

## (Reactive) Eccrine Syringofibroadenoma with Foci of Squamous Cell Carcinoma *in situ*: A Case Report

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**ABSTRACT** We describe a rare case of an eccrine syringofibroadenoma with a foci of squamous cell carcinoma *in situ*, which has to best of our knowledge been reported only twice in the English literature. An excisional biopsy of an elevated, lobular tumor of the lower leg in an 86-year-old male patient was performed. Histologic examination revealed a tumor consisting of anastomosing strands of epithelial cells originating from the epidermis, occasionally showing ductal eccrine differentiation. Foci of squamous cell carcinoma *in situ* were observed within the described lesion. The diagnosis of eccrine syringofibroadenoma with squamous cell carcinoma *in situ* was established. Eccrine syringofibroadenoma is a rare lesion, mostly considered to be a reactive process arising secondarily in association with other cutaneous diseases such as dermatoses or neoplasms, although some researchers do not exclude the possibility that it is a primary neoplasm with a potential for malignant transformation.

**KEY WORDS:** eccrine syringofibroadenoma, squamous cell carcinoma *in situ*, immunohistochemistry

### INTRODUCTION

Eccrine syringofibroadenoma is an uncommon benign adnexal lesion, characterized by proliferation of cords and strands of epithelial cells with ductal differentiation. It is considered to be a reactive process, therefore it is also known under the synonym “eccrine syringofibroadenomatous hyperplasia”. Another synonym for it is “acrosyringial nevus”, since it can appear in a nevoid pattern with variable presentation, ranging from solitary lesions to multiple papules and nodules arranged in symmetrical or linear fashion. Histological features include anastomosing strands of epithelial cells arising from the epidermis, enclosing a fibrovascular stroma often rich in lymphoplasmacytic cells and mucopolysaccharides.

We describe a rare case of a patient with an eccrine syringofibroadenoma showing foci of squamous cell

carcinoma *in situ*. To the best of our knowledge, only two cases have been previously described in the English literature (1,2).

### CASE REPORT

An 86-year-old male patient with a long-term chronic obstructive pulmonary disease was admitted to the hospital for treatment of newly discovered chronic myeloid leukemia. During hospitalization, an erythematous skin lesion of the left lower leg measuring 15x15 cm was observed, and the patient was referred to dermatological examination. A slightly elevated, skin colored, suspicious tumor measuring up to 2 cm was discovered in the previously described erythematous area. Dermatoscopically, the lesion was permeated by numerous blood vessels but had

no other special characteristics. The patient denied having any pre-existing skin conditions.

An excisional biopsy was performed, and a skin sample with an elevated lobular tumor on the surface, up to 2.2 cm in diameter, was sent to pathology.

Microscopic examination revealed a lesion consisting of anastomosing strands of epithelial cells originating from the epidermis, occasionally showing ductal eccrine differentiation. Stroma between the strands was fibrovascular, sparsely infiltrated by inflammatory mononuclear cells (Figure 1, A). Within the described lesion, foci of nuclear atypia, mitoses, and loss of cell polarization spanning the whole thickness of the epidermis were observed, which corresponded to squamous cell carcinoma *in situ* (Figure 1, B). The basal membrane was preserved, and no signs of dermal invasion were found. The described tumor did not reach the margins of the excision, and

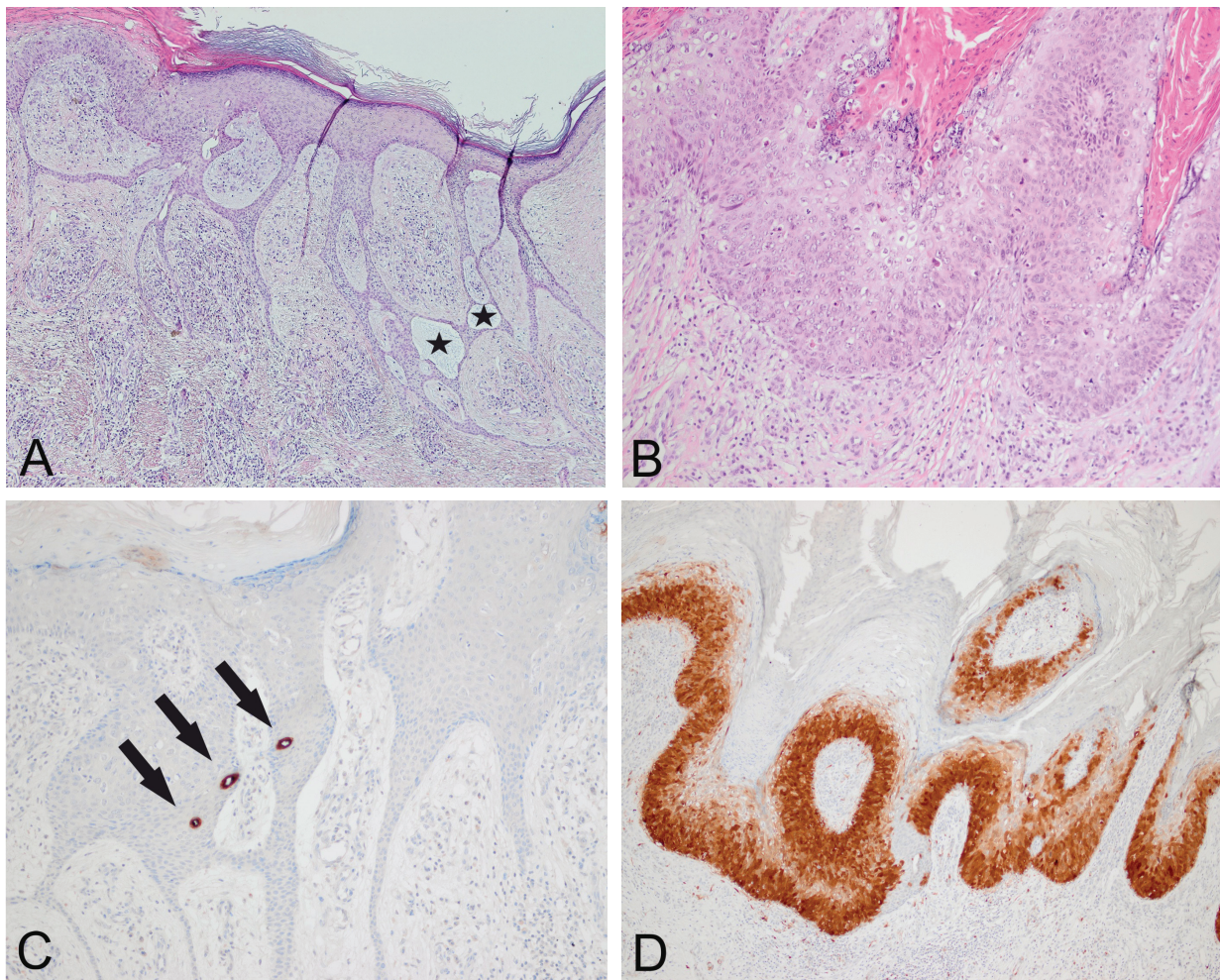
the squamous cell carcinoma *in situ* was 1 mm from the nearest lateral margin.

