The American Journal of Dermatopathology *24(4): 294–304, 2002*

Sebaceoma and Related Neoplasms With Sebaceous Differentiation

A Clinicopathologic Study of 30 Cases

Noriyuki Misago, M.D., Ichiro Mihara, M.D., Shin-ichi Ansai, M.D., and Yutaka Narisawa, M.D.

The classification of benign sebaceous neoplasms has been challenged both by the assertion that sebaceous adenomas are really carcinomas and by difficulties in drawing the boundaries between sebaceomas and other lesions. We performed a clinicopathologic study of 30 cases of basaloid neoplasms with sebaceous differentiation, excluding cases of definite sebaceous carcinoma with severe nuclear atypia invading deep within the subcutaneous tissue and those of ocular sebaceous carcinoma. We tried to classify sebaceous neoplasms in six categories with defined histopathologic criteria. All the neoplasms were characterized by aggregations of basaloid cells admixed with sebocytes and sebaceous duct-like structures located in the dermis with or without connection to the epidermis. The categories were 1) sebaceoma (14 cases); 2) trichoblastoma with sebaceous differentiation (3 cases); 3) apocrine poroma with sebaceous differentiation (2 cases); 4) low-grade sebaceous carcinoma (6 cases); 5) sebaceous carcinoma (4 cases); and 6) basal cell carcinoma with sebaceous differentiation (1 case). The sebaceoma was further subclassified as classic type (12 cases) or verruca/seborrheic keratosis type (2 cases). Although most sebaceomas can be distinguished from other lesions, there are problematic cases. We discuss the histopathologic diagnostic problems associated with sebaceoma and also argue in favor of the concept of sebaceous adenoma.

Key Words: Sebaceoma—Trichoblastoma with sebaceous differentiation—Apocrine poroma with sebaceous differentiation—Sebaceous carcinoma—Basal cell carcinoma with sebaceous differentiation—Sebaceous adenoma—Sebaceous epithelioma.

From the Division of Dermatology, Department of Internal Medicine (N.M., Y.N.), Saga Medical School, Saga; Mihara Clinic of Dermatology (I.M.), Tsuruoka; and the Department of Dermatology (S.A.), Akita University School of Medicine, Akita, Japan.

Address correspondence and reprint requests to Noriyuki Misago, M.D., Division of Dermatology, Department of Internal Medicine, Saga Medical School, Nabeshima 5-1-1, Saga 849-8501, Japan. E-mail: misago@post.saga-med.ac.jp

In the past, many authors have suggested that the distinction and classification of cutaneous neoplasms with sebaceous differentiation are often vague and difficult and that such classification and histopathologic diagnosis may occasionally be arbitrary (1–3). In addition, the criteria that have been used in such neoplasms with sebaceous differentiation were often poorly defined, and the definitions of the terms used for these neoplasms have varied among authors; a typical example of a confused term is *sebaceous epithelioma*. In 1984, Troy and Ackerman (4) created a stir by proposing the term *sebaceoma* for what they considered a distinct benign neoplasm with sebaceous differentiation. Despite their proposal, some confusion has remained concerning sebaceoma and its related neoplasms with sebaceous differentiation (5–7).

We appreciate the fact that Troy and Ackerman's proposal (4) provided a clear understanding of the classification of neoplasms with sebaceous differentiation and hoped to resolve some of the continuing confusion surrounding sebaceoma. We herein report a clinicopathologic study of 30 cases of basaloid neoplasms with sebaceous differentiation, in which we tried to classify these neoplasms in six categories with defined histopathologic criteria to challenge the continuing confusion.

MATERIALS AND METHODS

We collected 30 cases of basaloid neoplasms with sebaceous differentiation from 29 patients in a multicentric study. We excluded cases of definite sebaceous carcinoma invading deep within the subcutaneous tissue with severe nuclear atypia and those of ocular sebaceous carcinoma. All the basaloid neoplasms were characterized by aggregations of basaloid cells admixed with sebocytes and sebaceous duct-like structures located in the dermis with or without connection to the epidermis. We classified them in six categories: 1) sebaceoma; 2) trichoblas-

 DOI: 10.1097/01.DAD.0000021443.86177.A6

toma with sebaceous differentiation; 3) apocrine poroma with sebaceous differentiation; 4) low-grade sebaceous carcinoma; 5) sebaceous carcinoma; and 6) basal cell carcinoma with sebaceous differentiation. Sebaceoma was further subclassified as the classic type or the verruca/seborrheic keratosis type. The histopathologic criteria of each of the categories were as follows.

Sebaceoma (Classic Type)

The criteria for sebaceoma were generally defined according to the original description by Troy and Ackerman (4). The architectural pattern is characterized by sharp circumscription, smooth borders, and symmetry. The lesions have aggregations of basaloid undifferentiated sebocytes admixed with single or small clusters of mature vacuolated sebocytes, often in association with sebaceous duct-like structures and dense eosinophilic sclerosis. They are cytologically composed of basaloid cells with small, monomorphous, oval nuclei without prominent nucleoli, they are not pleomorphic, and they contain only a few mitotic figures. The ratio of basaloid undifferentiated sebocytes to mature vacuolated sebocytes varies from case to case as well as from field to field in the same case. The ratio of the two cell types has no bearing on the criteria. Although the aggregations with vacuolated sebocytes usually do not form the gland-like lobular structures vaguely resembling normal sebaceous lobules, the formation of these lobular structures can occur in some foci of the lesions. These lobular structures are not relatively normal and uniform in size and shape, however, unlike those of senile sebaceous hyperplasia. Necrosis en masse as the result of holocrine secretion is often seen, although necrosis en masse of neoplastic cells is rare. There is no palisaded arrangement of nuclei at the peripheries of the aggregations.

Sebaceoma (Verruca/Seborrheic Keratosis Type)

Basically, the architectural pattern and cytology are similar to those of the classic type except for the upper part of the lesion, which is always connected to hyperplastic infundibula. The upper part of the lesion is characterized by proliferation of infundibular keratinocytes (basaloid cells and/or squamous cells) associated with hypergranulosis and tunnels of cornified cells mimicking verruca or seborrheic keratosis. The basaloid cells are similar to those of seborrheic keratosis.

Trichoblastoma With Sebaceous Differentiation

The basic histopathologic features are those of the large nodular type of trichoblastoma (i.e., large nodular aggregations made up of follicular germinative cells associated with highly fibrocytic stroma, benign by silhouette, and with palisading borders in the aggregations). Limited differentiation toward follicular germs and rudimentary papillae is seen. In addition to those features of large nodular type trichoblastoma, sebocytes and sebaceous duct-like structures are observed within the basaloid aggregations.

Apocrine Poroma With Sebaceous Differentiation

This neoplasm is fundamentally a poroma. The basaloid aggregations are composed of poroid cells and cuticular cells associated with tubular structures. In addition, sebocytes and sebaceous duct-like structures are observed within the basaloid aggregations.

Low-Grade Sebaceous Carcinoma

Although the architectural pattern is characterized by relatively sharp circumscription, somewhat symmetric and cytologically neoplastic cells show large, crowded, heterochromic or vesicular nuclei with prominent nucleoli, and moderate pleomorphism and occasional mitoses (frequent mitoses in some parts) are seen. Confluence of aggregations of neoplastic cells of various shapes and sizes resulting in an irregularly anastomosing pattern as well as ulceration favors the diagnosis of a malignant neoplasm. The findings of basaloid cells arranged in a palisade at the periphery of aggregations and separated from adjacent stroma by clefts are not seen.

