ORIGINAL ARTICLE

Eccrine Porocarcinoma: Clinical and Histopathological Study of 14 Patients with Special Emphasis on Sentinel Lymph Node Biopsy

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Eccrine porocarcinoma is a rare skin adnexal tumour that affects elderly people. Most eccrine porocarcinomas are stage I or II according to the American Joint Committee on Cancer. The prognosis is good in early stages, but worsens when advanced. Since information on the use of sentinel lymph node biopsy in these patients is scarce, this study examined the records of all patients with eccrine porocarcinoma treated at Helsinki University Hospital during a 17-year period and focused on sentinel lymph node biopsy patients. The study identified 14 patients (9 male, 5 female). There were 2 metastases to the lymph nodes and 2 recurrences at initial referral to our institution. All primary tumours had wide local excision and 6 patients also had sentinel lymph node biopsy, of whom none had positive lymph nodes. There were no new metastases or recurrences during follow-up. Three patients died of causes other than eccrine porocarcinoma. When comparing the wide local excision only and wide local excision with sentinel lymph node biopsy groups, no parameters reached statistical significance. The decision process of the multidisciplinary tumour board meeting on whether to perform sentinel lymph node biopsy was not clear, perhaps due to the limited knowledge of eccrine porocarcinoma. Further studies and international collaboration are warranted.

Key words: eccrine porocarcinoma; sentinel lymph node biopsy; case series.

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SIGNIFICANCE

Eccrine porocarcinoma is a rare skin cancer originating from the sweat gland and affecting the elderly. The prognosis of local disease is good but worsens when spread to distant organs. We examined the records of all porocarcinoma patients treated at our institution during a 17-year period. We identified 14 patients of which two had metastases and two had recurrences at initial evaluation. All primary tumours were surgically removed and six patients had sentinel lymph node biopsy, of whom none had metastatic lymph nodes. During follow-up no new metastases, recurrences or porocarcinoma deaths were observed. To conclude, it seems prognosis of eccrine porocarcinoma is good when treated at early stage.

Eccrine porocarcinoma (EPC) is a rare malignant adnexal skin tumour that arises from the terminal sweat gland duct. EPC was initially described by Coburn & Smith in 1956 alongside hidroacanthoma simplex as its malignant homologue (1). In 1963, Pinkus & Mehregan named this tumour "epidermotropic eccrine carcinoma, or more precisely malignant eccrine poroma" (2). Mishima & Morioka subsequently showed that this tumour originates from the intraepidermal part of the sweat gland duct and gave it its current name, eccrine porocarcinoma (3). The age-adjusted incidence varies from 0.04 for males and 0.03 for females in the Netherlands (4) to, 0.15 for men and 0.10 for women (recent rates in Finland) (5) per 100,000 person-years (by European Standard Population).

EPC mostly affects elderly subjects (median reported age 65–78 years) (4, 6–9). The clinical presentation of EPC is commonly a firm nodule or a plaque, coloured violet, reddish or brown or an erythematous nodule with or without surface ulceration (10–13). EPC is most commonly located in the lower limb and the head and neck region (4, 7, 9, 10, 14–16). Due to its rarity, EPC is difficult to diagnose clinically and can be misdiagnosed as benign poroma, or more common non-melanoma skin cancers, pyogenic granuloma, sebaceous carcinoma, or amelanotic melanoma (9, 10, 14).

The reported lymph node involvement at the time of diagnosis varies greatly (8.1–42%) (6, 7, 13, 16–19). The disease progression to the regional lymph nodes has been observed in 8–25% (6, 9, 14, 18) and to the distant organs in 4–12% and even up to 33% of cases (6, 13, 14). However, in 2 recent (7, 8), and 1 slightly older (20), database studies, most EPCs were either stage I (56.2–61.1%) or stage II (21.0–30.5%) according to the American Joint Committee on Cancer (AJCC) (21). Deaths related to EPC occur in 7–33% of cases (9, 13, 14, 16, 18). The prognosis worsens with more advanced disease; the 5-year disease-specific survival (DSS) is 97.4% for stage I and 66.1% for stage III disease (8).

