

Eccrine Porocarcinoma of the Head: An Important Differential Diagnosis in the Elderly Patient

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Key Words

Eccrine porocarcinoma · Malignant eccrine poroma · Squamous cell carcinoma · Basal cell carcinoma

Abstract

Background: Eccrine porocarcinoma is a rare malignant tumor of the sweat gland, characterized by a broad spectrum of clinicopathologic presentations. Surprisingly, unlike its benign counterpart eccrine poroma, eccrine porocarcinoma is seldom found in areas with a high density of eccrine sweat glands, like the palms or soles. Instead, eccrine porocarcinoma frequently occurs on the lower extremities, trunk and abdomen, but also on the head, resembling various other skin tumors, as illustrated in the patients described herein. **Observations:** We report 5 cases of eccrine porocarcinoma of the head. All patients were initially diagnosed as having epidermal or melanocytic skin tumors. Only after histopathologic examination were they classified as eccrine porocarcinoma, showing features of epithelial tumors with abortive ductal differentiation. Characteristic clinical, histopathologic and immunohistochemical findings of eccrine porocarcinomas are illustrated. **Conclusion:** Eccrine porocarcinomas are potentially fatal adnexal malignancies, in which extensive metastatic dissemination may occur. Porocarcinomas are commonly overlooked, or misinterpreted as squamous or basal cell carcinomas as well as other common malignant and even benign skin tumors. Knowledge of the clinical pattern and histologic

findings, therefore, is crucial for an early therapeutic intervention, which can reduce the risk of tumor recurrence and serious complications.

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Introduction

Eccrine porocarcinoma is a rare malignant tumor of the eccrine sweat gland, producing protean clinical and pathologic findings. The tumor was first described in 1963 by Pinkus and Mehregan [1] as epidermotropic eccrine poroma. The term eccrine porocarcinoma was introduced in 1969 by Mishima and Morioka [2], who identified the intraepidermal portion of the eccrine sweat duct (i.e. the acrosyringium) as the point of origin of this tumor. Since then, eccrine porocarcinomas have been reported in fewer than 300 cases worldwide [3–5].

The peak incidence of porocarcinomas is in the seventh decade of life, and they appear to be slightly more common among males than females [4]. Patients usually present with a nodule, a verrucous infiltrative plaque, or an ulcerated polypoid lesion that is often mistaken for a squamous or basal cell carcinoma [5]. However, eccrine porocarcinomas can also mimic many other cutaneous malignancies, including Bowen's disease, amelanotic melanoma, cutaneous metastasis of a visceral carcinoma, or common benign lesions such as seborrheic keratosis, verruca vulgaris or pyogenic granuloma [3, 5]. The diagnosis

of eccrine porocarcinoma, therefore, most often relies upon identification of several of its more typical histopathologic and immunohistochemical features [5–7], as was the case with our patients.

The potential for local recurrence and metastasis of eccrine porocarcinoma has been emphasized in many previous reports and case series [4, 8]. There is a high risk of multiple relapses and particularly intracranial or intracerebral extension, when eccrine porocarcinoma is localized on the head [3, 8–10]. In the follow-up period of our patients (18–30 months) no tumor recurrences or metastases were observed. Nevertheless, long-term surveillance of eccrine porocarcinomas is required, because prognosis of the tumor is guarded [4, 8, 11]. Here, a review of clinical and pathologic manifestations and current treatment options for eccrine porocarcinoma are presented and discussed.

Case Reports

Patient 1

A 64-year-old female patient with a 10-year history of multiple myeloma was admitted to hospital with an exophytic tumor of the head for evaluation of possible squamous or basal cell carcinoma. The tumor had steadily increased for 4 years, but displayed a rapidly accelerated growth during the last 6 months. On examination, she had a partly erosive erythematous tumor, with a sharp irregular border, approximately 3 cm in diameter and located

