

CLINICAL AND HISTOPATHOLOGICAL STUDIES ON SPOTTED GROUPED PIGMENTED NEVI WITH SPECIAL REFERENCE TO ECCRINE-CENTERED NEVUS

Takafumi Morishima, Mikio Endo, Ichiro Imagawa and Sadao Morioka

From the Department of Dermatology, Nihon University School of Medicine, Tokyo, Japan

Abstract. Clinical and histopathological studies on 16 cases of spotted grouped pigmented nevus resulted in this disease being classified into at least three types. Characteristic findings of each type are described in this paper, in particular that nevus cell proliferation, a finding common to each type, is closely related pathogenetically to skin appendages, especially with eccrine sweat ducts. The eccrine-centered nevus characterized by Mishima corresponds to the third type, according to the present authors' classification. The similar characteristic histopathological finding was also observed in a specimen taken from a black papule in a case of giant pigmented nevus with disseminated pigment cell nevi. We would like to consider that the cells of eccrine-centered nevus are derived from nevoclasts present in the walls of sweat ducts.

Key words: Pigmented nevus, spotted grouped; Eccrine-centered nevus; Pigmented nevus, giant; Sweat duct; Skin abrasion

Spotted grouped pigmented nevus, a peculiar clinical type of pigmented nevus, was first studied by Mishima (6) histopathologically in 1970, and it has been established that the spotted pigmentation in this nevus is based on an eccrine-centered proliferation of the nevus cells. In 1971, Yoshinaga et al. (9) reported that the eccrine-centered nevus cell proliferation was observed in only half of all such nevus cases. This fact suggests a possibility that this affliction can be differentiated into several types and that the eccrine-centered nevus characterized by Mishima (7) may represent a distinct clinical picture. The purpose of our research was to resolve the above doubt by means of clinical and histopathological studies on 16 cases of this nevus.

Table I. Findings in 16 cases of spotted grouped pigmented nevi

Case	Age at 1st exam.	Age at onset	Sex	Site of Affection	Histological classification	Type
1	21	At birth	♂	R. buttock	Intradermal nevus	I
2	12	At birth	♀	R. buttock	Intradermal nevus	I
3	19	At birth	♂	R. loin	Intradermal nevus	I
4	31	At birth	♂	R. leg	Intradermal nevus	I
5	37	At birth	♀	R. thigh	Intradermal nevus	I
6	11	At birth	♀	R. thigh	Intradermal nevus	I
7	4	At birth	♂	R. chest	Compound nevus	II
8	6	At birth	♀	R. leg	Intradermal nevus	II
9	21	At birth	♂	R. chest	Intradermal nevus	II
10	6	At birth	♀	R. abdomen	Intradermal nevus	II
11	5	At birth	♀	L. thigh	Junction nevus	III
12	12	At birth	♀	L. thigh	Compound nevus	III
13	41	At birth	♂	R. chest	Intradermal nevus	III
14	33	At birth	♂	R. thigh	Intradermal nevus	III
15	37	At birth	♀	R. forearm	Intradermal nevus	III
16	14	At birth	♀	Abdomen	Intradermal nevus	III

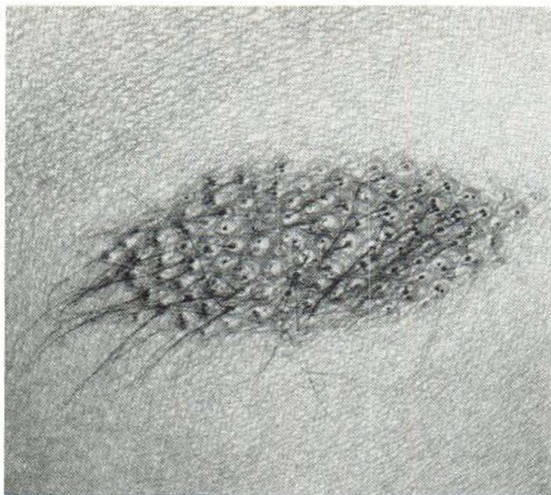


Fig. 1. Clinical finding of spotted grouped pigmented nevus type 1. On an elliptical brown pigment spot, many same-sized follicular blackish papules accompanying hairs are grouped at equal intervals, and intense staining is observed at the sites pierced by the hairs (Case 2).