The most common treatment for EPC is surgical excision of the tumour (4, 6, 8, 20). In 2 different cohorts of 206 and 203 patients with EPC, surgery alone was the most common treatment (73.8% and 83.7% of patients,

respectively) (6, 20). Radiotherapy was mostly given in combination with other treatments and varied from 4.4 to 7.3% of patients (6, 20) and was rarely given as sole treatment (0.5%) (6). Rates of chemotherapy use varied from 1.3 to 8.3% (6, 8, 22); chemotherapy was usually given in combination with other treatments. Interestingly, chemotherapy was used in up to 33% (13) and 54% (16) of patients with EPC in smaller case series; however, all of these patients had metastatic or recurrent disease.

Sentinel lymph node biopsy (SLNB) is rarely reported in the treatment of EPC. The sample sizes in case series with SLNB are small (12–28 patients); not all patients in those series had SLNB (13, 16–18). In a study by Goyal et al. information on whether a SLNB procedure was performed was retrieved from only 35.6% (229/644) of the patients (8). Of these 229 patients, only 21.8% had SLNB (8).

This study reviewed all patients treated for EPC at Helsinki University Hospital during a 17-year period and describes our experience. A further aim was to focus on patients who had SLNB.

METHODS

The local review board approved this retrospective chart review study and its plan. Patients treated for EPC at the Department of Plastic Surgery in Helsinki University Hospital during 1 January 2000 to 31 December 2016 were included. Medical records of patients fulfilling the inclusion criteria were reviewed in detail by 1 author (ASM) for demographics, comorbidities, tumour characteristics and anatomical location, surgical procedure(s), imaging, and follow-up time. Clinical information on surgical treatment, margin status, pre- and postoperative imaging and adjuvant therapy was extracted. The patients for SLNB were selected after a multidisciplinary tumour board meeting. The protocol for SLNB was as follows: all patients were injected with 99mTc nanocolloid adjacent to the primary tumour or the scar of the removed/biopsied primary tumour. Imaging (either single-photon emission computed tomography/computed tomography [SPECT/CT] or scintigraphy) was performed 30–60 min after the injection.

The biopsies or diagnostic removals of the tumours were conducted at various healthcare facilities, including primary healthcare centres, general surgical departments in regional hospitals, plastic surgery departments, and other specialized departments, such as gynaecological and urological departments, as well as private clinics. In healthcare centres, it was typically a general practitioner who performed the biopsy, while in surgery departments it could have been a specialist or a surgeon in training. All pathological samples were evaluated in the Department of Pathology, Helsinki University Hospital.

All histological slides were re-evaluated by a dermatopathologist (MVW-B). The slides were all stained with haematoxylin and eosin (HE) and the following immunohistochemical stains were used as needed to verify the EPC diagnosis: melanocytic markers, such as HMB-45, S-100 and Mart-1, were used to rule out melanoma, Ber-EP4 to rule out basal cell carcinoma, carcinoembryonic antigen (CEA) and epithelial membrane antigen (EMA) stains to demonstrate ductal structures, adipophilin to rule out sebaceous carcinoma and Mib-1 to show proliferation rate. Depth of invasion was measured from the granular cell layer (or ulcerated surface) to the deepest point of invasion of tumour. In fragmented specimens the thickest region measurable on the slide was noted. The number of mitoses was calculated per square millimetre.

Clinical and histological data for the SLNB patients were compared with data for the wide local excision (WLE) patients. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 28.0 (Armonk, NY: IBM Corp). Because the variables were not normally distributed, Mann-Whitney U test was used for the comparisons of groups. p-values <0.05 were considered statistically significant.

