

# NEOPLASMS WITH ECCRINE DIFFERENTIATION

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## SUMMARY

In the present article emphasis is given on four entities with eccrine differentiation that may pose problems in interpretation and classification: adenoid-cystic hyperplasia of eccrine glands, eccrine syringofibroadenomatosis, malignant giant eccrine acrospiroma and eccrine epithelioma.

## KEY WORDS

*neoplasms, eccrine differentiation, eccrine glands, syringofibroadenomatosis, malignant acrospiroma, eccrine epithelioma, case reports*

In this article emphasis will be given on four entities with eccrine differentiation that may pose problems in interpretation and classification:

- Adenoid-cystic Hyperplasia of Eccrine Glands
- Eccrine Syringofibroadenomatosis
- Malignant Giant Eccrine Acrospiroma
- Eccrine Epithelioma

## ADENOID-CYSTIC HYPERPLASIA OF ECCRINE GLANDS

### CASE REPORT

A 66-year-old female presented with multiple papules on the face which rapidly increased 18-months ago. The patient suffered from chronic polyarthritis since 15 years and during these years she received several medications including gold, corticosteroids, azathioprin

and various non-steroidal antirheumatics. Physical examination revealed numerous, small, skin-colored papules on the face clinically suggestive of multiple syringomas. However, histopathologic examination of a biopsy specimen showed several eccrine glands in the deep reticular dermis that were dilated 3 to 5 fold in size when compared to 'normal' eccrine glands. Besides the increase in size the eccrine glands did not show any obvious morphologic changes. There were no signs of decapitation secretion nor any hint for a communication of the cystic structures with pre-existing follicles. The histopathologic findings were interpreted as adenoid-cystic hyperplasia of eccrine glands.

### COMMENT

Adenoid-cystic hyperplasia of eccrine glands is a very rare event and to the best of our knowledge only few similar cases have been reported in the

literature. In 1987 Lerner et al. in a paper entitled "syringomatous hyperplasia and eccrine squamous syringometaplasia associated with Benoxaprofen therapy" described two patients with comparable clinical and histopathologic findings [1]. The authors concluded that this previously unreported cutaneous reaction probably is due to Benoxaprofen, a nonsteroidal anti-inflammatory medication that is no longer in clinical usage. They speculate that Benoxaprofen is secreted in sweat and therefore is concentrated in eccrine keratinocytes, which may be stimulated by Prostaglandin E2 a promotor of epidermal DNA synthesis in humans. In 1982 Findlay and Hull reported on "eruptive tumours on sun-exposed skin after Benoxaprofen" in four patients [2]. These lesions, however, represent a "tumor-forming transformation of the hair follicle infundibulum" and were clearly distinct from our observation. Although our patient has not received Benoxaprofen, several other nonsteroidal anti-inflammatory medications were administered orally during the course of her chronic polyarthritis, which may have induced the adenoid-cystic hyperplasia of eccrine glands [3].

## ECCRINE SYRINGOFIBROADENOMATOSIS

### CASE REPORT

A 64-year-old male patient presented with painless and non-itching skin lesions on both lower legs and the dorsum of both feet. On clinical examination, the lesions represented confluent pink plaques that were moist and spongy to palpation. The surface of



Fig. 1. Clinical features of eccrine syringofibroadenomatosis on the dorsum of the distal left foot with the characteristic mosaic or "tapioca pudding-like" appearance.

the plaques revealed a mosaic or "tapioca pudding-like" appearance (Fig. 1). No peripheral arterial vascular disease and no venous insufficiency was noted. Moreover a chronic lymphedema of the lower legs was not evident clinically. The clinical differential diagnosis included pachydermia vegetans and papillomatosis cutis. A shave biopsy was performed to rule out an early squamous-cell carcinoma. The histopathologic examination showed a netlike arrangement of epithelial cords and columns extending from the undersurface of a hyperplastic epidermis (Fig. 2). Within some of these netlike epithelial cells tubular lumina lined by an eosinophilic cuticle like those of eccrine ducts were observed. In addition to these epithelial changes there was a highly vascular, edematous and mucinous stroma with an infiltrate of lymphocytes and some plasma cells. The histopathologic findings were interpreted as eccrine syringofibroadenoma.