MATERIALS AND METHODS

Though the clinical concept of spotted grouped pigmented nevus has not fully been clarified, the present authors have defined this nevus as being a specific type of pigment cell nevus present at birth and consisting of a grouping of blackish-brown to black papules or pigment freckles on or without a brownish spot. Sixteen cases of this disease known to us for 4 years were examined at the dermatology clinic of Surugadai Nihon University Hospital, and the following results were obtained (see Table 1) concerning sex, age at onset, age at first examination, histological classification, and clinical types mentioned below. The skin specimens taken from these cases were microtomed into serial vertical and horizontal sections, and stained with hematoxylin-eosin, Weigert, and Masson-Fontana stainings. A study was made of the relationship between the nevus cell proliferation and the skin appendages, especially the eccrine sweat ducts, in contrast with the clinical findings.

Skin abrasion technique was the treatment chosen. The diseased skin was abraded down to the upper layer of the reticular dermis, and the presence of pigment on the abraded surface was examined macroscopically.

RESULTS

Spotted grouped pigmented nevus can be classified into at least three types, according to the results obtained in this study. The clinical and histopathological features of each type of this nevus are as follows.

Type 1. Of the 16 cases, 6 belonged to this type.

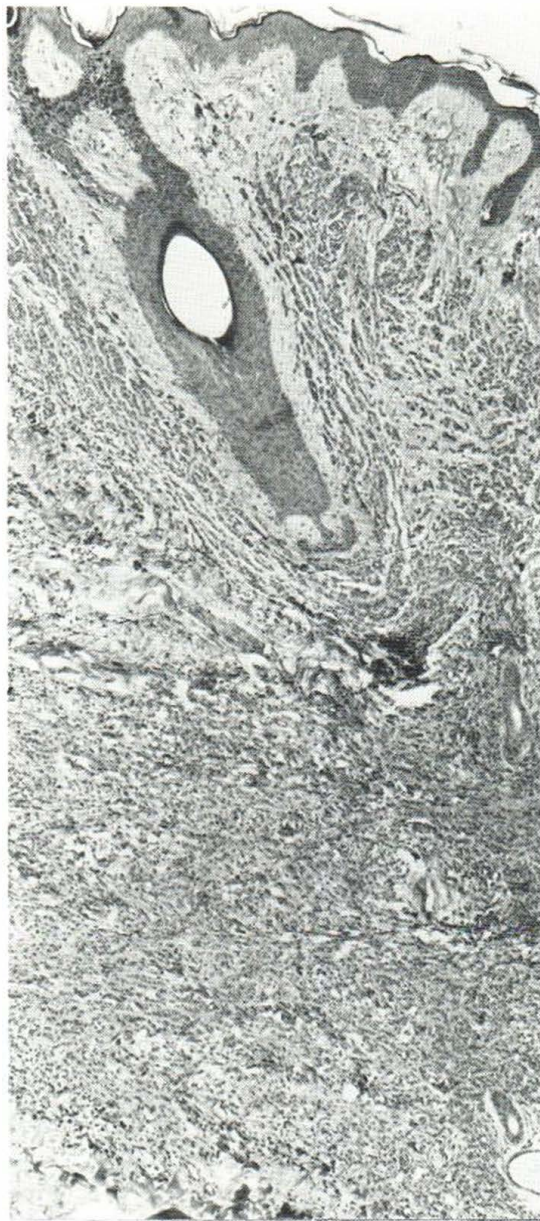


Fig. 2. Histopathological finding of spotted grouped pigmented nevus type 1. Follicle-centered nevus cell nests in the upper dermis and nevus cell nests in band-like arrangement from the middle to lower dermis are observed, and many eccrine sweat ducts are found among them (Case 3, hematoxylin-eosin, original magnification $\times 29$).

The age groups at first examination consisted of 3 patients in their teens, 1 in the twenties, and 2 in the thirties. The affected sites were the loin in 1 case, buttocks in 2 cases, thighs in 2 cases, and leg in 1 case. The sex ratio was 3:3.

