Eccrine syringofibroadenoma: A rare case report in a patient with chronic lymphedema.

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ABSTRACT:

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Eccrine syringofibroadenoma (ESFA) is an uncommon adnexal tumor of eccrine ductal differentiation with variable clinical presentations and characteristic histopathological features. ESFA usually presents as a solitary, large hyperkeratotic verrucous nodule affecting the extremities. Histopathological findings show anastomosing cords and strands of uniform cuboidal cells embedded in fibrovascular stroma. It can be classified into 5 categories: solitary ESFA, multiple ESFA with hidrotic ectodermal dysplasia, multiple ESFA without associated cutaneous finding, unilateral linear ESFA and reactive ESFA. We report a case of reactive eccrine syringofibroadenoma in a patient with chronic lymphatic obstruction.

Key words: eccrine syringofibroadenoma, lymphedema

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บทคัดย่อ :

ปวงใจ วราภรณ์พิพัฒน์, กอบกุล อุณหโชค รายงานผู้ป่วยโรค ECCRINE SYRINGOFIBROADENOMA ในผู้ป่วยที่มีภาวะ CHRONIC LYMPHEDEMA วารสารโรคผิวหนัง 2560; 33: 180-185.

สาขาตจวิทยา กองอายุรกรรม โรงพยาบาลพระมงกุฎเกล้า

เอ็กครายไซริงโกไฟโบรอะดีโนมา (Eccrine syringofibroadenoma, ESFA) เป็นโรคเนื้องอกของผิวหนังที่พบไม่บ่อย เนื้องอกชนิดนี้เกิดจากความผิดปกติของท่อของต่อมเหงื่อ ซึ่งมีอาการแสดงที่หลากหลายแต่มีลักษณะทางพยาธิวิทยาที่จำเพาะ ผู้ป่วยมักมาพบแพทย์ด้วยก้อนเนื้อขนาดใหญ่ผิวขรุขระซึ่งเกิดขึ้นที่แขนขา และพยาธิสภาพของชิ้นเนื้อพบเซลล์รูปทรงลูกแต๋ที่มีรูปร่างและขนาดเดียวกัน เรียงตัวเป็นแถบและประสานกันเป็นร่างแหอยู่ใน fibrovascular stroma. ESFA สามารถจำแนกได้เป็น 5 ประเภทคือ solitary ESFA, multiple ESFA ซึ่งพบร่วมกับ hidrotic ectodermal dysplasia, multiple ESFA ซึ่งไม่พบอาการแสดงทางผิวหนังชนิดอื่น, ESFA ซึ่งเรียงตัวเป็นแถบบริเวณซีกใดซีกหนึ่งของร่างกาย (unilateral linear ESFA) และ reactive ESFA. รายงานนี้ได้นำเสนอ ผู้ป่วย reactive eccrine syringofibroadenoma ซึ่งพบร่วมกับภาวะท่อน้ำเหลืองอุดตันเรื้อรัง

คำสำคัญ: เอ็กครายไซริงโกไฟโบรอะดีโนมา, น้ำเหลืองอุดตัน

Case report

A 79-year-old Thai man from Chachoengsao came to Phramongkutklao hospital with a mass on the right lateral malleolus for 2 years. He had a 5-year history of recurrent and progressive edema of both legs. Neither pain, redness, warmth nor fever was observed. Three years later, he developed an asymptomatic mass that was slowly enlarged on his right lateral malleolus. He denied history of previous trauma. His underlying diseases were uncontrolled hypertension for 8 years, stage III chronic kidney disease and urinary incontinence.

Physical examination revealed bilateral, symmetrical, non-pitting edema of both legs and feet with a solitary well-defined erythematous verrucous mass on the right lateral malleolus (Figure 1). There was no palpable lymphadenopathy. Other physical examination was unremarkable.

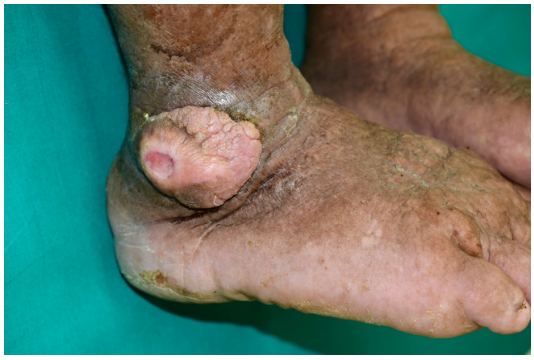

Figure 1 A verrucous mass on the right lateral malleolus.

