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Leukemia cutis and eccrine squamous syringometaplasia

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Abstract

Eccrine squamous syringometaplasia (ESS) is a histological term describing a mature squamous metaplasia of the eccrine ducts. Eccrine squamous syringometaplasia is not an infrequent histological finding and may be associated with chemotherapy or with a variety of non-specific conditions including infections, neoplastic conditions, and inflammatory skin diseases. We report a 75-year-old man who developed ESS within lesions of leukemia cutis (LC). The patient had an inaugural diagnosis of acute myeloid leukemia (AML) and he was not on chemotherapy when the biopsy was performed.

Keywords: eccrine, leukemia cutis, metaplasia, squamous syringometaplasia

Introduction

Syringometaplasia is an adaptive, benign, metaplastic cellular process that affects the eccrine ducts and glands in response to diverse physiological and pathological stimuli [1,2]. Different subtypes of syringometaplasia have been described, including squamous, mucinous, and adenomatous types. Eccrine squamous syringometaplasia (ESS), or syringosquamous metaplasia, is the most common observed type in the skin and is characterized by the transformation of the eccrine sweat duct cells into mature squamous cells with keratinization [3]. The first known case of ESS was described by Donald King and Ronald Barr in 1979 [4]. Three years later, in 1982, Santa Cruz et al. reported ESS changes in chemotherapy- and radiotherapy- treated patients [5]. Since then, ESS has been reported in association with multiple well-defined entities as an incidental finding, but it is mainly seen after chemotherapy for malignant neoplasms [1,6].

Herein, we present a 75-year-old man with an inaugural diagnosis of acute myeloid leukemia (AML) presenting with skin papules and plaques whose biopsy showed infiltration by AML cells and characteristic features of ESS.

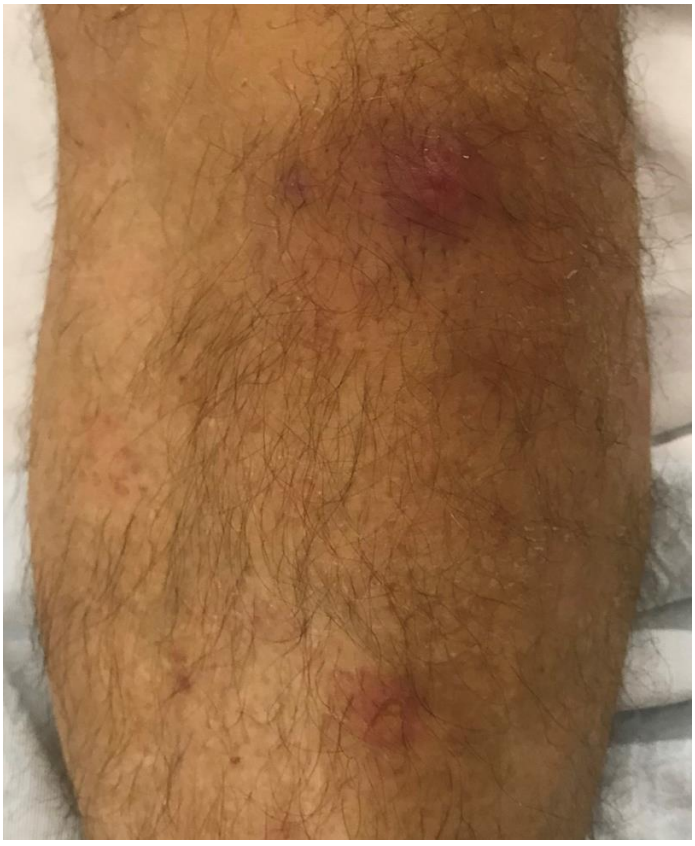

Figure 1. *Leukemia cutis, clinical picture: Well-delimited, erythematous papules and plaques on the anterior side of the patient's legs.*