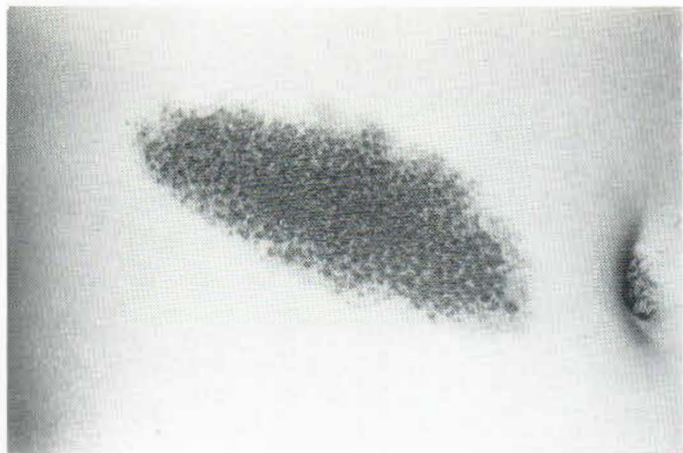


Fig. 3. Clinical finding of spotted grouped pigmented nevus type II. On an elliptical brown pigment spot, same-sized blackish pigment freckles not accompanying stiff hairs are grouped and coalesce to form a diffuse black pigment spot at the central portion (Case 10).

Clinical findings (Fig. 1). Numerous follicular blackish papules of roughly the same size, pierced by 1 or 2 hairs, are grouped on an oval, brown pigment spot at nearly equal intervals. Skin abrasion of the lesion reveals follicular pigmentation on the abraded surface. This finding suggests that the site of spotted pigmentation is follicle-centered.

Histopathological findings (Fig. 2). Histology revealed intradermal nevus in all cases. Many nevus cell nests were found around the hair follicles, from the upper to the lower reticular layer. In the connective tissue from the middle to the lower reticular layer, there were also observed nevus cell nests arranged parallel to the skin surface. In case 2, junction activity was observed in an infundibular portion of the follicle. Many eccrine sweat ducts were found among the nevus cell nests, and often

along the follicles. Abundant melanin granules were observed in the keratinocytes lying in the basal cell layer to the prickle cell layer of the infundibular portion of the follicle and adjacent epidermis, and in the nevus cells situated around the hair follicles in the upper reticular layer. From the above findings, it was considered that spotted pigmentation of this type derives from the nevus cell proliferation around the skin appendages, especially the hair follicles.

Type II. Of the 16 cases, 4 belonged to this type. The ages at first examination were: under 10 in 3 cases and the twenties in 1 case. The sites of affection were the chest in 2 cases, abdomen in 1 case, and leg in 1 case, and the sex ratio was 2:2.

Clinical findings (Fig. 3). On an oval brownish

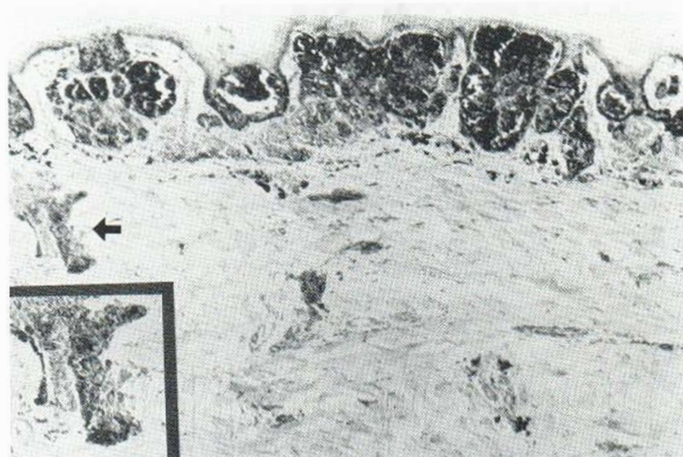


Fig. 4. Histopathological finding of spotted grouped pigmented nevus type II. Nevus cells are found in masses in the upper dermis and are localized around the eccrine sweat ducts thereunder. *Inset:* higher magnification of the part indicated by arrow (Case 7, Masson-Fontana stain, original magnification $\times 24$).