Sebaceous Carcinoma

The diagnostic criteria for sebaceous carcinomas are a silhouette of malignancy (asymmetry, poor circumscription, and marked variance in size and shape of the neoplastic aggregations), severe nuclear atypia with frequent mitoses, or both seen in the basaloid neoplasms with sebaceous differentiation. The findings of basaloid cells arranged in a palisade at the periphery of aggregations and separated from adjacent stroma by clefts are not seen.

Basal Cell Carcinoma With Sebaceous Differentiation

Both the architectural pattern and cytology of the neoplastic cells are those of basal cell carcinoma. Within the aggregations of basal cell carcinoma, sebocytes and sebaceous duct-like structures are seen.

RESULTS

According to the previously-defined histopathologic criteria, 30 cases of basaloid neoplasms were diagnosed and classified in six categories, resulting in 14 cases of sebaceoma (12 cases of classic type and 2 cases of verruca/seborrheic keratosis type), 3 cases of trichoblas-

toma with sebaceous differentiation, 2 cases of apocrine poroma with sebaceous differentiation, 6 cases of low-grade sebaceous carcinoma, 4 cases of sebaceous carcinoma, and 1 case of basal cell carcinoma with sebaceous differentiation. The clinical data of these 30 cases are summarized in Table 1. Most of the lesions occurred on the face and head in elderly people more than 50 years old, and there were no patent clinical differences between the six categories except for larger size in the sebaceous carcinoma category and more frequent ulceration in the low-grade sebaceous carcinoma and sebaceous carcinoma categories than in the other categories. Neither recurrence nor metastasis of the neoplasm was observed during the follow-up period in any of the 30 cases.

Sebaceoma (Classic Type)

Three cases occurred within a lesion of nevus sebaceous, and the other nine cases had no associated disease. At scanning magnification, all the neoplasms showed sharply bordered basaloid aggregations in the dermis mimicking trichoblastoma or cylindroma/spiradenoma. The dermal basaloid aggregations in eight cases showed no connection to the epidermis and those in the other four cases were connected to the epidermis. Sclerotic stroma was often associated, and the basaloid aggregation in three cases showed a reticular, cribriform, or even labyrinth-like pattern (Fig. 1). Another case showed a rippled pattern, and this case has been reported elsewhere (8). The basaloid aggregations in all the cases contained single or small clusters of sebocytes and sebaceous duct-like structures to various degrees. One case associated the aggregations of sebaceoma with large clusters of sebocytes vaguely resembling normal sebaceous lobules, demonstrating the features of so-called sebaceous adenoma (Fig. 2). As a rule, the constituent cells had small, monomorphous, oval, basophilic nuclei without prominent nucleoli. In some cases (especially the cases associated with nevus sebaceus), however, the cells were relatively large and showed vesicular nuclei with distinct nucleoli and occasionally some pleomorphism (Fig. 3). One case associated with nevus sebaceus had a focus of trichoblastoma within the lesion of sebaceoma, and this case has been reported elsewhere (9).

Sebaceoma (Verruca/Seborrheic Keratosis Type)

Both of the two cases showed the connection to the hyperplastic infundibula and had typical histopathologic features of classic type sebaceoma in the middle to lower part of the lesion. One case was an exoendophytic lesion and showed hypergranulosis, vacuolated cells, and large pale cells within the hyperplastic infundibula associated with capillaries in thin dermal papillae, demonstrating verruca-like features (Fig. 4). Another case was mostly

TABLE 1. *Summary of clinicopathologic findings in 30 cases*

Case	Diagnosis	Age (years)	Sex	Location	Size (cm)	Ulceration	Association
1	Sebaceoma (classic)	85	F	Scalp	2.5 + 2.0	–	
2	Sebaceoma (classic)	73	F	Face	0.8 × 0.8	–	
3	Sebaceoma (classic)	78	M	Nose	1.0 × 0.8	–	
4	Sebaceoma (classic)	71	F	Eyelid	2.5 × 2.0	–	
5	Sebaceoma (classic)	52	M	Eyelid	0.8 × 0.7	–	
6	Sebaceoma (classic)	62	M	Head	6.0 × 4.0	–	
7	Sebaceoma (classic)	58	M	Face	1.0 × 1.0	–	
8	Sebaceoma (classic)	48	F	Face	0.4 × 0.3	–	
9	Sebaceoma (classic) (8)	71	F	Head	1.2 × 1.0	+	
10	Sebaceoma (classic)	70	F	Head	1.8 × 0.8	–	Nevus sebaceus
11	Sebaceoma (classic)	48	F	Head	1.8 × 0.9	–	Nevus sebaceus
12	Sebaceoma (classic) (9)	73	F	Head	0.8 × 0.6	–	Nevus sebaceus
13	Sebaceoma (verruca/seborrheic keratosis)	87	F	Face	0.5 × 0.4	–	
14	Sebaceoma (verruca/seborrheic keratosis)	65	F	Face	1.1 × 1.0	–	
15	Trichoblastoma with sebaceous differentiation	85	F	Face	1.4 × 1.2	–	
16	Trichoblastoma with sebaceous differentiation	57	F	Face	1.6 × 1.4	–	
17	Trichoblastoma with sebaceous differentiation	51	M	Face	2.0 × 1.0	–	
18	Apocrine poroma with sebaceous differentiation	22	F	Face	0.2 × 0.2	–	
19	Apocrine poroma with sebaceous differentiation	74	F	Face	0.6 × 0.5	–	
20	Low-grade sebaceous carcinoma	74	F	Neck	Cutaneous horn	+	
21	Low-grade sebaceous carcinoma	74	F	Face	0.8 × 0.5	–	
22	Low-grade sebaceous carcinoma	66	F	Face	0.5 × 0.5	+	
23	Low-grade sebaceous carcinoma	58	M	Face	0.5 × 0.5	–	
24	Low-grade sebaceous carcinoma (10)	59	F	Face	1.5 × 1.2	+	Muir-Torre syndrome
25	Low-grade sebaceous carcinoma (11)	54	M	Nose	2.5 × 2.0	+	
26	Sebaceous carcinoma	85	F	Face	2.2 × 1.3	+	
27	Sebaceous carcinoma	61	F	Face	2.2 × 2.0	+	
28	Sebaceous carcinoma	65	F	Head	2.3 × 2.2	+	Nevus sebaceus
29	Sebaceous carcinoma (9)	73	F	Head	2.2 × 2.5	+	Nevus sebaceus
30	Basal cell carcinoma with sebaceous differentiation	77	M	Head	2.0 × 1.5	–	

* Case 12 and case 29 are from the same patient.
F, female; M, male.