RESULTS

All patients

Fourteen EPC patients were treated during the study period (9 male, 5 female). Median age at the time of EPC diagnosis was 64.5 years (range 19–82 years). Most of the primary tumours located in the lower limb (7 patients), followed by the trunk (including buttocks and genitalia; 3 patients), head and neck area (2 patients) and the upper limb (1 patient) (**Table I**).

Table I. Demographics and tumour-related data of eccrine porocarcinoma (EPC) patients

	All patients	WLE + SLNB	WLE only	Lymph dissection only
Total, *n* (%)	14	6 (43)	6 (43)	2 (14)
Male, *n* (%)	9 (64)	5 (83)	2 (33)	2 (100)
Female, *n* (%)	5 (36)	1 (17)	4 (67)	0
Age, years, median (range)	64.5 (19–82)	59.0 (19–74)	74.0 (22–80)	71.5 (61–82)
Tumour[a]				*n* = 1
Size, mm median, (range)	10.0 (4–15)	11.0 (4–15)	9.5 (9–12)	12.0
Thickness mm, median, (range)	5.0 (2–15)	7.0 (2.5–15)	5.0 (2–8)	5.0
Mitoses/mm^2, median (range)	2 (0–8)	2 (0–7)	4 (1–8)	2
Location of the primary tumour[a,b]	*n* = 13			*n* = 1
Lower limb, *n* (%)	7 (54)	3 (50)	3 (57)	1 (50)
Trunk, *n* (%)	3 (23)	1 (17)	2 (29)	
Upper limb, *n* (%)	1 (8)	1 (17)	0	
Head and neck, *n* (%)	2 (15)	1 (17)	1 (14)	
RLN metastasis, *n* (%)	2 (14)	–		2
Recurrence, *n* (%)	2 (14)	–	2 (33)	–
Deaths (of other causes than EPC), *n* (%)	3 (21)	–	3 (50)	–

[a]One patient with only lymph node metastasis and no primary tumour is not included. [b]Buttocks and genitalia are included in the trunk. Inguinal area is included in the lower limb.
WLE: wide local excision; SLNB: sentinel lymph node biopsy; RLN: regional lymph node.

Table II. Detailed histological and clinical data of the patients with eccrine porocarcinoma

Patient	Age/sex	Location	Size (mm)	Tumour thickness (mm)	Mitoses (/mm^2)	SLN location	Removed SLNs	Follow-up (years)	Metastases, recurrence	Other treatments	Outcome (at 1 December 2020)
1	76/F	Buttock	9	2	1			18	Recurrence	–	Dead
2	80/F	Inguinal area	9	8	2			8.5	Recurrence	–	Dead
3	61/M	Foot	12	5	2			16.6	Inguinal and parailiacal metastases[a]	Radiotherapy inguinal area preoperatively	Alive
4	63/M	Foot	13	5	0	Inguinal, parailiacal	2, 3	12.7	–	–	Alive
5	55/F	Thigh	4	2.5	0	Inguinal	2	9.5	–	–	Alive
6	66/M	Back	15	13	2	Inguinal, parailiacal	1, 1	8.9	–	–	Alive
7	59/M	Foot	12	8	1			8.8	–	–	Alive
8	72/F	Scalp	11	2.5	5			7.6	–	–	Alive
9	80/M	Genitalia	10	7	8			4.0	–	–	Dead
10	82/M	n/a	n/a	n/a	n/a			4.1	Inguinal metastases[b]	–	Alive
11	40/M	Arm	9	9	7	Axillary	1	4.1	–	–	Alive
12	22/F	Foot	9	3	6			0.7[c]	–	–	Alive
13	74/M	Thigh	15	15	2	Inguinal	1	4.1	–	–	Alive
14	19/M	Scalp	5	5	4	Occipital, retroauricular	4, 3	10.9	–	–	Alive

[a]In this patient an older skin lesion removed 3 years earlier was re-diagnosed as eccrine porocarcinoma. [b]In this patient no primary tumour was found. [c]This patient moved to a different hospital district area and the follow-up was to be continued up to 2 years.
SLN: sentinel lymph node; M: male; F: female; n/a: not applicable.