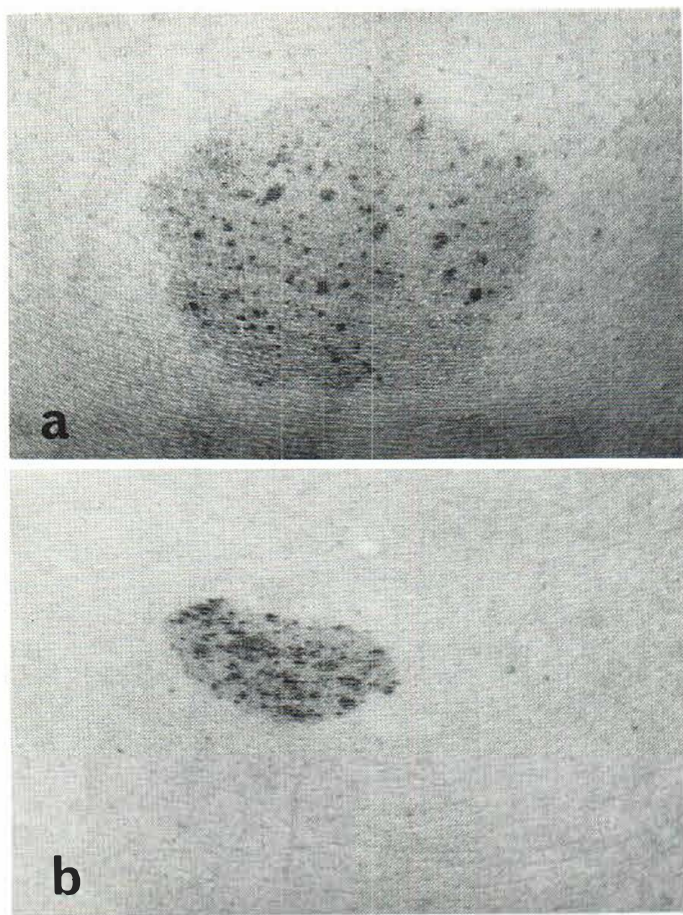


Fig. 5. Clinical finding of spotted grouped pigmented nevus type III. On chestnut-shaped (a), stomach-shaped (b) brown pigment spots, many various-sized dark brown to blackish brown pigment freckles are irregularly developed without stiff hairs (a, Case 16; b, Case 13).

pigment spot, without stiff hairs, many black pigment freckles of nearly the same size are grouped together, and in the central portion coalesce to form a diffuse black pigment spot. After skin abrasion, no pigment is observed on the abraded surface.

Histopathological findings (Fig. 4). Intradermal nevus was revealed in 3 cases, and compound nevus in 1 case. In the papillary layer, and also in the subpapillary to upper reticular layer, nevus cells rich in melanin were arranged in nests. Corresponding to the clinical findings, the nevus cell nests showed a tendency to localization in the peripheral portion and to coalesce towards the center. Though there are many cases in which the association of nevus cell proliferation with the skin appendages cannot be pointed out distinctly in the portions of such nevus cell nests facing the epidermis, the nevus cells in the upper to middle dermis are

arranged mostly around eccrine sweat ducts and in some places around follicles. This finding suggests the important role played by these skin appendages in the development of the nevus cells to the lower dermis. In the epidermis overlying the nevus cell nests, rete ridges are elongated and in some portions are absent, and abundant melanin granules are seen in the basal to prickle-cell layers. In case 7, junction activity was observed in the infundibular portion of the follicle and in the rete ridges, through which eccrine sweat ducts penetrate. The spotted pigmentation was assumed to be due to the nevus cell nests localized in the superficial dermis being closely related pathogenically with eccrine sweat ducts and in some cases with follicles.

