



## CASE REPORT

# Eccrine Syringofibroadenoma Associated with Bowen's Disease: A Case Report and Review of the Literature

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Eccrine syringofibroadenoma (ESFA) is a rare, benign adnexal neoplasm which usually manifests as a solitary nodule on the extremities of elderly patients. Few case reports have described an association between ESFA and carcinomas including squamous cell carcinoma, porocarcinoma, and basal cell carcinoma. A 66-year-old male presented with a pruritic, erythematous brownish solitary plaque with crusted and verrucous surface on the extensor side of the right thigh. The lesion developed 6 to 7 years ago, and had been growing slowly. Biopsy revealed anastomosing epithelial strands which were composed of 2 areas: the upper area consisting of dysplastic cells with prominent nucleoli and abundant mitoses, and the lower area consisting of oval and round cells, and occasionally small luminal ducts. Dysplastic cells comprised almost the entire epidermis but did not invade into the dermis. Benign syringofibroadenomatous lesion surrounded the dysplastic cells in the lowermost portion of the epidermis. Although it is still unclear whether ESFA undergoes malignant transformation or it is a reactive change to carcinoma, complete excision should be performed to prevent malignant transformation with unknown risk. (*Ann Dermatol* 32(1) 57~63, 2020)

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## -Keywords-

Basal cell carcinoma, Bowen's disease, Eccrine syringofibroadenoma, Porocarcinoma, Squamous cell carcinoma

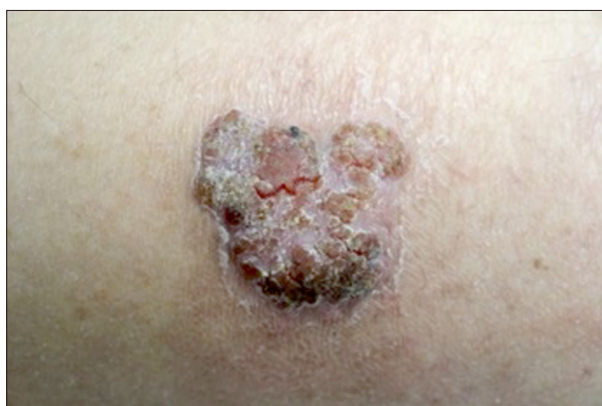
## INTRODUCTION

Eccrine syringofibroadenoma (ESFA) is a rare, benign adnexal neoplasm which shows eccrine differentiation<sup>1,2</sup>. Few case reports have described an association between ESFA and carcinomas including squamous cell carcinoma (SCC), porocarcinoma, and basal cell carcinoma (BCC). It is still unclear whether ESFA undergoes malignant transformation or if it is a reactive change secondary to carcinoma<sup>3</sup>. Here, we describe a rare case of ESFA associated with Bowen's disease (SCC *in situ*) on the thigh of a 66-year-old male and review the published 17 cases of ESFA associated with carcinoma. We received the consent from patient about publishing all photographic materials.

## CASE REPORT

A 66-year-old male presented with a pruritic, 3×2 cm-sized, erythematous brownish solitary plaque with crusted and verrucous surface on the extensor surface of the right thigh (Fig. 1). The lesion developed 6 to 7 years ago, and had been growing slowly. There was no palpable inguinal lymph node enlargement, and the patient had been otherwise healthy. Biopsy revealed epithelial strands extending down to the dermis, forming anastomoses (Fig. 2A). Epithelial strands were composed of 2 areas: the upper area consisting of dysplastic cells with prominent nucleoli and abundant mitoses, and the lower area consisting of oval and round cells, and occasionally small luminal ducts (Fig. 2A~C). Dysplastic cells comprised almost the entire epidermis but did not invade into the dermis (Fig. 2A). There

was a sharp contrast and demarcation between the upper dysplastic lesion and the benign adenomatous lesion immediately surrounding the dysplastic keratinocytes in the lowermost portion of the epidermis (Fig. 2A). In immuno-

