Sebaceous Neoplasms in Siriraj Hospital, Mahidol University: A 9-Year-Retrospective Study

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Background: *Sebaceous neoplasms are adnexal neoplasms that contain a varying number of sebocytes, i.e. large cells with lipid-laden vacuolated cytoplasm, soap-bubble in appearance, and crenate nuclei. They are uncommon compared to other adnexal neoplasms. Various sebaceous neoplasms with complex histopathologic features and varying degree of sebaceous cells differentiation have been described in the literature.*

Objectives: *To study the prevalence of sebaceous neoplasms, i.e. nevus sebaceus, sebaceous hyperplasia, sebaceous adenoma, sebaceoma, sebaceous epithelioma, superficial epithelioma with sebaceous differentiation, and sebaceous carcinoma diagnosed in the Department of Pathology, Siriraj Hospital, Mahidol University during the 9-year-period between 1997 and 2005. To study the prevalence of tumor transformation that occurs in nevus sebaceus.*

Material and Method: *A retrospective study of all sebaceous neoplasms including Nevus sebaceous, sebaceous hyperplasia, sebaceous adenoma, sebaceoma, sebaceous epithelioma, superficial epithelioma with sebaceous differentiation, sebaceous carcinoma, and all neoplasms containing the term "sebaceous" was performed. All slides were re-analyzed and re-diagnosed, without knowledge of the previous diagnosis or any clinical data, according to the criteria described in the standard textbooks of dermatopathology by Elder, McKee. Comparison between the previous diagnoses and the reviewed diagnoses was performed to assess the initial accuracy of all sebaceous neoplasms diagnosed. Small-sized biopsies or biopsies that possess incomplete sebaceous differentiation, in which the sebocytes were few and subtle, sometimes are difficult to diagnose. In these instances, the clinical correlation was needed for positive diagnosis. Afterwards, these reviewed diagnoses were recorded and classified according to the patient's age, gender, and localization.*

Results: *Two hundred seven sebaceous neoplasms (2.34%) from the 8819 skin biopsies that were taken in the Department of Pathology, Siriraj Hospital during the 9-year-period, were included. After exclusion of some authentically non-sebaceous neoplasms, 182 sebaceous neoplasms were found. Nevus sebaceus (n = 85, 46.7%) and sebaceous hyperplasia (n = 64, 35.1%) were the two most common benign lesions. The others were sebaceoma (n = 3, 1.6%), sebaceous adenoma (n = 2, 1.1%), sebaceous epithelioma (n = 1. 0.5%), sebaceous carcinoma (n = 26, 14.3%), and one unclassified sebaceous lesion that could not be considered a neoplasm. Tumor degeneration was found in 14 nevus sebaceus in which 21 neoplasms existed, namely, trichilemmoma (wart)-like lesion (n = 4), primitive follicular induction (n = 7), syringocystadenoma papilliferum (n = 3), trichoblastoma (n = 3), and one of each of trichoepithelioma, sebaceous adenoma, tumor of follicular infundiculum, and mucoepidermoid carcinoma.*

Conclusion: *Twenty-six sebaceous carcinomas out of 182 sebaceous neoplasms, occurring mostly on the patients' eyelids, were found. The most common sebaceous neoplasm was nevus sebaceus (n = 85); the prophylactic excision of this lesion was recommended as tumor degeneration was frequent (14 out of 85 cases). Epithelial membrane antigen (EMA) usually decorated both normal and abnormal sebocytes. It was very helpful in the detection of sebocytes in basaloid cells in sebaceous neoplasms and among lymphoid cells within metastasized lymph nodes and a discriminant between sebaceous and non-sebaceous neoplasms.*

Keywords: *Sebaceous neoplasms, Retrospective study*

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Sebaceous glands are holocrine glands that are widely distributed all over the body except on the palms and soles. They are particularly abundant on the face, scalp, in the midline of the back, and about the perineum. These sebaceous glands are composed of sebaceous lobules usually locating beside the hair follicles. Each sebaceous lobule is typically composed of 1-2 layers of small cuboidal or flattened basophilic germinative cells at the periphery, that give rise to the sebocytes at the center. These cells possess lipid content in their cytoplasm and will present as large cells with lipid-laden vacuolated-cytoplasm and centrally located crenate nuclei.

