

Development of Six Tumors in a Sebaceous Nevus of Jadassohn: Report of a Case

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Nevus sebaceus of Jadassohn is a congenital cutaneous hamartoma comprised of multiple skin structures. It has the potential to develop into variety of neoplasms of various epidermal adnexal origins. While multiple tumors may occasionally arise, it is unusual for more than four tumors to arise simultaneously within a single sebaceous nevus. Here in, we report a case of a 70-year-old woman with six neoplastic proliferations including a syringocystadenoma papilliferum, pigmented trichoblastoma, tubular apocrine adenoma, sebaceoma, tumors of follicular infundibulum and superficial epithelioma with sebaceous differentiation arising in a long standing nevus sebaceus on the scalp. Our case is extraordinary because a single nevus sebaceus contained six neoplastic proliferations with differentiation toward the folliculosebaceous-apocrine unit.

Key Words: Syringocystadenoma papilliferum; Pigmented trichoblastoma; Tubular apocrine adenoma; Sebaceous differentiation; Nevus sebaceus of Jadassohn

Nevus sebaceus of Jadassohn (NS) or organoid nevus is a complex cutaneous hamartoma involving not only the pilosebaceous follicle but also the epidermis and often other adnexal structures.¹ It may present at birth or develop in early childhood. Nearly all lesions occur on the scalp, forehead or face and appear clinically as smooth yellowish, hairless patches.^{1,2} Most lesions are plaques of 1-6 cm in diameter.¹ Characteristic morphologic changes occur with puberty and lesions assume a verrucoid appearance.²

In adulthood, various types of appendageal tumors, malignant and/or benign, such as basal cell carcinoma (BCC), syringocystadenoma papilliferum (SCAP), trichoblastoma (TB), and hidradenoma may develop secondarily within lesions of NS.^{1,3} The progression and frequency of tumors increases with age of the patient.^{4,5}

While up to four different tumors may be present, this is quite rare.^{1,2,6} Mehregan and Pinkus⁷ described a series of 150 patients with NS, including 4 that had three coexisting tumors and one

that had 4 tumors. In another series of 140 patients with NS, Jones and Heyl⁸ found only 1 patient with 3 tumors.

We report a case of the simultaneous occurrence of 6 tumors including SCAP, pigmented trichoblastoma (PT), tubular apocrine adenoma (TAA), sebaceoma, tumor of follicular infundibulum (TFI), and superficial epithelioma with sebaceous differentiation within a single nevus sebaceus.

CASE REPORT

A 70-year-old woman presented to our outpatient clinic with a verrucous growth on her scalp measuring 2.5×1.8 cm. The lesion presented at birth. While she was unaware of any specific changes in the lesion for decades, she noticed a rapid progression in the last two years. She was generally healthy and had no accompanying symptoms. The patient had no previous history of cutaneous or internal malignancies and a complete systems review was negative. There was no family history of malignancy.

The lesion of NS was completely excised with a free margin of 0.2 cm and submitted for histopathological evaluation. Mac-

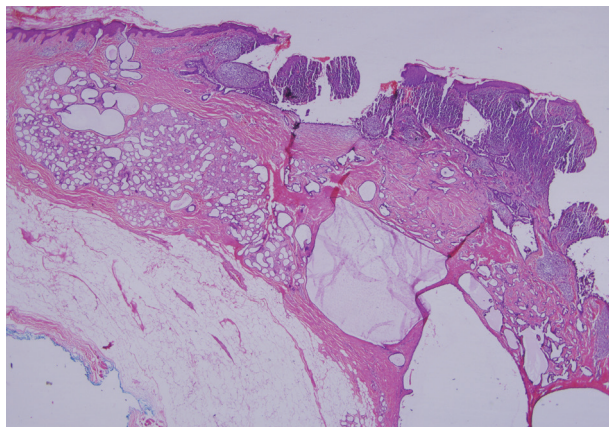


Fig. 1. Syringocystadenoma papilliferum in the superficial part of the lesion. Tubular apocrine adenoma and cystic dilate glands in the deeper part.

roscopic examination of the lesion revealed a 2.5 × 1.8 cm, yellowish, verrucous plaque devoid of hair. One large, vegetative plaque with a hemorrhagic crust lay within the yellowish plaque.