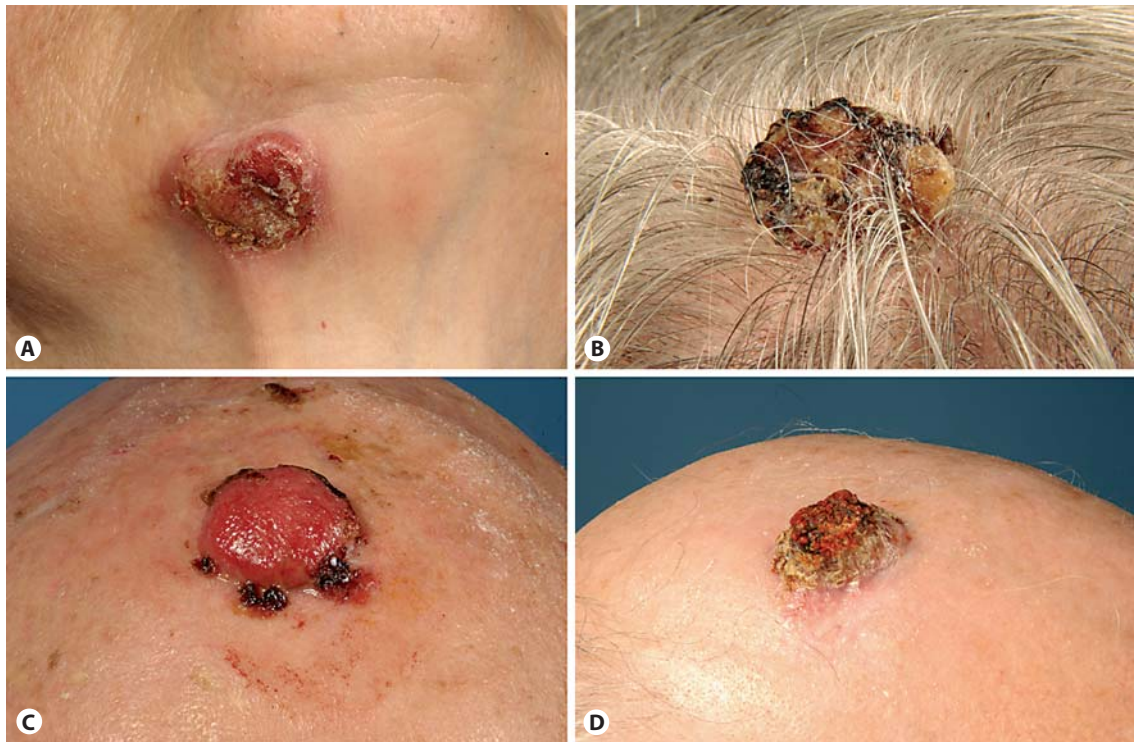


Fig. 1. Clinical aspects of eccrine porocarcinoma. **A** Partly erosive, erythematous tumor in patient 1 with multiple myeloma, mimicking squamous or basal cell carcinoma. **B** Rapidly progressive, exophytic tumor with superficial erosion and crusting in patient 2, mimicking squamous cell carcinoma or cutaneous metastasis. **C** Continuously growing, erosive tumor in patient 3, mimicking amelanotic melanoma or pyogenic granuloma. **D** Conical, hyperkeratotic tumor with typical aspects of a cutaneous horn in patient 4, mimicking a proliferating verruca vulgaris.

in the right submandibular region (fig. 1A). Computed tomography (CT) scans of the head, neck, trunk and abdomen revealed no metastases of a solid tumor. The patient underwent wide surgical excision of the skin lesion.

Patient 2

This 77-year-old male patient presented with a sharply bordered, hairless, exophytic, red-brown tumor, 2 cm in diameter on the vertex of his scalp with superficial erosion and crusting (fig. 1B). His admission was precipitated by rapid tumor growth for the last 2 months and frequent bleeding of the lesion after combing his hair. He denied any fevers, night sweat or weight loss. In this case, the tumor was resected under the clinical diagnosis of squamous cell carcinoma or cutaneous metastasis. A neck ultrasound study, a chest radiograph as well as an abdominal ultrasound study showed no evidence of metastasis.

Patient 3

An 80-year-old male patient was referred to our clinic with a 3-year history of a continuously growing and frequently bleeding tumor on the front of his scalp. Examination revealed a round, erythematous, erosive tumor, approximately 3 cm in diameter (fig. 1C). Four months before, the tumor had shown accelerated growth following a minor trauma. This tumor was initially interpreted as amelanotic melanoma or pyogenic granuloma. Before surgical excision, a CT scan of the head and neck was done, which showed no significant abnormality and no evidence of tumor metastasis.

