



## SYRINGOCYSTADENOMA PAPILLIFERUM IN CO-EXISTENCE WITH KERATOACANTHOMA AND APOCRINE NEVUS

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### ABSTRACT

Syringocystadenoma papilliferum is a rare cutaneous adnexal benign neoplasm of apocrine or eccrine type with characteristic histological features and varied, non-distinct clinical findings. It occurs singly or in association with other tumours, most commonly nevus sebaceous (of Jadassohn). We report the first case, to our knowledge, of syringocystadenoma papilliferum associated with keratoacanthoma and apocrine nevus, a case of a lesion of the scalp in an adult male, which was clinically diagnosed at first as keratoderma, but was later histologically confirmed as keratoacanthoma with foci of syringocystadenoma papilliferum, without pre-existing nevus sebaceous but with an underlying apocrine nevus.

### INTRODUCTION

Syringocystadenoma papilliferum (SCAP) is a rare benign hamartomatous adnexal tumour, which originates from the apocrine or the eccrine sweat glands and commonly occurs on the scalp and neck. It is relatively a rare neoplasm, predominantly a childhood tumour [1]. The lesions usually measure under 4cm in diameter. SCAP is thought to arise from either pluripotential appendageal cells or apo-eccrine glands. Histologically, it is characterized by funnel-shaped epidermal invaginations demonstrating a gradual transition from keratinizing squamous epithelium at the surface to variable layers of glandular epithelium within subjacent cystic spaces. This epithelial transition mirrors the physiologic epithelial transition of the apocrine gland to the follicular infundibulum [2]. In the healthy apocrine gland there are two layers of bland epithelial cells, an inner luminal layer and an outer basal layer. Immunohistochemically, SCAP has been reported to show CEA and EMA expression at the apical portion of the luminal cells as well as CK7 positivity

in the luminal cells, whereas the basal cells express other keratins, such as CK5/6 and CK14, with patchy SMA staining [2].

We herein present a case where an acquired type of keratoderma of uncertain aetiology was clinically suspected, but was later histologically diagnosed as keratoacanthoma (KA), within which a focal presence of a different neoplasm was recognized as SCAP, as well as a third dermal lesion as an apocrine nevus (AN).

### MATERIAL AND METHODS

#### a. Clinical Data

A 55-year-old male presented with a prominent bleeding lesion on his scalp. The patient could not recall at which point in time the lesion had appeared. The lesion was surgically excised completely with a normal margin of around 0.5cm and with a depth also up to 0.5cm into the subcutaneous plane. The patient did not show recurrence or any other lesion in follow-up.



## b. Gross Data

On gross examination the 2.5x1.5x0.5cm sized spindle-shaped skin sample showed an exophytic-like, ulcerated, flesh-colored, dome-shaped, hard lesion with everted margins, which measured 2.3x1.2x0.9cm above the surface. The cut surface showed that the lesion appeared to sit over the dermis. Sections of the specimen were fixed in formalin, embedded in paraffin and stained with hematoxylin and eosin. Several 2µm-thick, serially cut sections were studied morphologically and immunohistochemically.