The histopathologic hallmark is that the sebaceous neoplasms will contain lipid-laden sebocytes characteristically centrally-placed, with crenate nuclei and vacuolated, soap-bubble cytoplasm. By immunological studies, these cells are typically epithelial membrane antigen (EMA) positive and carcinoembryonic antigen (CEA), S100 protein negative. Sebaceous neoplasms are relatively rare compared to other adnexal neoplasms and could be subdivided into hamartomatous lesions, namely, sebaceous hyperplasia and Nevus sebaceous (of Jadassohn), benign neoplasms, *i.e.* sebaceous adenoma, sebaceoma, sebaceous epithelioma, superficial epithelioma with sebaceous differentiation, and malignant neoplasm, to wit, and sebaceous carcinoma. The diagnosis depends on their architectural patterns and, as a rule, the varying number of sebocytes contained inside. Some sebaceous neoplasms, *i.e.* sebaceoma and sebaceous epithelioma in which the sebocytes are less and inconspicuous, might be difficult to diagnose. In this instance, the immunostudy of epithelial membrane antigen (EMA) is helpful in detection of these occult sebocytes, which will be strongly EMA-positive.

Nevus sebaceus, although is a hamartomatous lesion, possesses some important aspects because many benign and malignant neoplasms have been reported arising within this lesion. Sebaceoma and sebaceous epithelioma share common histopathologic features, *i.e.* well-defined lobules of predominant small basaloid cells in common to those in basal cell carcinoma as well. It is necessary to diagnose sebaceoma and sebaceous epithelioma with certainty because they possess a better prognosis when compared to basal cell carcinoma. Sebaceous carcinoma, a malignant sebaceous neoplasm, usually presents as an ulcerative or non-ulcerative nodular lesion commonly on or about the eyelids. The diagnosis of sebaceous carcinoma is occasionally difficult to assess by clinical examination alone since many lesions are mistaken for basal cell carcinoma, squamous cell carcinoma, and even a chalazion or blephalo-conjunctivitis. This malignancy displays a high metastatic rate as well as a subsequent high mortality rate. The organs often affected include the regional lymph nodes, lung, liver, and brain.

Material and Method

The review of all sebaceous neoplasms under Nevus sebaceous, sebaceous hyperplasia, sebaceous adenoma, sebaceoma, sebaceous epithelioma, superficial epithelioma with sebaceous differentiation, sebaceous carcinoma, and all neoplasms containing the term "sebaceous" retrieved from the computer filing system in the Department of Pathology, Siriraj Hospital, Mahidol University between 1997 and 2005 was performed. All slides were re-analyzed and re-diagnosed, without the knowledge of the previous diagnosis or any clinical data, according to the criteria described by Elder, McKee[1,2] and recorded according to the patient's age, gender, and localization in the patients' data forms. The accuracy of the diagnoses, done by comparing between the previous diagnoses and the reviewed diagnoses of all these sebaceous neoplasms had been completed as well. Clinical correlation and immunostudies of epithelial membrane antigen (EMA) were done in sebaceous lesions with less differentiation or of small sample-size, in which the sebocytes were few, subtle, and difficult to diagnose to highlight the inconspicuous sebocytes.

Results

Two hundred seven sebaceous neoplasms (2.34% of the 8,819 skin biopsies) collected from the data file were included. Among these were nevus sebaceus (n = 89), sebaceous hyperplasia (n = 81), sebaceous adenoma (n = 5), sebaceoma (n = 3), sebaceous epithelioma (n = 1), and 28 sebaceous carcinomas. Agreement with the previous diagnoses was noted in 78 nevus sebaceus (87.6%), 58 sebaceous hyperplasias (71.6%), 2 out of 5 sebaceous adenomas (40%), 26 out of 28 sebaceous carcinomas (92.8%), all sebaceous epithelioma, and all sebaceoma (Table 1). The major disagreement was in sebaceous hyperplasia (n = 23, 28.2%) in which the reviewed diagnoses appeared to be nevus sebaceus (n = 9), seborrhiec keratosis (n = 3), fibrous papule (n = 2), and one of each of intradermal nevus, trichoepithelioma, comedone, hemangioma, wart, actinic keratosis, phimosis, lentigo,

nevus, and chronic dermatitis (Table 2). Eleven disagreed nevus sebaceus were finally confirmed to be sebaceous hyperplasia (n = 4), seborrheic keratosis (n = 2), actinic keratosis (n = 2), and unclassified follicular or sebaceous lesions (n = 3) (Table 3). Two out of five sebaceous adenomas and all three sebaceomas agreed with the previous diagnosis. (Table 3). Twenty-six out of 28 sebaceous carcinomas corresponded to the original diagnosis and the remaining two were changed into sweat gland carcinoma and lymphadenoma (lymphoepithelial-like carcinoma) (Table 4, 5).