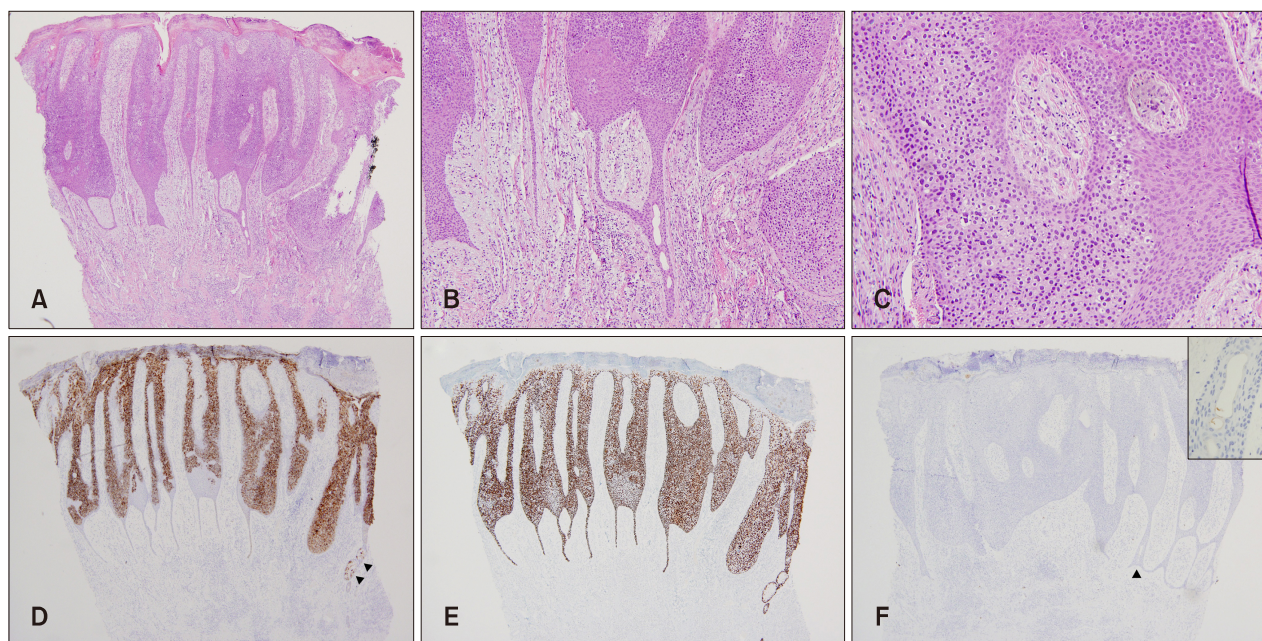


**Fig. 1.** Pruritic solitary mass on the extensor surface of the right thigh. A 3×2 cm sized, well-circumscribed, erythematous brownish plaque with verrucous and partially crusted surface.

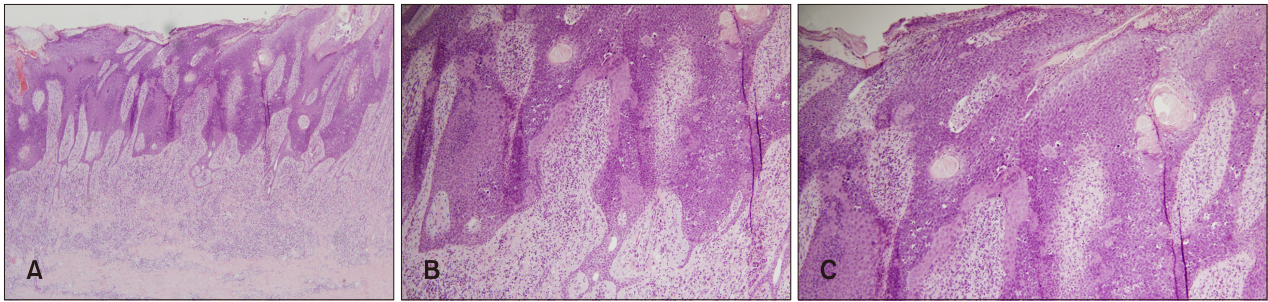
histochemical stains, epithelial membrane antigen (EMA) was positive in the dysplastic cells and weakly positive in the ductal structures in the adenomatous lower portion (Fig. 2D). p63 was more intensely positive in the dysplastic cells than in the adenomatous cells (Fig. 2E). Carcinoembryonic antigen (CEA) stain was weakly positive in the ductal structures in the adenomatous lower portion (Fig. 2F). The lesion was diagnosed as a reactive ESFA associated with Bowen's disease and was completely excised with free margins of the tumor. Histopathology of excised tissues was also consistent with reactive ESFA associated with Bowen's disease (Fig. 3).