Histopathological findings of the lesion by hematoxylin and eosin staining showed acanthosis, papillomatosis, sebaceous gland hyperplasia, and immature hair follicles in the dermis in the peripheral parts of the lesion. These findings were consistent with a diagnosis of NS. In addition, there were 6 adnexal tumors in the lesion including SCAP, PT, TAA, sebaceoma, TFI, and superficial epithelioma with sebaceous differentiation (SESD). The majority of the lesion was composed of SCAP, PT, and TAA. The tumors were separated from each other by loose fibrillary connective tissue stroma. These benign tumors were partly intertwined (Figs. 1, 2A).

Cytomorphologically, the SCAP was composed of irregular papillary projections covered by double layers of epithelium and stratified squamous epithelium with stroma containing

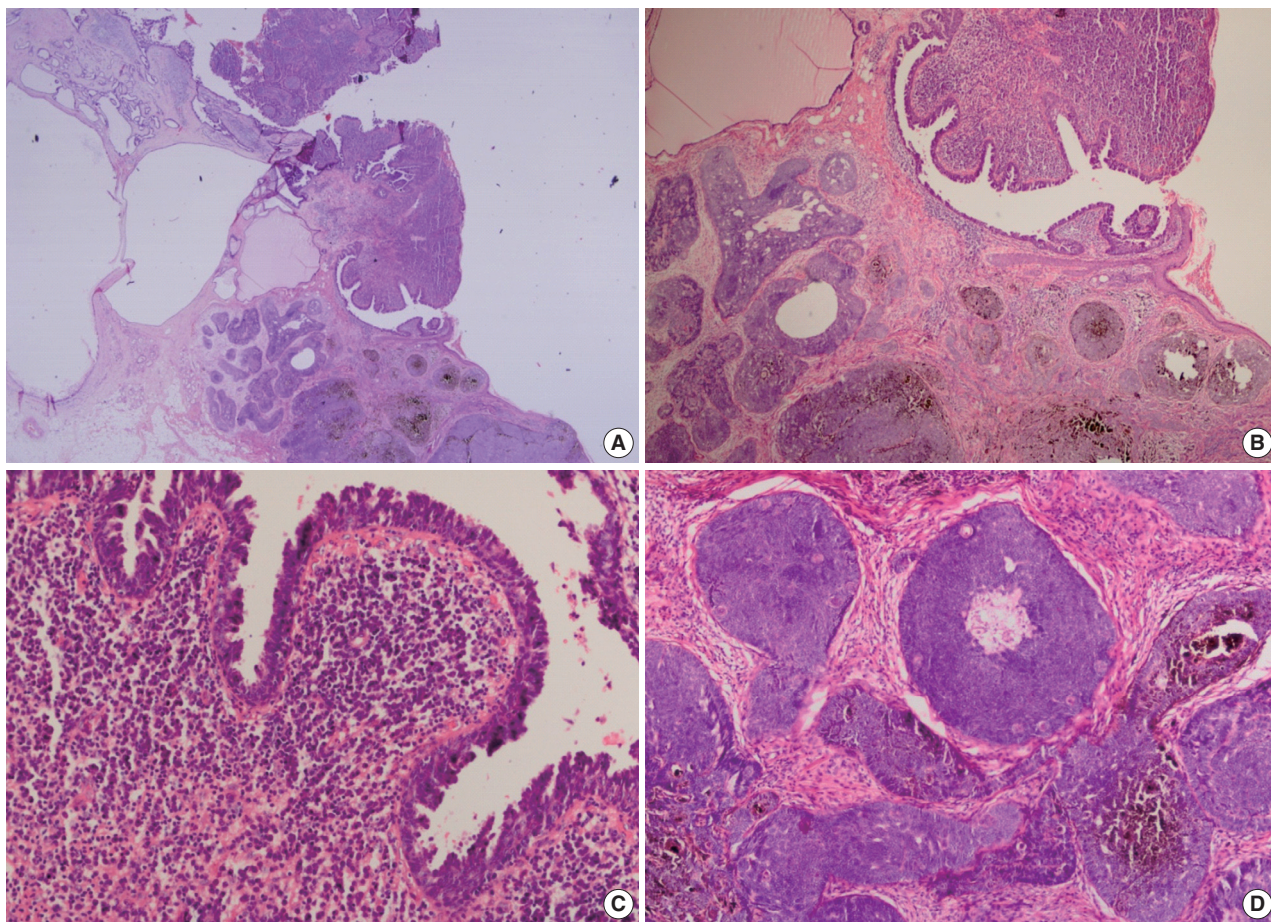


Fig. 2. Syringocystadenoma papilliferum in the superficial part of the lesion. (A) Pigmented trichoblastoma and cystic dilate glands in the deeper part. (B) Pigmented trichoblastoma in the deeper part. (C) Typical features of syringocystadenoma papilliferum. (D) Pigmented trichoblastoma; lobules of basaloid aggregates with peripheral palisading.