After exclusion and review, 182 sebaceous tumors, namely, nevus sebaceus (n = 85), sebaceous hyperplasias (n = 64), sebaceomas (n = 3), sebaceous adenomas (n = 2), sebaceous epithelioma (n = 1), sebaceous carcinomas (n = 26), and one unclassified

Table 1. Prevalence of various sebaceous neoplasms after revision

Neoplasms	Total (before revision)	Agreement	Total (after revision)
Nevus sebaceus	89 (42.9%)	78	85 (46.7%)
Sebaceous hyperplasia	81 (39.1%)	58	64 (35.1%)
Sebaceous adenoma	5 (2.41%)	2	2 (1.1%)
Sebaceous carcinoma	28 (13.5%)	26	26 (14.3%)
Sebaceous epithelioma	1 (0.48%)	1	1 (0.5%)
Sebaceoma	3 (1.44%)	3	3 (1.6%)
Unclassified sebaceous lesion			1 (0.5%)
	207	168	182

Table 2. Comparison of the previous diagnoses and the reviewed diagnoses of sebaceous hyperplasia

Neoplasm	Total (before revision)	Agreement	Disagreement	Revised diagnosis
Sebaceous hyperplasia	81	58	23	Nevus sebaceus (n = 9) Seborrheic keratosis (n = 3) Fibrous papule (n = 2) Lentigo (n = 1) Phimosis (n = 1) Intradermal nevus (n = 1) Comedone (n = 1) Trichoepithelioma (n = 1) Wart (n = 1) Hemangioma (n = 1) Actinic keratosis (n = 1) Chronic dermatitis (n = 1)
Percentage	100	71.6	28.4	

Table 3. Comparison of the previous diagnoses and the reviewed diagnoses of nevus sebaceus (of Jadassohn)

Neoplasm	Total (before revision)	Agreement	Disagreement	Revised diagnosis
Nevus sebaceus	89	78	11	Sebaceous hyperplasia (n = 4) Seborrheic keratosis (n = 2) Actinic keratosis (n = 2) Hair hamartoma (n = 2) Unclassified sebaceous lesion (n = 1)
Percentage		87.6	12.4	

Table 4. Comparison of the previous diagnoses and the reviewed diagnoses of sebaceous adenoma

Neoplasm	Total (before revision)	Agreement	Disagreement	Revised diagnosis
Sebaceous adenoma	5	2	3	Sebaceous hyperplasia (n = 2) Chronic dermatitis (n = 1)
Percentage	100	40	60	

Table 5. Comparison of the previous diagnoses and the reviewed diagnoses of sebaceous carcinoma

Neoplasm	Total (before revision)	Agreement	Disagreement	Revised diagnosis
Sebaceous carcinoma	28	26	2	Sweat gland carcinoma (n = 1) Lymphoepithelial-like carcinoma (n = 1)

Table 6. Sebaceous neoplasms (n = 182) in relation to gender and location

All sebaceous neoplasms	Total number (%)
Gender	
Female	97 (53.2%)
Male	85 (46.7%)
Location	
Scalp	38 (20.9%)
Eyelid	30 (16.4%)
Face	20 (10.9%)
Nose	19 (10.4%)
Forehead	18 (9.8%)
Cheek	17 (9.3%)
Others	40 (21.9%)
Total cases	182 (100%)

Table 7. Nevus sebaceus (n = 85) in relation to age, gender and location

Nevus sebaceus	Total number (%)
Gender	
Females	38 (44.7%)
Males	47 (55.3%)
Mean age	21.94
(at the time on the biopsies performed)	
Prepubertal (≤ 10)	14 (16.5%)
Pubertal (11-17)	32 (37.6%)
Postpubertal (≥ 18)	38 (44.7%)
Unknown	1 (1.1%)
Location	
Scalp	34 (40%)
Forehead	11 (13%)
Face	11 (13%)
Cheek	5 (5.9%)
Neck	4 (4.7%)
Chin	4 (4.7%)
Others	16 (18.8%)

sebaceous lesions that could not be considered a neoplasm, were found. Females: males were 97:85 (n = 97). In general, most sebaceous neoplasms occurred on the scalp and face (n = 142) while the remainder (n = 40) presented on the other sites (Table 6).