Patient 4

This 78-year-old male patient with no notable medical history had a verrucous tumor on his left temporoparietal area (fig. 1D). He reported a massive trauma of his scalp approximately 30 years ago and a 1-year history of tumor development in

the same location. He consulted a physician and, after a skin biopsy, a diagnosis of proliferating verruca vulgaris was made. On admission, he showed an irregularly but sharply bordered, exophytic, hyperkeratotic tumor, approximately 4 cm in diameter, resembling a cutaneous horn. A neck ultrasound study, chest radiography, as well as an abdominal ultrasound study, showed no evidence of metastasis, and a wide excision of the lesion was performed.

Patient 5

A 79-year-old male patient with a 12-year history of chronic lymphocytic leukemia who had had an exophytic tumor for 1 year was admitted to our hospital for investigation. He also had multiple actinic keratoses on all light-exposed areas of the skin. Clinical examination revealed a partly erosive, multinodular tumor of approximately 3 cm in diameter, localized in the left retroauricular region with close as-

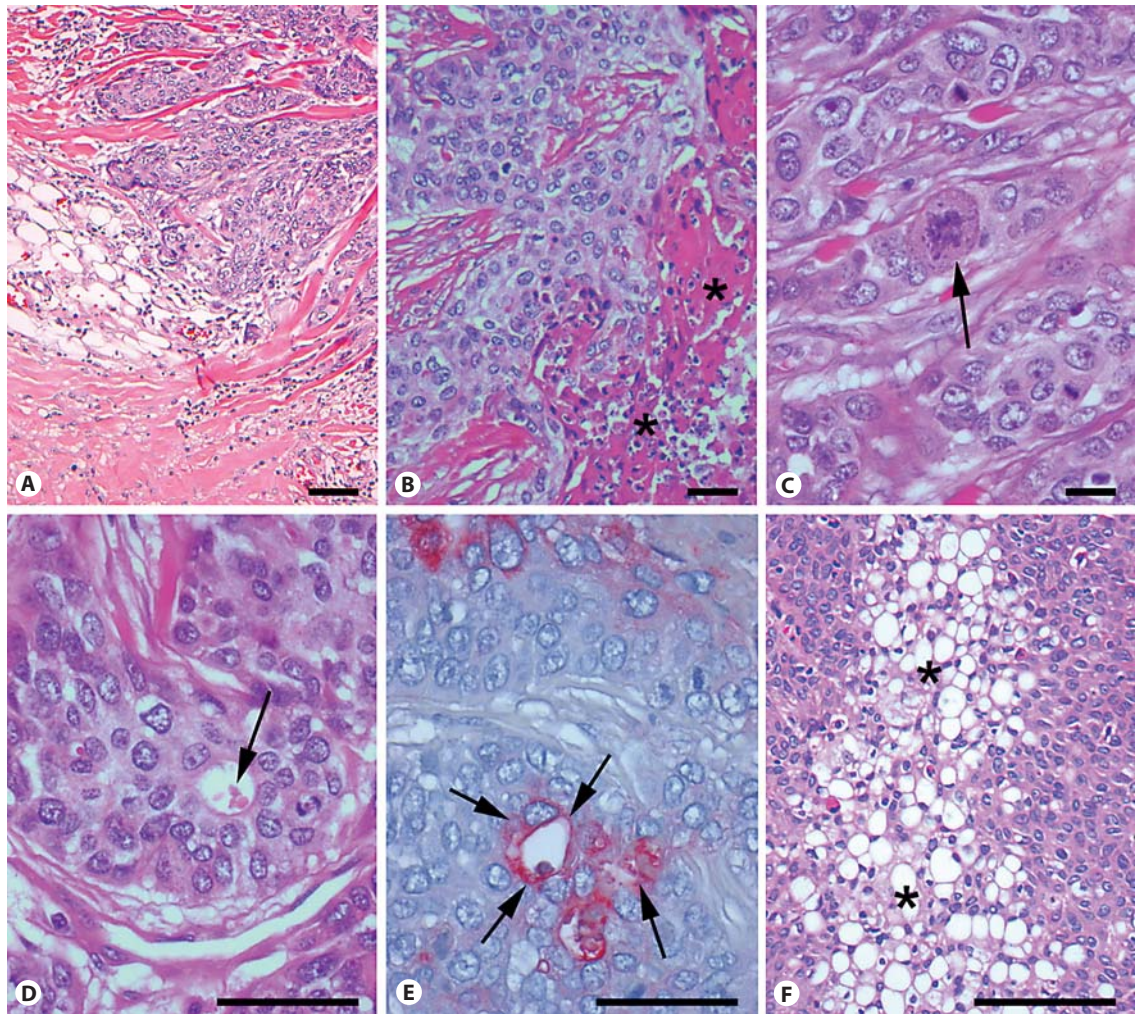


Fig. 2. Histomorphologic aspects of eccrine porocarcinoma. **A** Solid aggregates of invasive tumor cells growing deep into the dermis and adjacent subcutis. **B** Areas of necrosis (stars) and prominent nuclear pleomorphism. **C** Abnormal mitotic figures (arrow). **D** Abortive ductal differentiation (arrow) is highlighted by carcinoembryonic antigen immunostaining (**E**, arrows). **F** Focus of clear cell changes due to glycogen deposition (stars). Bars = 100 μ m.

sociation to his earlobe. The patient was given a presumptive diagnosis of squamous cell carcinoma. A neck ultrasound study, CT scans of the head and neck, chest radiography and an abdominal ultrasound study were unremarkable. The patient underwent wide local excision of the lesion.

Histopathology and Immunohistochemistry

Histopathological examination of all tumors revealed features consistent with the diagnosis of eccrine porocarcinoma (fig. 2A–F): solid aggregates of small epithelial tumor cells replaced the epidermis and grew in anastomosing bands deep into

the adjacent dermis. Peripheral nuclear palisading and retraction artifacts were not observed. All the tumors showed nuclear pleomorphism and prominent mitotic activity with abnormal mitotic figures. Abortive ductal differentiation was evident in all tumors and could be highlighted by epithelial membrane antigen as well as carcinoembryonic antigen immunohistochemistry. Some tumor cells contained glycogen, sometimes producing foci of clear cell changes.

