

Metastasizing Eccrine Porocarcinoma Of The Nose: Case-Report With Immunohistochemical Study And Review Of The Literature

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Abstract

Eccrine Porocarcinoma (EP) is a rare malignancy of eccrine sweat gland. It mostly affects old people. Clinical diagnosis is difficult and lesions are often mistakenly identified as squamous cell carcinoma. The majority of EPs occur on the soles of the lower extremities, but can also be found on palms, trunk, upper extremities. In the Literature twenty-nine cases have been reported in the head and neck region and only four cases involve the nose. The majority of EPs were associated with locally aggressive disease and a poor outcome with a variable rate of distant metastasis. Early diagnosis with immunohistochemistry and wide surgical excision are basic. There are no data to support the use of adjuvant therapy. A case of EP of the nasal pyramid in a cardiac transplant recipient metastasizing to femoral bone is presented to emphasize the problems in the differential diagnosis, the treatment's modalities and the poor prognosis.

INTRODUCTION

First described by Pinkus and Mehregan in 1963 (1) as an "Epidermotropic eccrine carcinoma", Eccrine Porocarcinoma (EP) is a rare malignant neoplasm arising from eccrine sweat glands, usually presenting as a long-standing growth on the lower extremities. This tumor has a multitude of synonyms (hidroacanthoma simplex, sweat gland carcinoma, malignant intraepidermal eccrine poroma, eccrine poroepithelioma, dysplastic poroma, malignant syringoacanthoma, porocarcinoma) and the current term of EP was introduced in 1969 by Mishima and Morioka (2).

The Authors present an unusual case of EP of the nasal pyramid following heart transplantation, and review the world literature, underlining the clinical and cytohistological findings and emphasizing the problems of the differential diagnosis and treatment of this unusual neoplasm.

CASE-REPORT

On May 2005 a 67-year-old man came to our Otorhinolaryngology Unit with a 5-months history of a single, asymptomatic, ulcerated nodule of the right ala of the nasal pyramid that recently increased in size. On 1985 this patient underwent heart transplantation for severe dilated cardiomyopathy. Since that time he developed multiple squamous skin cancer and actinic keratosis of the head and

the limbs, treated successfully with surgical excision. After transplantation the patient was treated with immunosuppressive agents and prednisone.

Physical examination revealed a 1.5 cm, irregular, ulcerative, roundish lesion of the right nasal ala, with overlying erythema. Regional lymphadenopathy was not present. CT and MRI of the head and neck not revealed any bony erosion. Videorhinoscopy not showed any intranasal or rinopharyngeal extension of the tumor.

The patient underwent a wide local tumour-resection with skin graft nasal reconstruction under local anaesthesia. The surgical specimen showed a skin-covered nodule, measuring 1,5 x 1,5 cm with the surface partially ulcerated. H&E (Hematoxylin and Eosin) sections were studied (figg. 1-2).

Figure 1

Figure 1: Eccrine porocarcinoma of the nose. Infiltrative cords, tubules and lumen-forming profiles of compact and uniform polygonal cells are seen in the dermis. (Hematoxylin and Eosin, [H&E], X4).

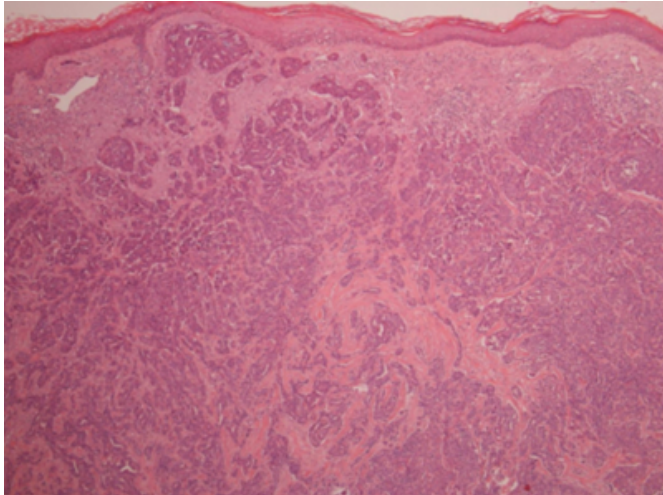
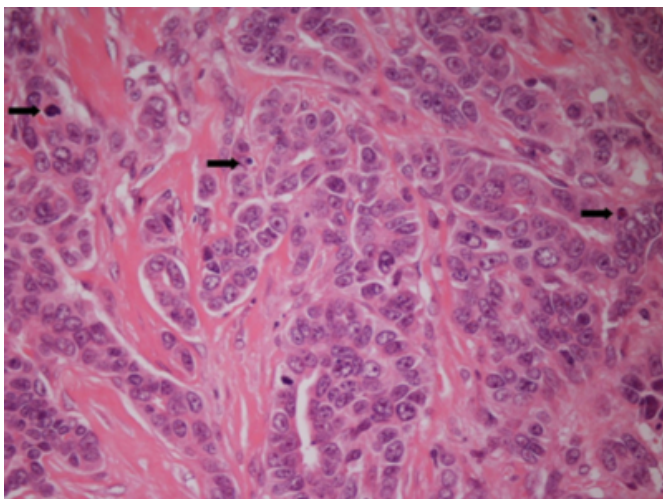


