Dermatology Practical & Conceptual

Eccrine Porocarcinoma of the Face is a Great Imitator With Aggressive Behavior

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ABSTRACT

Introduction: Eccrine porocarcinoma (EPC) is a rare subtype of non-melanoma skin cancer developing in the intraepithelial portion of eccrine sweat glands. It is branded with a highly metastatic potential and increased rate of local recurrence after treatment. EPC showcased a trend of developing on the extremities, with presentation on the face sparse.

Objectives: Aim of the study was to evaluate the frequency, clinical features, and course of this malignancy presented on the face.

Methods: A retrospective review of the skin cancers excised between January 2010 and June 2021 was conducted in the plastic surgery department of a tertiary hospital. Patients were included in the study if EPC on the face was histologically confirmed. A prospectively maintained clinic database and the pathological reports were used to collect data.

Results: 4 EPC cases on the face out of 3984 confirmed skin cancers were identified. None of the cases was suspected clinically, but the diagnosis was established following the histopathologic examination. An aggressive postoperative behavior was confirmed in 2 cases.

Conclusions: The variance in the clinical presentation and the non-specific characteristics are perplexing clinical diagnosis, with the histopathologic examination representing the current standard for confirmation. Early diagnosis and adequate surgical resection are recommended as treatment cornerstones. Clinical awareness ought to be raised and a definitive treatment protocol be established for optimized results.

Introduction

Skin cancer is the most common type of cancer encountered worldwide. However, skin malignancies originating from the sweat glands account only for 1% of these lesions [1]. Eccrine porocarcinoma (EPC) is a very rare subtype, representing only 0.005% of cutaneous tumors [2]. Most often witnessed in people aged over 60 years, it is characterized by a highly metastatic potential and increased rate of local recurrence, even after excision. EPC showcased a trend of developing on the extremities, with presentation on the face sparse [2].

Objectives

Aim of the current study was to evaluate the frequency, clinical features, and course of EPC presented on the face, shedding light on this rare malignancy.

Methods

An observational cohort study was conducted in the Plastic Surgery Department of a tertiary hospital, using a predetermined protocol, which conformed to the ethical guidelines of the 1975 Declaration of Helsinki, approved by the local ethical committee and adhered to the STROBE statement for cohort studies. All patients who underwent excision of a skin cancer in the department between January 2010 and June 2021 were identified. Patients were included in the study if EPC on the face was histologically confirmed. A prospectively maintained clinic database and the pathological reports were used to collect data. Outcomes of interest were the EPC incidence, the clinical and pathological characteristics and the postoperative course of the sample.

Results

Four cases of EPC out of 3984 confirmed skin tumors (frequency: 0.1%) were revealed. None of the cases was suspected clinically, but they were resected as non-melanoma skin tumors with 5-mm surgical margins (Figure 1) [3]. The diagnosis was established following the histopathologic examination, based on the presence of irregular dermis-infiltrating malignant cell clusters that showed an invasive architectural pattern (Figure 2). Tumor cells were demonstrating marked nuclear pleomorphism and prominent nucleoli, they were large polyhedral to cuboid with moderate to abundant eosinophilic and more rarely clear cytoplasm, as well as many mitotic figures (up to 6-7/HPF). Other observed features included squamous differentiation, without keratinization, ductal differentiation and focally desmoplasia. No tumor displayed granular cells or decapitated lumens, ruling out the possibility of apocrine differentiation. Ducts were revealed with Periodic acid–Schiff stain and immunohistochemically with CK19, CEA and EMA.