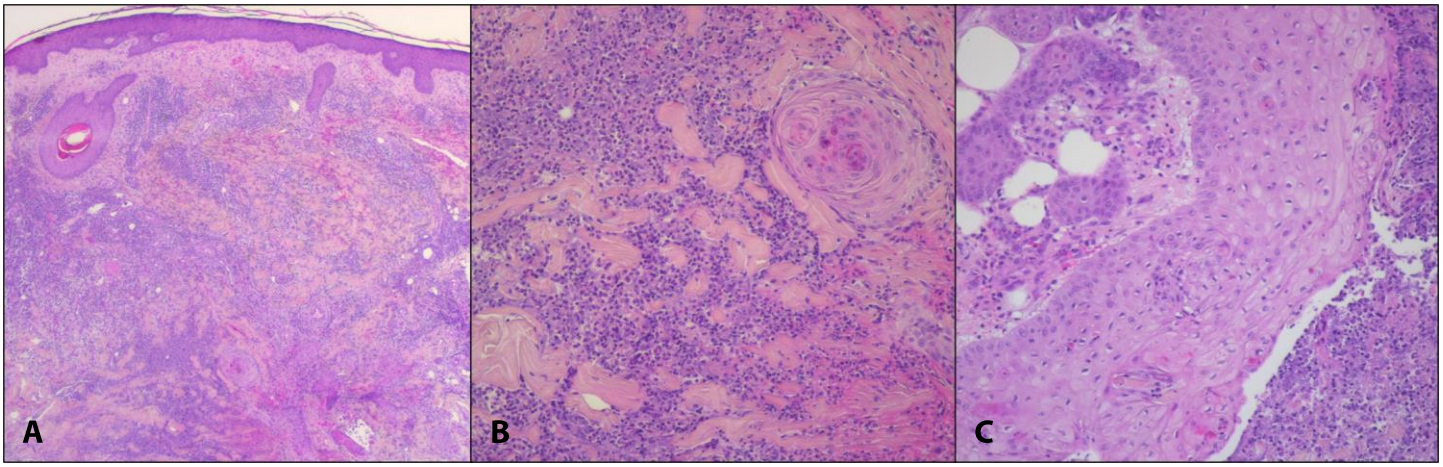

Figure 2. *Leukemia cutis and eccrine squamous syringometaplasia, histopathological aspects:* ***A)*** *Diffuse infiltrate of leukemic cells involving the dermis. A grenz zone of uninvolved upper dermis is also noted. H&E 25×.* ***B)*** *The infiltrate is composed of leukemic mononuclear cells with high nuclear-to-cytoplasmic ratio and prominent nucleoli. Eccrine squamous metaplasia with gland duct obliteration is also observed. H&E, 40×.* ***C)*** *Eccrine glands with dyskeratotic cells and epithelial lining with dense eosinophilic cytoplasm. H&E, 100×.*

Case Synopsis

A 75-year-old man was seen for a one-month history of mildly pruritic erythematous papules and plaques on the back and legs. The lesions had developed suddenly and had increased in number and size over the course of one week. The patient also noted fever (maximum axillary temperature of 38.2C) over the last three days. His past medical history was relevant for hypertension. Physical examination revealed multiple well-delimited, erythematous papules on the back and inferior legs (**Figure 1**). An ulcerated erythematous plaque on his left leg was also observed. He had no palpable lymph nodes or other significant skin lesions.

Routine blood tests revealed microcytic hypochromic anemia (hemoglobin 8.7g/dL, N>13) and leukocytosis (23.3×10^9 cells/L, N<11) with 23% of circulating blast cells and elevated D-Dimer levels (39.33mg/L, N<0.5). A skin biopsy of the leg lesions was performed. Histological examination revealed a diffuse infiltrate of large mononuclear cells with a high nuclear-to-cytoplasmic ratio and prominent nucleoli, involving the dermis and subcutaneous tissue. The epidermis was spared and a grenz zone of uninvolved dermis was observed (**Figure 2A**, **B)**. Immunohistochemical staining was positive for myeloperoxidase (MPO) and CD43, suggesting the myeloid origin of the leukemic cells (**Figure 3B)**.

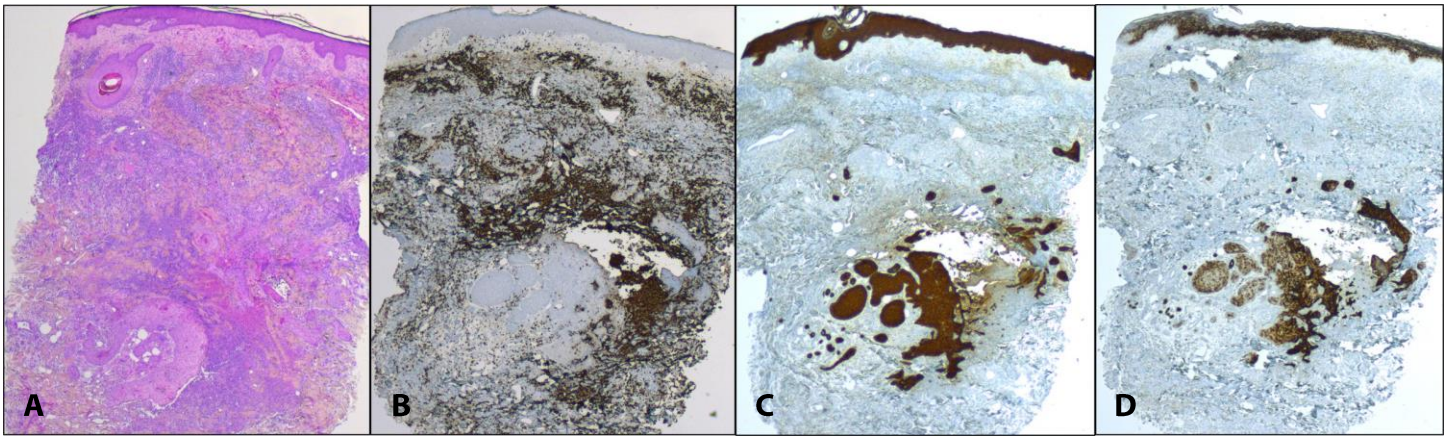

Figure 3. *Leukemia cutis and eccrine squamous syringometaplasia, immunohistochemical picture:* ***A)*** *Diffuse leukemic infiltrate with eccrine squamous metaplasia. H&E, 16×.* ***B)*** *Positive immunostaining of leukemic cells for MPO, 16×. Positive immunostaining for* ***C)*** *AE1/AE3 and* ***D)*** *EMA in areas of eccrine squamous metaplasia, 16×.*