Immunohistochemically, both tumor components were positive for epithelial membrane antigen (EMA), while carcinoembryonic antigen (CEA) was positive only in the ductal structures (Figure 1, C). The foci of squamous cell carcinoma *in situ* showed p16 positivity (Figure 1, D).

On the basis of histological and immunohistochemical analysis, the diagnosis of an eccrine syringofibroadenoma with foci of squamous cell carcinoma *in situ* was established.

## DISCUSSION

The association of eccrine syringofibroadenoma and squamous cell carcinoma *in situ* was reported only twice in the English literature, by Bjarke *et al.*



**Figure 1.** (A) The tumor was composed of anastomosing strands of epithelial cells originating from the basal layer of the epidermis with focal ductal eccrine differentiation (asterisk) (hematoxylin and eosin (HE),  $\times 100$ ). (B) A sharply demarcated focus of squamous cell carcinoma *in situ* within the syringofibroadenoma (HE,  $\times 200$ ). (C) Ductal eccrine differentiation was highlighted immunohistochemically by carcinoembryonic antigen (CEA) (arrows) (CEA,  $\times 100$ ). (D) P16 positivity was limited to foci of squamous cell carcinoma *in situ* (p16,  $\times 100$ ).

(1) and recently by Lee *et al.* (2). There have also been reports of an association with other malignant neoplasms such as squamous cell carcinoma (1-11), basal cell carcinoma (12), porocarcinoma (2,13,14), and verrucous carcinoma (15). Overall, this association of eccrine syringofibroadenoma and malignant neoplasms is very rare, with only 19 reported cases (1-15). In some published cases, a connection between HPV infection and squamous cell carcinoma in syringofibroadenoma was proposed (4,6). Our case showed strong p16 positivity only within the foci of squamous cell carcinoma *in situ*, which could also indicate a possible role of HPV infection in malignant transformation of syringofibroadenoma.

Five clinical subtypes of eccrine syringofibroadenoma have been proposed so far: 1) solitary eccrine syringofibroadenoma, 2) multiple eccrine syringofibroadenoma associated with ectodermal dysplasia, 3) multiple eccrine syringofibroadenoma without associated cutaneous findings, 4) nonfamilial unilateral linear eccrine syringofibroadenoma, and 5) reactive eccrine syringofibroadenoma (1,3,5,10,14-17). The first case of eccrine syringofibroadenoma was described by Mascaro *et al.* in 1963 (18), while French *et al.* (16) described the reactive subtype in 1997, associating it with various skin conditions, inflammatory dermatoses, or neoplasms.

Reactive eccrine syringofibroadenoma is considered to be a rare and unusual ductal hyperplastic epithelial change or hamartomatous process complicating other cutaneous diseases, such as inflammatory dermatoses or neoplasia, as a result of repeated and prolonged damage to the eccrine structures (1,8,12,15,17). There is a great number of reported and described dermatological and systemic diseases or conditions associated with eccrine syringofibroadenoma, such as ectodermal dysplasia, venous stasis, nail trauma, chronic skin ulcerations, diabetic foot ulcer, burn scars, leprosy, bullous pemphigoid, erosive lichen planus, epidermolysis bullosa, peristomal dermatopathy, hyperkeratotic eczema, nevus sebaceous, primary cutaneous amyloidosis, etc. (8,11,15,17).

The pathogenesis of reactive eccrine syringofibroadenoma is not yet fully understood. In earlier publications, some considered it to be a reactive epithelial proliferation instead of a neoplasm of the eccrine glands, as spontaneous regression has been described after successful treatment of the associated underlying inflammatory condition (15,19). Recurrences are not common, but malignant transformation within a longstanding eccrine syringofibroadenoma was also reported (1,5,8). It is therefore difficult to determine whether eccrine syringofibroadenoma is a reactive

process arising at a location of another cutaneous disease or a malignant neoplasm, a benign neoplasm with a potential for malignant transformation, or just a benign tumor arising concurrently at the same localization.

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