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Short Communication

Outcomes of Surgically-Resected Eccrine Porocarcinoma with Low-Risk Histologic Features

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Abstract

Background: Eccrine porocarcinoma has been reported as an aggressive tumor with metastatic potential and mortality rates of up to 33%. However, there is no consensus on appropriate work up and treatment regarding the need for staging or surveillance imaging or sentinel lymph node biopsy, with wide variability in published clinical outcomes.

Aim: We report a series of seven cases of porocarcinoma identified over 12 years in an attempt to further define its clinical course and the role of treatment or staging following excision.

Method: Seven cases from were retrospectively identified and confirmed histopathologically. The medical records were reviewed to establish treatment course and clinical outcome.

Results: Only 1 case displayed aggressive histologic features (depth >7 mm, mitoses >14/mm2 and lymphovascular invasion). All patients were treated with excision or Mohs micrographic surgery without baseline surveillance imaging or sentinel lymph node biopsy. Disease specific survival was 100% during a medianfollow-up of 55.2months.

Conclusions: Our series suggests that in the absence of aggressive histology, a "low risk" form of eccrine porocarcinoma exists, which does not require treatment or staging beyond complete surgical excision.

ABBREVIATIONS

EPC: Eccrine Porocarcinoma; MMS: Mohs Micrographic Surgery; SLNB: Sentinel Lymph Node Biopsy

INTRODUCTION

Eccrine porocarcinoma, also known as malignant eccrine poroma, is a rare malignancy of the eccrine sweat glands. It is a variant of eccrine carcinoma, thought to arise from the acrosyringium [1]. Eccrine porocarcinoma (EPC) was first described by Mehregan and Pinkus in 1963 on the ankle of an 82 year-old woman who subsequently died of widespread metastasis [2]. Since that time, fewer than 300 cases have been reported in the literature. EPC is typically a disease of the elderly, with the mean age at presentation of 60 to 80 years, although rare cases have been reported in children [3,4]. It is thought to arise *de novo*, but reports of an adjacent benign component on histology suggest that it can also be associated with a pre-existing benign poroma [4]. The presentation is extremely variable, and initial clinical impression is seldom accurate [4].

The most common reported locations for EPCs are the lower extremities and head and neck [4-6]. Histologically, EPC demonstrates nests of atypical cells, which extend from the epidermis into the dermis and exhibit ductal differentiation [4]. Confirmatory immunohistochemical stains are lacking, often making these tumors difficult to differentiate from other forms of non-melanoma skin cancer, especially squamous cell carcinoma [4,5].

Surgical excision is generally regarded as the appropriate first step for treatment of EPC [7,8]. Published surgical margins range from 0.5 to 3.0 cm but are largely unreported. Thus, there is no consensus on appropriate clinical margins or whether Mohs micrographic surgery (MMS) is indicated over conventional wide local excision [6,9,10]. The risk for local recurrence has been reported to range from 4% to 33% according to various case series, and rates of lymph node (4% to 50%) and distant metastasis (1% to 33%) are similarly variable in the published literature [1,4-7,10,11]. Furthermore, there are no guidelines or consensus on whether a staging workup, including baseline imaging or sentinel lymph node biopsy, is warranted following

diagnosis, in the absence of clinical signs or symptoms of metastasis. In an attempt to improve the understanding of EPC, we report a retrospective case series of seven patients with this rare entity.

