INTRODUCTION

Nevus sebaceous of Jadassohn (NSJ) is a congenital cutaneous hamartoma that usually appears shortly after birth. It has the potential to generate a variety of secondary neoplasms of different lineages, and the risk increases with patient age. Although multiple neoplasms may occasionally arise within the same lesion, the coexistence of more than five secondary tumors is extremely rare. Here we report a case of seven secondary tumors including syringocystadenoma papilliferum, desmoplastic trichilemmoma, sebaceoma, trichoblastoma, pigmented trichoblastoma, sebaceous adenoma, and tumor of follicular infundibulum arising within a nevus sebaceous. The complete diagnosis relies on the histopathological analysis of multipoint biopsies and delineate pathological sections.

Abbreviations: BCC, basal cell carcinoma; CK, cytokeratin; DT, desmoplastic trichilemmoma; MTS, Muir-Torre syndrome; NSJ, nevus sebaceous of Jadassohn; SCAP, syringocystadenoma papilliferum; TB, trichoblastoma; TFI, tumor of follicular infundibulum

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ored, alopecic verrucous plaque on her left temporoparietal scalp (Fig. 1), which contained several grayish-yellow papules and three erythematous ulcerated nodules. Under the clinical diagnosis of NSJ with possible malignant change, the lesion was totally excised with a 3 mm free margin for histopathological evaluation.

Microscopic examination of the main lesion revealed acanthosis, hyperkeratosis, and papillomatosis of the epidermis. Sebaceous gland hyperplasia, immature hair follicles, and ectopic apocrine glands were present in the dermis, which were consistent with a diagnosis of NSJ. Histopathologically, two connecting ulcerative nodules (Fig. 1, arrows) showed features of partially intertwined syringocystadenoma papilliferum (SCAP) and desmoplastic trichilemmoma (DT) (Figs. 2, 3). Features of sebaceoma were detected in an ulcerated nodule in the central part of the lesion (Figs. 1 arrowhead, 4). Trichoblastoma (TB), pigmented TB, sebaceous adenoma and tumor of follicular infundibulum (TFI), which were separated by connective tissue stroma, were identified in the area containing grayish-yellow papules under higher magnification (Figs. 5-8).

The simultaneous presence of two sebaceous neoplasms raised concern for Muir-Torre syndrome (MTS). The initial laboratory work-up for occult malignancy revealed a normal complete blood count, electrolytes, urine analysis, and renal

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**Fig. 1.** A linear, skin-colored, alopecic verrucous plaque measuring 7×1.5 cm on the scalp. The plaque contained three erythematous ulcerated nodules (white arrows and arrowhead) and several grayish-yellow papules.

**Fig. 2.** Syringocystadenoma papilliferum demonstrating papillary structures lined by double layers of cuboidal epithelium and stroma containing numerous plasma cells (H&E, ×20).

**Fig. 3.** Desmoplastic trichilemmoma comprising a well-defined lobular tumor with dense desmoplastic stroma occupying the central portion of the lesion. There is focal clear cell differentiation (black arrow) surrounded by a basement membrane. The irregular epithelial strands without cellular atypia are admixed in a desmoplastic stroma (white arrow) (H&E, ×40).

**Fig. 4.** Sebaceoma demonstrating a basaloid dermal tumor with cyst formation, superficial ulceration, and hemorrhage. Ductal structures lined by an eosinophilic cuticle are visible. Note the random admixture of basaloid cells and mature sebocytes (black arrow) (H&E, ×40).
and liver function. A further regular work-up was recommend-
ed to the patient, including colonoscopy, mammogram, pelvic
exam, and chest X-ray. There was no recurrence of the scalp tu-
mor 1 year after the surgery.

DISCUSSION

NSJs have the potential to generate a variety of secondary neo-
plasms of both sebaceous and non-sebaceous (e.g., follicular,
apocrine, eccrine, muscle) lineages [5]. Histopathologically, it is
also common to find proliferating basaloid cells or basaloid tu-
mors within NSJs, which may be related to mutations in genes
encoding PTCH and p53 [6,7]. As noted, NSJs rarely develop
multiple secondary tumors simultaneously, and our patient ap-
pears to be the first such reported case containing seven sec-
ondary benign neoplasms with follicular, sebaceous, and sweat
gland differentiation (Table 1).

According to previous studies, SCAP and TB are the most
common benign tumors associated with NSJ [8]. Histopatho-
logically, SCAP is composed of irregular papillary projections
lined by double layers of glandular epithelium, with numerous
plasma cells in the stroma. TB comprises benign basaloid epi-
thelial cells with abundant fibrous stroma and focal clefts be-
tween collagen fibers. It should be differentiated from basal cell
carcinoma (BCC), which is characterized by clefts between ba-
saloid aggregations and surrounding mucinous stroma. In ad-
tion, TB typically contains papillary mesenchymal bodies,
which are usually absent in BCC. Several immunohistochemis-
try markers (e.g., CD10, cytokeratin [CK] 15, CK19, CK20,
Ber-EP4) can be used to assist in distinguishing benign follicu-
lar tumors from BCCs [9]. In our case, the lesion diagnosed as
TB was focally positive for CK20 and negative for Ber-EP4.

