

# A Clinicopathologic Study on Nevus Sebaceus

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**Background :** Nevus sebaceus of Jadassohn is a complex anomaly involving the epidermis, dermis, apocrine glands and hair follicles, as well as the sebaceous glands, and a variety of benign and malignant tumors and neurologic abnormalities may be associated with it; however, only a few studies on it have been reported in the Korean literature.

**Objective :** The objectives of this study was to document clinical and histopathologic features of nevus sebaceus in Koreans and compare them to those in the previously reported studies.

**Method :** Clinical records and histopathology of 53 cases of nevus sebaceus diagnosed at Ewha Womans University Tongdaemun Hospital during a period of 18 years were reviewed and analyzed.

**Results :** The average incidence rate of nevus sebaceus among new patients was 0.03%. The male-to-female ratio was 1.04 and the average age at visit, 16.5 years. The lesions had been present since birth or had developed before age 10 in 85% of the cases. All lesions were situated on the head, and the most common site was the scalp. Linear lesions (20.8%) were mostly facial lesions. Histopathologically, the incidence of sebaceous and apocrine glandular hyperplasia was most notable in the 13-18 and over-18 age groups. The sebaceous glands showed small punched out defects or "holes" in 24.5%; ectopic apocrine glands were found in 24.5%. Mature hair follicles were absent or greatly reduced in number in 75.5%. Acanthosis nigricans-like pattern of acanthosis and mild papillomatosis were the dominant changes in the epidermis. Hyperplasias and neoplasms were associated in 15.1%, which included 5 cases of primitive follicular induction and 1 trichoblastoma.

**Conclusion :** In this series, no examples of malignant neoplasms were identified; however, an early total excision before age 13 is recommended since a variable "deficit malformation" of the follicles with hyperplasia of the epidermis and sebaceous glands becomes more prominent after that age. (Ann Dermatol 13(1) 32~38, 2001).

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**Key Words :** Nevus sebaceus of Jadassohn, Clinical and histopathological study

Surprisingly few clinicopathologic studies have been done in Korea concerning the nevus sebaceus of Jadassohn or "organoid nevus", as Mehregan and Pinkus put it<sup>1</sup>. Considering that nevus sebaceus is not such a rarity among out-patients and that it has a characteristic life history with

possible secondary development of various tumors, we thought it relevant to document the features of the entity and compare them to those in previous reports.

## MATERIALS AND METHODS

This study is based on a review of clinical information and histological findings in 53 cases of organoid nevi that were biopsied and diagnosed in the Department of Dermatology at Ewha Womans University Tongdaemun Hospital between 1982 and 1999.

### Clinical data

The age at diagnosis and sex of each patient, the

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duration, precise anatomic location, gross appearance of the lesion, symptom and clinical diagnoses were documented.

#### Histopathological data

We divided our material into four age groups, according to when the biopsy specimens were removed: birth to 6 years (10 cases), 7-12 years (7 cases), 13-18 years (16 cases), and over 18 years (20 cases) as done by Mehregan and Pinkus<sup>1</sup>. The histologic specimens were fixed and stained in routine fashion and analyzed for the state of development of sebaceous glands, ectopic apocrine glands, hair follicles and epidermis, and the degree of dermal infiltrate. In sebaceous glands, increase or decrease in number and size of the glands, and abnormalities in the arrangement and maturation of the glands, including the presence of localized defects or "holes" were recorded. Hair follicles were classified as mature or immature by observing the general state of maturation of the whole specimen. As for the epidermis, acanthosis was recorded as "marked" when there were around 20 prickle cell layers, "mild" when there was no acanthosis or mild acanthosis nigricans-like changes only, and "moderate" when the degree of acanthosis was in-between. Hyperkeratosis was determined to be "mild" when the normal basket-weave pattern of orthokeratosis or dense but thin stratum corneum was seen, and when the keratin layer was thickened out of proportion compared to the granular layer, "marked." With hypergranulosis, stratum granulosum consisting of 4 layers or less was recorded as "mild", and more than 4, as "marked." The presence of secondary tumors or anomalies was noted.

