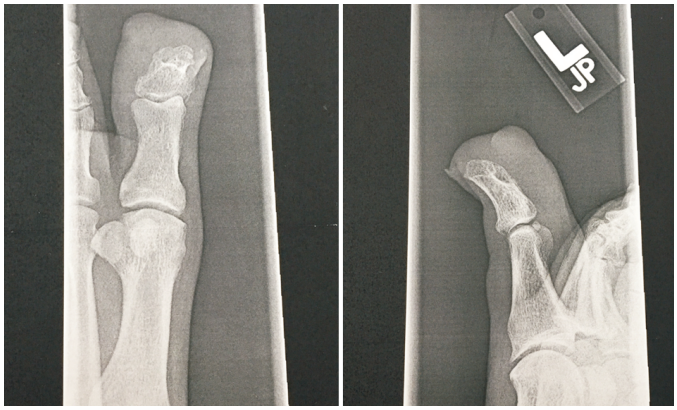

Figure 1. Preoperative radiographs of the left hallux showing soft tissue mass, as well as possible cystic changes in the distal phalanx.

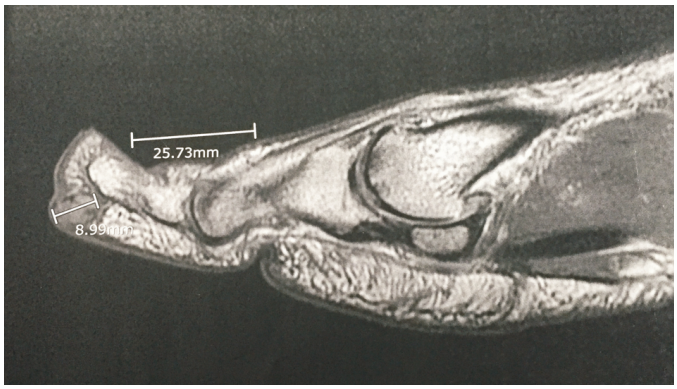

Figure 2. Magnetic resonance image of the left forefoot showing a plantar distal soft tissue mass.

and a consult from dermatopathology was requested. The dermatopathologist subsequently determined that the lesion was a malignant eccrine poroma. Based on the MRI reading of the lesion, this ellipsed area should have been sufficient to excise the mass, however, surgical pathology showed that malignant cells were present extensively at the margins of the specimen and they recommended re-excision to achieve clear margins. It was also noted that although an eccrine porocarcinoma with >14 mitoses per high power field require a more aggressive clinical course, the biopsy pathology in this case shows mitotic activity much lower than this without evidence of lymphovascular invasion.

Given the inherently malignant nature of the neoplasm and its propensity for spread, the decision was made to move forward with re-resection. The option of wide excision versus partial hallux amputation was discussed at length with the patient. At the time of preoperative evaluation, due to the concern for recurrence, the patient desired to proceed with a more definitive partial left hallux amputation with concomitant left groin sentinel lymph node biopsy, by a general surgeon. The surgery was carried out approximately 1 month following the primary surgery, and the pathology returned with no residual neoplasm, clean margins, and negative lymph node biopsy.

Initially, upon diagnosis of malignant eccrine porocarcinoma, it was recommended that the patient establish care at an academic center, which may have more resources and funding available, however, he was unable to do so due to prolonged wait times. The patient was subsequently referred to hematology and oncology in December 2017, who recommended referral to dermatology. They also recommended follow-up with a dermatology specialist at an institution several hours away who had previously treated 6 similar cases. Unfortunately, due to access, he was unable to follow-up with this dermatologist. Upon finally establishing care with dermatology, the patient was advised to see a physician every 3-6 months for skin surveys, and was referred to a second specialist in hematology and oncology, outside of the referring institution, for recommendations regarding adjuvant therapy and imaging guidelines. The outside specialist determined that there was no need for adjuvant therapies, or routine imaging at this time.

DISCUSSION

Perhaps the reason for the seemingly aggressive nature of this lesion is the fact that there is a wide differential diagnosis and difficulty in identification of these lesions, leading to delay in definitive diagnosis. In many cases, the differential diagnosis does include other epithelial malignancies such as squamous cell carcinoma, basal cell carcinoma, and amelanotic melanoma and in these cases, perhaps they are caught sooner, as the standard of care is to biopsy or excise this type of lesion, leading to early identification via pathology.

