CASE REPORT

Eccrine porocarcinoma: A rare case of an in situ tumor with lymph node metastases

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INTRODUCTION

Eccrine porocarcinoma (EPC) is a rare skin malignancy that represents around 0.01% of all skin tumors.1,2 There is a wide range of clinical presentations of this neoplasm such as papules, plaques, and nodules. Most tumors appear in the head and neck region or on the lower extremities, but all body parts can be involved. EPC is frequently clinically misdiagnosed as squamous cell carcinoma or Bowen disease because the tumors have similar clinical presentations. Therefore, histopathologic examination prior to therapy is required.

EPC is known for its high recurrence and metastatic rate of both 20%. Metastases are mostly found in the regional lymph nodes and mortality among patients with EPC with nodal metastasis is high (67%). The survival period for patients with distant metastasis is reported to be 5 to 24 months.1

At this moment, no therapy exists as the gold standard because of the rarity of the disease, although surgery (wide local excision or Mohs micrographic surgery) is the common treatment for local disease. In case of metastatic and/or recurrent disease, it is suggested to add chemotherapy and/or radiotherapy. There is no consistency about which chemotherapy should be added due to the rarity of the disease.1,2

Here we present a patient with EPC in situ with lymph node metastases.

CASE REPORT

A 58-year-old man was referred by his general practitioner to the dermatology outpatient clinic of our hospital with a skin lesion on his right hip. The lesion existed for 11 years, and 2 previous biopsies performed by the general practitioner both showed Bowen disease. The lesion was subsequently repeatedly treated with cryotherapy without complete response. A few weeks before his first visit to our department, the lesion increased in size and thickness. No other skin lesions were present and the medical history was negative for any other skin disease.

Besides the skin lesion, 18 months earlier the patient had biopsy-proven lymph node metastases of the right groin, parailiac, and para-aortic right. The lymph node biopsies showed a non—small cell carcinoma of unknown primary origin. The tumor cells were initially found positive for CKAE1/AE3, CK7, EMA, GATA3, and p40, and negative staining was found for SOX10, CD15, and OCT4. Based on this immunohistochemical profile, the case was signed out as a non—small cell carcinoma of unknown primary origin. Based on the p401 and GATA31 staining, a suggestion of metastatic poorly differentiated squamous cell carcinoma or urothelial carcinoma was made. Extensive clinical workup in search for a primary tumor with computed tomography, positron emission tomography, and cystoscopy failed to detect a primary tumor. The patient was subsequently treated with chemotherapy (cisplatin-etoposide and carboplatin-etoposide).
At the time of dermatologic total body inspection, we noticed an erythematous nummular superficial plaque with central hyperkeratosis on the patient’s right hip (Fig 1). No other skin lesions were seen.

A diagnostic excision of the whole lesion was performed. Histopathologic examination found an intraepidermal proliferation with large expansile epithelial nests with central comedonecrosis. The epithelial nests were composed of poroid cells showing nuclear polymorphism and nuclear hyperchromasia. In areas, the proliferation showed cystic foci of ductal differentiation with presence of an inner EMA-positive cuticle layer (Fig 2, A and B). Also, abortive duct differentiation was focally observed in the form of intracytoplasmic lumina. P53 showed an aberrantly high expression in lesional cells. Altogether, the histopathologic features are consistent with eccrine porocarcinoma in situ.

Although invasive growth was not found, we reasoned that the previously diagnosed lymph node metastases could be metastases of the porocarcinoma in situ. Both the earlier biopsies of the skin lesion and the earlier lymph node biopsies were reviewed. In the skin biopsies, the diagnosis of a porocarcinoma in situ was confirmed instead of the previously diagnosed Bowen disease. Review of the lymph node biopsies confirmed the metastases of a non—small cell carcinoma. In retrospect, however, the tumor cells in both biopsies focally showed abortive duct differentiation with the presence of a intracytoplasmic lumina (Fig 3, A). The luminal cuticular layer was highlighted by epithelial membrane antigen (EMA) staining that confirmed the ductal differentiation (Fig 3, B). Additional molecular analysis using targeted next-generation sequencing of both the porocarcinoma in situ and the metastasis found an identical hotspot TP53 exon 7 missense mutation (c.743G>A,p.R248Q (NM 000546)) with a variant allele frequency of 77% in the porocarcinoma in situ and 17% in the lymph node metastasis.
(estimated tumor cell percentages 80% and 40%, respectively). This hotspot mutation has previously
been identified in porocarcinoma; however, this hotspot mutation is also commonly found in other
tumors. Single-nucleotide polymorphism analysis showed loss of the wild-type TP53 allele in both
tumors. Furthermore, strong aberrant nuclear p53
immunohistochemical staining was present in both
lesions supporting our molecular findings. Importantly, single-nucleotide polymorphism anal-
ysis identified additional chromosomal losses (chromosome 3p, 10q, and 13q) that were shared by both
lesions.