Metastatic disease at presentation

Two patients were referred to the Helsinki University Hospital because of a mass found at the inguinal area, which was subsequently confirmed as lymph node metastasis. The first patient (**Table II**, patient 3) had inguinal and parailiacal lymph node metastasis. The primary tumour had been removed 3 years earlier and misdiagnosed. When re-evaluating this previous histological sample, it was re-diagnosed as EPC. The second patient (Table II, patient 10) presented with inguinal lymph node metastases, but no primary tumour was found.

Recurrent tumours at presentation

In 2 patients, the tumours presented at initial evaluation at our institution were recurrences (Table I and Table II, patients 1 and 2). Patient 2 had a previous skin tumour at the same location 2 years prior to the current EPC. This previous tumour was also later confirmed as EPC; the current tumour was therefore a recurrence. Patient 1 was referred to our institution after the tumour had recurred twice at the same location. The previous resections were performed in a primary healthcare centre by general practitioners.

Time between tumour presentation and diagnostic biopsy

Time from initial presentation of the tumour to diagnostic biopsy ranged from a few months to over 10 years; this information was precisely stated for 8 patients. It is uncertain whether the clinically noticeable tumour had been malignant porocarcinoma from the beginning or a benign poroma that has transformed to porocarcinoma. The clinical presentation varied significantly; 3 were reddish lesions, 2 were atheroma-like nodules with oozing, 2 were only described as nodules, 1 was a skin lesion since childhood that started to grow, 1 was a hyperkeratotic lesion, 1 resembled a skin tag, and 4 were not specified. The median skin tumour size at the time of diagnostic removal was 10.0 mm (range 4.0–15.0 mm) (Table I).

Preoperative imaging

All patients had chest X-rays preoperatively, which was routine protocol for general anaesthesia at the time of this study. In addition, 4 patients had ultrasound imaging of the lymphatic basins with normal findings.

Patient 3 with inguinal and parailiacal metastasis at initial evaluation was first referred to the oncological department where the aetiology of the metastasis was thoroughly investigated with computed tomography (CT) and positron emission tomography-computed tomography (PET-CT) scans. The metastasis was subsequently excised and the location irradiated. A follow-up CT scan revealed more metastatic lymph nodes in the same inguinal area and the patient was then referred to the plastic surgery department for inguinal lymph node evacuation and removal of 1 metastatic parailiacal lymph node. Patient 10 with inguinal lymph node metastasis had ultrasound and magnetic resonance imaging (MRI) preoperatively (**Table III**).

Surgery

Twelve patients had WLE of the primary tumour with 1–2 cm clinical margins with or without SLNB. The median microscopic margin of the removed primary tumours ($n=13$) was 10.9 mm (range 2–20 mm). Median depth of invasion was 5 mm (range 2–15 mm). The median number of mitoses was 2 (range 0–8). Detailed

Table III. Detailed information on imaging and operations of the patients with eccrine porocarcinoma (EPC)