## RESULTS

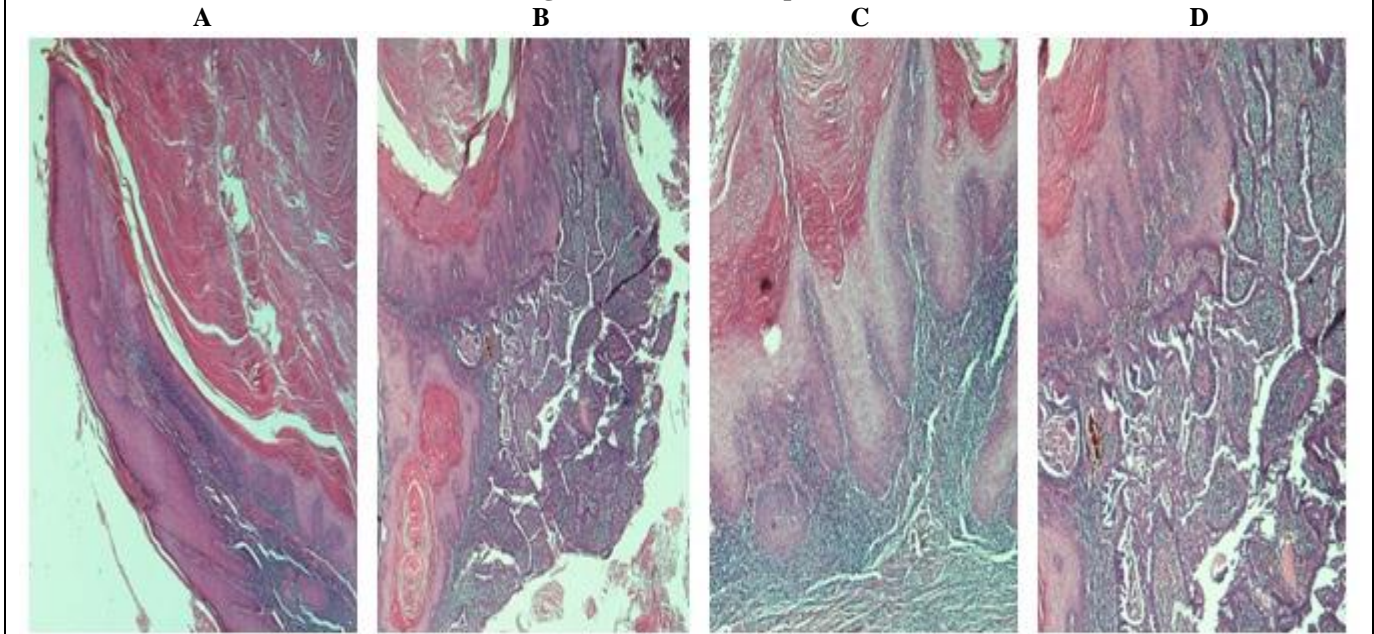
Histologic examination revealed prominent hyperkeratosis and hyperacanthosis in an exophytical growth of the epidermis, which seemed to form a crater-like concavity, filled with desquamated keratin plugs. There was sharp demarcation between tumour and stroma, and a deep but distinct collar-like front of the epithelium. The epithelial bands at the two edges of the lesion seemed to converge towards the middle. The epithelial masses consisted of basal type and squamous type cells with low mitotic rate and minimal pleomorphism, with micro-abscesses of neutrophils approaching the surface, but no granular layer (Fig.1). Both stained positively with keratin cocktail 34βE12 (CK903) and only the former with p63. At least two areas just beneath the epithelial border of the lesion present cleft-like, papillary projections, lined by basically two layers of glandular epithelium: tall columnar luminal cells and cuboidal basal cells. They show oval nuclei and a pale eosinophilic cytoplasm (Fig.2). The glandular epithelium demonstrates signs of decapitation

secretion. Its stroma contains a dense mononuclear cell infiltrate which comprises predominantly of plasma cells. Immunohistochemically, the luminal cells show a strong expression for CK8/18, CK7, CEA and EMA, whereas the basal cells are positive for 34βE12 and p63. A patchy SMA stain highlights foci of myoepithelial basal cells (Fig.3). In certain regions, the neoplasm seems connected to the epidermal surface and the epithelium displays a gradual transition of stratified squamous epithelium at the surface to glandular epithelium within the cystic space.

