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Large eccrine angiomatous hamartoma: a novel clinical presentation of disease

Uffe Nygaard[1], *Søren Dalager*[2], *Eva Spaun*[2], *Lene Hedelund*[1]

1. Department of Dermatology and Venerology, Aarhus University Hospital, University of Aarhus, 8000 Aarhus, Denmark;
2. Institute of Pathology, Aarhus University Hospital, University of Aarhus, 8000 Aarhus, Denmark.

Corresponding author:

Uffe Nygaard, MD

Department of Dermatology and Venerology, Marselisborg Centre, Aarhus University Hospital

P.P. Ørumsgade 11, DK-8000 Aarhus, Denmark

E-mail: *uffenygaard@clin.au.dk*

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Abstract

Background: Eccrine angiomatous hamartoma is a rare benign cutaneous malformation with a diverse clinical appearance, therefore likely to be misdiagnosed and underreported.

Main observations: A 44-year-old man presented with a congenital erythematous hyperhidrotic plaque on the left upper back measuring 18 x 25 cm. No pain or tenderness nor hypertrichosis were observed. Histopathology was consistent with the mucinous variant of eccrine angiomatous hamartoma. Intralesional injection of botulinum toxin type A greatly reduced localized sweating, improving patient quality of life.

Conclusions: This article describes a novel clinical presentation of eccrine angiomatous hamartoma: large, erythematous, and slightly indurated plaque localized on the upper back. It emphasizes the role of histopathology in the diagnostic process and botulinum toxin as a viable treatment option. (*J Dermatol Case Rep*. 2015; 9(3): 58-61)

Introduction

Eccrine angiomatous hamartoma (EAH) comprises a most uncommon benign nevoid malformation. Patients typically present with a solitary nodule or plaque, or, less commonly, a macule on the extremities though reports of multiple lesions and those occurring in more unusual sites exist. It usually appears at birth or arises during childhood, less frequent during puberty or adulthood. EAH may be associated with hypertrichosis, tenderness/pain, hyperhidrosis and itching. It can be red, violaceous, blue, brown, or skin-coloured. Enlargement often occur and is usually in concordance with the growth of the patient disclosing a median size, at time of diagnosis, ranging from 4-15 mm.[1-3] EAH is characterized by the proliferation of eccrine glands and numerous vascular channels, and a variable presence of pilar structures, fatty tissue, mucin deposition, and/or lymphatic configurations.[4] It is important to recognize the hamartoma as a benign clinical entity, for which aggressive management is not necessary, yet treatment including surgery or topical therapies is occasionally needed to alleviate pain or hyperhidrosis.[2,3,5-9] While clinical examination can give meaningful clues, the diagnosis is based on the histologic criteria for EAH, which is defined as (1) proliferation of mature, normal or dilated eccrine glands, (2) intimate association of the eccrine structures with benign vascular proliferation, and (3) varying occurrence of pilar, lipomatous, mucinous, and/or lymphatic structures.[1,2,4,10] We present a case of EAH disclosing distinct histopathological features of the previously reported, though rare, mucinous EAH variant but of extraordinary size several hundred times larger than commonly seen.

Case report

A 44-year-old man was referred to our outpatient clinic with a congenital naevus. He presented with a well-defined erythematous plaque on his upper back, with a flattened domelike shape, measuring 180 x 250 mm (Fig. 1A). It had increased in size proportionate with growth of the patient. The lesion displayed profuse hyperhidrosis (Fig. 1B), but no hypertrichosis or pain at palpation. Within the last two years the thickness of the lesion and the localized sweating had

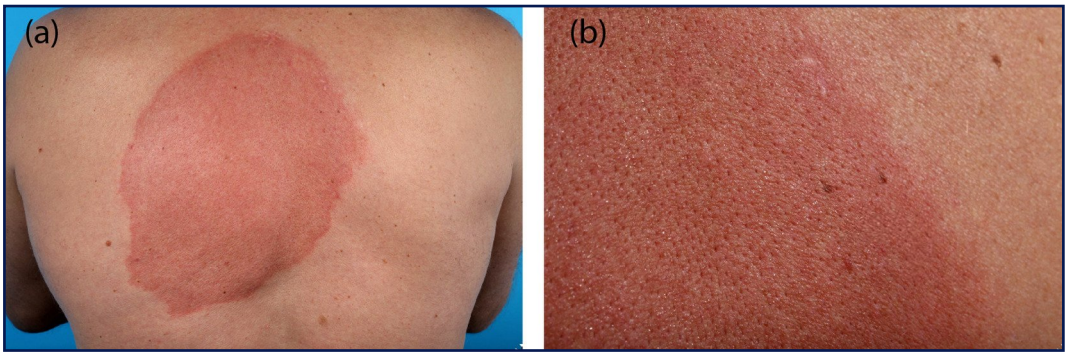

Figure 1

Eccrine angiomatous hamartoma, clinical presentation. The patient presented a dome-shaped, well demarcated, 180 x 250 mm large, erythematous, and slightly indurated plaque on the upper back (A). Close-up revealed accentuated sweat pores and profuse hyperhidrosis (B).