METHODS

Following Institutional Review Board approval, patients were identified through retrospective review of pathology records from January 1991- September 2013 at the Veterans Affairs Palo Alto Health Care System and Stanford University Medical Center, in which the terms "eccrine porocarcinoma" or "malignant poroma" were noted in the initial histologic differential diagnosis. Eleven cases were initially identified and re-reviewed by two dermatopathologists (BME, KER), independently. The diagnosis of EPC was confirmed based the criteria of *Robson et al.,* (2001), including the presence of atypical cells exhibiting ductal differentiation in the epidermis or extending from the epidermis into the dermis. Four cases, which did not include all of these features, were excluded, leaving 7 in the case series [4]. Histologic features including border type (pushing or infiltrative), host response, mitotic rate per millimeters squared, depth of invasion, and presence of lymphovascular or perineural invasion were recorded. Depth of invasion was measured from the granular layer to the deepest portion of the tumor, analogous to Breslow thickness measurement. In keeping with definitions by *Robson et al.*, "pushing border" was defined as a broad advancing edge of cells extending into the dermis, while an "infiltrative border" was defined as cords or strands of cells invading the dermis [4]. Given the variability in the literature for the definition of what constitutes a high-powered field on microscopy, we measured the mitotic index as the number of mitoses per millimeter squared. To allow for comparison to prior case series, we utilized the definition proposed by to *Burton AL et al.,* in the melanoma literature, which described a practical conversion of 1 mm^2 as equivalent to 10 high-powered fields [12]. Immunohistochemistry was performed on select cases; however, given the lack of consistent confirmatory stains for porocarcinoma, these results were not used as part of our diagnostic criteria [5].

The medical record was reviewed in each case to denote details regarding initial presentation, surgical treatment and extent of clinical margin, performance of sentinel lymph node biopsy or imaging, development of local clinical recurrence via follow up physical exams and/or metastasis. The follow-up period was calculated based on the most recent visit to a dermatologist, oncologist or primary care physician.

RESULTS

Seven cases of eccrine porocarcinoma were identified from January 1, 1991 to August 31, 2013. The characteristics of each patient and their treatment courses are noted in Table 1. The median age at presentation was 82 years (range 68 to 87 years). Tumor location included the head and neck, trunk, and extremities. The appearance was variable, ranging from an 8 mm papule to a 2.8 cm ulcerated nodule. EPC was not included in any of the initial clinical differential diagnoses, which instead favored basal cell carcinoma, squamous cell carcinoma, seborrheic keratosis, or nevus. The clinical appearance of case 4, for which a diagnosis of basal cell carcinoma was favored, is shown in Figure 1. One case was excised on biopsy without further treatment. Three patients underwent surgical excision with clinical margins of 2 to 5 mm. Three patients underwent Mohs micrographic surgery for clear histologic margins, 2 of which were excised in 1 or 2 stages. One patient presenting with a 2.8 cm clinically-apparent nodule on the forehead required 5 stages of MMS for complete excision, with a post-operative defect measuring 4.1 by 3.6 cm.

Histologic features for each tumor are noted in Table 2. All tumors were <7 mm in depth. No cases displayed lymphovascular invasion, although 1 case had foci suspicious for perineural invasion. All but 1 case had a mitotic index <14/mm^2, with the exception demonstrating a mitotic index of 40/mm^2. This latter patient underwent surgical excision with 2 mm margins, without additional staging work up or imaging and remained disease-free at 43.5 months follow up. None of the patients underwent sentinel lymph node biopsy, baseline or surveillance imaging for metastatic work-up, or adjuvant radiation or systemic therapy.

The median follow-up time was 55.2 months (range 13.5 – 112.0 months). No patients developed local recurrence, regional or distant metastasis, and overall disease-specific survival was 100% during the follow-up period. Only one patient (case 1) died during the study from an unrelated malignancy.

Table 1: Clinical Characteristics.

Case	Age/sex	Site	Treatment	Margins	Follow up (mo)	Outcome
1	82m	forearm	Excised on biopsy, re-excision not performed	Narrow histologic	82.8	Died of other malignancy
2	63m	forehead	Excision	5mm	35.4	Lost to follow up
3	84m	lower back	Excision	5mm	63.9	Ongoing follow up
4	87m	forehead	MMS (1 stage)	NA	13.5	Ongoing follow up
5	80m	foot	MMS (2 stages)	NA	112.0	Lost to follow up
6	83f	lower leg	Excision	2mm	55.2	Ongoing Follow Up
7	68f	forehead	MMS (5 stages)	NA	26.0	Ongoing Follow Up
			Median follow up/Survival (mo):		55.2	