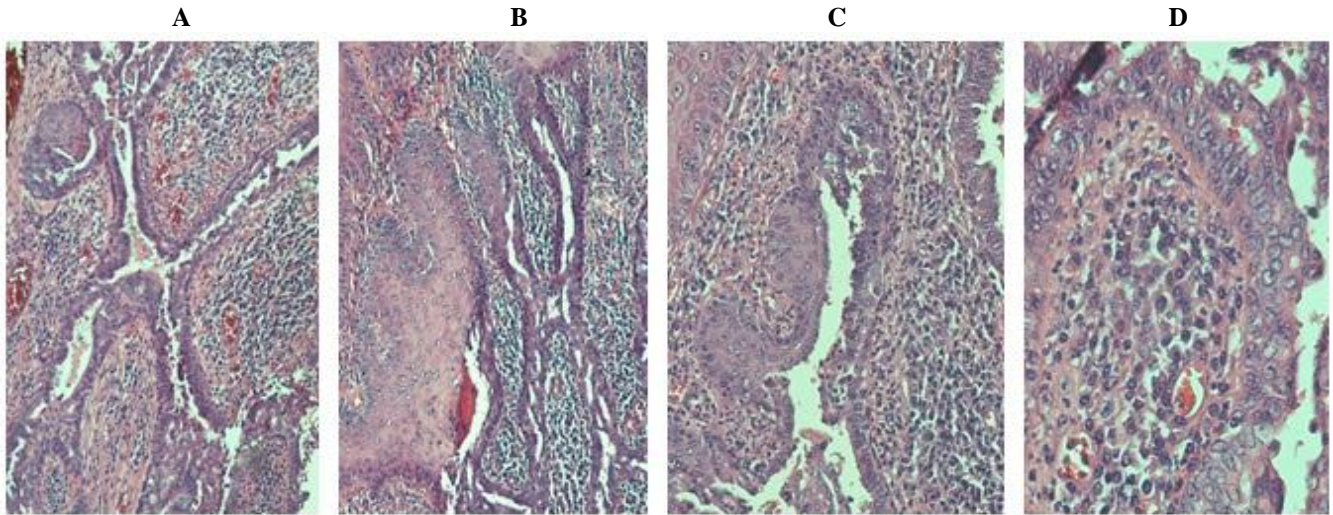
The findings in the first lesion were interpreted as stable phase KA, while those in the focal areas as SCAP.

Around the dermoepidermal junction dense bands of lymphoplasmacytic infiltrations can be observed, with one nodular lymphocytic gathering forming a germinal centre. The dermis includes adnexal elements, such as hair follicles, sebaceous glands and sweat glands. The adjacent sebaceous and eccrine structures are normal. Interestingly, a large central area of the reticular dermis is occupied by a third underlying lesion that consists of prominent glandular and ductal structures, some of them cystically dilated and surrounded by a thin fibrous sheath, composed of irregularly columnar luminal cells with eosinophilic cytoplasm arranged in an organoid pattern within a fibrous stroma filling the reticular dermis and extending into the subcutaneous plane (Fig.4). The glandular luminal cells display 'apical snouts' (decapitation secretion). No atypia was seen in either the glandular structures or the stroma. They show immunohistochemical expression of GCDFP-15 (BRST-2), as does at least partially the overlying lesion of SCAP. These findings were found compatible with apocrine gland hyperplasia as in AN.