## RESULTS

#### Clinical details

From 1982 through 1999, the total number of patients who visited our institute was 1,039,331, including 243,386 new patients, or approximately 14,000 new patients per year. During this period, the number of patients with nevus sebaceus was 53 (27 males, 26 females), with male-to-female ratio of 1.04. The average incidence rate was 0.03% among the new patients, and the rate showed an increasing trend. The majority of patients were adolescents or young adults. Briefly, 10 cases (18.9%)

were included in the first age group, 7 cases (13.2%) in the second one, 16 cases (30.2%) in the third one, and 20 cases (37.7%) in the fourth one. The average age of the patients at initial visit was 16.5 years. Thirty-four patients (64.2%) said that their lesions had been present since birth; in eleven patients (20.7%), the lesions developed before 10 years of age. Only 8 patients (15.1%) had first noticed their lesions after 10 years of age. All lesions were situated on the head. The most common site was the scalp (45.3%), followed by the cheek (18.9%), forehead and temple (9.4% each). In most patients the nevi occurred as solitary circumscribed round or oval patches, grouped papules or plaques with warty or mammilated surface. The color ranged from yellowish to orange, erythematous or brownish. Lesions of the scalp were almost invariably hairless. Eleven (20.8%) lesions were linear. Of them, only 1 occurred on the scalp; the others were all facial lesions, and all of the chin lesions were linear. Many of the lesions became more prominent and troublesome in adolescence and young adult life. In two patients the lesions were pruritic; others were all symptomless. No cerebral or other systemic malformations were associated in any of our patients. The most common clinical diagnosis was nevus sebaceus (42 cases; 79.2%), followed by epidermal nevus (5 cases; 9.4%), and 1 case each of xanthoma, nevus lipomatosus superficialis, compound nevus, congenital ectodermal defect, lipoma and rhinophyma.

#### Histopathological findings

The abnormalities affecting the epidermis or the appendages are listed in Table 1. The sebaceous glands were not present in 3 cases, which occurred in children with ages of 14 months, 5 and 6 years. As the age of the lesion increased, the number of small immature glands decreased and more large, mature sebaceous glands developed. The incidence of hyperplasia was most notable in the 13-18 and over-18 age groups, reflecting the response of the glands to the hormonal stimuli of puberty. The most common change was a grouping of hyperplastic glands in an abnormally high position in the dermis where they were often apparently unconnected with normal follicular canals. In 13 cases (24.5%), sebaceous glands opened directly into the epidermis. In 13 nevi (24.5%), the sebaceous glands showed a number of small punched

out defects or "holes", usually situated at the periphery of a lobule (Fig. 1). Ectopic apocrine glands were found in 13 (24.5%) cases. Only two patients before the age of 13 had them, and marked proliferation was seen only among the patients over the age of 13. Eccrine-derived abnormalities were found in 4 cases: the occurrence of areas resembling syringoma in 2 cases and those resembling a component of papillary eccrine adenoma in another two. In 40 (75.5%) nevi, mature hair follicles were absent or greatly reduced in number. In

the earliest stage, numerous small and incompletely formed hair follicles and sebaceous glands were seen. In the older lesions, many normal-appearing hair follicles with well-developed hair shafts were present. However, connected to the lower border of the epidermis or pilosebaceous structures, there were buds of undifferentiated basaloid cells surrounded by fibrous connective tissue stroma. The infundibula were often widened and plugged by compact orthokeratotic cells. Table 2 shows the state of epidermis and the degree of dermal infiltrate

**Table 1.** State of development of sebaceous glands, apocrine glands and hair follicles according to aging in 53 cases of nevus sebaceus