Figure 2

Figure 2: Eccrine porocarcinoma of the nose. The sections showed an ulcerated epidermis with atypical poroid cells extending into the dermis and hypodermis as anastomosing bands and dermal tumor islands. Poroid cells had large and hyperchromatic nuclei, with an increased number of mitotic figures (see arrows). (Hematoxylin and Eosin, [H&E], X40).



The sections showed an ulcerated epidermis with atypical poroid cells extending into the dermis and hypodermis as anastomosing bands and dermal tumor islands. Poroid cells had large and hyperchromatic nuclei, with an increased number of mitotic figures. Areas of squamous differentiation mimicking squamous cell carcinoma were also present. Immunohistochemically the tumour cells were strongly positive for CKMNF 116, CK 7 (fig.3), EMA (fig.4) and

focally for S100 protein, but were negative for CK 20, PSA, TTF1, chromogranin A, and synaptophysin. The final histological diagnosis was eccrine porocarcinoma.

Figure 3

Figure 3: Eccrine porocarcinoma of the nose. Immunohistochemical study 25X. Tumoral cells stain strongly positive for CK7 (cytokeratin 7).

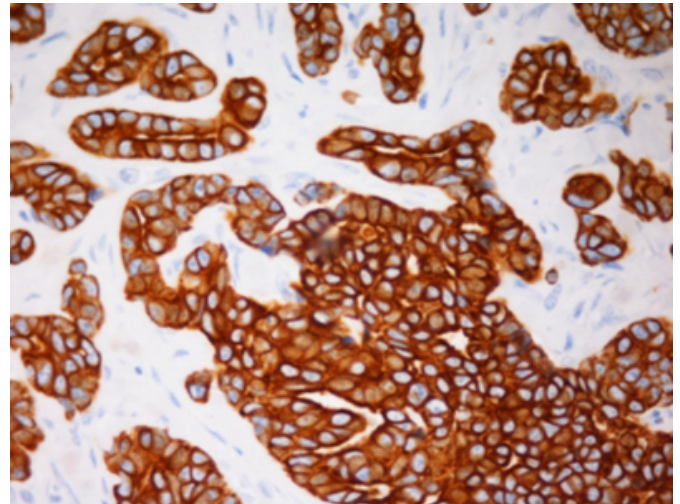
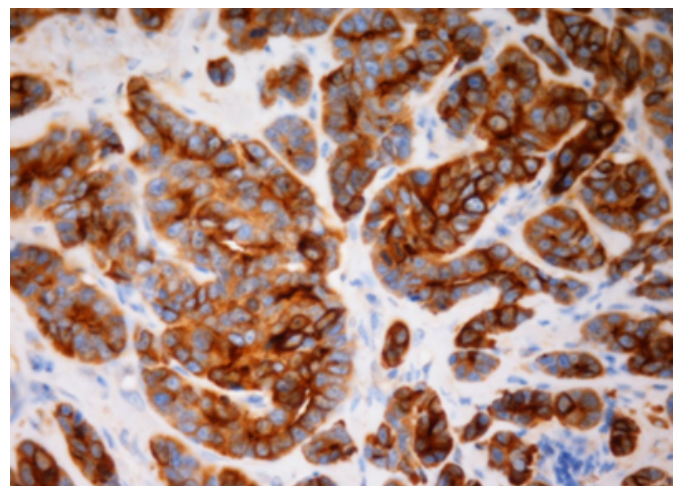


Figure 4

Figure 4: Eccrine porocarcinoma of the nose. Immunohistochemical study 25X. Tumoral cells stain strongly positive for EMA (Epithelial Membrane Antigen).



Two months later the patient underwent a biopsy which resulted negative for recurrence. Eighteen months later a pathologic fracture of femoral bone occurred and the patient underwent a surgical reduction. The microscopic examination and immunohistochemical stain of bone specimen demonstrated the presence of metastasis of EP. The patient started radiotherapy and chemotherapy with docetaxel and interferon-alpha 2a without response. The

patient died nine months after the diagnosis of bone metastasis and twenty-seven months after the initial diagnosis of EP.