lymphocytes and large numbers of plasma cells (Fig. 2B, C). The deeper portion of the SCAP consisted of tubular structures with two layers of epithelial cells. While the luminal cells of the tubules were columnar and showed decapitation secretion, the outer layer was composed of flattened cells. These tubules were surrounded by a fibrous stroma. TAA was diagnosed from these findings (Fig. 1).

The PT was characterized by a well-circumscribed large basoid dermal tumor without an epidermal connection. There were dispersedly brown pigmentation fields in the center of large tumor islands (Fig. 2B, D).

In our case, small foci of follicular infundibulum, sebaceoma and SESD were observed. The TFI was composed of a plate like growth of basoid keratinocytes with several points of attachment to the epidermis (Fig. 3). A collection of benign basoid sebaceous cells suggestive of a sebaceoma was present and the sebaceoma existed as two types: superficial and deep in the dermis. There were cysts containing debris from holocrine degeneration

(Fig. 4). The SESD was characterized by a sharply defined and well-circumscribed plate-like epidermal growth. Merging with the superficial keratinocytes was a cytologically bland

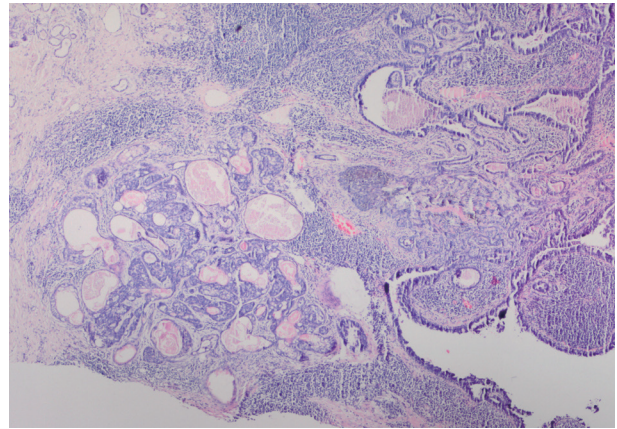


Fig. 4. Syringocystadenoma papilliferum in the superficial part, pigmented trichoblastoma and sebaceoma in the deeper part.