## DISCUSSION

Although ESFA most often presents as a slowly growing, solitary, flesh- or reddish-colored nodule or plaque on the extremities of elderly patients, it has various clinical appearance ranging from a solitary erythematous scaly patch to multiple verrucous papules, nodules, and plaques<sup>1,2</sup>. The distribution other than extremities includes face, trunk



**Fig. 2.** Histopathology of the solitary mass. (A) Anastomosing epithelial strands extended down to the dermis and were composed of 2 different areas, i.e., dysplastic cells comprising almost the entire epidermis but not invading into the dermis and benign adenomatous lesion immediately surrounding the dysplastic keratinocytes in the lowermost portion of the epidermis (hematoxylin and eosin [H&E], ×40). (B) Epithelial strands were surrounded by mucinous fibrous stroma, and small luminal ducts were embedded within the strands (H&E, ×100). (C) Dysplastic area was composed of atypical cells with prominent nucleoli and abundant mitoses. Adjacent benign adenomatous portion was composed of oval and round cells (H&E, ×200). (D) Epithelial membrane antigen (EMA) was positive in the cytoplasm of dysplastic cells and weakly positive in the ductal structures in the adenomatous lesion (arrowheads) (EMA, ×40). (E) A p63 was positive in the nucleus of dysplastic cells and weakly positive in the adenoma lesion (p63, ×40). (F) Carcinoembryonic antigen (CEA) stain was weakly positive in the ductal structures in the adenoma lesion (arrowhead and inset on the right upper corner) (CEA, ×40).



**Fig. 3.** Histopathology of excised tissues. (A) Epithelial strands formed anastomoses and ductal structures were observed within the epithelial strands extending down into the dermis (hematoxylin and eosin [H&E],  $\times 40$ ). (B, C) Immediately above and adjacent to the syringofibroadenoma lesion, almost the entire epidermis displayed dysplasia with atypical keratinocytes and numerous mitotic figures (H&E,  $\times 100$ ).

and rarely nails. ESFA is classified into 5 subtypes according to the clinical presentation: (1) solitary ESFA; (2) multiple ESFA with ectodermal dysplasia; (3) multiple ESFA without cutaneous findings; (4) unilateral linear ESFA; and (5) reactive ESFA. However, its histopathologic findings are peculiar and common to all subtypes. Typically, anastomosing strands and cords of monomorphous epithelial cells proliferate and are surrounded by abundant fibrous stroma. Occasionally small luminal eccrine ducts can be found within these cords<sup>2,4</sup>.

