

A Case of Sebaceous Naevus of the Leg with Secondarily Developed Trichoblastoma

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Sir,

Sebaceous naevi (organoid naevi) are hamartomatous proliferations that usually appear at birth or early in life, and are most commonly located on the scalp and face (1). They often present as round or oval lesions, and occasionally distribute in a linear pattern (2). Frequently, sebaceous naevi are complicated by the development of secondary tumours, such as syringocystadenoma papilliferum, trichoblastoma, and trichilemmoma. Except for systematized sebaceous naevi, sebaceous naevi on the legs are extremely rare, and only three cases have been reported so far (3–5). Therefore, it is difficult to make a diagnosis of sebaceous naevus when it occurs on the leg in a linear distribution that is rather characteristic of non-organoid (keratinocytic) epidermal naevi. We report here a case of sebaceous naevus on the leg complicated by trichoblastoma. Molecular investigations for *FGFR3* and *PIK3CA* mutations, both of which have been identified in non-organoid epidermal naevi (6, 7), were performed.

CASE REPORT AND GENETIC ANALYSIS

A 54-year-old Japanese woman presented in May 2008 with a one-year history of a slowly enlarging pigmented nodule, which had developed in a pre-existing linear lesion since birth, on her left thigh. She was otherwise in excellent health. Clinical examination revealed a dark-brown nodule 4 mm in diameter within yellowish-brown papules in a linear distribution (Fig. 1). Complete excision of the entire skin lesion was performed. Histopathology of the dark-brown nodule revealed a large well-circumscribed nodule composed of basaloid cells with marked melanin depositions in connection with the epidermis extending into the dermis (Fig. 2A). There were follicular germ-like structures, prominent fibrocytic stroma surrounding



Fig. 1. A dark-brown nodule (4 mm in diameter) on the left thigh and yellowish brown papules in a linear distribution.

the periphery of the nodule, and a cleft formation between the fibrocytic stroma and normal dermis. (Fig. 2B, C). Histopathology of the yellowish-brown papules demonstrated acanthosis, papillomatosis, and small numbers of abortive hair papillae-like proliferations and sebaceous glands, which was located at an abnormally high level within the dermis (Fig. 3). The lesion was diagnosed as trichoblastoma arising in sebaceous naevus.

We analysed the 2 specimens (trichoblastoma and sebaceous naevus) for *FGFR3* and *PIK3CA* hotspot mutations, which have been reported recently in non-organoid epidermal naevi, but not in sebaceous naevi (6, 7). We used a *FGFR3* SNaPshot multiplex assay covering 11 *FGFR3* hotspot mutations, including all recently described *FGFR3* mutations in non-organoid epidermal naevi (6). In addition, we directly sequenced exons 9 and 20 of *PIK3CA* (7). All samples displayed an *FGFR3* and *PIK3CA* wild-type status for the investigated loci.

DISCUSSION

Sebaceous naevi are frequently complicated by the development of secondary tumours, and its incidence has been reported to be approximately 15% (8). The most common secondary tumours are syringocystadenoma papilliferum, trichoblastoma, and trichilemmoma (2). Less commonly, malignant tumours, such as basal cell carcinoma, squamous cell carcinoma, and malignancies of apocrine, eccrine, and sebaceous origin have been reported (2).