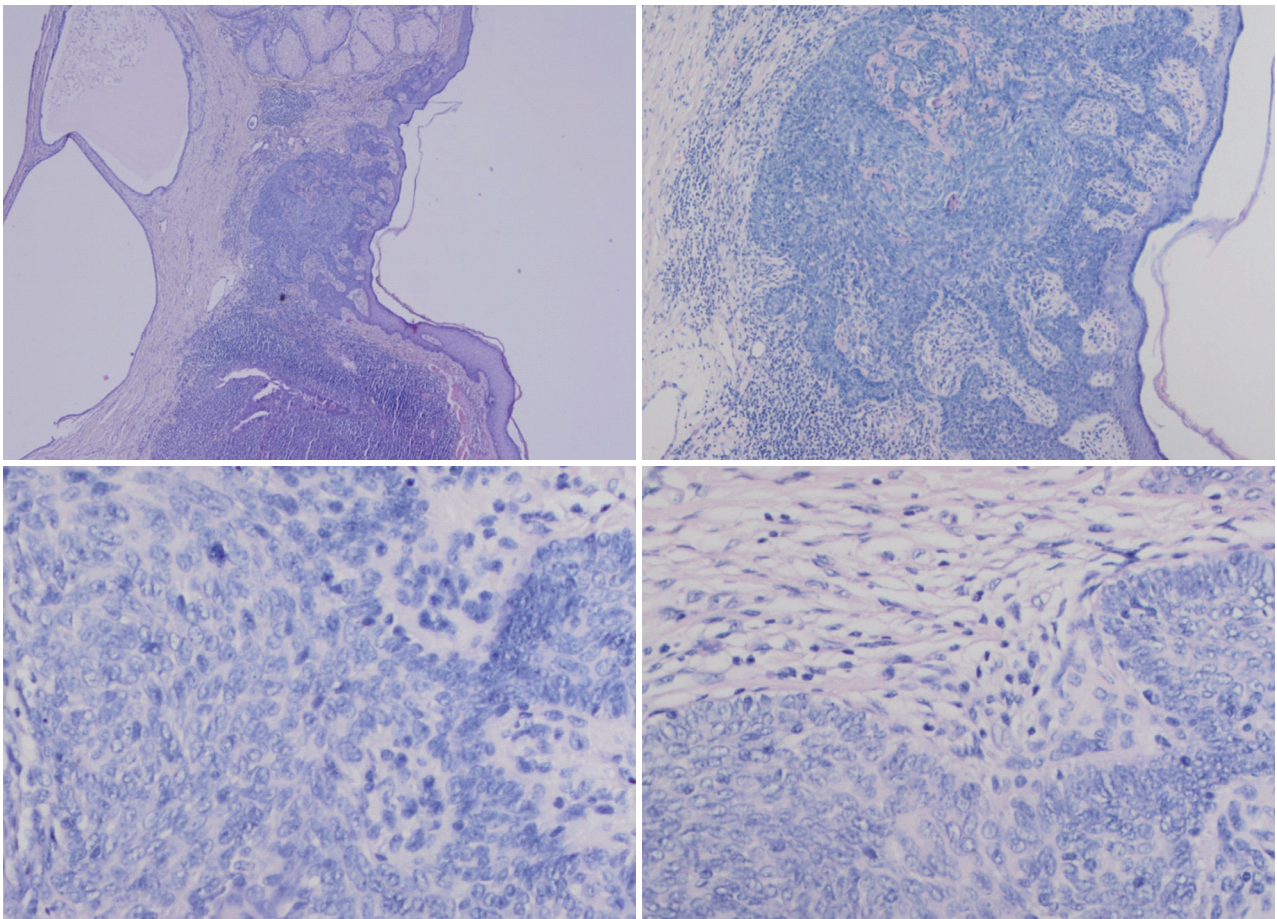


Fig. 3. Tumor of follicular infundibulum. Aggregates of small keratinocytes show multiple connections to the epidermis and form a superficial dermal plaque.