### COMMENT

Eccrine syringofibroadenoma has been originally reported by Mascaró in 1963, who described two patients with skin tumors that had histopathologic features of the fibroepithelioma of Pinkus but clearly showed eccrine ductal differentiation [4]. The designation "eccrine syringofibroadenomatosis" has been coined by Aloï and Torre, who observed this characteristic histopathologic pattern in 1 patient with hidrotic ectodermal dysplasia [5]. The clinical and histopathologic features of our patient are similar to the cases reported by Hurt et al. and Lui et al., and may represent a distinct hamartoma within the spectrum of proliferative acrosyringeal lesions [6,7]. It

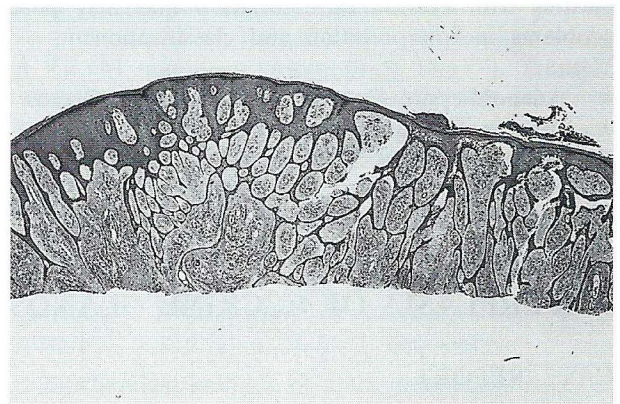


Fig. 2. Eccrine syringofibroadenomatosis: Typical histopathologic findings with a netlike arrangement of epithelial strands emanating from the undersurface of a hyperplastic epidermis.



is important, however, to rule out an underlying disease process such as chronic venous insufficiency or chronic lymphedema following recurrent erysipelas [8].

## MALIGNANT GIANT ECCRINE ACROSPIROMA

### CASE REPORT

A 60-year-old male patient was admitted to our department with a nodule on the trunk that had been present since 40 years. Clinical examination revealed on the left side of the chest a 6x5 cm large brownish red, ulcerated nodule situated on a plaque-like base. A total excision of the lesion was performed. Histopathologic examination showed an epithelial, solid-cystic neoplasm with multiple epidermal connections. The tumor was composed of basaloid cells and intermediate-sized squamous cells. Occasionally ductlike structures lined by epithelial cells or eosinophilic cuticles were seen. At the base of the lesion neoplastic cells arranged in irregular nests, cords and strands were embedded in a fibrotic stroma. In addition, neoplastic cells were found in perineurial location and also within small vessels. Cytomorphologically little or no nuclear atypia could be detected. Mitotic figures were prominent in focal areas near the center and base of the tumor. The histopathologic diagnosis of malignant transformation of a pre-existing benign eccrine acrospiroma was made. After a follow-up time of 1 year no recurrence has been observed.

### COMMENT

In 1969 Johnson and Helwig introduced the term eccrine acrospiroma to define a cutaneous neoplasm that had previously been reported under a variety of terms and was considered to be related to the epithelial cells of eccrine ducts [9]. Abenoza and Ackerman, however, stated that eccrine acrospiroma, as described by Johnson and Helwig, is not a single neoplasm, but an assortment of neoplasms with eccrine and apocrine differentiation, including eccrine and apocrine hidradenomas [10]. Recently, Hunt et al. reported upon giant eccrine acrospiromas and stressed the point that unusually large eccrine acrospiromas, especially with gross cyst formation, often represent benign lesions despite the fact that these lesions may foster concerns of malignancy [11]. Our case, however, which represents case 4 in their publication, is best interpreted as malignant transformation of a long-standing benign eccrine