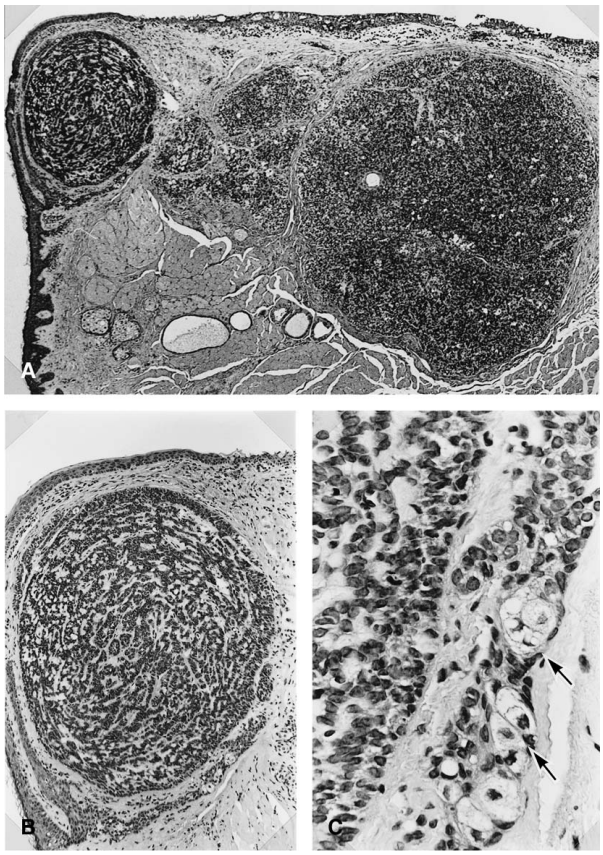

FIG. 1. Histopathologic features of sebaceoma (classic type) (Case 5). **(A)** Two large basaloid aggregations and a few small basaloid aggregations within the tarsal plate in the upper eyelid. **(B)** The basaloid aggregation demonstrates a labyrinth-like pattern. **(C)** The constituent cells are small, monomorphous, oval, basophilic nuclei without prominent nucleoli associated with single or small clusters of sebocytes (*arrows*).

endophytic, and basaloid cells and squamous cells associated with tunnels of cornified cells were seen within the hyperplastic infundibula, demonstrating seborrheic keratosis-like features (Fig. 5).

Trichoblastoma With Sebaceous Differentiation

All three cases showed histopathologic features of large nodular type trichoblastoma. Although fibrocytic stroma was not so prominent, follicular germs and rudimentary follicular papillae, a partial palisading border in the neoplastic aggregations, an appreciable component of fibrotic stroma, and clefts within stroma itself were seen in these three cases. Characteristically, sebocytes in clusters of various sizes and sebaceous duct-like structures were observed within the basaloid aggregations (Fig. 6).

Apocrine Poroma With Sebaceous Differentiation

Both cases showed a connection to the epidermis, and the basaloid aggregations were mainly composed of poroid cells with some cuticular cells in association with tubular structures, some of which showed hints of decapitation secretion. Additionally, sebocytes in small clusters and sebaceous duct-like structures were seen within the aggregations (Fig. 7).

Low-Grade Sebaceous Carcinoma

Four cases showed the connection to the ulcerated epidermis and were composed of one or a few large aggregations with relatively sharp circumscription and confluence of aggregations of neoplastic cells in various shapes and sizes, resulting in the characteristic irregularly anastomosing pattern. One of the four cases manifested a cutaneous horn-like shape (Fig. 8). The other two cases had no connection to the epidermis and were composed of some intradermal basaloid aggregations of various shapes and sizes with relatively sharp circumscription. In all six cases, the constituent cells (both basaloid cells and sebocytes) showed large, crowded, and

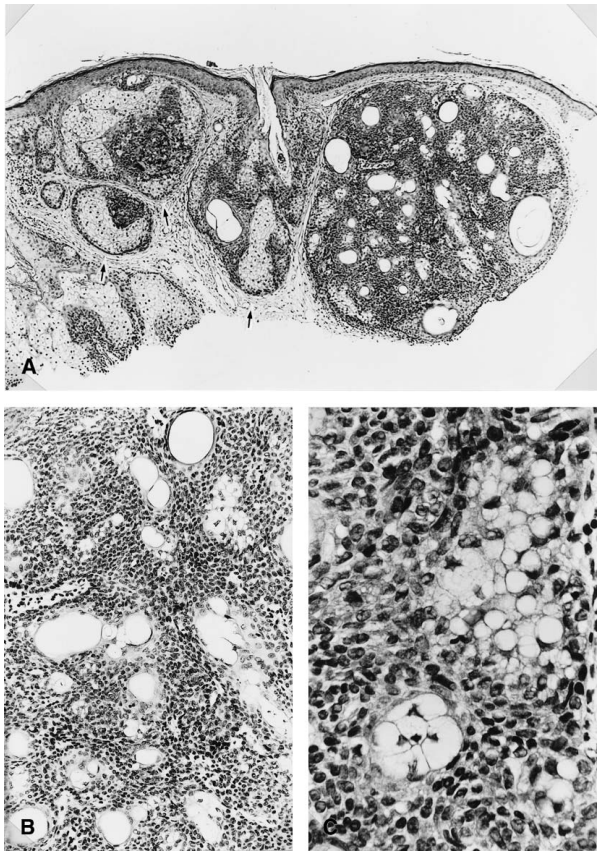

FIG. 2. Histopathologic features of sebaceoma (classic type) (Case 8). **(A)** A small lesion composed of a basaloid aggregation and a few small aggregations vaguely resembling normal sebaceous lobules (*arrows*) in the upper dermis. **(B)** The basaloid aggregation is composed of basaloid cells and vacuolated cells in association with sebaceous ductal structures. **(C)** The constituent basaloid cells are small and monomorphous, and the vacuolated cells have the features of sebocytes.

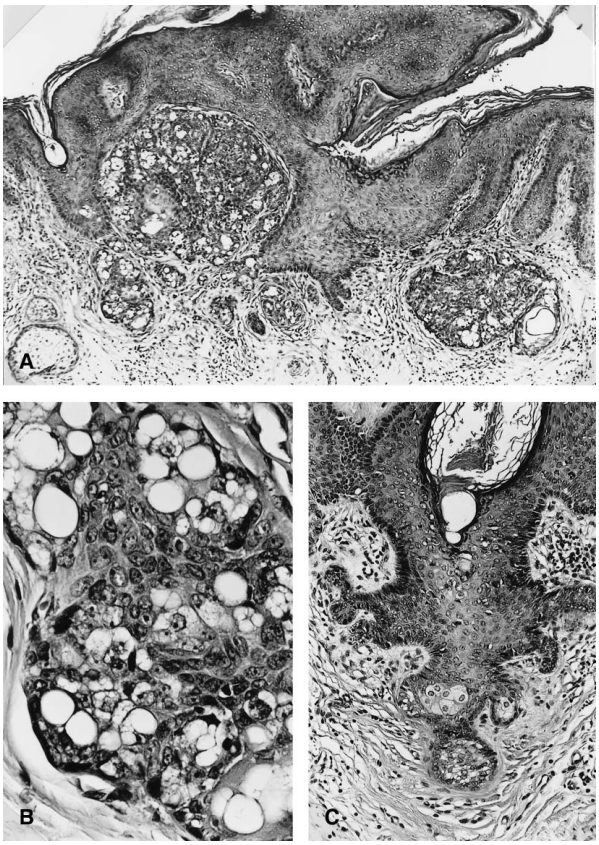

FIG. 3. Histopathologic features of sebaceoma associated with nevus sebaceus (classic type) (Case 11). **(A)** A few basaloid aggregations in the upper dermis. **(B)** The constituent basaloid cells are relatively large and vesicular nuclei with distinct nucleoli and have some pleomorphism. **(C)** Abnormal and primitive sebaceous budding adjacent to this sebaceoma within the lesion of nevus sebaceus.

heterochromic or vesicular nuclei with prominent nucleoli in association with moderate pleomorphism and occasional mitoses, and frequent mitoses were observed in some parts of the lesions (Fig. 8). Immature sebocytes characterized by large, eosinophilic, granular cytoplasm were often observed among the constituent cells in all six cases (Fig. 8). Large clusters of sebocytes vaguely resembling normal sebaceous lobules were seen in three cases (Fig. 8). One case associated with the Muir-Torre syndrome was reported previously (10), and another case demonstrating apocrine differentiation was also reported elsewhere (11). We faced a diagnostic dilemma of benign or malignant (namely, sebaceoma or low-grade sebaceous carcinoma) in several of these six cases (10,11); the confluence of aggregations of neoplastic cells and ulceration as well as more pleomorphic nuclei favored the latter diagnosis.