Unfortunately, the differential diagnosis also includes some benign processes, as was the case with our patient, which results in the lesion being allowed to develop and spread. This more benign differential includes pyogenic granuloma, verruca vulgaris, dermatofibroma, seborrheic keratosis, and of course benign eccrine poroma (4). In the case of a malignant eccrine poroma, the location of the lesion does not necessarily correlate with the areas of highest concentration of eccrine glands, as the benign lesions would (3). Eccrine porocarcinoma often appears as a pedunculated tumor, which is typically less aggressive, whereas ulceration, and multinodularity tend to be signs of a more aggressive lesion, which lends itself to higher risk of recurrence and metastases. Apart from this wide differential, the rarity of the lesion also likely contributes to the difficulty in identification.

The diagnosis of eccrine porocarcinoma can only truly be made by biopsy and histological evaluation, and dermatopathology consultation should be considered because diagnostic error often occurs due to the wide variety of histologic features. For example, eccrine porocarcinoma can often show basal or squamous differentiation (4). Belin et al noted that in their study of 24 patients with eccrine porocarcinoma, 37% of the specimens sent to pathology were misdiagnosed, initially (6). Histologically, it has been suggested that the upper portion of the dermal eccrine duct seems to play a role in the oncogenesis (2), and the pathology usually reveals an irregular tumor with cell clusters showing an invasive pattern, with ductal and eccrine differentiation (4). Invasion is often defined as cytologic atypia, desmoplasia, and the presence of irregular dermis with infiltrating basaloid cell clusters (4). The intracytoplasmic lumina tend to be smaller and ill-formed compared to their benign counterparts. It is differentiated from apocrine glands, as it does not show granular cells or decapitated lumens. In a study by Robson et al involving review of 69 cases, approximately 68% of the tumors demonstrated mature, well-formed ducts and approximately 18% seemed to arise from an existing benign poroma (5). Immunohistochemical techniques are often less helpful than morphology, and therefore not necessary, but in some cases, may help confirm the diagnosis. Based on current literature review a more aggressive clinical course is recommended when there are >14 mitoses per high power field, which along with lymph node involvement, and a depth of >7 mm predicted death with a confidence interval of 95% (5).

Another important, although less definitive, means of diagnosis is by way of advanced imaging. MRI is the current diagnostic imaging of choice; however, it is better for surgical planning, evaluating extent of invasion and depth,

rather than accurately diagnosing the lesion. One means of imaging, which has been reviewed in the literature is that of positron emission tomography-computer tomography (PET/CT). The purpose of PET/CT is to help identify body changes at a cellular level. Again, this is not diagnostic, however, it is useful in staging, follow-up, and detection of recurrence and metastases (7-9).

When the diagnosis of eccrine porocarcinoma is made, the current treatment of choice is wide local excision, or ≥2mm margins, which has been noted to have a cure rate of about 70-80% (2). If there is known lymph node involvement, then these too must be cleared. Unfortunately, there is no clear recommendation in the literature regarding appropriate wide surgical margins for eccrine porocarcinoma, and therefore it may be difficult to determine a successful resection until the surgical pathology is returned showing clear margins. There is a high incidence of local recurrence, 20%, and this seems to occur more frequently in more infiltrative type tumors (1,6). Recurrences have been reported to occur anywhere from 4 months to 12 years later, and it is possible that in many of these cases, adequate excision was not performed at the primary surgical intervention (1).

Beyond wide excision, other intervention options include Mohs surgery, local destruction, and electrocoagulation. Mohs microsurgery is an excellent surgical option, particularly when there is concern for larger soft tissue deficits with wide excision. Patients who receive Mohs microsurgery may require multiple stages of treatment to fully clear the neoplasm. In a case series of 5 patients treated with Mohs, 4 of the patients required 2 stages, and there have been no recurrences demonstrated at an average 1.7 year follow-up (1). In a similar case series of 5 patients undergoing Mohs microsurgery, 1 patient required 1 stage of treatment, 3 required 2 stages of treatment, and 1 required 3 stages of treatment. None of these patients have demonstrated recurrence in a mean follow-up of 11 months (10). These are small numbers of patients, however it is important to keep in mind that this is a very rare lesion, and these outcomes are already demonstrating greater success than wide excision. Although these results are reassuring, in reality this tells us very little about the efficacy, as the lesions can recur decades down the line.

Belin et al, in their study of 24 patients, found that, while there is no consensus in surgical management, they designed an algorithm that they find to be successful. The algorithm is based upon the histological subtypes; pushing and infiltrative, which were originally proposed by Robson. The authors proposed that infiltrative or pagetoid porocarcinoma should undergo excision with additional modified Mohs, while "pushing" porocarcinoma usually demonstrates good response and less recurrence with surgical wide excision. It has been suggested that, for the infiltrative type of tumor, the patient would be better served by undergoing one or several treatments with Mohs microsurgery, as wide margins do not seem to change the recurrence rate for that particular type (6).