acrospiroma. Similar observations have been reported by Galadari et al. in previously benign eccrine tumors, particularly long-standing eccrine spiradenomas and cylindromas [12]. In our case the diagnosis of malignant transformation in a pre-existing giant eccrine acrospiroma is reflected by the complex clinical appearance. The histopathologic findings characterized by irregularly sized and shaped nests and cords of neoplastic cells embedded in a fibrotic stroma at the base of the lesion, perineurial and angiolymphatic "invasion" finally confirmed the diagnosis of malignant eccrine acrospiroma. However, cytomorphology and mitotic counts do not allow to differentiate between benign and malignant acrospiromas as demonstrated in our case. In this context it is worth mentioning that Hernández-Pérez and Cestoni-Parducci reported a young boy who died with widespread pulmonary metastases but had entirely benign-appearing biopsy specimens of both the primary tumor and its cervical lymph node metastases [13]. On the other hand, the presence of nuclear atypia does not necessarily indicate malignancy, because it can be seen in tumors that are otherwise clinically and histopathologically benign [14].

## ECCRINE EPITHELIOMA

### CASE REPORT

The patient was a 59-year-old man who presented with a slowly growing plaque on the scalp. No further clinical data were available. The histopathologic examination of a total excision showed numerous ductal structures with variation in size and shape that were distributed diffusely throughout the dermis and in fibrous septae of the subcutaneous fat. In addition to the ductal structures that are lined by one or two layers of basaloid cells, aggregations of neoplastic cells with a solid and cribriform pattern were observed. The mostly tubular basaloid aggregations were focally embedded in a dense sclerotic fibrous stroma. Higher magnification revealed medium-sized, rather uniform cells with hyperchromatic nuclei and scanty basophilic cytoplasm. No cornification and no decapitation secretion was observed. In some areas infiltration of the perineurium was clearly evident. Moreover no connection with the overlying epidermis nor with pre-existing follicular structures was present. The histopathologic diagnosis of eccrine epithelioma was made.

### COMMENT

Malignant eccrine tumors with syringoma-like features may often pose considerable diagnostic difficulties,



because they are very rare and various authors categorize histopathologically similar lesions in different ways within the major groups of eccrine neoplasms [15]. In 1969, Freeman and Winkelmann described two neoplasms that showed "features analogous to a basal-cell epithelioma in their morphology and behavior" and because there was evidence of eccrine ductal differentiation the designation "basal-cell tumor with eccrine differentiation" or "eccrine epithelioma" was introduced [16]. Syringoid eccrine carcinoma described by Mehregan et al. refers to a "relatively well-differentiated form of eccrine carcinoma" and may represent a mixture of eccrine epithelioma and adenoid cystic carcinoma [17]. Furthermore in the last years cases of eccrine epithelioma have been reported under different names such as basal-cell carcinoma with eccrine derivation, adenocarcinoma of eccrine sweat glands, syringal hidradenoma, atypical

syringoma, and eccrine basalioma. Abenzoza and Ackerman in their recently published monography on "neoplasms with eccrine differentiation" came to the conclusion that eccrine epithelioma and syringoid eccrine carcinoma simply can be summarized under the diagnosis of moderately differentiated syringomatous carcinoma [10]. They argue that no criteria have been set forth to differentiate between these two variants of eccrine neoplasms and we completely agree with their statement. The histopathologic differential diagnosis of eccrine epithelioma includes adenoid cystic carcinoma, microcystic adnexal carcinoma, basal-cell carcinoma and syringoma [15]. However, besides all the above mentioned semantic problems in categorizing these malignant neoplasms with ductal differentiation it is extremely important, especially in poorly differentiated cases, to rule out a primary adenocarcinoma in any other organ.

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