Sebaceous Carcinoma

Although the lesions were located in the dermis without invading deep within the subcutaneous fat, the silhouette and cytology demonstrated malignancy in all three cases. One case was a broad and endophytic lesion characterized by many highly elongated and bulbous aggregations of various shapes and sizes oriented mostly vertical to the skin surface and connected to the infundibula—a typical example of superficial sebaceous carcinoma (Fig. 9). This case associated the aggregations with large clusters of sebocytes vaguely resembling normal sebaceous lobules, demonstrating the features of so-called sebaceous adenoma. Two other cases were composed of several intradermal basaloid aggregations of various shapes and sizes associated with ulcerated epidermis (Fig. 10), and both were associated with nevus sebaceous. One of the two cases was reported elsewhere (9). In another case, immature basaloid neoplastic cells with severe pleomorphism and frequent mitoses were predominant, but neoplastic sebocytes with vacuolated and bubbly cytoplasm and sebaceous duct-like structures could be seen in some parts (Fig. 10).

Basal Cell Carcinoma With Sebaceous Differentiation

Only one case showed histopathologic features of basal cell carcinoma. Within the aggregations of basal cell carcinoma, sebocytes and sebaceous duct-like structures were seen. Apocrine duct-like structures were also seen, and precise histopathologic features will be discussed elsewhere in detail (12).

DISCUSSION

Through diagnosis and classification of the 30 presented cases of basaloid neoplasms with sebaceous differentiation in six categories, we confirmed the significance and usefulness of the concept and entity of sebaceoma as a distinct benign neoplasm with sebaceous differentiation. Just as trichoblastoma is mostly composed of follicular germinative cells (13,14), sebaceoma is considered to be mostly composed of sebaceous germinative cells. Both trichoblastoma and sebaceoma histopathologically show a benign nature in their silhouette (4,13,14). As a rule, the nuclei of neoplastic cells in trichoblastoma are small, basophilic, and monomorphous. Nevertheless, nuclei are occasionally large and even pleomorphic (13,14). The current study suggests that the same can be said with regard to the nuclei of neoplastic cells in sebaceoma. It may be argued that in sebaceoma, constituent cells with small and monomorphous nuclei are immature germinative cells in mantles and those with relatively large and vesicular nuclei with conspicuous nucleoli are some of the mature germinative cells at the periphery of sebaceous lobules because of similar cytologic features between the two cell types in each of the events (8). Although the significance of the entity of sebaceoma was confirmed as a distinct benign neoplasm with sebaceous differentiation in this study, it

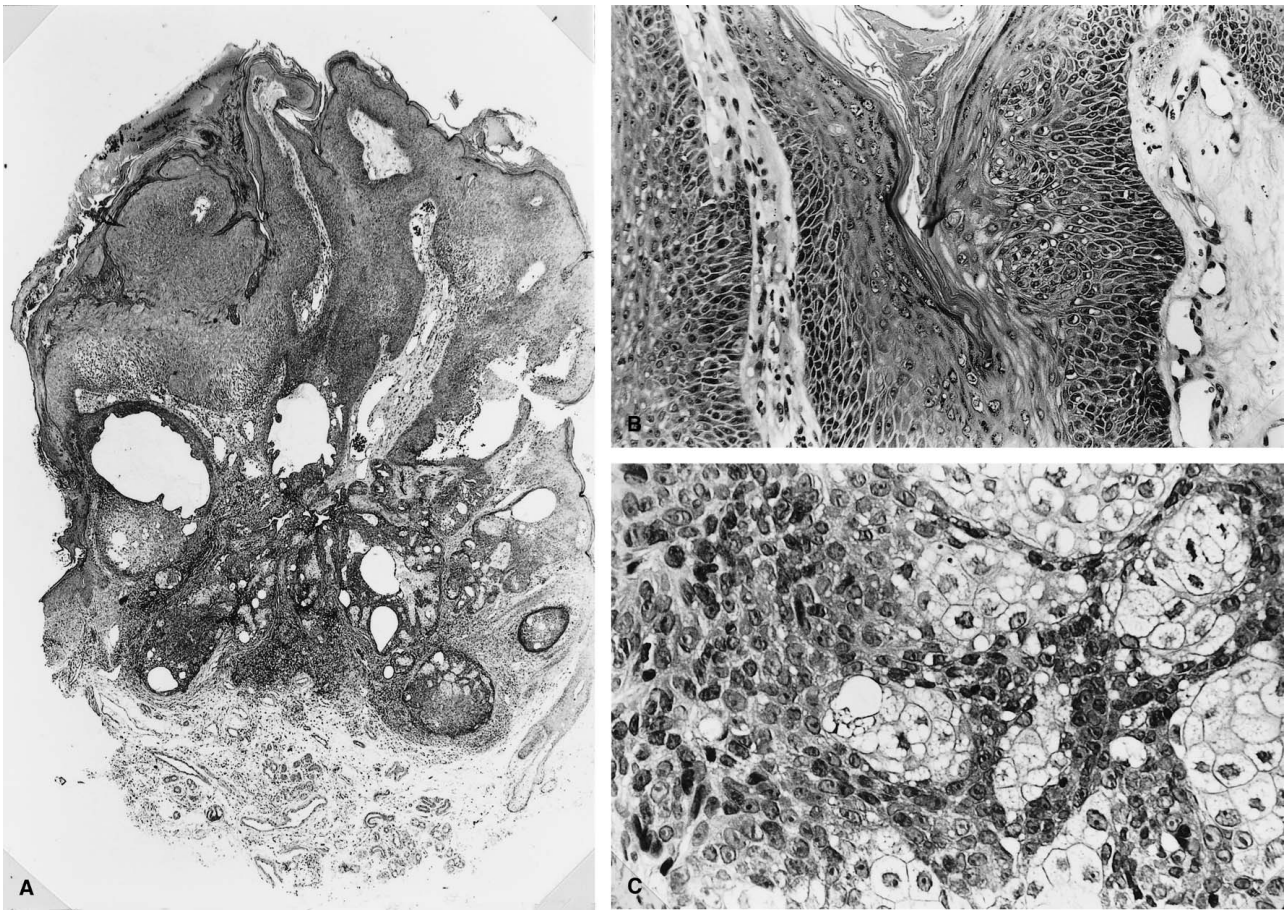

FIG. 4. Histopathologic features of sebaceoma (verruca/seborrheic keratosis type) (Case 17). **(A)** An exoendophytic lesion with hyperplastic infundibula and several dermal basaloid aggregations. **(B)** Hypergranulomatosis, vacuolated cells, and large pale cells within the hyperplastic infundibula associated with capillaries in thin dermal papillae, demonstrating verruca-like features. **(C)** The dermal basaloid aggregations have typical histopathologic features of classic type sebaceoma.

is also true that some difficulties were encountered in the diagnosis of the cases of sebaceoma and its related neoplasms.