Patient	Primary tumour location	Preoperative imaging	Operation(s)	Complications	Follow-up imaging
1	Buttock	Chest X-ray	Re-excision and direct closure	No	None
2	Inguinal	Chest X-ray	Re-excision and direct closure	No	None
3	Foot	Body CT scan, PET-CT scan	Excision and direct closure (3 years previously), evacuation of inguinal lymph nodes	No	Body CT scan
4	Foot	Chest X-ray	Re-excision and skin graft, SNLB	Skin graft infected. Swelling of the lower extremity	None
5	Thigh	Chest X-ray, ultrasound of the groin	Re-excision and direct closure, SLNB	No	None
6	Back	Chest X-ray	Re-excision and direct closure, SLNB	No	Ultrasound of the lymphatic basins, body CT scan
7	Foot	Chest X-ray	Re-excision and skin graft	No	None
8	Scalp	Chest X-ray, ultrasound of lymphatic basins	Re-excision and skin graft, later rotation flap	Necrosis of the skin graft leaving the skull visible. Later prolonged healing of the rotation flap.	None
9	Genitalia	Chest X-ray, ultrasound of the inguinal area	Re-excision and direct closure	No	None
10	n/a	Chest X-ray, ultrasound of the inguinal tumour, MRI of the inguinal area.	First diagnostic removal of the tumour and later inguinal lymph node evacuation. Sartoriusplasty operation for the seroma complication.	Wound infection and dehiscence. Wound closure with NPWT. Prolonged seroma requiring multiple punctions, corticosteroid injections, and surgery. Swelling of the lower extremity.	Body CT scan
11	Arm	Chest X-ray	Re-excision and direct closure, SLNB	No	Ultrasound of the lymphatic basins and abdomen
12	Foot	Chest X-ray, ultrasound of the inguinal area	Amputation	No	None
13	Thigh	Chest X-ray	Re-excision and direct closure, SLBN	Infection and dehiscence of the primary tumour removal site. Closure with NPWT.	
14	Scalp	Chest X-ray	Re-excision and direct closure, SLNB	Not known	Not known

CT: computed tomography; SLNB: sentinel lymph node biopsy; NPWT: negative pressure wound therapy; n/a: not applicable.

histological and clinical data are shown in Tables II and III. None of the primary tumours exhibited lymphovascular invasion.

Patient 3 with inguinal and parailiacal lymph node metastasis had the primary tumour removed 3 years previously with minimal margins in another hospital and had only inguinal lymph node evacuation and removal of the parailiacal lymph node metastasis at our hospital.

Patient 10 with inguinal lymph node metastasis had only evacuation.

Nine sites were closed directly after removal of the primary tumour. Three excision defects were reconstructed with split thickness skin grafts and 1 patient had amputation of a toe. Four patients (29%) had complications after surgery. Of these, 2 patients needed surgical interventions. Detailed data of imaging, operations, and complications are shown in Table III.

Follow-up

Median follow-up time for all patients was 8.6 years (range 8 months to 18 years). Two patients had routine ultrasound imaging and 2 patients had routine body CT scans during follow-up. One patient had body CT scans when reporting symptoms of back pain (Table III). No further metastasis or new recurrences were observed during the follow-up period. The patients with lymph node metastasis were alive at the end of follow-up. Three patients died due to causes other than EPC.

Patients with sentinel lymph node biopsy

Starting from 2008, 6 patients (5 male, 1 female) also had a SLNB performed in addition to WLE of the primary tumour. All cases were evaluated in a multidisciplinary tumour board meeting and the decision to perform a SLNB was based on their recommendation. In 2 patients, the recommendation was based on the literature that suggested that EPC has an aggressive nature. No detailed decision process was described for 4 patients.

In all patients, preoperative lymphoscintigraphy and SLNB operations were successful. In 1 patient, blue dye was also injected preoperatively adjacent to the biopsy scar in addition to the 99mTc nanocolloid injection, as this was routine protocol at the time of the surgery. There were no positive sentinel lymph nodes (SLN). Follow up of SLNB patients was uneventful (median 9.2 years, range 4–12.7 years).

Comparison of the wide local excision only and wide local excision plus sentinel lymph node biopsy groups

When comparing the SLNB group with the WLE group, none of the parameters reached statistical significance, although some differences were observed. The median age of the patients in the SLNB group was lower than in the WLE group (59.0 and 74.0 years, respectively; $p=0.149$).

The median size of the primary tumour was larger in the SLNB group than in the WLE group (11.0 and 9.5

mm, respectively; $p=0.806$). The tumour invaded deeper in the SLNB group than in the WLE group (median 7.0 and 5.0 mm, respectively; $p=0.227$). The median number of mitoses of the primary tumour was lower in the SLNB group compared with the WLE group (2 and 4 per mm^2, respectively; $p=0.418$) (Table I).