Abbreviations: mo: Months; m: Male; f: Female; AKs: Actinic Keratosis, NMSC: Non-Melanoma Skin Cancer; BCC: Basal Cell Carcinoma; SCCIS: Squamous Cell Carcinoma in situ; MMS: Mohs Micrographic Surgery; NA: Not Applicable

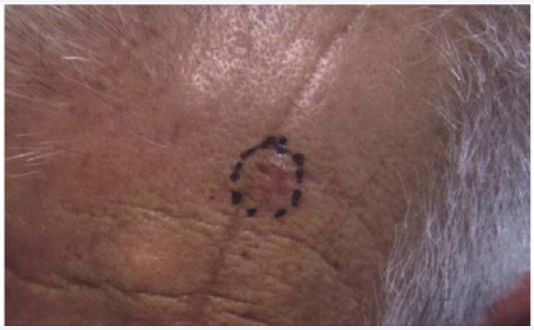

Figure 1 Clinical presentation of case 4 with surrounding black ink, left forehead.

Table 2: Histologic Characteristics.

Case	Border	Mitotic Index (per mm2)	Depth (mm)	LVI	Stains	Perineural Invasion
1	pushing	3	2.45	no		no
2	infiltrative	6	2.00*	no	CEA+, PAS+	no
3	infiltrative	6	4.45	no	CEA and PAS negative	suspicious areas
4	infiltrative	2	2.35*	no	CEA+, P16+	no
5	non-infiltrative, in situ	4	0.80	no		no
6	pushing	40	4.80	no	BerEP4+, EMA+	no
7	infiltrative	10	2.25	no	CEA+, P16 negative, Ki67 20%	No

*Depth is at least
Abbreviations: LVI: lymphovascular Invasion; mm: Millimeter; CEA: Carcino Embryonic Antigen; PAS: Periodic Acid Schiff; EMA: Epithelial Membrane Antigen

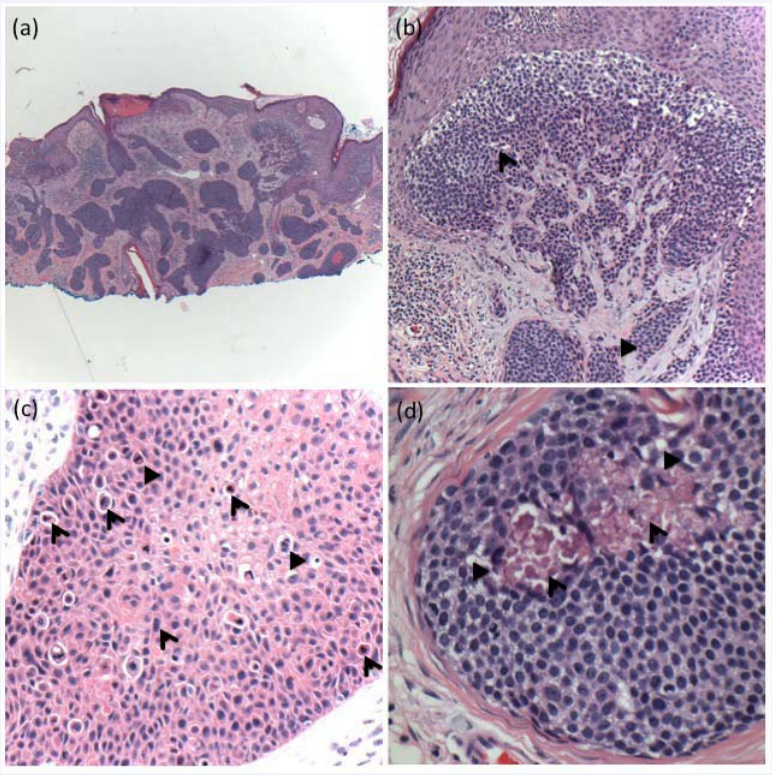

Figure 2 Case 7: A) Tumor extending from the epidermis with an infiltrative border, 4x. B) Tumor cells invading the dermis from the epidermis, prominent fibrosis (solid arrowhead) and ducts (open arrowhead), 20x. C) Numerous mitoses (solid arrowhead) and single cell necrosis (open arrowhead), 40x. D) Prominent tumor necrosis (open arrowhead) and ducts (closed arrowhead), 60x.