Histopathological examination of 4-mm punch biopsy specimen taken from the center of the lesion showed reticular, thin, anastomosing

epidermal cords and strands, connected to the undersurface of the epidermis (Figure 2). These cords are composed of small cuboidal cells with basophilic appearance. Foci of ductal formation (Figure 3) and eccrine miliaria were seen (Figure 4).

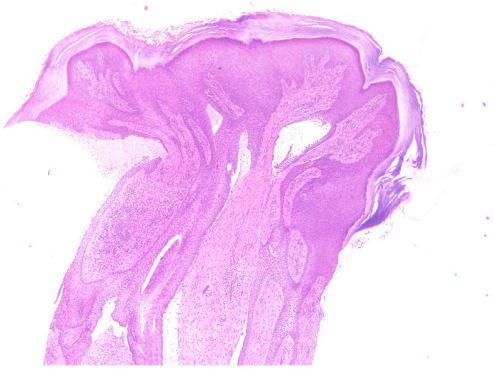

Figure 2 H&E section showed reticular, thin anastomosing cords and strands of epidermis.

Further laboratory investigations including doppler ultrasonography showed absence of deep vein thrombosis of both lower extremities. Lymphatic scan revealed lymphatic obstruction of his right leg and multidetector computed tomography showed multiple subcentimeter lymph nodes along bilateral femoral and inguinal regions. He was diagnosed as reactive eccrine syringofibroadenoma secondary to chronic lymphedema. We have already referred him to a surgeon who planned to excise the tumor after conservative management. However the patient denied to have surgery. Meanwhile the lesion remained stable in size and shape after 1 year followup.

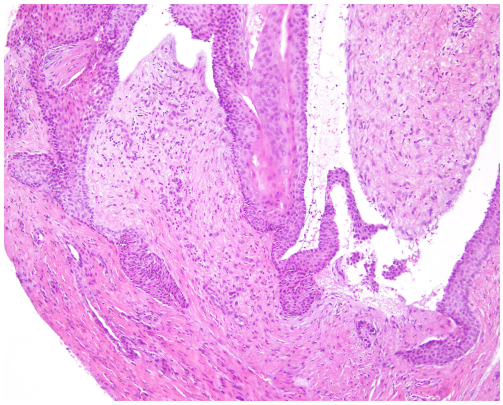

Figure 3 Foci of ductal formation was seen.

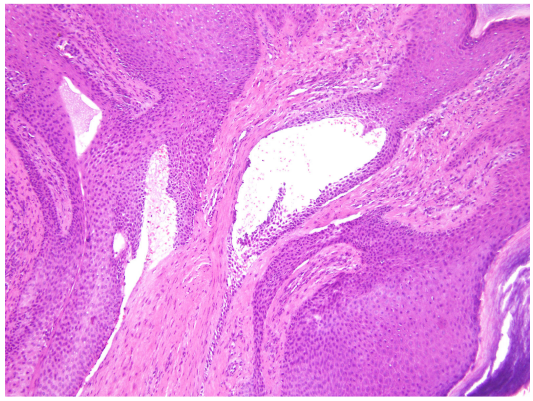

Figure 4 Area of eccrine miliaria.

Discussion:

Eccrine synringofibroadenoma (ESFA) is an uncommon adnexal tumor of eccrine ductal differentiation that was firstly described by Mascaro in 1963.[1] ESFA usually manifests as a solitary nodule on an extremity in patients over 40 years of age.[2] However, it can have a variety of clinical presentations, ranging from a verrucous papule or nodule to solitary or multiple nodules with symmetric distribution. Lesions can be coalesced to plaque or have linear arrangement. The clinical presentations

should be differentiated from other cutaneous malignancies such as squamous cell carcinoma, verrucous carcinoma, amelanotic melanoma, benign adnexal tumors, soft tissue tumors, or cutaneous metastasis. Chronic infections of the skin including tuberculosis verrucosa cutis, other atypical mycobacterial infections and deep mycoses are also included in the differential diagnosis.[3] The variety of clinical features of ESFA can be classified into 5 categories according to Starink[4] and French.[2]

Solitary ESFA, the most common type, typically presents as a nonhereditary solitary nodule or verrucous mass which is usually found on the lower extremities of middle-aged and elderly patients. Multiple ESFA associated with hidrotic ectodermal dysplasia (HED) called Schopf-Schulz-Passarge syndrome which onset of the lesions generally occurs between 15 and 25 years. The patients typically have multiple erythematous verrucous papules on the palms and soles and may have other cutaneous signs such as eyelid apocrine hidrocystoma, hypotrichosis, hypodontia and nail dystrophy. Multiple ESFA without associated cutaneous finding which is considered to be a forme fuste or incomplete form of Schulz syndrome[4] usually presents with nonfamilial palmoplantar lesions. Unilateral linear ESFA is a rare form that probably represents a genetic mosaicism caused by postzygotic mutation in an early embryonic stage.[4] Reactive ESFA is associated with chronic inflammatory dermatoses or neoplastic dermatoses such as chronic lymphedema (elephantiasis), venous stasis or insufficiency[3], burn scar ulcer[3], erosive palmoplantar lichen planus[3], diabetic neuropathy with chronic ulcer[3,5], leprous neuropathy[3], bullous pemphigoid[3,6], epidermolysis bullosa[3], peristomal dermopathy[7] and epithelioid hemangioendothelioma.[8] This form of ESFA is usually single and acrally located.