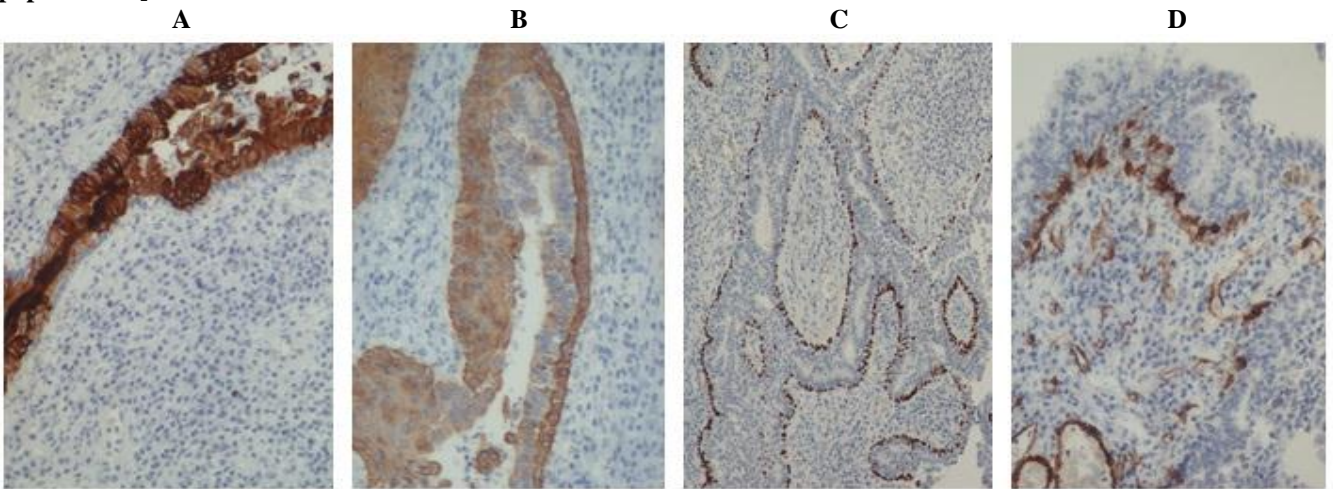
**Fig. 1. Findings of the central lesion. Epidermal crater filled with keratin plugs and acanthotic masses (A) in an inflammatory stroma (A, C), containing cystic invagination lined by glandular epithelium with papillary projections (B, D) and connected to the skin surface through the infundibular epithelium. (H&E, A-B: ×20, C-D: ×40).**



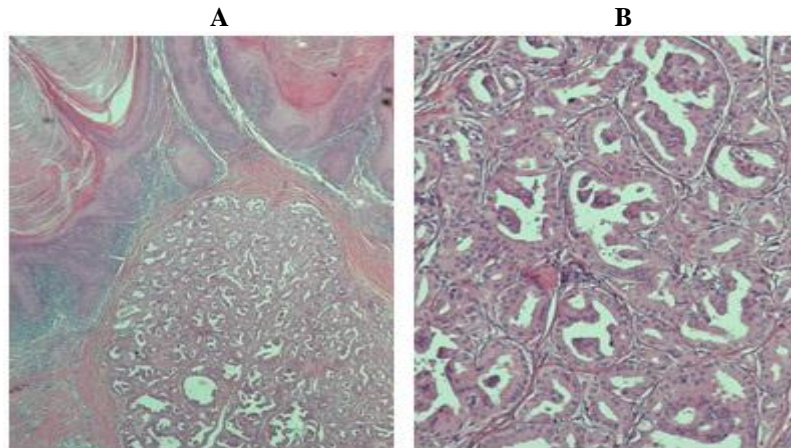
**Fig. 2. Findings of the focal lesion. Papillary projections lined by a bilayered glandular epithelium and packed with plasmacytic infiltrates. Note the gradual transition to stratified squamous epithelium. (H&E, A-B:  $\times 100$ , C:  $\times 200$ , D:  $\times 400$ ).**



**Fig. 3. Immunohistochemical stains of SCAP. Luminal cell layer strongly positive for CK8/18 (A). Basal cell layer positive for 34 $\beta$ E12 (B), p63 (C) and focally SMA (D). (H&E, A, B, D:  $\times 200$ , C:  $\times 100$ ). [SCAP: syringocystadenoma papilliferum]**



**Fig. 4. Findings of the underlying lesion. Compact group of hyperplastic apocrine glands in an organoid pattern. (H&E, A:  $\times 20$ , B:  $\times 100$ ).**



## DISCUSSION

SCAP usually occurs de-novo or within a nevus sebaceous (NS). However, it occasionally co-exists with other tumours such as basal cell, squamous cell and verrucous carcinoma, sebaceous epithelioma, apocrine hydrocystadenoma, trichoepithelioma, eccrine spiroadenoma, papillary hydradenoma, clear cell syringoma, trichilemmoma, apocrine adenoma, follicular poroma [1,3,4]. Thus, its association with hamartomatous lesions of follicular or sebaceous origin is evident. SCAP is believed to derive from the apocrine or eccrine sweat glands and thus considered a hamartoma that recapitulates the formation of the folliculo-apocrine unit [3].