Type III. Of the 16 cases, 6 belonged to this type. The ages of the patients at first examination were: under 10 years in 1 case, in the teens in 2 cases,

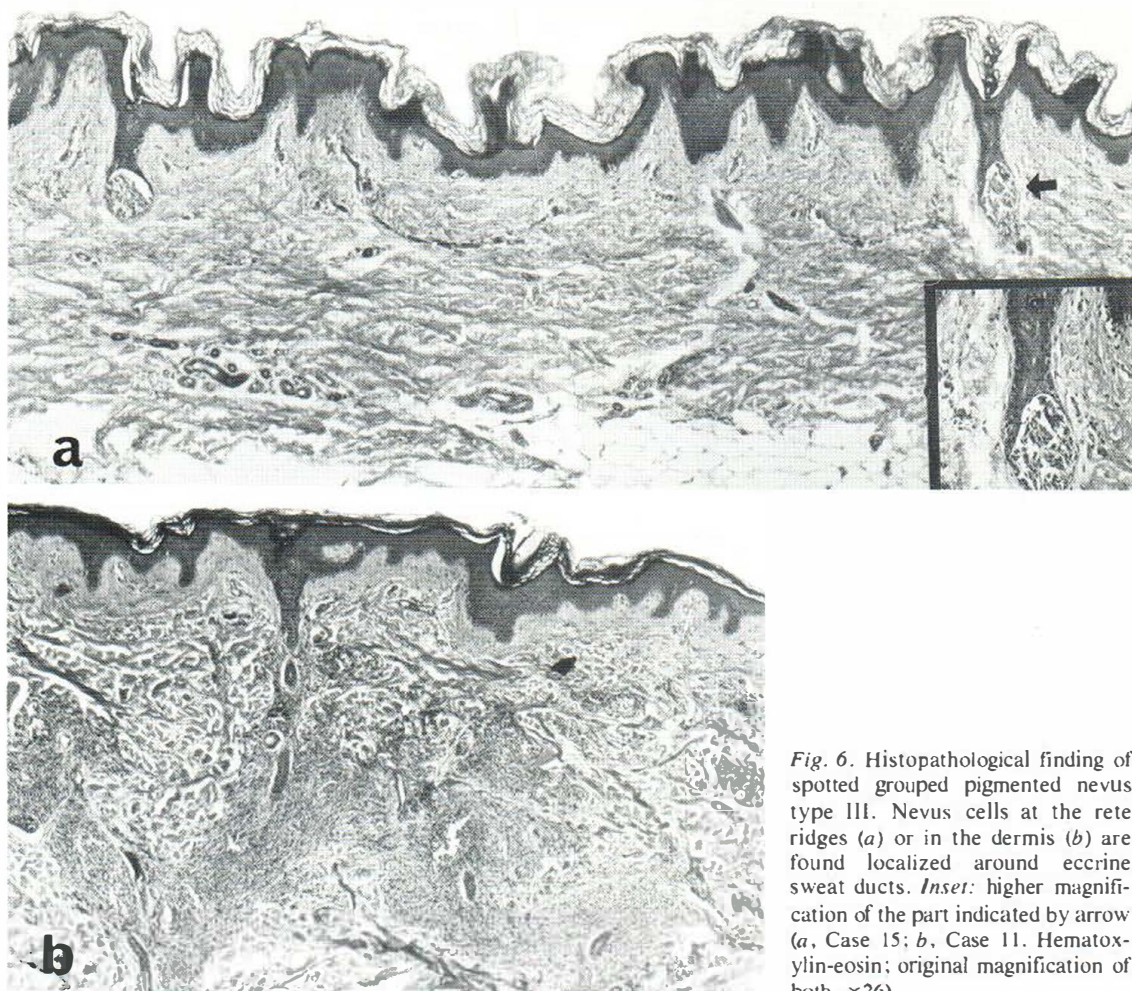


Fig. 6. Histopathological finding of spotted grouped pigmented nevus type III. Nevus cells at the rete ridges (a) or in the dermis (b) are found localized around eccrine sweat ducts. *Insert*: higher magnification of the part indicated by arrow (a, Case 15; b, Case 11. Hematoxylin-eosin; original magnification of both, $\times 26$).

in the thirties in 2 cases, and in the forties in 1 case. The affected sites were: the thighs in 3 cases, and the leg, chest, abdomen, in 1 case each.

Clinical findings (Fig. 5). The clinical picture differs from that of types I and II. That is to say, on irregular-shaped (such as ovoid, stomach-shaped, or chestnut-shaped) brown pigment spots there are many dark brown to blackish brown pigment freckles varying in size and irregularly developed, without stiff hairs. After the skin abrasion procedure, no pigment could be seen on the abraded surface.