All three cases of trichoblastoma with sebaceous differentiation were large nodular type trichoblastomas without prominent fibrotic stroma, which could not be easily differentiated from sebaceoma. In these three cases, however, the presence of follicular germs and rudimentary follicular papillae, a partial palisading border in the neoplastic aggregations, and an appreciable component of fibrotic stroma excluded a diagnosis of sebaceoma. If no follicular differentiation and palisading border in the neoplastic aggregations are seen in this situation, sebaceoma is the preferred diagnosis. Difficulty and disagreement in the distinction between sebaceoma and trichoblastoma (large nodular type) with sebaceous differentiation sometimes occurs (8,15,16), because sebaceoma and trichoblastoma are highly related neoplasms (9,17). Pluripotent stem cells in the folliculosebaceous-apocrine unit may give rise to follicular germinative cells and sebaceous germinative cells (11). In some instances, we believe that the distinction between these two neoplasms was ambiguous.

It may be better that verruca/seborrheic keratosis type sebaceoma is called verruca vulgaris with sebaceous differentiation or seborrheic keratosis with sebaceous differentiation when the features of verruca vulgaris or those of seborrheic keratosis, respectively, are prominent (18–20). In our two cases, however, the histopathologic features in the middle to lower part of the lesion are those of sebaceoma; thus, we consider these two cases to be examples of sebaceoma. There may be a difference in histogenesis between the classic and verruca/seborrheic types of sebaceoma, but we could not find any fundamental histopathologic differences between the two types except in the superficial part of the lesion. The distinction between sebaceoma (especially of verruca/seborrheic type) and apocrine poroma with sebaceous differentiation has been controversial because of the similarity and degree of overlap in the histopathologic

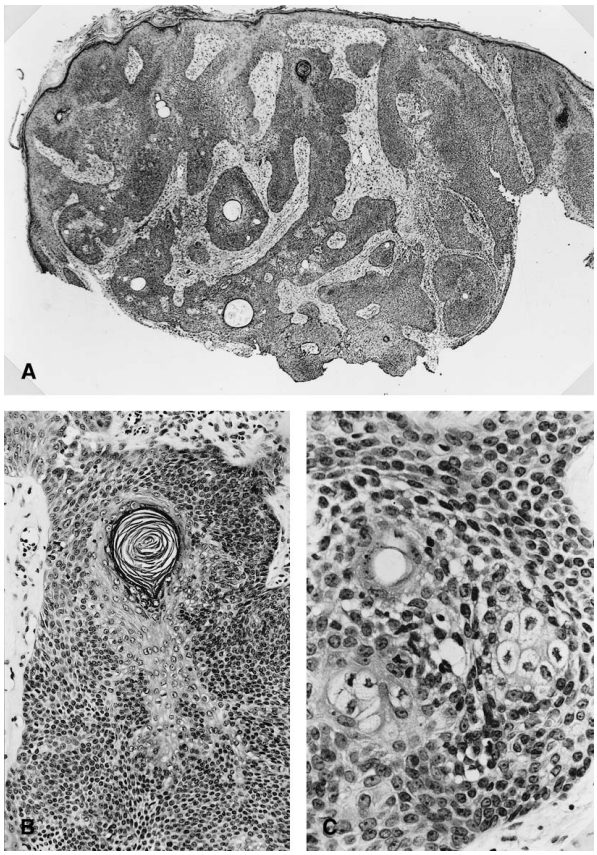

FIG. 5. Histopathologic features of sebaceoma (verruca/seborrheic keratosis type) (Case 13). **(A)** A mostly endophytic lesion with hyperplastic infundibula and several dermal basaloid aggregations. **(B)** Basaloid cells and squamous cells are associated with a tunnel of cornified cells within the hyperplastic infundibula, demonstrating seborrheic keratosis-like features. **(C)** The dermal basaloid aggregations have typical histopathologic features of classic type sebaceoma.

features of these two neoplasms (18–23). As Harvell et al. (23) have suggested, the distinction can be made by the following points: 1) the neoplastic constituent cells are not basaloid sebaceous germinative cells but poroid cells, and tubular structures are seen in apocrine poroma with sebaceous differentiation; and 2) horn pseudocysts and prominent hypergranulosis are often seen within the hyperplastic infundibula in verruca/seborrheic keratosis type sebaceoma.

With regard to sebaceous carcinoma, only aggressive and invasive sebaceous carcinomas may have been emphasized so far, and sufficient attention may have not been given to superficial sebaceous carcinoma. Based on the silhouette of malignancy and/or severe nuclear atypia with frequent mitoses, we could confidently diagnose four cases as sebaceous carcinoma in this study, and one of these four cases was a typical example of superficial sebaceous carcinoma. A major diagnostic challenge in this study was presented by the cases of low-grade sebaceous carcinoma. The choice of benign or malignant was difficult in some cases (10,11), namely, sebaceoma or low-grade sebaceous carcinoma, because of relatively large nuclei having distinct nucleoli with some pleomorphism seen in rare cases of sebaceoma and relatively sharp circumscription in low-grade sebaceous carcinomas. Concerning the diagnosis of the cases of low-grade sebaceous carcinoma, we suppose that some colleagues would agree with our diagnosis and others would not (24–34). Some of the neoplasms would be classified as examples of sebaceoma, and the diagnosis of low-grade sebaceous carcinoma would not be acceptable to others, even with our criteria for sebaceoma and low-grade sebaceous carcinoma. Many authors have suggested that the distinction between well-differentiated sebaceous carcinoma and sebaceous epithelioma is difficult in some cases and may be arbitrary, although the definition of the term *sebaceous epithelioma* by most of these authors was not clearly documented (35–39). In some instances, there may be neoplastic progression (sebaceoma to low-grade

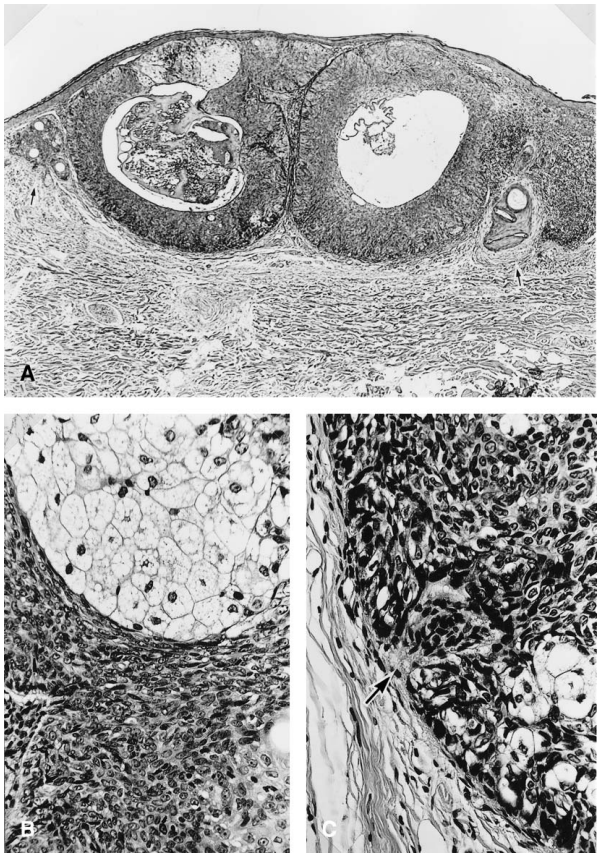

FIG. 6. Histopathologic features of trichoblastoma with sebaceous differentiation (Case 14). **(A)** Two large basaloid aggregations with cystic degenerations and a few small aggregations with infundibulocystic structures (*arrows*) in the dermis. **(B)** Follicular germinative cells and a large cluster of sebocytes in the basaloid aggregation. **(C)** Rudimentary follicular germs and follicular papillae (*arrow*) are seen.