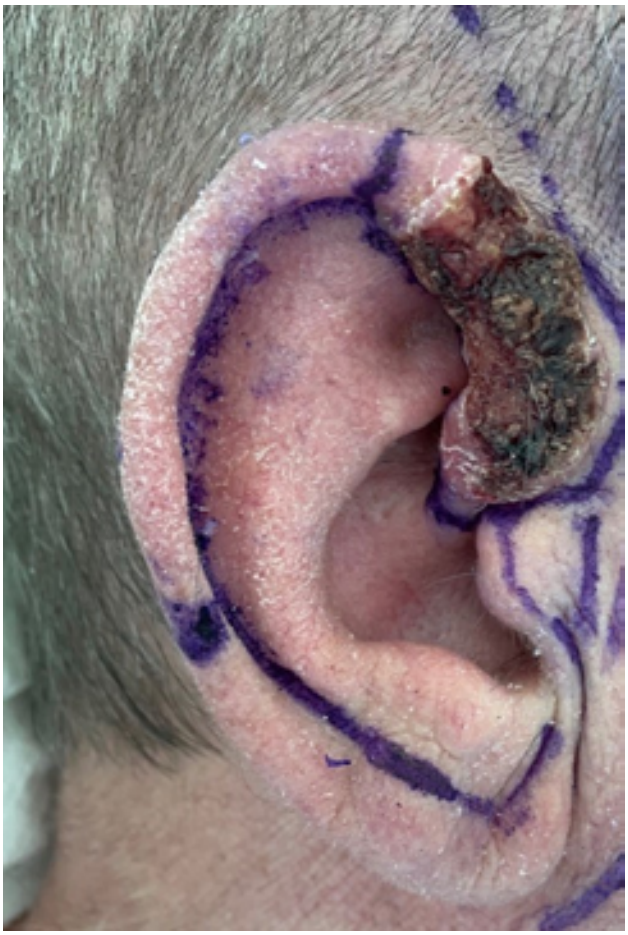

Figure 1. Eccrine Porocarcinoma - Macroscopic appearance of patient 4.

The characteristics and clinical course are depicted in Table 1. An aggressive behavior with local recurrence was revealed in 2 cases, despite the excision with clear margins in both cases and the radiotherapy course, which followed (Figure 3).

Conclusions

EPC is considered one of the rarest skin tumors a surgeon can encounter. Although it develops often on the extremities, the face in particular the auricle is considered an extremely rare location. Salih et al reviewed 453 EPC cases, with 40% of these located on the head and neck, but 7 cases only on the ear [4]. The cases we encountered concerned male patients exclusively, thus confirming the predilection of facial EPC towards the male gender [5]. Misdiagnosis of EPC due to its atypical presentation is highly probable. It could also be attributed to the diversity of total number of sweat glands on different parts of the body. However, current data annul this idea, as EPC occurrence is not correlated with the