DT is an uncommon histological subtype of trichilemmoma,
Sebaceous adenoma, syringocystadenoma papilliferum, tumor of follicular infundibulum, trichoblastoma

| Author          | Age (yr)/sex | No. of Tumors | Benign tumors                                                                 | Malignant tumors                                      |
|-----------------|--------------|---------------|-------------------------------------------------------------------------------|-------------------------------------------------------|
| Miller et al. [1] | 45/F         | 5             | Trichoepithelioma, trichoblastoma, syringocystadenoma papilliferum              | Sebaceous carcinoma, basal cell carcinoma              |
| Gozel et al. [2] | 70/F         | 6             | Syringocystadenoma papilliferum, pigmented trichoblastoma, tubular apocrine adenoma, sebaceoma, tumors of follicular infundibulum, superficial epithelioma with sebaceous differentiation | Sebaceous carcinoma, basal cell carcinoma              |
| Kantrow et al. [3] | 66/F        | 6             | Tumor of the follicular infundibulum, superficial trichoblastoma, syringofibroadenoma, sebaceoma | Metastasizing adenocarcinoma, basal cell carcinoma    |
| Manonukul et al. [4] | 38/F       | 4             | Sebaceous adenoma, syringocystadenoma papilliferum, tumor of follicular infundibulum, trichoblastoma | Sebaceous carcinoma, basal cell carcinoma              |
| Wang et al. [10] | 40/F         | 4             | Syringocystadenoma papilliferum, trichilemmoma, sebaceoma                    | Basal cell carcinoma                                  |
| Dore et al. [11] | 63/M         | 4             | Trichoblastoma, syringocystadenoma papilliferum, desmoplastic trichilemmoma, tumor of the follicular infundibulum with signet-ring cells | Sebaceous carcinoma                                  |
| Wang et al. [12] | 48/F         | 4             | Sebacea, trichoblastoma, poroma                                             | Sebaceous carcinoma                                  |
| Namiki et al. [13] | 67/F        | 4             | Syringocystadenoma papilliferum, sebaceoma, trichoblastoma                  | Basal cell carcinoma                                  |
| Basu et al. [14] | 67/F         | 4             | Syringocystadenoma papilliferum, prurigo nodularis, apocrine cystadenoma, sebaceoma | Basal cell carcinoma                                  |
| Our case        | 50/F         | 7             | Syringocystadenoma papilliferum, desmoplastic trichilemmoma, sebacea, trichoblastoma, pigmented trichoblastoma, sebaceous adenoma, tumor of follicular infundibulum | Basal cell carcinoma                                  |

F, female; M, male.

and only 10 cases of DT arising within NSJ have been described [8,11,15,16]. Histopathologically, DT presents as a well-defined lobular tumor with typical features of trichilemmoma at the periphery and a central desmoplastic stroma. The presence of admixed irregular epithelial strands and nests in a dense sclerotic stroma may cause misdiagnosis as squamous cell carcinoma or morpheaform BCC. A correct diagnosis relies on the absence of cellular atypia and mitotic activity, and the presence of lobules of clear epithelial cells surrounded by an eosinophilic hyaline mantle. In difficult cases, CD34-positive epithelial strands may facilitate the differential diagnosis of DT over other desmoplastic tumors of the skin [17].

The NSJ in our patient also included areas resembling sebacea and sebaceous adenoma. Sebaceoma is composed of a random admixture of germinative basaloid cells and mature sebocytes lacking an organized lobular architecture [18]. Sebaceous adenoma comprises irregular sebaceous lobules with a rim of basaloid cells peripherally and mature sebocytes centrally [4]. Although neither neoplasm typically exhibits cytological atypia or a significantly increased mitotic rate, some benign sebaceous neoplasms in MTS are supposed to have a high potential for malignant transformation [19]. In our patient, there was no family history of internal malignancy, and the initial work-up for occult malignancy related to MTS yielded negative results. Further regular work-ups for cutaneous and internal malignancies may be warranted in this patient.

A TFI was also identified in our case, which is characterized by anastomosing islands of basophilic cells with multiple points of attachment to the overlying epithelium. The basaloid features and peripheral palisading in TFI may be similar to a superficial BCC or superficial portion of an infundibulocystic BCC. In contrast to BCC, the tumor cells in TFI are pale staining due to glycogen and lack hyperchromatic nuclei, peripheral clefting, and Ber-EP4 expression [2]. They may also include scattered CK20-positive Merkel cells, which are usually absent in BCC [20].

In conclusion, this report highlights the diverse neoplastic potential of NSJ toward adnexal tumors of different lineages and supports the hypothesis that NSJ develops from the pluripotent primary epithelial germ cells. The proliferation of these pluripotent germ cells into different lineages may explain the development of multiple secondary tumors. Clinically, for a longstanding NSJ with multiple tumor growth, multipoint biopsies and delicate pathological sections should be obtained to make a complete diagnosis and exclude the possibility of malignant transformation. It is important to select the appropriate biopsy site and size when evaluating the secondary neoplasms. Additional tissue sampling or pathological sections may be essential if the pathology findings do not entirely correlate with the clinical presentation. Although prophylactic excision may not be necessary for every adult patient with NSJ, close clinical surveillance and appropriate pathological examinations are warranted to monitor the development of neoplasms.
NOTES

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

Ethical approval
The study was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (IRB No. KSVGH20-CT12-21).

Patient consent
The patient provided written informed consent for the publication and the use of her images.

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