Other histologic hints include the decapitation secretion that provides evidence of apocrine differentiation. Many authors believe that SCAP is a mainly apocrine derived tumour due to the occasional presence of this decapitation secretion in some of the luminal cells of the tumour and the frequent presence of tubular glands with large lumina and decapitation secretion beneath the tumour [5]. In this regard, the apocrine tubular glands found closely beneath the SCAP lesion in our case cannot be interpreted as a random appearance, but rather as a strong indication of its origin and as a cellular formation which plays a certain role in the appearance of the overlying neoplasm. In some lesions, where there are no apocrine glands in the dermis, the papilliferous structures represent eccrine proliferation.

Dermal apocrine glands originate from the follicular infundibulum, characteristically exhibiting a gradual transition from multilayered squamous epithelium at the epidermal surface to a bilayered intradermal duct. This characteristic epidermal transition found in SCAP implies apocrine differentiation and indicates its potential to recapitulate the physiologic relationship of the apocrine gland to the infundibulum of the hair follicle [2].

Histogenetically, various results of light/electron microscopic, immunohistochemical and anatomic studies appear contradictory. Immunohistochemistry supports an apocrine origin, whereas ultra-structural analysis favours an eccrine derivation [6]. SCAP probably derives from both apocrine and eccrine glands. The exact mechanism is still uncertain. Most authors agree that this hamartoma develops from undifferentiated pluripotential appendageal cells. This would support a mix of apocrine and eccrine elements. The presence of cells with apocrine characteristics was confirmed in this case by immunoreactivity to GCDPF-15 antibody, which was expressed in the upper portion of the cyst walls.

Association of SCAP with keratinizing squamous epithelium most likely differentiating towards the infra-infundibulum has also been reported [7]. This relationship as well as the one between SCAP and squamous cell carcinoma has not been adequately investigated. It is mostly syringocystadenocarcinoma papilliferum (SCACP) that has shown association with squamous epithelium [8,9]. However, although earlier reports suggested

malignancy in syringocystadenoma papilliferum-like lesions or benign syringocystadenoma papilliferum with lymph node metastases [2], the diagnosis remains controversial because some authors maintain that there have been no well-documented cases of malignant transformation in syringocystadenoma papilliferum [10]. Albeit, SCACP cannot be an issue here due to the lack of cytologic malignancy, such as higher nuclear/cytoplasmic ratio, nuclear irregularity, coarse chromatin and increased mitotic activity, a ductal hyperplasia pattern or evidence of infiltration of tumour cells into deep dermis or subcutaneous fat. The general impression as well the specific features of the squamous lesion here were those of KA rather than of verrucous carcinoma, since overhanging edges, keratin-filled crater and hemispheric shape are the most important features in differentiating from squamous cell carcinoma. The lesion is also not compatible with the morphological characteristics of the histologic entity described by Kishimoto et al. as *apocrine acrosyringal keratosis* due to the presence of epidermal collarettes and the absence of keratohyalin granules amongst other features [11]. The presence of KA could imply here an abnormal development of a squamous element of the infundibular epithelium towards the surface in combination with an abnormal development of the glandular element, considering that KA is described as a benign, borderline or malignant proliferation of squamous epithelium caused by infundibular hyperplasia and squamous metaplasia of sebaceous glands [12]. Observational and experimental data about the biological behaviour of KA have suggested that the outer root sheath of the hair follicle infundibulum is the origin of this lesion, since pilous follicles naturally evolve through cycles comprising phases of activity/growth, transition and resting/loss.