Staging and Outcome

Initial and follow-up staging examinations (including CT and ultrasound stud-

ies) showed no evidence of lymph node or visceral metastasis of any solid tumor. Furthermore, no local tumor recurrences were observed so far. However, it must be noted that the follow-up periods in our patients were rather short (12–24 months) at the time of publication.

Discussion

Eccrine porocarcinoma, also known as malignant eccrine poroma, is a rare adnexal tumor that accounts for 0.005% of epidermal skin neoplasms [9]. Eccrine porocarcinoma may occur de novo as a pri-

mary tumor or, as in nearly 50% of cases, develop from preexisting benign poromas after a long latency. The malignant transformation may be induced by immunosuppression or ionizing radiation [10].

Eccrine porocarcinomas are certainly rare skin malignancies, but the reported incidence may be an underestimation because many porocarcinomas are overlooked or misinterpreted as squamous or basal cell carcinoma [5]. Moreover, eccrine porocarcinomas may also resemble various common benign skin tumors, including verruca vulgaris or pyogenic granuloma [5, 7], as was the case with our patients. Furthermore, Akiyoshi et al. [8] described a single case of zosteriform tumor appearance. Clinicians, therefore, need to be aware of this rare entity, as porocarcinomas often show a marked morphologic variability, which has led to misdiagnosis and delayed treatment with disastrous consequences in previously reported cases [5–7].

Eccrine porocarcinoma of the head, as in our cases, is a rare clinical manifestation. The most common sites affected are the lower limbs, the trunk, abdomen or the upper extremities [9]. Notably, some authors reported eccrine porocarcinomas occurring in unusual localizations, like scars [12], the vulva, the scrotum, the penis or the periungual region [13]. In areas exhibiting a high density of eccrine sweat glands, like the palms or soles, porocarcinomas occur surprisingly seldom [8].

The vast majority of patients with eccrine porocarcinomas are elderly people [4], although the tumor may also affect younger patients. Poiars Baptista et al. [6] report on a case observed in a 12-year-old patient with xeroderma pigmentosum, and Valverde et al. [14] report on an 8-year-old girl with eccrine porocarcinoma, representing the youngest patient so far. A 16-year-old Iraqi soldier, injured by a poison gas explosion, developed metastatic porocarcinoma 8 years later, suggesting that eccrine porocarcinoma could be an additional variant in the spectrum of skin malignancies as late complications of contact with poison gas [15].