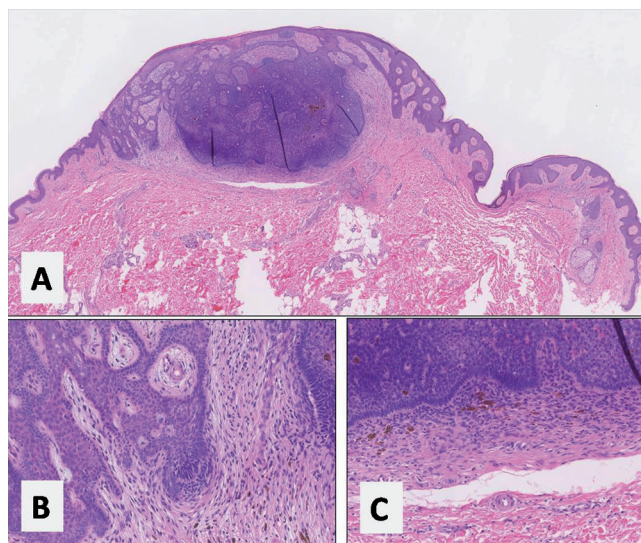


Fig. 2. Histopathology of the dark brown nodule. (A) A well-circumscribed nodule with remarkable melanin depositions (haematoxylin and eosin (H&E), original magnification $\times 12.5$). (B) A follicular germ-like structure (H&E $\times 100$). (C) Peripheral prominent fibrocytic stroma and a cleft formation between the fibrocytic stroma and normal dermis (H&E $\times 100$).

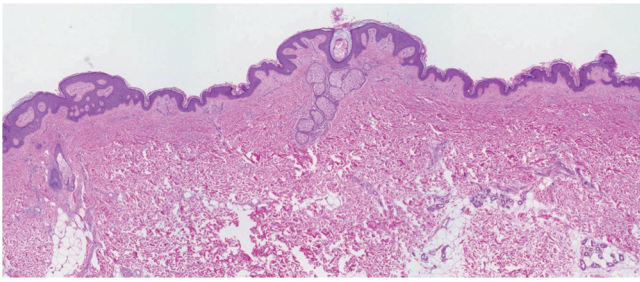


Fig. 3. Histopathology of the yellowish brown papules. Acanthosis, papillomatosis, and small numbers of abortive hair papillae-like proliferations and sebaceous glands, located at an abnormally high level in the dermis (haematoxylin and eosin (H&E), original magnification $\times 12.5$).

Sebaceous naevi and non-organoid epidermal naevi have several common features. Both are usually present at birth and often display as verrucous plaques. Despite such similarities, it is important to differentiate them considering the higher frequency of secondary tumours in sebaceous naevi than in non-organoid epidermal naevi (9). Histologically, sebaceous naevi are composed of many organoid epithelial structures, such as the epidermis, hair follicle, sebaceous and sweat glands. The foci of abortive hair papillae-like proliferation are common findings of sebaceous naevi (10). Because of the linear distribution and sparse density of organoid components in our case, it was difficult to differentiate it from non-organoid epidermal naevus. However, we have diagnosed it as sebaceous naevus based on the existence of abortive hair papillae-like proliferations and hyperplastic sebaceous glands. In addition, it should be borne in mind that in systematized sebaceous naevi involving the trunk or the limbs, the organoid components may be minimal or even absent (11). Thus, partial biopsy might not be sufficient to make a definite diagnosis of sebaceous naevi. The genetic basis of sebaceous naevi remains unknown because previous findings that *PTCH* gene mutations have been involved in its pathogenesis were not confirmed by others (12, 13). Likewise, the molecular pathogenesis of trichoblastoma remains elusive. In contrast to basal cell carcinoma, *PTCH* mutations could not be identified in sporadic trichoblastomas (14). Recently, *FGFR3* mutations were identified in a large proportion of non-organoid epidermal naevi, whereas sebaceous naevi of the head did not show these mutations (6). In addition, *PIK3CA* mutations were also found to be common in non-organoid epidermal naevi (7). There is a case report of non-organoid epidermal naevus with wild-type status in *FGFR3* and *PIK3CA* genes accompanied by basal cell carcinoma displaying a *PIK3CA* mutation (15). Molecular investigations of *FGFR3* and *PIK3CA* mutations in our case showed wild-type status in both samples. Since only a proportion of non-organoid epidermal naevi showed *FGFR3*

or *PIK3CA* mutations, the wild-type status in our case does not necessarily exclude the diagnosis of this naevus type. However, these molecular genetic investigations might be helpful in the differential diagnosis of non-organoid epidermal naevi and could explain the diversity of clinicopathological features between sebaceous naevi and non-organoid epidermal naevi.

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