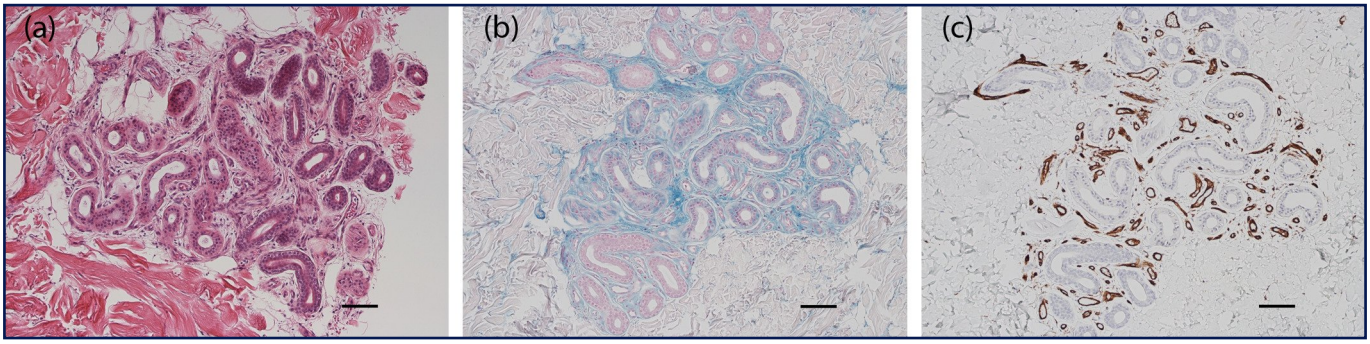

Figure 2

Histopathological profile of lesional skin. Histological examination showed an increased number of normally calibrated eccrine ducts and acini (haematoxylin and eosin, x100)(A). Abundant interlobular deposition of mucin (alcian-blue PAS, x100) (B). Irregular collection of small CD31 lined vessels, interspersed between the sweat glands coils within the lobules (CD31, x100) (C). Scale bars, 100 µm.

reached an intolerable level, profoundly hampering the professional life of the patient. The clinical examination was otherwise unremarkable. As all prior punch biopsies, taken solely from the edge of the element, had not given a specific diagnosis, a deeper biopsy from the central part of the plaque was obtained. Histopathological analyses were in accordance with those of the mucinous variant of EAH. Topical treatment with antiperspirants was discarded due to localization, as was surgical extirpation due to size. With the patients consent intralesional treatment with botulinum toxin type A was performed. A total of 100 U was administered in a single course of intradermic injections each containing about 2 U per intradermic injection, at intervals of 2 cm distributed evenly across the entire element. To date, 1 year after treatment, a significant decrease of localized sweating is still observed and improvement of patient quality of life maintained.

Ten and 4 mm punch biopsies from lesional and adjacent normal skin were formalin-fixed and embedded in paraffin using routine histopathological techniques. Sections of 4 µm were cut and stained with H&E (for general morphology), colloidal iron and alcian-blue PAS (for mucin). In addition, 4 µm sections were cut for immunohistochemical demonstration of S-100 protein, carcinoembryonic antigen (CEA), pan-cytokeratin (KL-1), vascular endothelium (CD31), and smooth muscle actin (SMA) using standard techniques including heat-induced epitope retrieval. DAB (3,3'-Diaminobenzidine) was used as a chromogen. Appropriate positive controls were included on each slide.

The punch biopsies from lesional skin included epidermis, dermis, and subcutaneous tissue. Epidermis was apart from a minimal hyperpigmentation unremarkable showing only slight orthokeratosis and acanthosis. The dermis and subcutaneous tissue contained 3 large lobules of coiled eccrine sweat gland ducts and secretory units. Each lobule featured an increased amount of ducts as well as acini, both of normal calibre. In the immediate vicinity of a hair follicle and the corresponding sebaceous gland, the biopsy from the lesion showed an irregular collection of small vessels, interspersed between the sweat glands coils within the lobules (Fig. 2). A cuboidal two-cell layer lined the eccrine ducts, with the luminal margin CEA positive and the luminal cell layer KL-1 positive. S-100 protein and SMA was negative in the eccrine ducts.

The eccrine glandular units were also two-layered, with the outer layer consisting of more elongated S-100 and SMA positive myoepithelial cells while the luminal cell layer consisted of taller secretory cells with more abundant eosinophilic cytoplasm and a CEA positive luminal margin. Both layers were positive for KL-1.The many intralobular dilated vessels were lined by a CD31 positive endothelium (Fig. 2). Some dilated CD31 lined vascular channels were also present in the deeper dermis and subcutis, but the pathological significance of this latter finding was doubtful. Mucin was abundant within the lobules judged by the stains for colloidal iron and alcian-blue PAS (Fig. 2). Dermis was relatively fibrous, but this finding could not be regarded as of any definitive pathological significance.

In comparison, the punch biopsy from the surrounding normal tissue contained only a single small lobule of fewer and smaller eccrine ducts and secretory units. Almost no mucin was present within the lobule, which contained a few interspersed small non-dilated vessels. Only very few vessels were present in the deeper dermis and subcutis. The immunohistochemical profile was comparable with lesional skin.