In addition, an association with lymphocyte dysfunction has been recognized in a previous report of an 81-year-old patient, and has been implicated in tumorigenesis [7]. Of particular interest in this case was the dysfunction of interleukin 2 production and interleukin 2 receptor expression of peripheral lymphocytes, which

have been related to the patient's exceptional clinical manifestation with extensive cutaneous metastasis. Similar observations, though uncommon, have been noted in some cases in previously published series [16, 17]. Taken together, the role of lymphocyte dysfunction in the development of eccrine porocarcinoma is currently unclear, but it is interesting to note that 2 of our elderly patients also had disorders with functional lymphocyte impairment, such as multiple myeloma and chronic lymphocytic leukemia.

Although in some cases the diagnosis of eccrine porocarcinoma can be made on typical history and clinical findings (i.e. preexisting poroma), the definitive proof is histological. Deriving from the intraepithelial ductal portion of eccrine sweat glands, histopathology reveals a tumor with ductal differentiation and significant cytologic pleomorphism. Eccrine porocarcinoma is most typically characterized by the downgrowth of broad anastomosing bands of epithelium showing small epithelial cells united by small intercellular bridges and lacking any tendency towards peripheral palisading (dermal type). Occasionally, the tumor grows horizontally and may produce extensive pagetoid infiltration in the overlying epidermis. This intraepidermal or epidermotropic type has been reported to exhibit a worse prognosis with either locally recurrent or metastatic disease [18, 19]. It is standard practice to ascertain the origin of malignant cells by additional immunohistochemical staining. Thus, ductal differentiation and intracytoplasmic lumen formation of eccrine porocarcinomas can be highlighted with the use of diastase-PAS reaction or the immunocytochemical demonstration of epithelial membrane antigen or carcinoembryonic antigen expression [13].

Despite their sometimes innocuous histologic appearance, eccrine porocarcinomas are aggressive lesions, which require wide local excision of the primary tumor with dissection of regional lymph nodes if they are clinically involved [4]. The role of an elective lymph node dissection, especially in recurrent or poorly differentiated tumors, is still under debate. The recurrence rates in porocarcinomas after excision are approximately 20% and depend on completeness of removal, depth of tumor invasion (>7 mm), and pathological grading [4, 8, 11]. With regard to tumor staging, a recent report highlights the diagnostic value of ¹⁸F-fluorodeoxyglu-

cose positron emission tomography to detect residual tumor, recurrent lesions and metastasis to regional lymph nodes or distant organs [20].

The prognosis of eccrine porocarcinoma has been discussed controversially. Robson et al. [4] presented the largest series of cases to date with a poor prognosis in 30% of the patients experiencing lymph node (20%) or distant metastases (10%). Akiyoshi et al. [8] reviewed 21 cases with as many as 48% of patients developing metastases. Matloub et al. [21] described the development of cutaneous, lymph node or visceral metastases in 39% of 79 reviewed cases. In contrast, Poiars Baptista et al. [6] as well as Perna et al. [11] each reported on only 1 out of 24 cases (4%), who developed metastases in the course of their disease. However, once the tumor has metastasized, the outlook is poor, because no definitive treatment exists. When lymph node metastases occur, the mortality rises up to approximately 65% [4]. The survival time in 6 patients with distant metastases was 5–24 months [3]. Radiotherapy seems of little benefit and systemic chemotherapy is of uncertain value [5, 22], although responses of metastatic tumors have recently been described after treatment with docetaxel (Taxotere) [22] as well as paclitaxel (Taxol) combined with systemic immunotherapy (interferon α) [23]. One case report indicated that metastatic porocarcinoma improved substantially with interferon α and interleukin 2 injected perilesionally [24]. There is, however, no evidence to suggest a beneficial effect of an adjuvant therapy. Overall, careful follow-up is needed in patients with eccrine porocarcinoma. None of our 5 cases has shown tumor recurrence, lymph node or distant metastases (18–30 months follow-up) so far, but a long-term follow-up is required.

To summarize, the diagnosis of eccrine porocarcinoma may be delayed, especially in cases of atypical presentation, leading to protracted illness and serious complications. Even though rare, and diagnosed most often only by histology, our report highlights the fact that eccrine porocarcinoma should enter the list of differential diagnosis when considering skin tumors in the elderly.

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