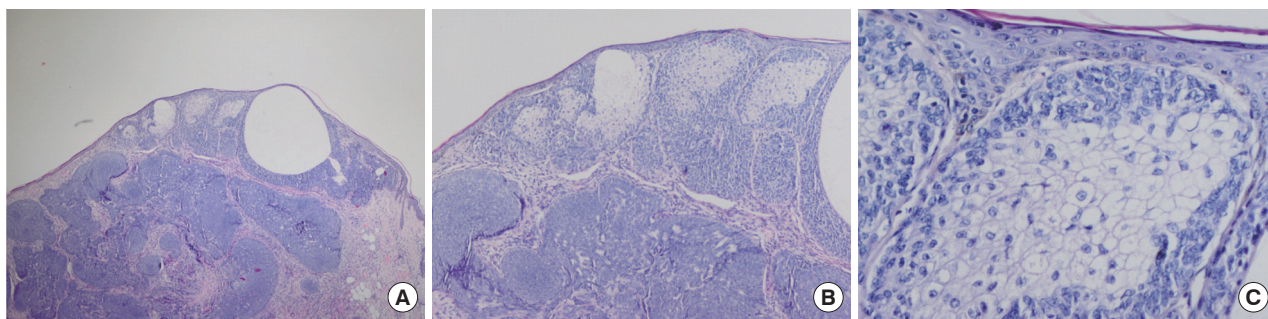


Fig. 5. (A) Superficial epithelioma with sebaceous differentiation above the trichoblastoma. (B) Superficial epithelioma with sebaceous differentiation. (C) Sebaceous differentiation in the superficial epithelioma.

basaloid cell population in which admixed mature sebocytes were present in clusters (Fig. 5).

DISCUSSION

While multiple neoplasms may occasionally arise within the same lesion of NS, it is rare for four or more neoplasms to occur simultaneously.⁹ There are only three articles in the English medical literature describing the development and progression of 5 neoplasms in a solitary lesion. Our case is the second involving 6 neoplasms in a solitary lesion.^{2,5,10} This is not surprising considering that the skin adnexal structures arise from pluripotent stem cells.

The 6 benign tumors arising within the nevus sebaceus of our patient included SCAP, TB, TAA, TFI, sebaceoma, and SESD. SCAP and TB are the most common neoplasms associated with nevus sebaceus.⁴

TBs are fibroepithelial tumors composed of benign basaloid epithelial cells with cellular fibrous stroma. There are histopathologic overlaps between TB and BCC. The main distinction between pigmented TB and pigmented BCC is the stroma of TB shows a tight association with basaloid epithelial cells. In addition, no clefts or retractions are seen between epithelium and stroma as is characteristic of BCC. Mitoses and apoptotic bodies can occur in TB but are not as common as in BCC.^{5,11}

TAAAs are benign tumors with glandular differentiation. They tend to be centered in the dermis and are well-circumscribed. The important issue is to distinguish adenomas from well differentiated adenocarcinomas. In the majority of cases, this distinction is straight forward because many carcinomas are large, infiltrative and show significant cytologic atypia.¹

The fourth tumor in our patient was TFI. The tumor cells had basaloid features and resembled a superficial BCC and superficial portion of an infundibulocystic BCC. In contrast with

BCC, TFI lacks hyperchromatic nuclei, myxoid stroma and peripheral clefting.¹

The fifth tumor in our patient was sebaceoma. Sebaceoma, as presented in our case, should be differentiated from mantleoma and sebaceus carcinoma. In our case there was no atypia observed in the sebaceus carcinoma. The mantleoma is a tumor of the sebaceus mantle. Histopathologically, early neoplasms consist only of cords and columns of undifferentiated epithelial cells that radiate from an infundibulum. In late stages, these cords interweave in a retiform pattern that contains sebocytes of varying degrees of vacuolization and sebaceus ductal structures. In our case, there were multiple nests of basaloid cells with a random admixture of sebaceous cells. In addition, cysts and duct like structures containing debris from holocrine degeneration are suggestive of sebaceoma.¹

The sixth tumor in our patient was SESD. SESD is very closely related to reticulated acanthoma with sebaceous differentiation but is a distinct tumor. Reticulated acanthoma with sebaceous differentiation (RASD) is mainly characterized by proliferation of spinous cells, aggregates of mature sebocytes in the bottom of the strand of epithelium, bridging of the bases of the epithelium by those mature sebocytes and lack of pseudocysts and melanin granules.^{12,13} Utilizing features like sebaceous aggregates located only at the basal aspects without a reticulated pattern, our case was differentiated from RASD.