Differential diagnosis

The increased number of eccrine sweat gland lobules composed of an increased number of oversized sweat gland coils indicated an eccrine naevus. Subdivision into "classic" eccrine naevus, EAH or mucinous eccrine naevus is based on small variations. Compared to "classic" eccrine naevus, EAH, contains an additional component of increased number of vascular elements associated to the eccrine lobule. EAH may also contain other epithelial components as well as fatty tissue and mucinous stroma, though while the mucinous eccrine naevus always show increased stromal mucin within the lobule a total absence of the vascular component is conclusive.

In the present case, we observed vascular abnormalities as well as deposition of mucin accompanying an increased amount of large eccrine lobules; hence the diagnosis mucinous variant of EAH is appropriate.

Discussion

EAH is an extremely rare variant of eccrine naevus, with only 73 cases previously reported and the mucinous variant is even less frequent.[7] The most common presentation is a painful, hyperhidrotic and solitary element on the distal extremities with a median size of 4-15 mm.[6,7] Several things differ in our case; localisation on the upper back, no pain or tenderness nor hypertrichosis and a size far surpassing that of preceding reports. Hyperhidrosis of EAH is presumably an expression of its eccrine components and occurs in one third of all patients with EAH, as it was the case in our patient, it is seen in response to the typical triggers of eccrine secretion such as heat or emotional stimuli. However, it can also occur spontaneously or after manipulation of the lesion, a phenomenon we could not reproduce.[3,10,11] The exact pathogenesis of EAH is unknown, but theories revolve around abnormal induction of heterotypic dependency leading to malformation of adnexal and mesenchymal elements although this can not explain cases appearing later in life.[11] The spectrum of clinical differential diagnoses of EAH is broad, due to its heterogeneous clinical aspect, therefore one must consider: vascular lesions, eccrine nevus, sudoriparous angioma, fibrous hamartoma of infancy, and smooth muscle hamartoma.[10] Hence diagnosis should rely on comprehensive histopathological analyses on representative lesional tissue that includes deep dermis. As it difficult to attain definitive diagnosis we recommend 10 mm punch biopsies if localisation and estimated risk of scarring allows it.

Histopathologically, EAH is generally seated in the middle or deep dermis where it is well demarcated but not encapsulated.[4] The histologic criteria for EAH include hyperplasia of normal or dilated eccrine glands; close association of the eccrine structures with capillary angiomatous foci; and the variable presence of pilar, lipomatous, mucinous, and/or lymphatic structures.[1,2,4,10] Our histopathological conclusion matched all criteria and included mucin deposition. Mild fibroblastic hyperplasia can present in the dermis, a sign we also might have encountered. The epidermis is largely not affected, though can show hyperkeratosis, papillomatosis or hyperplasia, in our case only slight orthokeratosis and acanthosis with minimal hyperpigmentation were observed. Immunohistochemical analysis of EAH has only been carried a few times showing positive staining of the eccrine glands with S100, carcinoembryonic antigen (CEA) and epithelial membrane antigen (EMA). The ductal components stained positively for CEA and cytokeratin 1 and weakly positively for EMA. The vascular elements were labeled positively for anti-Ulex europaeus and anti-factor VIII antigens. Immunohistochemical analyses have demonstrated no definite difference between normal eccrine glands and those in EAH.[4,6,12] We found a similar pattern with the addition CD31 lined vessels, CEA and KL-1 positive ducts and SMA and KL-1 positive glands. Importantly, the immunohistochemical profiles of EAH and non-lesional skin were comparable on these parameters as well.

The natural course of EAH is that of enlargement commensurate with growth of the patient but sometimes, sudden enlargement in response to hormonal stimulation as occurs during puberty or pregnancy.[2,12,13] We disclosed no anamnestic, clinical or paraclinical clues to the sudden enlargement and increased hyperhidrosis in our patient.

Treatment is typically not required, but indicated if severe drug-resistant pain, disabling sweating, or progressive enlargement with cosmetic concern occurs. For most cases, surgical removal is the first choice and the definitive treatment.[2,3,5-7] Non-invasive treatments comprise of topical antiperspirants or intralesional injections of botulinum toxin type A.[8] As surgery was rejected due to size and topical ointments due to location, botulinum toxin type A was preferred. In this case rapid relieve of hyperhidrosis was achieved resulting in an increase in patient quality of. We registered a sustained effect of treatment 12 months after treatment though no changes in size or shape. The efficacy is due to blocking of the release of neuronal acetylcholine from the presynaptic junction of both neuromuscular and cholinergic autonomic neurons. When hindering the release of acetylcholine, botulinum toxin can temporarily diminish sweat production.[14] The effect can persist for three to nine months or even longer as seen in our patient.[14]

Conclusions

Our report adds to the small number of cases reported in the literature and consolidates the use of histopathology in the diagnostic process. Furthermore it explores new im-

munohistochemical targets and describes and validates the use of botulinum toxin in a much different setting than previously tested. Lastly, we present a phenomenal clinical presentation of this entity and further extend the clinical spectrum of disease.

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