Among 85 nevus sebaceus, 47 males and 38 females were found, the most common site was the scalp (n = 34, 40%) followed by face (n = 31, 36.5%), and neck (n = 4, 0.5%) (Table 7). Clinically, this lesion usually presents as well-defined, linear verrucous plaque (Fig. 1). All showed the typical histopathologic features, *i.e.* acanthosis, papillomatosis, hyperkeratosis, and abundant mature sebaceous glands in the upper dermis (Fig. 2). Ectopic apocrine glands were also present in some samples (Fig. 3). Various cutaneous neoplasms had been reported in association with this lesion (Fig. 4) and usually occurred after puberty

Table 8. Neoplasms in association with nevus sebaceus

Neoplasm	Total
Primitive follicular induction (basaloid follicular proliferation)	7
Syringocystadenoma papilliferum	3
Trichilemmoma (wart)-like lesion	4
Trichoblastoma	3
Trichoepithelioma-like lesion	1
Sebaceous adenoma	1
Tumor of follicular infundiculum	1
Mucoepidermoid carcinoma	1
Total	21

(Table 8). In the present study, complicated tumor transformation was noted in 14 nevus sebaceus (n = 14, 15.8%), in which 21 neoplasms had been arising, *i.e.* primitive follicular induction (n = 7) (Fig. 5), syringocystadenoma papilliferum (n = 3) (Fig. 6), trichilemmoma (wart)-like lesion (n = 4) (Fig. 7A, B), trichoblastoma (n = 3) (Fig. 8), and one of each of trichoepithelioma-like lesion, sebaceous adenoma, tumor of follicular infundibulum, and mucoepidermoid carcinoma. More than one neoplasm within a lesion of nevus sebaceus was found in two patients. Primitive follicular induction, trichoepithelioma, and trichoblastoma were found in one patient (Fig. 4). Interestingly, multiple neoplasms as trichilemmoma, trichoblastoma, sebaceous adenoma, syringocystadenoma papilliferum, tumor of follicular infundibulum, and mucoepidermoid carcinoma occurred within two lesions of nevus sebaceus (Fig. 9A-E).

Sixty-four sebaceous hyperplasias (29 males, 35 females) were found and patients' ages ranged from 5 to 79 years (mean age 47.3 years). This neoplasm is common in elderly persons (n = 47, 73.4%). The most common site was the nose (n = 18, 28.1%) followed by cheeks (n = 11, 17.2%), face (n = 8, 12.5%), forehead (n =7, 10.9%), and eyelid (n = 5, 7.8%) (Table 9). All sebaceous hyperplasias showed groups of hyperplastic mature sebaceous glands located higher in the dermis. Each sebaceous gland composed of 1-2 layers of germinative basaloid cells at the

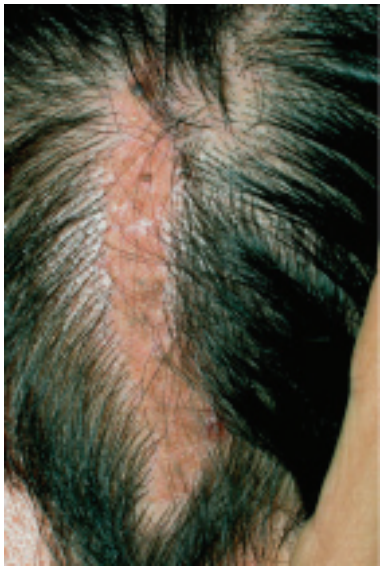

Fig. 1 Nevus sebaceus: the lesion characteristically presents as linear verrucous patch or plaque