Seborrheic keratosis with sebaceous differentiation was also included in the differential diagnosis. However, this lesion showed features of an acanthotic variant with only small numbers of mature sebaceous cells scattered randomly throughout the epithelium. There were no pseudohorn cysts and no melanin pigments.

SESD should also be distinguished from follicular infundibulum tumor. Tumor of follicular infundibulum is characterized by a plate-like epithelial proliferation suspended from the epi-

dermis. However, tumor trabeculae are characteristically thin, vacuolated and often surrounded by a thickened eosinophilic basement membrane.¹⁴ In terms of the differential diagnosis, it is important that our case did not have a reticular pattern.

In our case, there was no direct connection of sebaceous cells with the superficial epithelium as they were located only in the basal aspects of the epithelium. In addition, our lesion contained not only sebaceous cells but also basaloid cells.

As a result, many publications have discussed extensively whether SESD is a completely different entity. From our perspective, we believe SESD is unique as although it may have some similar features, it does not fit exactly into any of the other diagnoses. These kinds of cases are difficult to interpret since they are rare, are not published in a wide range of classical books and are not defined by exact diagnostic criteria. Therefore, it is important to create awareness on this issue and share information through the literature.

There have been recent reports of benign and malignant complex neoplasms arising within NS. Manonukul *et al.*¹⁰ reported TB, trichilemmoma, sebaceous adenoma, TFI, SCAP, and mucocystic carcinoma arising within 2 persistent lesions of NS. Kantrow *et al.*² reported a coexistence of tumor of the follicular infundibulum, basaloid proliferations resembling superficial TB, a focus reminiscent of syringofibroadenoma, a trichilemmoma, a sebaceous lesion consistent with sebaceoma/sebaceous epithelioma and an apocrine adenocarcinoma in a long-standing NS. Miller *et al.*⁵ also reported five tumors in a NS (sebaceous carcinoma, BCC, trichoadenoma, TB, and SCAP). The multiplicity of tumors was considered not to be coincidental and was attributed to histogenetic mechanisms of NS.⁹ Tumors complicating NS may arise from the pluripotential primary epithelial germ as a result of either dedifferentiation of NS cells or from embryonic cells that lie dormant until the onset of neoplasia.³

In their study, Xin *et al.*¹¹ concluded that the genetic defect at 9q22.3 might possibly also contribute to the development of other appendageal tumors in NS such as SCAP, primitive follicular germs and TBs. They also suggested that further studies needed to address whether patched (*PTCH*) deletion in NS is associated with progression to BCC and/or other appendageal tumors.¹¹

Sebaceous tumor existence is important in NS because sebaceous lesions are associated with two syndromes: linear sebaceous nevus syndrome and Muir-Torre syndrome.¹ Muir-Torre syndrome is characterized by the development of usually multiple sebaceous tumors in association with visceral neoplasms, usually gastrointestinal carcinomas and occasionally the genitourinary

system. A single skin tumor with sebaceous differentiation could be a sign of Muir-Torre syndrome.¹ Fortunately, in this case, careful examinations for internal malignancies were all negative.

Currently, the necessity of prophylactic excision or topical photodynamic therapy in NS has been discussed in many publications.^{2,5,9,10,15,16} Clinical features are not sufficient to make an exact diagnosis of benign or malignant secondary tumors.¹⁷ In our opinion, owing to the possibility of malignant tumor outgrowth from a NS and the increasing frequency of occurrence with age, it is necessary to conduct prophylactic excision especially in adulthood. If excision is not conducted, at a minimum, changes in the lesion should be monitored by close clinical follow-up.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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