Age range (years)		0-6	7-12	13-18	over 18	Total (%)
No. of cases		10	7	16	20	53 (100.0)
Sebaceous glands	Not present	3	0	0	0	3 (5.7)
	Slight proliferation	6	6	10	7	29 (54.7)
	Marked proliferation	1	1	6	13	21 (39.6)
Apocrine glands	Not present	8	7	11	14	40 (75.5)
	Slight proliferation	2	0	2	5	9 (17.0)
	Marked proliferation	0	0	3	1	4 (7.5)
Hair follicles	Immature	10	4	11	15	40 (75.5)
	Mature	0	3	5	5	13 (24.5)

**Table 2.** State of epidermis and frequency of dermal infiltrate according to aging in 53 cases of nevus sebaceus

Age range (years)		0-6	7-12	13-18	over 18	Total (%)
No. of cases		10	7	16	20	53 (100.0)
Acanthosis	Negative or mild	10	3	10	12	35 (66.0)
	Moderate	0	4	4	4	12 (22.6)
	Marked	0	0	2	4	6 (11.3)
Papillomatosis	Negative or mild	10	2	6	14	32 (60.4)
	Moderate	0	4	6	4	14 (26.4)
	Marked	0	1	4	2	7 (13.2)
Hyperkeratosis	Mild	9	3	9	14	35 (66.0)
	Marked	1	4	7	6	18 (34.0)
Hypergranulosis	Negative or mild	10	7	15	19	51 (96.2)
	Marked	0	0	1	1	2 (3.8)
	Mild	9	3	8	9	29 (54.7)
Dermal infiltrate	Moderate	1	4	8	7	20 (37.7)
	Marked	0	0	0	4	4 (7.5)

**Fig. 1.** Male, 13. Life-long nevus of scalp. A hole is seen in the sebaceous gland lobule (H & E,  $\times 100$ ).

**Fig. 3.** Male, 23. Scalp lesion. Sebaceous epithelioma is seen with a hole in one of the lobules (H & E,  $\times 100$ ).

**Fig. 2.** Female, 28. Eyebrow lesion. Primitive follicular induction is located right above a focus of ectopic apocrine glands (H & E,  $\times 100$ ).

**Fig. 4.** Female, 17. Scalp lesion. A large nodular trichoblastoma in a nevus sebaceus (H & E,  $\times 20$ ). Inset: Epithelial aggregations of basaloid cells with peripheral palisading and prominent fibrocytic stroma close to the epithelial aggregations (H & E,  $\times 200$ ).

**Table 3.** Hyperplasias and neoplasms associated with 53 cases of nevus sebaceus

Case	Age (year)	Sex	Location	Hyperplasias or tumors
1	7	M	scalp	primitive follicular induction
2	16	F	cheek	primitive follicular induction
3	20	F	scalp	primitive follicular induction
4	28	F	eyebrow	primitive follicular induction
5	51	F	scalp	primitive follicular induction
6	29	M	cheek	eccrine hidrocystoma
7	23	M	scalp	apocrine hidrocystoma
				sebaceous epithelioma
8	17	F	scalp	syringocystadenoma papilliferum
				trichoblastoma

in the 4 different age groups. Acanthosis, papillomatosis, hyperkeratosis, hypergranulosis and dermal infiltrate all gradually increase as the lesions age. With respect to the epidermis, an undulating acanthotic epidermis somewhat reminiscent of acanthosis nigricans was the dominant pattern in approximately 80% of the nevi, and most of them were counted as "mild" acanthosis. In 3 nevi (5.7%), the epidermis was thickened in a pattern similar to the acanthotic type of seborrheic keratosis. In 7 nevi (13.2%), the epidermal outline mimicked that of a simple epidermal nevus, which has a regular saw-tooth appearance due to regularly peaked papillae. A moderate to heavy inflammatory infiltrate, consisting mainly of lymphocytes, plasma cells, and some eosinophils, was present around the vessels of the superficial plexus and the adnexa in 24 cases (45.3%). The two pruritic lesions showed a moderate dermal infiltrate.