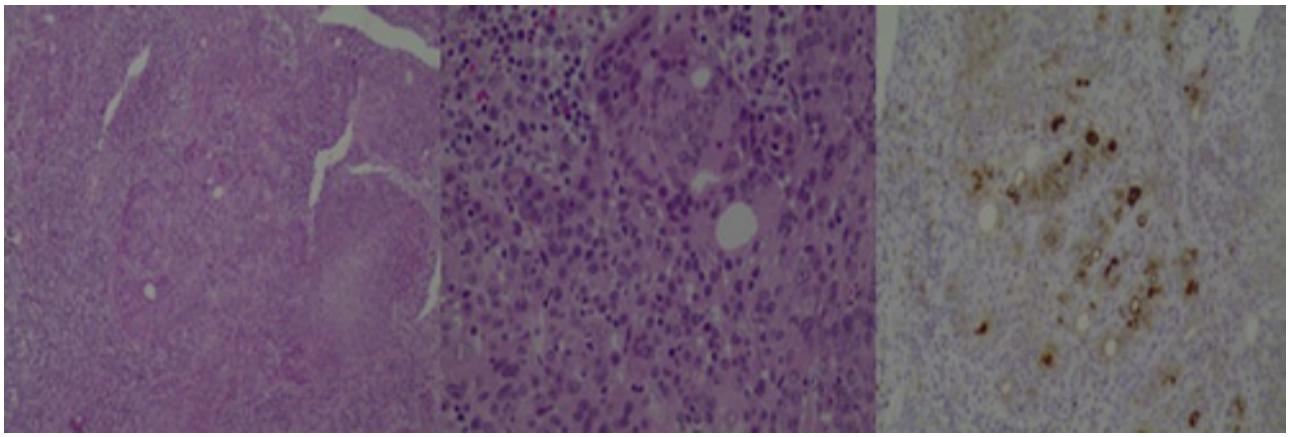

Figure 2. Eccrine Porocarcinoma – Histology. (A) Diffuse infiltrative pattern. (B) Duct formation, nuclear pleomorphism and prominent nucleoli. (C) Immunohistochemical expression of CEA in ducts.

Table 1. Characteristics of the EPC cases identified

Case	Month/ Year	Age (years)	Gender	Location	Diameter (mm)	Surgical Treatment	Adjuvant Treatment	Recurrence
#1	5/2012	69	M	Cheek	13	Excision -primary repair	-	In 6 months
#2	11/2018	80	M	Lower lid	30	Excision - eye exenteration-temporalis flap	Radiotherapy	In 4 months
#3	12/2019	84	M	Temple	10	Excision -FTSG	-	No
#4	3/2021	61	M	Ear	22	Excision -postauricular flap	Radiotherapy	No (5 months postoperatively)

FTSG = full thickness skin grafting; M = Male.

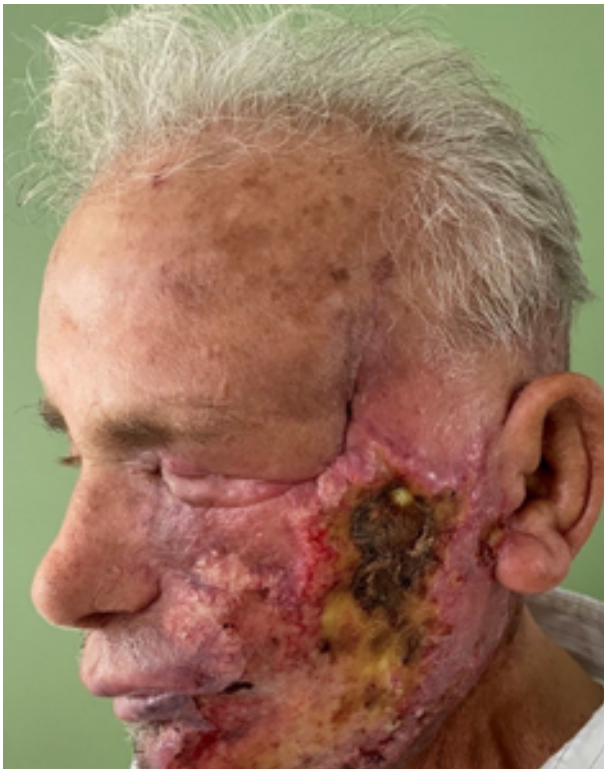

Figure 3. Eccrine Porocarcinoma – Locoregional metastasis of patient #2, 2 years following surgery and radiotherapy.

highest concentration of sweat glands (palmoplantar region) [5]. Underreporting of this entity remains also a possibility.

It is proposed that EPC emerges either de-novo or from a pre-existing benign poroma [2]. The ratio of malignant transformation was estimated around 18% [2]. Immunosuppression may be a contributing factor in EPC pathogenesis, as well as sun exposure [4]. Genetic predisposition may be also implicated, as p53 oncogene expression is witnessed in 88% of cases, while loss of retinoblastoma protein and overexpression of p16 gene, though not consistent, have been also reported [6,7]. None of these implicating factors could be associated with a predilection for EPC manifestation on specific areas.