Histopathological findings (Fig. 6). Junction nevus and compound nevus were observed in 1 case and intradermal nevus in 4 cases. The characteristic finding in this type is that the nevus cells situated

at the rete ridges or in the dermis are localized mostly around eccrine sweat ducts. In the cases of junction nevus and compound nevus, junction activity is present corresponding to the rete ridges through which eccrine sweat ducts run. In the sweat duct wall cells, however, no melanin is observed. In the cases of intradermal nevus as well as of compound nevus, nevus cells rich in melanin are often observed in cord-like arrangement or in masses localized around the eccrine sweat ducts lying in the upper to middle portions of the reticular layer. Around the eccrine sweat glands, however, this picture is not seen. In the overlying epidermis under which there are nevus cells, elongation of the rete ridges and abundant melanin granules are found, in contrast to the peripheral

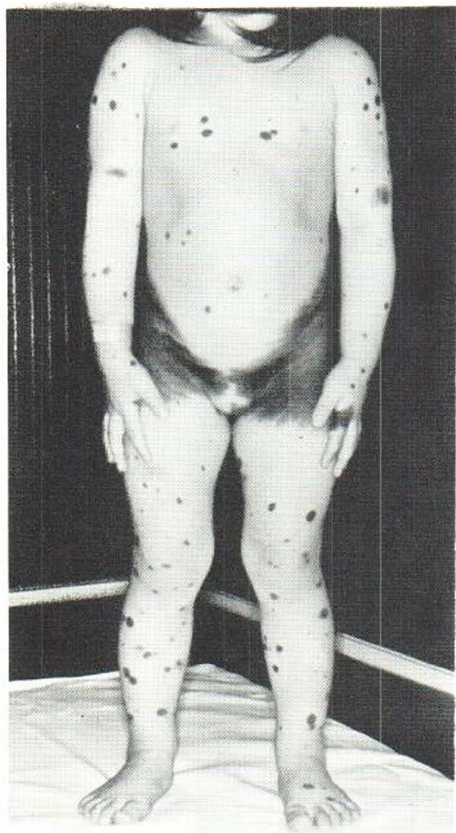


Fig. 7. Clinical finding of giant pigmented nevus combined with disseminated pigment cell nevi in a 3-year-old girl.

epidermis without nevus cells thereunder. The spotted pigmentation is assumed to be due to eccrine-centered nevus cell proliferation.

COMMENT

The first description of a case which corresponds to the spotted grouped pigmented nevus was by Scholtz (8) in 1932 who illustrated the clinical picture in Jadassohn's *Handbuch* with a diagnosis of "einseitiger aus Lentigines zusammengesetzter Nävus". In Japan, Matsumoto (5) first gave the name spotted grouped pigmented nevus to a peculiar case seen on the face. Kawamura (2) then described its clinical picture with the same diagnosis in the Japanese *Handbook of Dermatology*. Thereafter, this disease, spotted grouped pigmented nevus, seems to have been considered to be merely a special clinical type of pigmented

nevus, without having been precisely studied histopathologically.

On the other hand, it is a well-known fact that sweat duct wall cells lack melanin, in contrast to the keratinocytes surrounding them, as is seen in intra-epidermal sweat ducts. Little attention has been paid to the relationship between eccrine sweat ducts and melanin-producing cells. In certain sub-human primates (4), however, it has long been known that melanocytes and melanin can be found on the eccrine sweat ducts, and Lund & Kraus (3) illustrated the arrangement of nevus cells around sweat ducts as a finding seen during the development process of the pigmented nevus.

In 1970, Mishima (6) studied 3 cases of this nevus histopathologically and found that the spotted pigmentation to be observed clinically is a change based on an eccrine sweat duct-centered proliferation of nevus cells, and in 1973 he advo-



Fig. 8. Histopathological finding of the blackish pigment freckle on right forearm of the same girl as in Fig. 7. Nevus cell proliferation is localized around eccrine sweat ducts (hematoxylin-eosin, original magnification $\times 28$).

cated the term 'eccrine-centered nevus' (7). In 1971, Yoshinaga et al. (7) studied 18 cases of this nevus histopathologically, and reported that the nevus cell proliferation was eccrine-centered in 10 cases, though no association was noted between the nevus cells and the skin appendages in the remaining cases. This description by Yoshinaga et al. suggests that the histopathological change in this nevus is not necessarily compatible with the eccrine-centered nevus. The relationship between the clinical and the histopathological picture of this nevus remained unsolved. From the data obtained in our study, it can be concluded that this is due to the fact that there are at least three types of spotted grouped pigmented nevus and that these types have sometimes been confused.