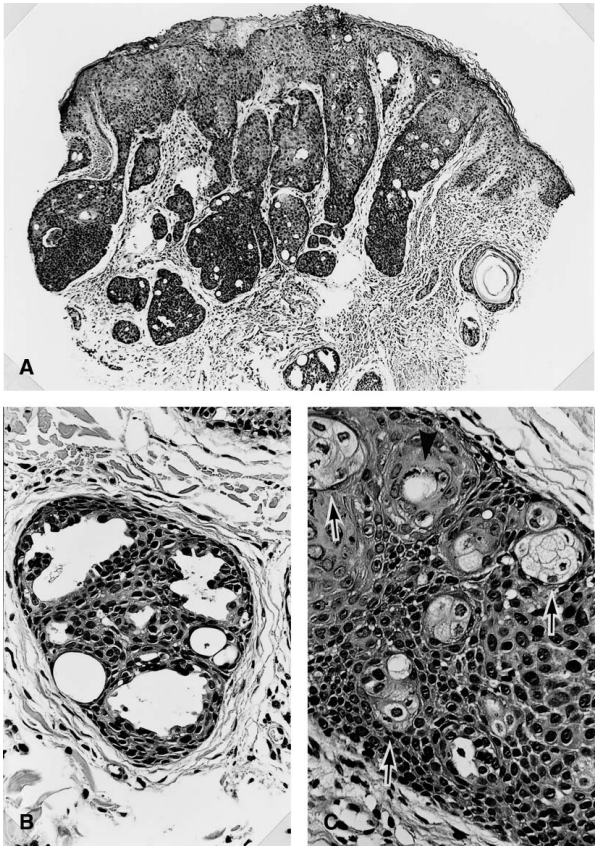

FIG. 7. Histopathologic features of apocrine poroma with sebaceous differentiation (Case 18). **(A)** Several basaloid aggregations are seen in the dermis, and some of them connect to the epidermis. **(B)** An aggregation mainly composed of poroid cells with some cuticular cells in association with tubular structures, some of which showed hints of decapitation secretion, demonstrating both ductal and glandular differentiation. **(C)** Sebocytes in small clusters (*arrows*) and duct-like structures formed by cuticular cells with keratohyalin granules (*arrowhead*), demonstrating differentiation toward apocrine acrosyringium within the aggregations of poroma.

sebaceous carcinoma to sebaceous carcinoma) (39) analogous to the morphologic progression according to genetic alterations in the colonic adenoma-carcinoma sequence (small adenoma to large adenoma with a certain degree of epithelial dysplasia-carcinoma) (40–44) as Rütten et al. (45) have pointed out. Conversely, low-grade sebaceous carcinoma may be a malignant neoplasm from the outset. Nevertheless, if the lesions are completely excised, there should be no clinical problem for most patients with low-grade sebaceous carcinoma regardless of whether it is classified as benign or malignant. As Graham et al. (36) have suggested, however, when it is difficult to assign cases as benign or malignant (especially in cases occurring in the eyelids), we prefer the diagnosis of low-grade sebaceous carcinoma without recourse to the term *sebaceous epithelioma*. We follow up carefully after surgery, because cases diagnosed as sebaceous epithelioma have shown malignant transformation (46), recurred with cytologic atypia (47), or even showed metastasis (48).

The present study also revealed the rare existence of basal cell carcinoma with sebaceous differentiation, which should be differentiated from sebaceous carcinoma. This case was considered actually to be an example of basal cell carcinoma with folliculo-sebaceous-apocrine differentiation. However, there were some diagnostic problems in this case, therefore its precise histopathologic features will be discussed in the "Cases in Consultation" section of the journal (12). To sum up, basal cell carcinoma with sebaceous differentiation should have the histopathologic features of basal cell carcinoma, whereas sebaceous carcinoma (including

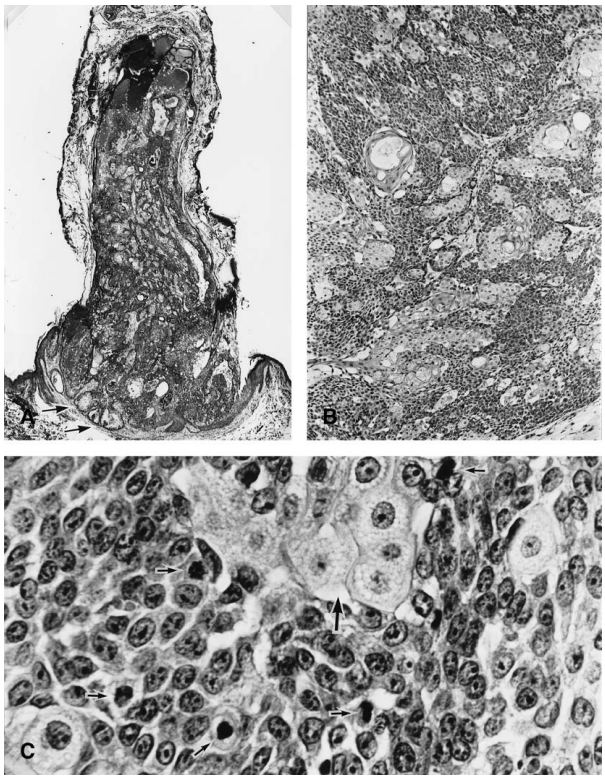

FIG. 8. Histopathologic features of low-grade sebaceous carcinoma (Case 20). **(A)** The confluence of aggregations of neoplastic cells with an anastomosing pattern forming a cutaneous horn-like shape in the epidermis and upper dermis. Large clusters of sebocytes vaguely resembling normal sebaceous lobules are seen (*arrows*). **(B)** Note the confluence of aggregations of neoplastic cells of various shapes and sizes with an irregularly anastomosing pattern. The confluent aggregations are composed of basaloid cells, sebocytes, and sebaceous duct-like structures. **(C)** The constituent cells (both basaloid cells and sebocytes) show large, crowded, and heterochromic nuclei with prominent nucleoli in association with moderate pleomorphism. In this part, frequent mitoses are seen (*small arrows*). Small clusters of immature sebocytes with eosinophilic and granular or vacuolated cytoplasm are often observed (*large arrow*).