Reactive ESFA, first described in 1997 by French<sup>5</sup> is a rare ESFA subtype associated with various inflammatory dermatoses or neoplasms. Venous stasis and ulceration is the most common dermatoses reported to be associated with ESFA<sup>6</sup>, and others include trauma, hyperkeratotic eczema, burn scars, lichen planus, elephantiasis, bullous pemphigoid, eccrine poroma, and hidroacanthoma simplex<sup>4,6</sup>. Even among the rare cases of reactive ESFA, ESFA associated with malignant neoplasm is extremely rare and there have been only 18 cases including the present case in the literature to date (Table 1)<sup>3,4,6-16</sup>. Of the 18 cases, SCC was the most commonly associated carcinoma, which was followed by SCC with porocarcinoma, porocarcinoma, BCC and Bowen's disease (SCC *in situ*). Metastasis or recurrence after excision has not been reported. All but 2 cases occurred at the age older than 65 years; exceptional 1 case (case 1) occurred in a male's heel with repeated minor trauma, and the other 1 case (case 12) occurred in a female who had a history of numerous actinic keratoses. Dorsum of feet or hands (including fingers) was the most common site, and all 3 cases which occurred on the soles involved the heel area. Extremities were also involved with its extensor surface. The lesion duration showed a wide distribution ranging from 6 weeks to several decades. In most cases, lesions had been growing slowly and recently became painful or

bled. Clinical appearance varied considerably ranging from palmoplantar keratoderma (case 2) to an exophytic mass approximately 10 cm in diameter (case 3). Histopathologic features were also variable. Five cases showed the histology of carcinoma with some benign ESFA foci, and conversely, 3 cases showed the histology of benign ESFA with some carcinomatous foci. In the other 10 cases, carcinomatous area and benign ESFA area were abutting contiguously; 1 case (case 3) showed SCC surrounded by ESFA, another 1 case (case 14) showed SCC alternating with ESFA, and other 2 cases (cases 8 and 9) showed mixed features of ESFA, SCC, and porocarcinoma. While there has been an attempt to distinguish carcinomatous area from benign ESFA with immunohistochemical stains, the results were inconsistent. CEA stains ductal structures regardless of whether it is benign or carcinomatous. Notwithstanding EMA, MNF116, p16, and p63 tend to stain carcinomatous area more strongly; however, they can stain benign ESFA area as well. It is still controversial whether ESFA precedes carcinoma and undergoes malignant transformation or if it is a reactive change secondary to carcinoma<sup>3</sup>. Whereas SCC occurs most frequently on the head and neck and the upper extremity, most of cases occurred on the lower extremity, especially dorsum of the foot, extensor of the leg, or the heel, where the sites were prone to trauma. These findings implicate that venous insufficiency<sup>7</sup> or repeated minor trauma<sup>2</sup> might be associated with ESFA. No cases of reactive ESFA associated with carcinoma occurred in the head and neck region, the most common site of SCC. Overall, it can be postulated that SCC emerges from ESFA or occurs together with ESFA due to repeated minor trauma. Cases with duration of several decades also support the claim that ESFA precedes carcinoma. Some authors even proposed the term of 'syringofibrocarcinoma' to describe carcinoma associated with ESFA in this regard<sup>8</sup>. In contrast,