DISCUSSION

Eccrine porocarcinoma has been reported to be a relatively aggressive tumor with a tendency to metastasize to regional lymph nodes [6,7,9-11]. The largest series to date of 69 cases reported a significant risk of both lymph node and distant metastasis at rates of 19% and 11%, respectively [4]. This same series showed that lymph node metastasis is a poor prognostic factor, with mortality rates up to 67% [4]. Despite this relatively high rate of metastasis, the role of sentinel lymph node biopsy for porocarcinoma staging at baseline is not defined,[7,8,13] although it has been suggested in the setting of tumors with a more aggressive histologic phenotype [6,14]

Robson et al., defined histologic features that portend a more aggressive phenotype of porocarcinoma with increased risk for metastasis as follows: depth >7 mm, mitoses >14/10 hpf and lymphovascular invasion [4]. Other than a single case with an elevated mitotic rate, these features were not observed in our cohort, and therefore, our findings are likely not applicable to tumors that exhibit more aggressive pathology. Robson et al suggested a low rate of positive SLNB for patients with eccrine porocarcinoma but that SLNB may be appropriate in cases with elevated mitotic rate or depth of invasion >7 mm. Our case series supports the existence of a subset of patients who may be considered "low risk" with an improved prognosis [4] and further suggests that lymph node evaluation and additional staging work-up is not necessary in the absence of lymphadenopathy, systemic symptoms, or aggressive histology.

No local recurrence, regional nodal or distant metastasis was observed in our cohort, with median follow-up of nearly 5 years. This positive outcome varies significantly from previous reports [6,7,9-11]. However, prior case series were characterized by lengthy duration of the lesion prior to diagnosis as opposed to our cohort, in which 3 of the patients were seen by a dermatologist at least annually for non-melanoma skin cancer screening or other dermatologic complaints prior to their porocarcinoma diagnosis, and 4 of the 7 patients presented for reasons other than the porocarcinoma. More frequent dermatology visits and referral for unrelated conditions may have led to earlier detection, shorter lesion duration preceding diagnosis, and improved outcome in our series compared to previous reports. In addition, immunosuppression, which may be a risk factor for a poorer outcome and more aggressive tumor, was not a factor in any of our patients [11].

An infiltrative border on histology (as opposed to pushing) has been shown to be a risk factor for local recurrence of porocarcinoma [4,9]. Interestingly, there were no instances of local recurrence in our cohort although the majority (57.14%) did display an infiltrative histologic border phenotype. Two cases with an infiltrative border underwent MMS as the primary treatment modality. Case 7, which required five stages for histologic clearance, highlights the need for wide surgical margins in certain cases and careful histologic assessment of the margin status regardless of border type. Previous authors have suggested that MMS may be the treatment of choice for porocarcinoma [9]. Given our small sample size, varied treatment modalities and the uniform positive outcome of our cases, our data neither support nor refute this assertion. However, as none of our cases treated with MMS developed local or distant recurrence, MMS may be an appropriate, tissue-sparing modality in select cases, particularly those with favorable histologic features. This is in accord with the recent appropriate use criteria established for MMS and eccrine carcinomas [15].

Our findings are limited by the small size of the series and the follow-up period, which ranged widely from 13.4 to 112.0 months. In addition, follow-up visits were not always with a dermatologist and therefore careful inspection for local recurrence may not have been performed in every case; however, this would not be expected to affect overall survival data. In addition, our determination of mitotic index using the conversion employed for melanoma histologic assessment may not be applicable to EPC, but was done to compare our series with prior reports. Despite these limitations, our results support the concept that in patients with EPCs that exhibit "lower risk" histology, staging with SLNB or PET-CT may not be warranted, and that treatment beyond MMS or conventional surgical excision with 0.5 to 1 cm margins, may not be necessary [4,9,14].

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