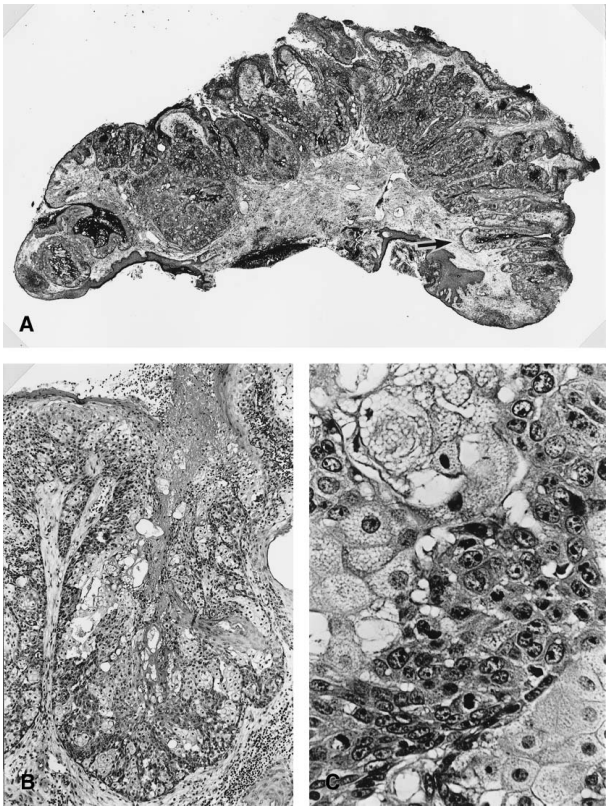

FIG. 9. Histopathologic features of superficial sebaceous carcinoma (Case 26). **(A)** A broad and endophytic lesion composed of many highly elongated and bulbous aggregations of varied shapes and sizes oriented mostly vertical to the skin surface and connecting to the infundibula. An aggregation vaguely resembling normal sebaceous lobules is observed (*arrow*). **(B)** The aggregation, consisting of basaloid cells, sebocytes, and sebaceous duct-like structures, with connection to the infundibula. **(C)** The neoplastic cells are large and heterochromic nuclei with prominent nucleoli in association with pleomorphism and frequent mitoses.

low-grade sebaceous carcinoma) and sebaceoma never have these features (12).

If the term *sebaceous adenoma* is defined as neoplastic dermal lobules composed of sebocytes with an architecture vaguely resembling that of normal sebaceous lobules, our study demonstrated that an aggregation of sebaceous adenoma could be seen in sebaceoma, low-grade sebaceous carcinoma, and sebaceous carcinoma, suggesting that when sebaceous differentiation is advanced in sebaceoma, low-grade sebaceous carcinoma, and sebaceous carcinoma, an architecture vaguely resembling that of normal sebaceous lobules can be observed in these neoplasms. We consider that sebaceous adenoma is sebaceoma in some cases, because we regard most small conventional sebaceous adenomas as sebaceomas with advanced sebaceous differentiation. Nevertheless, we also agree with Nussen and Ackerman's proposal that "sebaceous adenoma is sebaceous carcinoma" (7) in another set of cases, because we assume that most of the cases diagnosed as large cystic sebaceous adenomas or broad superficial sebaceous adenomas thus far are actually well-differentiated sebaceous carcinomas (including low-grade carcinoma). Briefly, the cases diagnosed as sebaceous adenoma hitherto include both sebaceomas with advanced sebaceous differentiation and well-differentiated sebaceous carcinomas (including low-grade carcinomas). We disagree with Nussen and Ackerman's idea that all sebaceous adenomas are actually sebaceous carcinomas (7). Many authors have noticed that an aggregation of sebaceous adenoma can be observed within the lesions of sebaceoma or sebaceous epithelioma (1–3) and have pointed out the existence of a spectrum of neoplasms ranging from sebaceoma to sebaceous adenoma (5). The possibility of two spectra (benign and malignant), namely, from sebaceoma to seba-

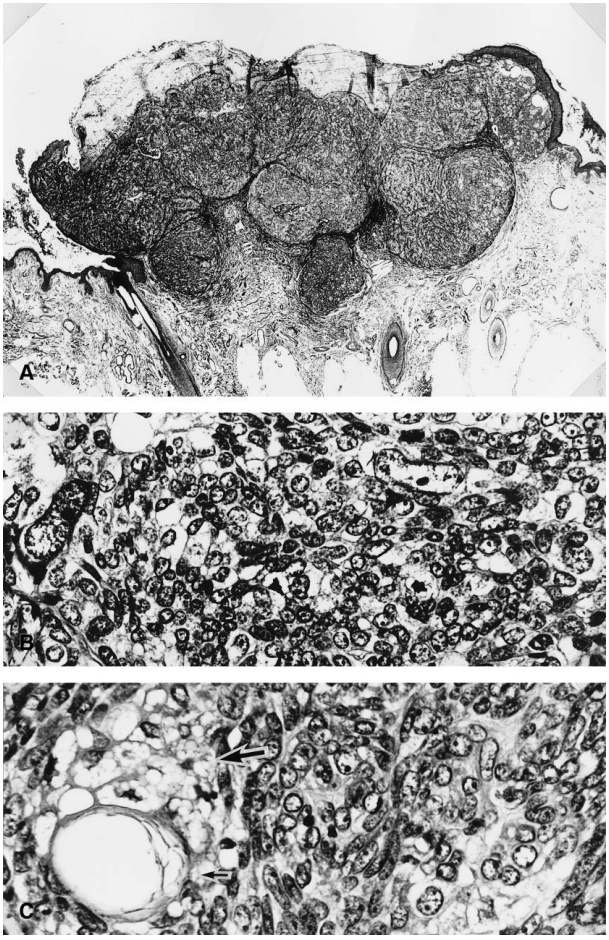

FIG. 10. Histopathologic features of sebaceous carcinoma associated with nevus sebaceus (Case 28). **(A)** A lesion composed of several intradermal basaloid aggregations of various shapes and sizes associated with ulcerative epidermis. **(B)** Immature basaloid neoplastic cells with severe pleomorphism and frequent mitoses are predominant. **(C)** In this part, the neoplastic sebocytes with vacuolated and bubbly cytoplasm (*large arrow*) and a sebaceous duct-like structure (*small arrow*) can be seen, demonstrating evidence of sebaceous differentiation.

ceous adenoma in some cases and from sebaceous carcinoma (including low-grade carcinoma) to sebaceous adenoma in a few other cases, has not been suggested previously. If the term *sebaceous adenoma* is preserved, it should be used in a benign spectrum, namely, sebaceoma with advanced sebaceous differentiation.

In closing this discussion, trichoblastoma is a neoplasm with follicular differentiation, and apocrine poroma is a neoplasm with apocrine differentiation. Basal cell carcinoma would be a neoplasm with follicular germinative differentiation (49). These three kinds of neoplasms are not authentic neoplasms with sebaceous differentiation in contrast to the other neoplasms included in this series. Practically, however, trichoblastoma with sebaceous differentiation, apocrine poroma with sebaceous differentiation, and basal cell carcinoma with sebaceous differentiation are easily confused with the authentic neoplasms with sebaceous differentiation and hence were included in this study. □

Acknowledgments: The authors thank Mr. Toyoji Tanamachi at the Photocenter of Saga Medical School (Saga, Japan) for performing photomicrography. One of the authors (N.M.) also thanks Dr. A. Bernard Ackerman (Director of Ackerman Academy of Dermatopathology, New York, NY) for his kind answer to repeated questions from the author about sebaceoma when they studied together at the Institute for Dermatopathology, Jefferson Medical College (Philadelphia, PA).