**Table 1.** Reported cases of eccrine syringofibroadenoma associated with malignant neoplasms

No.	Reference	Sex	Age (yr)	Duration	Location	Clinical feature	Histological feature	Immunohistochemical finding
1	D'Amato et al. (1996) <sup>10</sup>	M	51	12 yr	Plantar surface of the right heel	Slowly growing, painful, 3 cm, fungating mass; Patient spent much time on the feet as a football coach	Porocarcinoma with some benign ESFA foci	-
2	Starink (1997) <sup>11</sup>	F	78	55 yr	Bilateral palms and soles	Diffuse redness and scaling plaques with multiple fissures and flat papules; Patient had ectodermal dysplasia	SCC contiguous to benign ESFA	-
3	Lele et al. (1997) <sup>12</sup>	M	91	Many yr	Dorsum of the right foot	9 × 7 cm exophytic mass surrounded by a scaling hyperkeratotic plaque-like lesion	SCC contiguous to benign ESFA; SCC surrounded by ESFA	CEA and EMA positive in cells of strands
4	González-Serva et al. (1997) <sup>8</sup>	M	82	6 wk	Dorsum of the left hand	3 cm, crusted nodular lesion; Severely sun-damaged skin	SCC with some benign ESFA foci and above a trichoepithelioma	CEA positive in ductal cells
5	Katane et al. (2003) <sup>13</sup>	F	91	1 yr	Extensor surface of the left forearm	Slowly growing, asymptomatic, 3 × 2 cm, dome-shaped, reddish tumor	Benign ESFA with some SCC foci; Benign ESFA with central nest of SCC cells	Keratin 1, 5, 10, and 14 positive for in of strands
6	Bjarke et al. (2003) <sup>14</sup>	F	78	Since early childhood	Dorsal surface of left middle finger, hand, and wrist	Erythematous patches, slowly expanding and inflammation recurring from 20 years ago	Benign ESFA with some SCC foci	CEA positive in luminal ducts, EMA and MNF116 mainly positive in SCC parts
7	Bjarke et al. (2003) <sup>14</sup>	F	76	More than 10 yr	Dorsum of the right hand	Recently starting to grow and ooze, irregular shaped, verrucous hyperkeratotic lesion	Benign ESFA with some SCC foci	Same as above
8	Bjarke et al. (2003) <sup>14</sup>	M	70	More than 10 yr	Plantar surface of both heels	3 and 6 cm, partly ulcerated, hyperkeratotic lesion; Patient had ectodermal dysplasia	SCC contiguous to benign ESFA; Mixed areas with ESFA, SCC, and porocarcinoma	CEA positive in luminal ducts, EMA and MNF116 positive in ESFA and poroma parts, CEA negative, EMA variable, and MNF116 positive in SCC parts
9	Bjarke et al. (2003) <sup>14</sup>	M	75	2 yr	Right wrist	Slowly growing, 1 cm, ulcerated and crusted tumor	SCC contiguous to benign ESFA; Mixed areas with ESFA, SCC, and porocarcinoma	CEA positive in ducts, EMA and MNF116 positive in ESFA, poroma, and funnel structures of SCC parts
10	Bjarke et al. (2003) <sup>14</sup>	M	96	5 yr	Dorsal surface of the right thigh	3 cm nodular lesion on the 12 cm psoriatic lesion	Bowen's disease (SCC <i>in situ</i> ) contiguous to benign ESFA	CEA positive in ducts and funnel structures in SCC parts, EMA and MNF diffusely positive
11	Cho et al. (2005) <sup>15</sup>	F	76	2 mo	Dorsal surface of the left foot	Painful, walnut-sized, ulcerated and crusted, erythematous plaque	SCC contiguous to benign ESFA	-