DISCUSSION

We report here the clinical course of EPC in 14 patients treated at the Department of Plastic Surgery, Helsinki, Finland with data collected over a 17-year period. Metastases were found at initial evaluation in 2 (14%) patients, which is consistent with previously reported rates (6–8, 18, 19). No further metastases or new recurrences were observed during the follow-up. None of the patients in the current study died of EPC, which is significantly lower than the disease-specific deaths observed in other smaller case series (range 7–33%) (9, 13, 14, 16, 18). In our recent epidemiological study the 5-year relative survival rate for patients with EPC in Finland was 104%; which is similar to the general population (5). The 2 patients with lymph node metastases were alive at the end of the follow-up. The 5-year DSS is rather good, with stages I (97.4%) and II (95.2%), but decreases to 50.4% with positive SLN (8). In larger database studies, EPC is mostly diagnosed as a localized disease and not advanced to regional lymph nodes nor distant organs (7, 8, 20, 23), which may suggest that EPC is not as aggressive as previously believed. Since there were only 2 patients with metastases in our study and no primary tumour in the other patient, it cannot be concluded if any particular histological characteristics influence the disease progression. There are few case reports where the patients presented with lymph node metastases and the primary tumour had been previously misdiagnosed, usually as squamous cell carcinoma (24, 25). It is debatable whether a correct diagnosis in the beginning and appropriate management would have changed the course of the disease progression.

A clear recommendation to perform or not to perform a SLNB was difficult to extract from the multidisciplinary tumour board patient files. The rationale for SLNB was described only for 2 patients. This may be due to the paucity of knowledge on the use of SLNB in EPC treatment. There was a trend when comparing the histological characteristics of the SLNB and WLE only groups; it appeared that the tumours were larger and invaded deeper in the SLNB group, although this did not reach statistical significance. The patients in SLNB group were also younger. These characteristics may have influenced the decision process in the multidisciplinary tumour board meeting. Interestingly, Tsunoda et al. (16) reported in their case series that lymph node metastasis were also observed in shallow tumours and not only in deep invasive tumours.

None of our 6 patients had positive SLNs, and the disease did not progress any further during the follow-up. Information on the rate of positive SLNs in EPC is scarce and not readily combinable. In different case series, the SLN positivity rate ranged from 0% to 50%, but the number of patients in these articles ranged from 2 to 8 (13, 16–18, 26). Goyal et al. (8) retrieved information of SLN status for 229 patients. Of these 50 had SLNB and 18 (36%) had positive SLNs. In another database study by Avraham et al. (20), there were 203 EPC patients, but information on SLNB was available only for 33 patients (the positivity rate 42%; 14/33). In the literature, the rate for lymph node metastases at initial evaluation (6, 7, 13, 16–19) and progression to the regional lymph nodes (8–25%) (6, 9, 14, 18) varies greatly. However, these rates cannot readily be used to justify the SLNB procedure for EPC.

The limitations of the current study were that the design was retrospective and the patient population of 14 patients was rather small. Data were extracted from patients' files that were recorded for purposes other than research, which can limit the review and analysis of clinical diagnostic impressions.

The strengths of this study include the re-evaluation and confirmation of all histological samples from the primary tumours by the same dermatopathologist. Furthermore, the follow-up time was long (median 8.6 years).

Based on the current series, the false-negative rate of SLNB was zero, accentuated by the long follow-up of median 9.2 years (range 4.1–12.7 years) during no recurrences were detected. In other case series it seems that the disease of patients with EPC with negative SLNs infrequently progress in follow-up (13,1 6, 26–28). Due to the rarity of EPC and small number of patients in this series the real benefit of SLNB remains plausible. However, as in melanoma and breast cancer, SLNB gives unique information for staging and prognosis. It would be of interest to see whether SLNB has an impact on treatment protocols, follow-up, and prognosis in larger cohorts. In the future, multicentre international collaboration is needed to gather information to establish treatment protocols for this rare cancer.

The authors have no conflicts of interest to declare.

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