From a clinical standpoint, EPC usually presents itself as an asymptomatic solitary nodule or mass which can progress to ulceration and cause pain [2]. The lesion is typically noticed over a long period of time (up to several years), although cases of rapid growth in a few months were also noted. Considering its rarity, EPC needs to be differentiated from a plethora of skin conditions such as seborrheic keratosis, pyogenic granuloma, amelanotic melanoma, squamous cell carcinoma and verruca vulgaris [2]. This task becomes even harder for the dermatologist, as most of the aforementioned

skin lesions are encountered predominantly in older people, while no clear clinical characteristics for EPC have been reported and thus clinical diagnosis often fails.

The clinical characteristics of EPC act as an insurmountable impediment to the clinical diagnosis and shifted focus on the histological examination. The presence of cytologic atypia with advancing margin and poromatous basaloid cells displaying ductal differentiation confirmσ the diagnosis [2]. Robson et al has described 3 histological variants. "Infiltrative" is characterized by ill-defined lower limits with malignant clusters infiltrating the dermis and hypodermis, "pushing" by well-defined lower dermal border, and "pagetoid" by intraepidermal clusters of tumoral cells, mimicking Paget disease [2]. Immunohistochemistry can be a significant diagnostic aid, including various stains for CEA, EMA, CK-7 and S-100 protein [8].

EPC is regarded as a very aggressive malignancy exhibiting high metastatic potential [2]. A 31% of regional or distant metastasis was revealed, with the most common sites being the regional lymph nodes (57.7%), and the lungs (12.8%) [4]. Mortality increases drastically in case of metastatic disease, with overall survival ranging between 5 and 24 months [5]. Local recurrence after excision is also high, reaching 25%, with the "infiltrative" and "pagetoid" subtypes being implicated most often [2,9]. Indeed, 2 of our 4 patients manifested local recurrence few months following tumor excision. Multi-nodularity and ulceration are among the signs of aggressiveness, while pedunculated tumors are less aggressive [4]. Lympho-vascular invasion, positive tumor margins, high mitotic count (> 14/HPF) and tumor depth (> 7 mm) have been proposed as predictors of worse clinical outcomes [2].

Currently, no established treatment guidelines exist. Wide local resection with confirmation of clear margins remains the optimal treatment option, achieving therapeutic outcome in 70%-80% of cases [5]. Belin et al proposed a surgical algorithm, based on the histological type [2,9]. In particular, all lesions should be excised with 3-mm clear margins and a further 5-mm margin must be achieved using a modified Mohs technique, should the "infiltrative" or the "pagetoid" subtypes be confirmed [9]. Having high suspicion for an aggressive skin tumor but no access to Mohs surgery, we performed an excision with a 5-mm margin. Involvement of lymph nodes requires surgical clearance, but little data exists to support routine lymph node dissection [10]. Adjuvant treatments have been administered in metastatic disease, with both chemotherapy and radiotherapy provoking mixed responses, which is also supported by our data [5].

Limitations of the study include the small sample size and its retrospective nature. However, the data covering a long period, the dedicated to skin cancer plastic surgery department of a tertiary hospital and the long-term follow-up of the patients with confirmed EPC of the face enabled the analysis of such a rare malignancy, mitigating the potential effect of the study limitations to the outcomes of interest.

Overall, EPC is very rarely encountered. Based on this cohort and the pertinent literature review, the evidence regarding the pathophysiology, surgical and adjuvant treatment is inconclusive and call for further reporting and analysis. Currently, awareness should be raised by the clinician to properly recognize EPC and treat promptly, and vigilance is needed, due to its high malignant nature and mortality rates.

Learning points

- Eccrine porocarcinoma (EPC) is an extremely rare subtype of non-melanoma skin cancer, mostly presenting in the extremities of the elderly population.
- Underreporting and misdiagnosis of EPC occurring on the face are distinct possibilities accounting for its rarity.
- Histologic examination confirms the diagnosis and identifies the histologic subtype, essential for guiding further treatment.
- EPC is regarded as a very aggressive malignancy exhibiting high rates of local recurrence and metastasis.
- Wide local excision remains the optimal treatment option, without a clear treatment protocol established up to date.
- Vigilance is mandatory for prompt recognition and treatment to avoid the high mortality rates reported.

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