DISCUSSION

Carcinomas of the eccrine sweat gland represent a uncommon group of neoplasms with potential for local destruction and metastasis. The classification of these tumours is often incomplete and improbable because of the paucity of reported cases and also because of their histologic resemblance to mature eccrine glands. EP may originate de novo from any portion of the physiological eccrine apparatus or result from the malignant transformation of an existing benign eccrine tumour; generally, primary malignant EP derives from the intraepidermal ductal portion of the eccrine gland.

EP represent 0.005% to 0.01% of all skin tumours and in Literature approximately 140 cases have been reported. It is commonly found in old people with a slight predilection for men (55%) [3]. It was previously thought that the majority of EPs are found on the palms and soles, reflecting the high concentration of sweat glands. However, the distribution of these lesion appears to have no correlation with sweat gland density. The lower extremities are most usually affected (more than 50%). In Literature twenty-nine cases have been reported in the head and neck region and only four cases involve the nose (tab. I)

[3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23].

Local recurrence (25%) and metastasis to skin, local lymph nodes, breast, liver, bladder, ovary, adrenal glands, lung, peritoneum and bone may occur [12]. Early reports suggested that the majority of EP were associated with locally aggressive disease and a poor outcome with a variable rate of distant metastasis (11-50%). Once metastasized, prognosis is unfavourable with a mortality rate of 75-80% according to a large case series [5,8,10,11,14,24].

The tumour's pathogenesis is still unknown, but in Literature some Authors have described many factors which predispose its appearance on the skin: burns, trauma, radiotherapy, immunosuppression treatment post cardiac and renal transplant, AIDS, prolonged exposure to ultraviolet radiation. The most widely cited explanation for the increased risk of skin cancer after solid organ transplant is that immunosuppressive therapy impairs the tumour surveillance mechanism of lymphocytes, disrupting the balance between tumorigenesis and tumorilysis [25]. In a

recent retrospective review of appendageal tumors in organ transplant recipients, Harwood et al. suggest that patients who are immunosuppressed have a propensity to also develop cutaneous appendageal tumors over their immunocompetent counterparts, with increased rates of both benign eccrine tumors and malignant eccrine tumors [26].

Generally EP present as a single, asymptomatic, solitary nodule or plaque, occasionally ulcerated; this tumor grow either slowly over years or rapidly, reaching a size of several centimeters over a few months. It may arise de novo or develop as a malignant transformation of an eccrine poroma, nevus sebaceous, chronic lymphatic leukaemia and actinic lesions [12]. A long-standing tumor history is often encountered in patients with EP. This is probably due to the fact that some Eps arise from a preexisting benign eccrine poroma. The preoperative duration of the lesion varied from 2 weeks to 60 years with a mean of 9 years [14].

EPs were composed of eosinophilic and clear atypical cells arranged in solid-cystic lobular masses. These tumors were divided into 2 subgroups: horizontal porocarcinomas, showing a prominent intraepidermal component, and nodular porocarcinomas, which demonstrated predominant nodular growth [27].

Microscopic appearance show an asymmetrical tumor with cords and lobules of polygonal cells. Tumor cells may be limited to epidermis or may extend into dermis and hypodermis. Some islands of tumor cells may lie free in the dermis and there will be cystic lumina within tumor nests. There is nuclear atypia with frequent mitosis and necrosis. Epidermis may show acanthosis. Eccrine differentiation is indicated by spiralling ductular structures, ducts lined by cuticular material, zones of cytoplasmic glycogenation, intraepidermal cells in discreet aggregates often centred on acrosyringeal pores. Stroma may be fibrotic, hyalinised, highly myxoid or frankly mucinous. Malignant porocarcinoma in a poroma, on microscopy, will show areas composed of eccrine poroma cells with a benign appearance adjoining areas of anaplastic cells. Malignant cells have large hyperchromatic, irregularly shaped nuclei and may be multi-nucleated and are rich in glycogen [28].

The distinction between subtypes and even the designation of eccrine tumor may be difficult, if not impossible, in select cases based on light microscopy alone. In these instances, a stain of eccrine-type enzymes (eg, succinic dehydrogenase, amylophosphorylase) may be obtained. The presence of

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ferritin also is helpful in determining the eccrine origin of a tumor; such immunostains as EMA, EKH5, and EKH6 also may be used. Immunohistochemical studies, namely, P53 protein expression study, expression of angiotensin type 1 receptors and expression of CEA, if possible, should be done to confirm the diagnosis [3,15].

Notwithstanding EP shows a significant p53 protein expression, this marker cannot be accepted as a valuable parameter for malignancy [29]. Gu Li-Hong et al. report that detectable p16 protein and loss of RB protein are common occurrences in EP lesions. Moreover, overexpression of p16 protein may be an additional, simple and useful diagnostic marker for EP on routine laboratory screening [30]. As well DNA ploidy status evaluated with a flow cytometric analysis would have helped in understanding the progress of disease and further his management [31].