Because of the similar histopathologic findings of
the porocarcinoma in situ and the lymph node
metastases, together with an identical molecular
profile, it is highly suggestive that both lesions
represent the same entity.

Unfortunately, the lymph node metastases pro-
gressed under chemotherapeutic treatment, and the
patient died of metastatic disease half a year after the
EPC in situ was diagnosed.

DISCUSSION

There are several cases described in which an EPC
originated from the site of a pre-existing Bowen
disease. There are also cases described of lymph
node metastases with unknown primary tumor that
appeared to be metastasis of an eccrine porocarci-
noma. The uniqueness in this case is that the patient
was previously repeatedly given a diagnosis of
Bowen disease, which appeared to be a porocarci-
noma in situ and the primary tumor of lymph node
metastases. This case demonstrates the importance
of molecular analysis as a tool in search for the
primary tumor.

Several possibilities exist for how an in situ
carcinoma could cause lymph node metastases. The primary tumor most likely regressed from
infiltrative to in situ from chemotherapy, as
previously described in EPC. Another possibility is
that the innate or the adaptive immune system was
activated (upon metastasis) and caused spontaneous
regression of the invasive component of the primary
tumor. A third option is the chance that the
invasive component was sampled in the earlier biopsies and/or the latter skin excision but not
detected by light microscopy, as not all tissue is
routinely analyzed. In case there was an invasive
component at that time, it could be gone as a result
of the previous treatments with cryotherapy.

Here we report a rare case of an eccrine
porocarcinoma in situ that metastasized to the
regional lymph nodes. We recommend to critically
re-assess the patient’s clinical history and findings
when there is a metastatic disease with an un-
known primary tumor and a superficial or in situ
lesion.

REFERENCES

1. Nazemi A, Higgins S, Swift R, In G, Miller K, Wysong A. Eccrine porocarcinoma: new insights and a systematic
review of the literature. Dermatol Surg. 2018;44(10):
1247-1261.
2. Salih AM, Kakamad FH, Baba HO, et al. Porocarcinoma;
presentation and management, a meta-analysis of 453 cases.
Ann Med Surg (Lond). 2017;20:74-79.
3. Harms PW, Hovelson DH, Cani AK, et al. Porocarcinomas
harbor recurrent HRAS-activating mutations and tumor
suppressor inactivating mutations. Hum Pathol. 2016;51:
25-31.
4. Thuruthil RR, Jayalakshmy PS, Sukumar V. A case of recurrent
eccrine porocarcinoma with regional lymph nodal metastasis,
arising on a Bowen’s disease patch. Indian J Surg. 2015;
77(Suppl 1):182-184.
5. Lowney AC, Mc Aleer MA, O’Connor K, Fitzgibbon JF,
Bourke JF. Eccrine porocarcinoma arising within an area of
Bowen disease. Clin Exp Dermatol. 2012;37(2):136-138.
6. Hoshina D, Akiyama M, Hata H, Aoyagi S, Sato-Matsumura KC,
Shimizu H. Eccrine porocarcinoma and Bowen’s disease
arising in a seborrheic keratosis. Clin Exp Dermatol. 2007;
32(1):54-56.
7. Günhan O, Karsilioglu Y, Alomeroglu M, Berberoglu U. Eccrine
porocarcinoma: a case with an obscure primary tumor
diagnosed from lymph node metastasis. Am J Dermatopathol.
2007;29(2):176-179.

Fig 3. Lymph node metastasis shows fields of epithelial cells with cytonuclear atypia and focal
duct differentiation with presence of an eosinophilic inner cuticle layer (A) highlighted with
EMA (B).
8. Aaribi I, Mohtaram A, Ben Ameur El Youbi M, et al. Successful management of metastatic eccrine porocarcinoma. *Case Rep Oncol Med*. 2013;2013:282536.

9. Thomas JA, Badini M. The role of innate immunity in spontaneous regression of cancer. *Indian J Cancer*. 2011;48(2):246-251.

10. Mansfield AS, Heikkila P, von Smitten K, Vakkila J, Leidenius M. Metastasis to sentinel lymph nodes in breast cancer is associated with maturation arrest of dendritic cells and poor co-localization of dendritic cells and CD8+ T cells. *Virchows Arch*. 2011;459(4):391-398.