The common findings in these three types of this nevus are as follows: 1) clinically, black papules or small pigment freckles are observed on the basis of a brown pigment spot, and 2) pathogenically, nevus cell proliferation is closely related to eccrine sweat ducts, in view of the results obtained by Imagawa (1) in his study on the mechanism of recurrence after dermabrasion in types I and II of this nevus.

The eccrine-centered nevus characterized by Mishima (7) corresponds to type III according to the present authors' classification. However, the clinical picture of Mishima's case is a medium-sized plaque composed of a grouping of brown to blackish brown papules, 1-3 mm in diameter, and therefore differs from that of type III in respect to the presence of a brown pigment spot, to whether the grouped rash is of papules or pigment freckles, and to the mode of distribution. Consequently, it follows that there are at least two clinical types of eccrine-centered nevus. In our series, however, no cases are included similar to Mishima's case.

Histopathological studies were made to decide whether or not there is an eccrine-centered nevus in various pigmented nevi other than spotted grouped pigmented nevus, with the following finding. The histological feature as mentioned above was observed in a specimen taken from a blackish papule on the forearm of a 3-year-old girl who was diagnosed to have giant pigmented nevus with disseminated pigment cell nevi (Figs. 7 and 8). This fact suggests that a nevus which displays, histopathologically, the picture of an eccrine-centered nevus is not always found clinically to be a spotted grouped pigmented nevus. Mishima's case might be

a nevus composed of a grouping of such blackish papules.

What is the origin of eccrine-centered nevus cells? Concerning this problem, Mishima (7) states that it cannot be decided whether these nevus cells are derived from nevoclasts in eccrine sweat ducts, or result from the proliferation of specific syringotropic nevus cells. He emphasizes the greater likelihood of the former hypothesis, on the basis of other evidence. Imagawa (1) in his study on the mechanism of recurrence after skin abrasion of this nevus, type I and type II, judged the process to be the junctional activity of melanin-producing cells seen in regenerating eccrine sweat duct walls. This finding supports the hypothesis that the eccrine-centered nevus cells originate from nevoclasts of the sweat duct walls.

REFERENCES

1. Imagawa, I.: Mechanism of recurrence of pigmented nevi following dermabrasion. *Jap J Dermatol* 84: 273, 1974.
2. Kawamura, T.: Nevi and Phacomatosis. In *Japanese Handbook of Dermatology*, vol. 7, no. 2, p. 62. Kanehara Shuppan Co., Tokyo, 1957.
3. Lund, H. Z. & Kraus, J. M.: Melanotic tumor of the skin, p. F3-70. Armed Forces Institute of Pathology, Washington, 1962.
4. Machida, H. & Perkin, E. M.: The distribution of melanotic melanocytes in the skin of subhuman primates. In *Advances in Biology of the Skin* (ed. W. Montagna & F. Hu), p. 41. Pergamon Press, Oxford and Braunschweig, 1967.
5. Matsumoto, S.: *Dermatology*, p. 2. Nankodo, Kyoto, 1953.
6. Mishima, Y.: Eccrine centric nevus. *Jap J Dermatol* 80: 859, 1970.
7. — Eccrine-centered nevus. *Arch Dermatol* 107: 59, 1973.
8. Scholtz, W.: Naevi. In *Handbuch d. Haut- u. Geschlechtskrankheiten* (J. Jadassohn, ed.), vol. 12, no. 2, p. 580. Springer Verlag, Berlin, 1932.
9. Yoshinaga, K., Arakawa, H. & Morioka, S.: Eccrine centric nevus seen in spotted grouped nevi. *Rhinsho Derma* (Tokyo) 13: 630, 1971.

Received June 27, 1975

T. Morishima, M.D.
Department of Dermatology
Surugadai Nihon University Hospital
1-8-13, Surugadai, Kanda
Chiyoda-ku
Tokyo
Japan