Because the clinical manifestations of ESFA resemble those of primary cutaneous tumors or secondary metastatic tumors, the diagnosis of ESFA is based on histopathology characterized by proliferation of anastomosing strands and cords of monomorphous epithelial cells in reticular pattern with eccrine duct formations embedded in a fibrovascular stroma.[6] The histological differential diagnosis includes fibroepithelial tumor of Pinkus, eccrine poroma, tumor of the follicular infundibulum, pseudoepitheliomatous hyperplasia, papillary eccrine adenoma, reticulated seborrheic keratosis, squamous cell carcinoma, and artifacts of histologic processing.[7] Pathology of fibroepithelial tumor of Pinkus shows focal changes which are typical for basal cell carcinoma such as columns of basaloid cells with peripheral palisading, clefting artifact and loose fibromyxoid stroma. Eccrine poroma shows

a more uniform small epithelial cell proliferation with vertical broad sheets of cells streaming down from the epidermis extending into the dermis. Thin cords of basaloid cells are not usual features of eccrine poroma. Papillary eccrine adenoma consisted of dilated tubules lined by eccrine duct cells with intraluminal papillary projection which are usually not attached to the epidermis. In cases of reactive pseudoepitheliomatous hyperplasia, the underlying disease such as halogenodermas, deep mycoses, or granular cell tumors is usually clearly demonstrable. Moreover, on immunohistochemistry, the lesional cells of ESFA are positive for keratin 6, keratin 9, filaggrin and luminal borders are positive for carcinoembryonic antigen (CEA).[7]

Our patient presented with solitary asymptomatic erythematous verrucous mass on the right lateral malleolus 2 years after recurrent and progressive edema of his legs. The pathology showed reticular, anastomosing cords and strands of basophilic cuboidal epidermis with ductal formation that is typical for ESFA. We diagnosed the lesion in our patient as reactive ESFA secondary to chronic lymphatic obstruction.

Reactive ESFA associated with chronic lymphedema have been rarely reported. Rongioletti report the first case report of ESFA associated with elephantiasis from lymphatic obstruction.[8] Wendemagegn reported reactive change of eccrine structures in 10 biopsy specimens taken from fully developed podoconiosis, four of which showed reactive eccrine syringofibroadenoma.[9] Podoconiosis is a form of chronic lymphedema caused by long-term bared foot exposure to alkaline volcanic soil.[9]

Eventhough ESFA can be found at the periphery of squamous cell carcinoma and SCC is the most common tumor in patients with chronic lymphedema, the stable in size and shape of the lesion suggest that SCC is less likely. We planned to make a total excision of the mass but the patient denied.

Although, exact pathogenesis of ESFA is not yet completely understood and still unclear whether the lesion is neoplastic, hamartomatous, or reactive process in nature, some alteration in the cellular growth and differentiation of epidermal and adnexal structures have been suspected.[3] The pathogenesis of reactive ESFA includes repeated eccrine duct trauma resulting in eccrine duct remodeling and repair.[7]

The clinical course of ESFA is usually benign but malignant transformation to eccrine syringofibrocarcinoma or squamous cell carcinoma has been reported in nonreactive ESFA.[10] Spontaneous resolution can occur in the reactive type if the primary causes are

terminated.[11] Associated risk factors of malignant changes include advanced age of the patients with eight decade in average, more proportion of male patients, the extremities involvement and worrisome features such as pain, inflammation, new growth, ulceration with crusting and persistent disease despite extensive treatment.[7]

The treatment of ESFA depends on the number, location, and resectability of the lesions. Surgical excision has been the treatment of choice for solitary ESFA. If the lesions are unresectable, alternative treatment options are pulsed dye laser, carbon dioxide laser and radiation therapy. Because of the risk of malignancy, regular follow up and close observation should be done if the lesions are left without treatment.[3]

In summary, we report a patient with reactive eccine syringofibroadenoma secondary to chronic lymphedema. Since the clinical manifestation resembles various conditions, EFSA should be included in the differential diagnosis of the chronic verrucous skin lesion in the patient with chronic lymphatic obstruction.

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