We found 8 hyperplasias and neoplasms (15.1%) associated with nevus sebaceus in 53 patients (Table 3). Primitive follicular induction was the most common association. This induction mainly occurred in the adult patients, as is the case with other tumors. In all 5 cases with primitive follicular induction, sebaceous glands and rudimentary follicular structures were seen in the underlying dermis. In one of them, the follicular induction was located right above a focus of the ectopic apocrine glands (Fig. 2). In two patients, more than one tumor developed simultaneously from the lesions of nevus sebaceus. The area of hyperplasias or neoplasms was small and focal in all 8 cases (Fig. 3) except for trichoblastoma. The trichoblastoma was large, symmetrical and well circumscribed (Fig. 4). It also showed several superficial BCC-like proliferations in the epidermis overlying it, marked ectopic apocrine gland proliferations underneath, and a focal area of syringoma-like change as well as syringocystadenoma papilliferum. Ectopic apocrine glands were associated in 66.7% of the cases complicated by hyperplasias or tumors. Moderate cellular infiltrates were observed in the dermis in most of the cases complicated by tumors.

## DISCUSSION

This analysis of 53 cases of nevus sebaceus confirms a number of well-known features and reveals others not so well recognized in the literature. Nevus se-

baceus is a relatively rare lesion at our institute: it has a lower incidence (0.03%) than that of basal cell carcinoma (0.048%). The fact that our annual incidence of 0.03% is much lower than the 0.12% reported by Kyungpook National University<sup>7</sup> seems to be due to a higher number of new patients at our institute.

With respect to the location of the lesions, our findings confirmed that the scalp is the most common site of nevus sebaceus but lesions occurring on the cheek were twice as common as ones on the forehead or retroauricle, which is in contrast to a previous report.<sup>3</sup> Scalp lesions (50.9%) were also much less common than the previously reported 83.3%<sup>2</sup>, 71.3%<sup>1</sup> and 64%.<sup>3</sup> About 15% of the lesions have been reported to be linear, and nearly all of the retroauricular lesions were of this shape.<sup>4</sup> Our results confirm this, 21% being linear. In addition, all of the chin lesions were linear.

We were able to confirm the striking increase in the sebaceous gland component in adolescents and young adults. The presence of punched-out defects or "holes" in the abnormal sebaceous glands has been reported only once previously<sup>4</sup>; in that article, the holes were reported in 26.4% (37/140), similar to the 24.5% in our series. These holes are probably lipid-containing vacuoles arising as a result of breakdown of individual cells. Possibly some of the holes connected with the secretory duct of the gland, but the peripheral position of the holes in the glands makes this an unlikely explanation in most cases.

Ectopic apocrine glands are commonly present in the organoid nevi in adult cases, the reported incidences ranging from 32% to 54%.<sup>1-4</sup> The incidence of 24.5% in this series is lower than the previously reported figures but still shows an increasing trend with aging. The fact that apocrine glands were present much more frequently (66.7%) in the cases complicated by tumors seems logical since secondary tumors usually develop from nevus sebaceus in the adulthood phase. However, the case complicated by the trichoblastoma was a 17-year-old girl who already showed marked proliferation of apocrine glands. Also, tumors developed in half of the patients with marked apocrine gland proliferation, and in one case of primitive follicular induction, the induction occurred right on top of the apocrine gland proliferation. Although our series is too small for any speculations, it would do no

harm to follow up regularly on any organoid nevi that show proliferation of apocrine glands.

All cases before age 7 years were practically normal regarding the state of the epidermis and dermal infiltrate. Acanthosis, papillomatosis and hyperkeratosis all gradually became marked after that age. Hypergranulosis was not associated as much with aging. The degree of epidermal hyperplasia was generally lower than that reported in a Japanese study.<sup>5</sup> Marked dermal infiltrate was seen only in the over-18 age group. In the series reported by Mehregan and Pinkus<sup>1</sup>, 28% showed a moderate to heavy inflammatory infiltrate, which is relatively lower than the 45% seen in this series.