Surprisingly, transformation of the dermis eccrine cuboidal epithelium into layers of squamous cells with intraductal keratinization was also noted (**Figure 2B**, **C)**. There was no connection between the epidermis and the eccrine epithelium. The metaplastic ducts yielded positive staining for AE1/AE3, CEA, and EMA (**Figure 3C**, **D)**. These features favored the diagnosis of skin infiltration by AML cells and ESS. A bone marrow biopsy confirmed the diagnosis of AML with myelodysplasia-related changes. The patient was initiated on chemotherapy with azacytidine in a 5-day regimen. Disease progression was documented after two courses and thus venetoclax was added to azacytidine. A complete remission (with incomplete hematologic recovery) along with resolution of the skin lesions was achieved by the initiation of cycle 2. Currently, at 5 months follow-up, the patient is on the third course of azacytidine plus venetoclax. Bone marrow biopsy will be checked after cycle four and every six months thereafter, in the absence of clinical suspicion for disease relapse.

Case Discussion

Eccrine squamous syringometaplasia is a histological term describing the replacement of eccrine duct cuboidal epithelium by two or more layers of squamous epithelium with keratinization inside the duct [7,8]. This histological pattern has been found in association with several conditions and two types have been described. Type I occurs in patients receiving chemotherapy and the type II appears as an incidental finding in relation to infectious, neoplastic, and inflammatory skin diseases (**Box 1**), [1,2]. Clinically, both present as erythematodesquamative and edematous papules and plaques but with varying locations. Chemotherapy-related ESS lesions are symmetrically distributed and primarily involve eccrine cell rich areas (intertriginous areas, palms, and soles). In incidental ESS the location is variable, depending on the specific entity [9,10].

The pathogenesis of ESS is not fully elucidated and different etiopathogenic factors have been proposed according to the ESS type. In cases of chemotherapy-associated ESS, direct or immune-mediated toxic effects are believed to play a role [3,6,8-10]. In incidental ESS, local factors such as inflammation are postulated to contribute to indirect damage to sweat glands [3,9]. In our case, when the biopsy was performed the patient had not received any chemotherapeutic drug and the ESS was found as an incidental finding within the LC lesions [11,12].

Histopathology of ESS typically consists of dermally-located small, round, or comma-shaped nests of mature squamous epithelium showing evidence of keratinization [3]. This metaplastic change leads to loss of low molecular weight cytokeratins (such as CAM 5.2), that are normally expressed in normal eccrine glands [1]. On the other hand, antibodies against acidic and basic cytokeratin (AE1/AE3) and other epithelial markers, label the metaplastic

Box 1. *Conditions associated with eccrine squamous syringometaplasia (adapted from [1] and [9]).*

Neoplastic
- Keratoacanthoma
- Squamous cell carcinoma
- Syringotropic mycosis fungoides
- Fibrous hamartoma of infancy

Infectious
- Herpes virus
- Cytomegalovirus

Inflammatory
- Panniculitis
- Pyoderma gangrenosum
- Annular elastolytic granuloma
- Systemic lupus erythematosus
- Morphea
- Sclerodermatous graft-versus-host disease

Medications
- Chemotherapy*
- NSAIDs

Other
- Scars
- Ulcers
- Burns
- Areas of ischemia
- Areas of radiation

*Type 1 eccrine squamous syringometaplasia.
NSAIDs, nonsteroidal anti-inflammatory drugs.

epithelium [3]. ESS should be differentiated from squamous cell carcinoma. Preservation of the normal lobular architecture of the glands and ducts and the absence of epidermal dysplasia and true invasion help determine the correct diagnosis [1,3,4].

Conclusion

Eccrine squamous syringometaplasia is a histological term describing a benign cutaneous reaction characterized by transformation of the normal cuboidal epithelial cells of the eccrine sweat ducts into layers of squamous epithelial cells. It has been described in association with diverse well-defined entities and as an incidental finding, but it is mainly observed after chemotherapy for malignant neoplasms. We present a case of ESS unrelated to chemotherapy in a patient with an inaugural diagnosis of AML. To the best of our knowledge, the association of ESS with LC had not been hitherto reported.

Potential conflicts of interest

The authors declare no conflicts of interest.

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