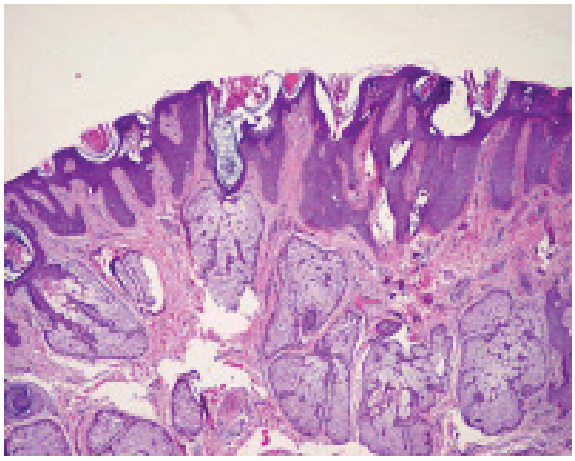

Fig. 2 Nevus sebaceus: the lesion commonly shows acanthosis, papillomatosis and sebaceous gland hyper-plasia; the typical histopathologic features (x10)

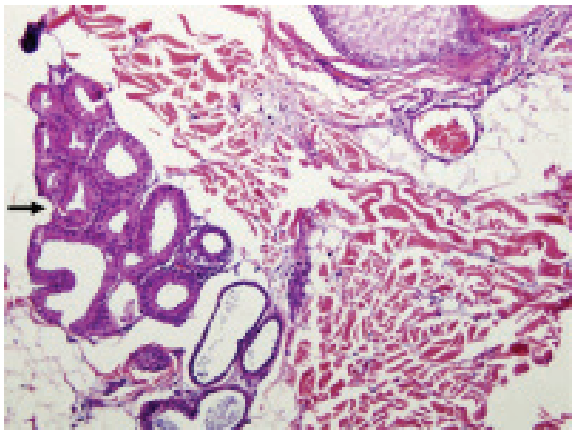

Fig. 3 Nevus sebaceus: ectopic apocrine glands are not uncommon in this lesion (x20)

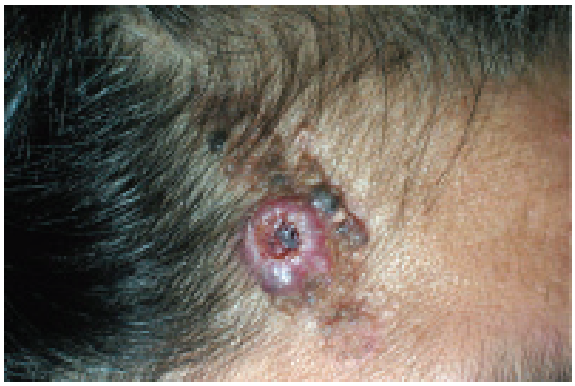

Fig. 4 Nevus sebaceus: postpubertal or tumoral phase; note the nodule arising from the lesion in which, in this patient, are trichilemmoma, syringocystadenoma papilliferum

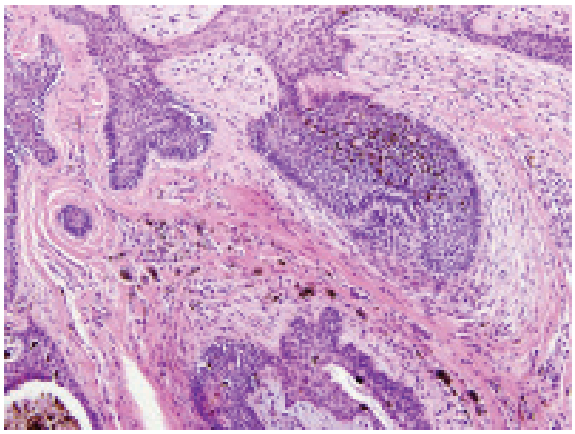

Fig. 5 Nevus sebaceus: in this example basaloid follicular proliferation composed of predominant basaloid cells with peripheral palisading like those found in basal cell carcinoma was present (x20)