In the incidence where a patient may have multiple lesions, making resection and surgical recovery more difficult, local destruction without surgical intervention may be an option. In 1 case study, a patient with multiple lesions of the bilateral feet was treated with topical diphencyprone (DPC), which promotes lymphocyte mediated tumor destruction and is also used to treat patients with melanoma metastases. The patient in question underwent a series of 6 treatments with the concentration of DPC increased each week, and after 6 weeks the nodules had completely resolved (11). Clinically, no recurrence was noted at 6 months. There is, however, little other evidence of the use of DPC for eccrine porocarcinoma.

With regard to adjuvant therapies, there is little literature reviewing the efficacy of radiotherapy and chemotherapy. In 2 individual case studies by Yamamato et al and Katsanis et al, each patient underwent radiotherapy with lymph node excision, with survival at 55 months and 19 months respectively (12,13).

Chemotherapy has been documented in some case studies although it is noted that treatment with methotrexate, cisplatin, Adriamycin, bleomycin and interferon alpha have shown partial or little response and there is currently little to no evidence to support their use (2). In one case, a patient with metastatic eccrine porocarcinoma was treated with single agent docetaxel, after demonstrating resistance to platinum, with good response both symptomatically and radiographically (3). One case report documents the author's experience with electrochemotherapy using bleomycin and electric pulses, which demonstrated good response of a local recurrence with no clinically macroscopic relapses (14). In a study by Shiohara et al, 4 of 12 patients with eccrine porocarcinoma underwent chemotherapy for local recurrence or metastasis (15). Three of these received intravenous therapy and 2 received oral therapy, all showing no improvement. Of these 12 patients, 3 of them underwent radiotherapy, 2 of which who had already received chemotherapy. In these 3 patients, good local control and pain response was demonstrated although the efficiency duration was fairly short in all cases. While it is used on occasion, chemotherapy needs to be reserved for the more resistant or severe cases, for which other treatment methods have failed. The prognosis, of course seems to be better if caught early with wide resection. However, if the localization of the tumor requires close surgical margins, or is nonresectable, chemotherapy and radiation therapy may be warranted. Similarly, if a lesion seems to be high risk microscopically, it is reasonable to initiate chemotherapy on a therapeutic basis and for metastasis suppression.

Again, these decisions would almost certainly be determined by an oncologist.

Although, the cause of eccrine porocarcinoma is unclear, and a large number may in fact be idiopathic, there are thought to be some risk factors. These risk factors include exposure to trauma, burning, or radiotherapy; immunosuppressive drugs, UV, and AIDS (16).

In an article by Elliot et al, the authors discuss the importance of referring patients to a specialist prior to biopsy, in the case of suspected soft tissue sarcoma (17). While eccrine porocarcinoma does not fall into soft tissue sarcomas, much of what they discussed should be considered. According to the authors, there is a statistically significant correlation between pre-referral procedures, such as biopsy, and complications. These complications are often associated with errors such as type of approach, type of biopsy, incomplete excision, and diagnostic errors. Probably the most important complication of biopsy is the possibility of contamination of a tumor naive compartment. Much of the information presented in our research is, of course, within the purview of the oncologist, to whom the patient should be referred as soon as possible following diagnosis. However, the goals of this article are two-fold: to allow the physician to form a more complete differential diagnosis at initial presentation, thus allowing earlier diagnosis and intervention; and to educate so that any physician can provide the patient with important information at the time of diagnosis.

Eccrine porocarcinoma is a rare, locally aggressive, soft tissue neoplasm that can potentially be fatal. While there are no formal recommendations supported by the literature guiding treatment and surgical intervention, we are able to make informed decisions based on the current literature. Diagnosis is almost exclusively based on pathology, and while imaging is by no means definitive, MRI is recommended to evaluate and stage the lesion. PET/CT scan is useful, particularly in the case of suspected aggressive lesions and metastases. While there is currently no published treatment guideline, wide surgical excision is recommended, and unfortunately this is often determined by clean, histological margins. Mohs microsurgery is an alternative intervention that should be considered for more aggressive lesions. Lymph node biopsy should also be considered, especially in infiltrative lesions. Wide excision may leave large defects, and therefore it may be best for the patient to be referred to dermatology, surgery or oncology. In the case of aggressive pathology, recurrence, or metastases the patient should be referred to an oncologist who will determine further evaluation and treatment measures.

In the case of our 53-year-old patient with eccrine porocarcinoma, there was an unknown delay in definitive diagnosis, as the lesion had been clinically misdiagnosed by previous health care providers. Once diagnosis was made, it required a relatively aggressive resection. This case also brings up several key points: timing of referral, and follow up. Ideally, our patient would have been seen by dermatology and oncology at the time of diagnosis, however there was some delay due to access although it was felt to not impact the outcome in this case. Lastly, follow-up at regular and short intervals is recommended given the high recurrence rate.

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