Secondary development of various types of adnexal tumors within the organoid nevi is well known. The reported incidences range from 22%<sup>1</sup> to 50%.<sup>5</sup> The lower incidence (15.1%) in this series may be due in part to the relatively younger age of our patients. Inflammatory cellular infiltration caused by repeated mechanical or inflammatory stimuli according to aging may influence follicles, sebaceous glands and apocrine sweat glands in the dermis, and develop various undifferentiated-differentiated types of tumors of the skin appendages.<sup>5</sup> In addition, the occurrence of these tumors may be greatly associated with the congenital potency of this disease as a pilo-syringo-sebaceous nevus to develop tumorous proliferation of the organs of the pilosebaceous system. Tumors such as syringocystadenoma papilliferum, sebaceous epithelioma, trichilemmoma, proliferating trichilemmal cyst, tumor of the follicular infundibulum (TFI), nodular hidradenoma, syringoma, chondroid syringoma, keratoacanthoma, basal cell carcinoma (BCC), squamous cell carcinoma and apocrine carcinoma may occur.<sup>6</sup> The vast majority of neoplasms associated with nevus sebaceus do not conform precisely to neoplasms that arise independent of nevus sebaceus.<sup>7</sup> Nearly all of these neoplasms are benign biologically, but, exceedingly rarely, neoplasms that develop in nevus sebaceus metastasize. In addition, we also observed focal tumor-like changes of the pilosebaceous components in several patients.

Primitive follicular induction is defined as buds of germinative follicular cells with adjacent clusters of fibrocytes, which represented follicular papillae, emanating from the undersurface of the epidermis.<sup>7</sup> In a recent study of 155 cases<sup>7</sup>, the induction

was seen in 9%, comparable to our 9.4%. This induction should be differentiated from TFI, which is characterized by the horizontal platelike organization of the tumor and the dense elastic network beneath the tumor. Two cases of TFI associated with sebaceous nevi were first reported in 1995.<sup>8</sup> However, the only histopathologic illustration provided by the authors showed features of primitive follicular induction but not quite the horizontal platelike pattern required for the diagnosis of TFI. The case reported by Alessi et al.<sup>9</sup> as a benign basal cell neoplasm with follicular differentiation probably shares a common histogenesis with primitive follicular induction. Similar to our cases of follicular induction, the two previously reported TFI overlying nevus sebaceus both showed a proliferation of heterotopic apocrine glands in the reticular dermis and sebaceous glands and rudimentary follicular structures in the papillary dermis.

Apart from syringocystadenoma papilliferum, other sweat gland tumors are a rare association.<sup>4</sup> In this series, syringocystadenoma papilliferum was as rare as other sweat gland tumors. As reported previously, all these lesions in our patients were small and relatively unimportant complications.

With the exception of the series of Wilson Jones and Heyl<sup>4</sup>, who made a distinction between true BCCs and basaloid proliferations, most of the published articles about nevus sebaceus reported BCC as the most frequently described malignancy. In contrast, Ackerman and coworkers<sup>9,10</sup> considered trichoblastoma the most common neoplasm associated with organoid nevus. Differential diagnosis between BCC and trichoblastoma is challenging; however, in contrast to BCC, trichoblastoma is a well-circumscribed and symmetrical neoplasm in which features of follicular differentiation in the form of follicular bulbs and papillae are readily seen, and it characteristically exhibits a highly fibrocytic stroma.<sup>7</sup> Steffen and Ackerman<sup>10</sup> believed that neoplasms reported as BCC originated within organoid nevus were actually examples of trichoblastoma, which was considered by them as the benign counterpart of BCC. We agree with them. Our example of trichoblastoma is large in size but shows symmetry and good circumscription with dense fibrocytic stroma, which is typical of the tumor. The lower incidence of secondary tumors in this series seems attributable to the relatively young age of our patients; the majority of

our patients were under 30, and only 1 patient was over 50.

Our results that a variable "deficit malformation" of the follicles with hyperplasia of the epidermis and sebaceous glands becomes more prominent after age 12 years and that tumors such as trichoblastoma occur as early as 17 years of age indicate that an early total surgical excision of nevus sebaceus before age 12 is the treatment of choice. However, malignancies such as BCC seem to develop less commonly than previously thought in organoid nevus.

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