**Table 1.** Continued

No.	Reference	Sex	Age (yr)	Duration	Location	Clinical feature	Histological feature	Immunohistochemical finding
12	Schadt and Boyd (2007) <sup>9</sup>	F	62	2 yr	Right lower leg	Occasionally pruritic, 1.5 cm, flesh-colored hyperkeratotic nodule with a keratotic horn; History of numerous actinic keratoses and a keratoacanthoma on the chin 8 years prior	SCC contiguous to benign ESFA	CEA, CAM5.2, and AE1 positive in ductal structures, EMA positive in cells of deep strands, AE1 moderately positive and AE3 diffusely positive in cells of strands
13	Watanabe et al. (2007) <sup>16</sup>	F	87	8 yr	Dorsal surface of the right index finger	Slowly growing, become painful over the previous few months, 5×3 cm, dark-red irregular nodule with erosion and bleeding	Porocarcinoma with some benign ESFA foci	-
14	Kacerovska et al. (2008) <sup>7</sup>	M	85	1 yr	Dorsal surface of the left index finger	Asymptomatic, 2.5 cm brown-colored ulcerated nodule with fragile bleeding surface	SCC contiguous to benign ESFA; SCC alternating with benign ESFA	CEA and EMA positive in ductal structures, EMA, AE1, and AE3 positive in SCC parts, p16 positive in the epithelium of SCC parts
15	Duffy et al. (2009) <sup>4</sup>	F	88	4 mo	Extensor surface of the right lower leg	Fast growing, 3×2.5 cm, indurated, erythematous plaque with central crust	SCC contiguous to benign ESFA	-
16	Fernandez-Flores et al. (2014) <sup>3</sup>	M	95	Several yr	Dorsal surface of the right hand	Recently become painful and bled easily, 1.5 cm, ulcerated and pedunculated tumor	SCC contiguous to benign ESFA	EMA positive in SCC and superficial layer of ESFA, AE1, AE3, and CK5/6 positive both in ESFA and SCC, p63 positive in SCC and lower two third of ESFA, p16 positive in SCC
17	Hays et al. (2018) <sup>6</sup>	M	77	3 yr	Extensor surface of the right lower leg	2.5 cm, erythematous plaque with ulceration; venous stasis	BCC with some benign ESFA foci	-
18	The present case	M	66	6~7 yr	Extensor surface of the right thigh	Slowly-growing, pruritic, 3×2 cm sized, crusted and verrucous plaque	Bowen's disease (SCC <i>in situ</i> ) with some benign ESFA foci	EMA mainly positive in SCC, p63 mainly positive in SCC, CEA weakly positive in ductal structures

M: male, F: female, ESFA: eccrine syringofibroadenoma, SCC: squamous cell carcinoma, -: not available, CEA: carcinoembryonic antigen, EMA: epithelial membrane antigen, MNF116: marker which stains keratins 5, 6, 8, 17, and probably 19, BCC: basal cell carcinoma, CAM5.2: marker that detects keratins 8 and 10, AE1: marker that detects keratins 10, 14~16, and 19, AE3: marker that detects keratins 1~8, CK, cytokeratin.

the hypothesis that ESFA is a secondary change to SCC seems reasonable with respect to cases of ESFA associated with numerous inflammatory or benign neoplastic dermatoses other than carcinoma.

Histopathologically, ESFA is similar to fibroepithelioma of Pinkus, poroma or porocarcinoma, hidroacanthoma simplex or malignant hidroacanthoma simplex, and SCC with ductal differentiation. However, in fibroepithelioma of Pinkus, epithelial strands are composed of basaloid cells with stromal retraction, ductal structures within the strands are rare, and scattered mast cells are usually observed<sup>9</sup>. Poroma shows epithelial strands which are similar to ESFA, but they rarely form anastomoses, and cystic and ductal structures are usually distinctly stained with EMA and CEA<sup>9,17</sup>. Porocarcinoma shows marked cytologic atypia and numerous mitotic figures<sup>9</sup>. An intraepidermal form of poroma and porocarcinoma is called hidroacanthoma simplex and malignant hidroacanthoma simplex, respectively. Although glandular proliferation is rarely observed in SCC, glandular components are typically negative for CEA, and prominent keratinization, keratin pearl and cytologic atypia are typically present in SCC in contrast to ESFA<sup>18</sup>.

The treatment of choice is complete surgical excision since it is impossible to exclude malignant transformation of ESFA<sup>1,2</sup>. When complete excision is difficult due to large involvement area or poor patient condition for surgery, close observation may be an alternative to early excision<sup>2</sup>. An ESFA lesion that increases in size faster than the initial tumor, becomes painful or bleeds, or forms ulcer or crust is more likely to be associated with malignancy.

This report describes a rare case of ESFA associated with Bowen's diseases with literature review. ESFA associated with carcinoma usually presents with a solitary nodule on the lower extremity of the elderly, usually older than 60 years of age. Although it is uncertain whether ESFA precedes carcinoma or emerges from carcinoma, complete excision should be preferred and potential adjacent malignancy should be meticulously checked for when ESFA is diagnosed.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

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