Clinical differential diagnoses include cutaneous squamous cell carcinoma, cutaneous lymphoma, Paget's disease, Bowen's disease, cutaneous metastases, amelanotic melanoma, other primary skin-appendage tumor or pyogenic granuloma. EP demonstrates an invasive cellular pattern with intraepidermal and dermal involvement. The intraepidermal cells grow in nests or islands within an acanthotic and hyperkeratotic epidermis and they are often confused with Bowen's disease and Paget's disease. The intradermal cellular pattern has similarly been misdiagnosed as squamous cell carcinoma, cutaneous metastases, amelanotic melanoma, other primary skin-appendage tumor or pyogenic granuloma.

Recommended treatment is wide local excision with regional lymph node dissection if involved. Management of the patient with clinically negative nodes remains controversial. Chang et al. report the efficacy of lymphoscintigraphy with sentinel lymph node biopsy in identifying microscopic metastasis of EP in primary lesions arising in the head and neck [32].

There are no data to support the use of adjuvant therapy (both radiotherapy and chemotherapy) in the management of EP. As our case, metastatic EP has proven resistant to radiotherapy and to many chemotherapeutic agents but some Authors have described encouraging therapeutical responses. Plunkett et al. have reported a marked symptomatic and radiological response to treatment with docetaxel in a female renal transplant patient aged 45 years with a metastatic EP resistant to epirubicin [33]. Oudit et al. have mentioned use of

Melphalan, intra-arterial infusion of 5-fluorouracil and hyperthermia. Perilesional injection of interferon-alpha and interleukin-2 has been reported to produce a partial response [3,34]. Arslan has mentioned use of docetaxel, interferon-alpha 2a and isotretinoin. DaSilva and Bleier have reported a successful outcome with post-operative radiotherapy [35].

In conclusion, the high incidence of skin cancer in the post-transplant period underlines the importance of implementing early and continued cancer surveillance regimens post-transplant. In transplant recipients, although previously reported lesions have arisen in long standing benign eccrine poromas, usually on the extremities, this report shows that EP may occur as a primary aggressive malignant tumour and it may involve an unusual location such as the nose.

Figure 5

Table 1: Eccrine Porocarcinoma of the head and neck region. Review of 29 cases reported in Literature.

AUTHORS	CASES	SEX	AGE	SITE	TREATMENT	OUTCOME
Shaw,82	3	F	30	Lip	Surgery	Unknown
		F	82	Chin	Surgery	Unknown
		M	41	Scalp	Surgery	Unknown
Mehregan,83	5	M	47	Face	Surgery	Unknown
		M	67	Cheek	Surgery	Unknown
		M	77	Scalp	Surgery	Unknown
		M	42	Postauricular	Surgery	Unknown
Labbe,89	1	-	-	Nasal tip	Surgery	-
		-	-	Auricle	Surgery	-
Snow, 92	1	M	36	Chin	Surgery	Free of disease
Poiares,93	1	-	-	Face	-	-
Van Heer,96	1	F	36	Cheek	Surgery	Unknown
Lozano,97	3	M	37	Eyelid	Surgery	Free of disease
		F	89	Cheek	Radiotherapy	Recurrence
		M	62	Postauricular	Surgery	Recurrence after 6 years
Grimme,99	1	M	47	Scalp	Surgery	Recurrence after 10 weeks
Ritter,99	1	M	78	Occiput	Surgery + Radiotherapy	No recurrence within 1 year
McMichael,99	1	F	71	Auricular	Surgery	No recurrence
Kacker,99	1	M	64	Postauricular	Surgery + Radiotherapy	Free of disease
Arslan,04	1	M	62	Nose	Surgery	-
Rana,05	1	F	50	Scalp	Surgery	Unknown
Kim,05	1	M	75	Eyelid	Surgery	No recurrence within 1 year
Bleier,06	1	M	55	Nose	Surgery + Radiotherapy	No recurrence within 1 year
Greco,06	1	M	70	Cheek, nose, eyelid	Surgery	No recurrence after 2 years
Bonadio,06	1	F	64	Eyebrow	Surgery	-
Kose,06	1	F	52	Scalp	Surgery	No recurrence within 1 year
Aydin,06	1	M	65	Ear lobule, Parotid gland	Surgery	No recurrence
Klenzner,06	1	F	60	Pinna of the ear	Surgery	-
Present case	1	M	67	Nose	Surgery + Radiotherapy + Chemotherapy	Bone metastasis after 18 months and death after 27 months

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