The histological features of the third underlying lesion are consistent with those of an AN. There are no hallmarks of NS, such as immature hair follicles and prominent sebaceous glands. This presence of an increased number of mature apocrine glands found closely beneath indicates an apocrine origin of this SCAP lesion and a component of a very rare hamartomatous apocrine gland hyperplasia as in AN, which has been associated with SCAP, rather than found isolated [13-15], and which is thought to develop itself a SCAP [14]. Morphology as well as immunohistochemistry of this organoid appendageal lesion strongly support the diagnosis of an apocrine nevus.

## CONCLUSION

In conclusion this case demonstrates that SCAP can arise without a NS background in adults in co-existence with benign or low-grade malignant squamous lesions of the type of KA and a background of an AN. Taking into account the related case reports in the English scientific literature it is postulated either that KA developed on a substrate of SCAP which developed from an AN or that both neoplasms arose synchronously during the abnormal development of a folliculo-apocrine or a pilo-sebaceous unit.



## Declarations of interest

No financial or other competing interests.

## REFERENCES

1. Xu D, Bi T, Lan H, et al. (2013). Syringocystadenoma papilliferum in the right lower abdomen, a case report and review of literature. *Onco Targets Ther*, 6, 233-236.
2. Leeborg N, Thompson M, Rossmiller S, et al. (2010). Diagnostic Pitfalls in Syringocystadenocarcinoma Papilliferum, Case Report and Review of the Literature. *Arch Pathol Lab Med*, 134, 1205-1209.
3. Sangma MMB, Dasiah SD, Bhat VR. (2013). Syringocystadenoma Papilliferum of the Scalp in an Adult Male – A Case Report. *J Clin Diagn Res*, 7, 742-743.
4. Fujita M, Kobayashi M. (1986). Syringocystadenoma papilliferum associated with poroma folliculare. *J Dermatol*, 13, 480-482.
5. Yoon JH, Ahn HH, Kye YC, et al. (2011). Syringocystadenoma Papilliferum in Co-existence with Tubular Apocrine Adenoma on the Calf. *Ann Dermatol*, 23, S175-178.
6. Yamamoto O, Doi Y, Hamada T, et al. (2002). An immunohistochemical and ultrastructural study of syringocystadenoma papilliferum. *Br J Dermatol*, 147, 936-945.
7. Kurokawa I, Mizutani H, Nishijima S, et al. (2005). Keratinizing squamous epithelium associated with Syringocystadenoma papilliferum differentiates towards infrainfundibulum, case report with immunohistochemical study of cytokeratins. *J Int Med Res*, 33(5), 590-593.
8. Zhang YH, Wang WL, Rapini RP, et al. (2012). Syringocystadenocarcinoma papilliferum with transition to areas of squamous differentiation, a case report and review of the literature. *Am J Dermatopathol*, 34(4), 428-433.
9. Kazakov DV, Requena L, Kutzner H, et al. (2010). Morphologic diversity of syringocystadenocarcinoma papilliferum based on a clinicopathologic study of 6 cases and review of the literature. *Am J Dermatopathol*, 32(4), 340-347.
10. Patterson JW, Wick MR. (2006). Nonmelanocytic Tumors of the Skin. Silver Spring, MD Armed Registry of Pathology, and Washington, DC, Armed Forces Institute of Pathology, 147-148. Atlas of Tumor Pathology; 4th series, fascicle 4.
11. Kishimoto S, Wakabayashi S, Yamamoto M, et al. (2000). Apocrine acrosyringal keratosis in association with syringocystadenoma papilliferum. *Br J Dermatol*, 142(3), 543-547.
12. Schwartz RA. (2004). Keratoacanthoma, a clinico-pathologic enigma. *Dermatol Surg*, 30, 327-333.
13. Cordero SC, Royer MC, Rush WL, et al. (2012). Pure apocrine nevus, a report of 4 cases. *Am J Dermatopathol*, 34(3), 305-309.
14. Numata Y, Okuyama R, Terui T, et al. (2006). Apocrine nevus in abdominal skin. *Dermatology*, 213, 46-47.
15. Misago N, Narisawa Y. (2006). Syringocystadenoma papilliferum with extensive apocrine nevus. *J Dermatol*, 33, 303-305.