REFERENCES

1. Zackheim HS. The sebaceous epithelioma. A clinical and histologic study. *Arch Dermatol* 1964;89:711–24.
2. Rulon DB, Helwig EB. Cutaneous sebaceous neoplasms. *Cancer* 1974;33:82–102.
3. Finan MC, Connolly SM. Sebaceous gland tumors and systemic disease: a clinicopathologic analysis. *Medicine* 1984;63:232–42.
4. Troy JL, Ackerman AB. Sebaceoma. A distinctive benign neoplasm of adnexal epithelium differentiating toward sebaceous cells. *Am J Dermatopathol* 1984;6:7–13.
5. Sáchez Yus E, Requena L, Simón P, et al. Sebomatricoma: a unifying term that encompasses all benign neoplasms with sebaceous differentiation. *Am J Dermatopathol* 1995;17:213–21.
6. Dinneen AM, Mehregan DR. Sebaceous epithelioma: a review of twenty-one cases. *J Am Acad Dermatol* 1996;34:47–50.
7. Nussen S, Ackerman AB. Sebaceous "adenoma" is sebaceous carcinoma. *Dermatopathol Pract Concept* 1998;4:5–14.
8. Misago N, Narisawa Y. Rippled-pattern sebaceoma. *Am J Dermatopathol* 2001;23:437–43.
9. Misago N, Kodera H, Narisawa Y. Sebaceous carcinoma, trichoblastoma, and sebaceoma with features of trichoblastoma in nevus sebaceus. *Am J Dermatopathol* 2001;23:456–62.
10. Misago N, Narisawa Y. Sebaceous neoplasms in Muir-Torre syndrome. *Am J Dermatopathol* 2000;22:155–61.
11. Misago N, Narisawa Y. Sebaceous carcinoma with apocrine differentiation. *Am J Dermatopathol* 2001;23:50–7.
12. Misago N, Mochizuki Y, Narisawa Y. Basal cell carcinoma with sebaceous differentiation. *Am J Dermatopathol.* In press.
13. Ackerman AB, De Viragh PA, Chongchitnant N. Trichoblastoma. In: *Neoplasms with follicular differentiation*. Philadelphia: Lea & Febiger, 1993:357–422.
14. Ackerman AB, Reddy VB, Soyer HP. Trichoblastoma. In: *Neoplasms with follicular differentiation*. New York: Ardor Scribendi, 2001:405–622.
15. Graham BS, Barr RJ. Rippled-pattern sebaceous trichoblastoma. *J Cutan Pathol* 2000;27:455–9.
16. Yamamoto O, Hisaoka M, Yasuda H, et al. A rippled-pattern trichoblastoma: an immunohistochemical study. *J Cutan Pathol* 2000;27:460–6.
17. Kaddu S, Schäppi H, Kerl H. Trichoblastoma and sebaceoma in nevus sebaceus. *Am J Dermatopathol* 1999;21:552–6.
18. Steffen CH, Ackerman AB. Neoplasms with combined sebaceous and apocrine differentiation. In: *Neoplasms with sebaceous differentiation*. Philadelphia: Lea & Febiger, 1994:469–84.
19. Steffen CH, Ackerman AB. Verruca vulgaris with sebaceous differentiation In: *Neoplasms with sebaceous differentiation*. Philadelphia: Lea & Febiger, 1994:279–327.
20. Steffen CH, Ackerman AB. Seborrheic keratosis with sebaceous differentiation. In: *Neoplasms with sebaceous differentiation*. Philadelphia: Lea & Febiger, 1994:433–47.
21. Hanau D, Grosshans E, Laplanche G. A complex poroma-like adnexal adenoma. *Am J Dermatopathol* 1984;6:567–72.
22. Zaim MT. Sebocrine adenoma. An adnexal adenoma with sebaceous and apocrine poroma-like differentiation. *Am J Dermatopathol* 1988;10:311–8.
23. Harvell JD, Kerschmann RL, LeBoit PE. Eccrine or apocrine poroma? Six poromas with divergent adnexal differentiation. *Am J Dermatopathol* 1996;18:1–9.
24. Ackerman AB. Serious limitations of a method. *Am J Dermatopathol* 2001;23:242–3.
25. Cowen EW, Helm KF, Billingsley EM. An unusually aggressive trichoblastoma. *J Am Acad Dermatol* 2000;42:374–7.
26. Helm KF, Cowen EW, Billingsley EM, et al. Trichoblastoma or trichoblastic carcinoma? [letter] *J Am Acad Dermatol* 2001;44: 547.
27. Chan JK, Ng CS, Tsang WY. Nodular desmoplastic variant of trichoblastoma. *Am J Surg Pathol* 1994;18:495–500.
28. Ackerman AB. Nodular desmoplastic variant of trichoblastoma. *Am J Surg Pathol* 2000;24:1033–4.
29. Foucar E. 'Individuality' in the specialty of surgical pathology. Self-expression or just another source of diagnostic error? *Am J Surg Pathol* 2000;24:1573–6.
30. Nichols PW, Cote RJ. Diagnostic 'individuality' [letter]. *Am J Surg Pathol* 2001;25:1100.
31. Ackerman AB. 'Individuality' in the specialty of surgical pathology [letter]. *Am J Surg Pathol* 2001;25:1100–1.
32. Ioachim HL. On variability, standardization, and error in diagnostic pathology [letter]. *Am J Surg Pathol* 2001;25:1101–3.
33. Sridhar SR. 'Individuality' in surgical pathology [letter]. *Am J Surg Pathol* 2001;25:1103–4.
34. Foucar E. Author's reply [letter]. *Am J Surg Pathol* 2001;25: 1104–6.
35. Schwartz RA, Flieger DN, Saied NK. The Torre syndrome with gastrointestinal polyposis. *Arch Dermatol* 1980;116:312–4.
36. Graham RM, McKee PH, McGibbon D. Sebaceous carcinoma. *Clin Exp Dermatol* 1984;9:466–71.
37. Oka K, Katusmata M. Intraepidermal sebaceous carcinoma: case report. *Dermatologica* 1990;180:181–5.
38. Elder D, Elenitsas R, Ioffreda M, et al. Sebaceous adenoma and sebaceous epithelioma (sebaceoma). In: *Synopsis and atlas of Lever's histopathology of the skin*. Philadelphia: Lippincott Williams & Wilkins, 1999:304–5.
39. Kiehl P, Richter K, Erdelkamp J, et al. DNA image cytometry in sebaceous tumors of the Muir-Torre syndrome. *Br J Dermatol* 1998;138:706–8.
40. Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. *Cell* 1990;61:759–67.
41. Speroni AH, Vanzulli SI, Meiss RP. Adenomas of the colon: overexpression of p53 protein and risk factors. *Endoscopy* 1998;30: 623–6.
42. Yang HB, Chow NH, Sheu BS, et al. The role of bcl-2 in the progression of the colorectal adenoma-carcinoma sequence. *Anticancer Res* 1999;19:727–30.

43. Iwabuchi M, Sasano H, Hiwatashi N, et al. Serrated adenoma: a clinicopathologic, DNA ploidy, and immunohistochemical study. *Anticancer Res* 2000;20:1141–7.
44. Bennett MW, O'Connell J, Houston A, et al. Fas ligand upregulation is an early event in colonic carcinogenesis. *J Clin Pathol* 2001;54:598–604.
45. Rütten A, Burgdorf W, Hügel H, et al. Cystic sebaceous tumors as marker lesions for the Muir-Torre syndrome. *Am J Dermatopathol* 1999;21:405–13.
46. Ohda C, Matsunaka M. A case of sebaceoma with malignant transformation [in Japanese]. *Skin Research* 1993;35:99–104.
47. Tsukada M, Ohara K. Sebaceous epithelioma [in Japanese]. *Rinsho Dermatol (Tokyo)* 1999;41:1325–7.
48. Burgdorf WHC, Koester G. Multiple cutaneous tumors: what do they mean? *J Cutan Pathol* 1992;19:449–57.
49. Ackerman AB, Reddy VB, Soyer HP. Trichoblastic carcinoma. In: *Neoplasms with follicular differentiation*. New York: Ardor Scribendi, 2001:625–1005.