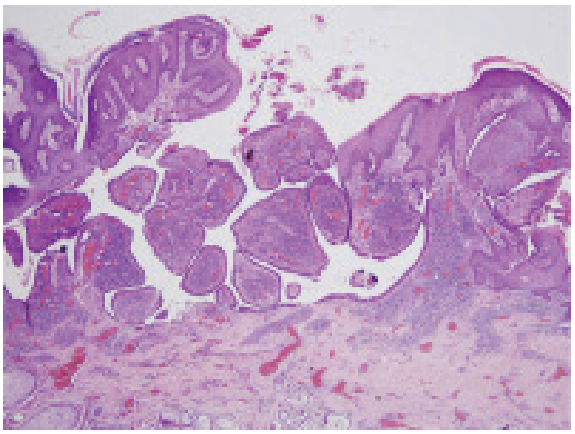

Fig. 6 Nevus sebaceus: an invagination typical of syringocystadenoma papilliferum was present in the center (x10)

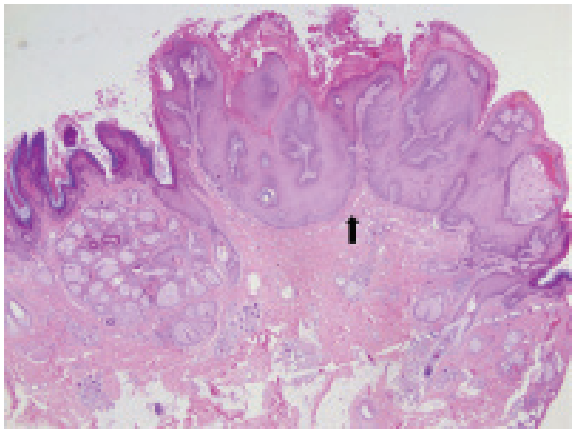

Fig. 7A Nevus sebaceus: a trichilemmoma was arising in the upper right corner of this field (x2)

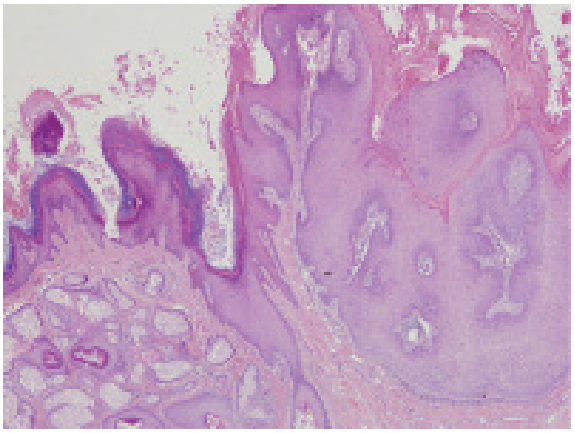

Fig. 7B Nevus sebaceus: note the characteristic lobulated mass composed of predominant clear cells (x10)

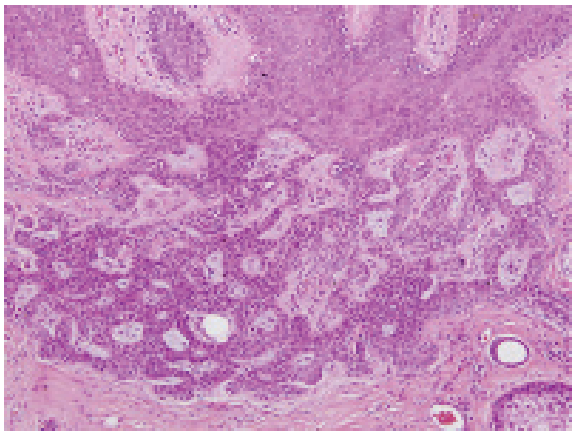

Fig. 8 Nevus sebaceus: trichoblastoma is also a common associated neoplasm, as was found in this patient (x10)

periphery and, centrally located, was a large amount of mature sebocytes. All these sebaceous glands drained into a dilated central duct (Fig. 10). Atypia, mitosis, or necrosis should be absent in this lesion.

Two sebaceous adenomas (1.1%), one male with lesion on his cheek, one female with lesion on the chin, were found. Both sebaceous adenomas presented as a multilobulated mass composed of sebaceous lobules being surrounded by collagenous pseudocapsule (Fig. 11A). At the periphery of each sebaceous lobule were multiple layers of small germinative (basaloid) cells with round or oval vesicular nuclei and scanty cytoplasm. These cells blended with centrally located, mature sebaceous cells (sebocytes) that were much larger and possessed pale-staining foamy cytoplasm with central crenate nuclei (Fig. 11B).

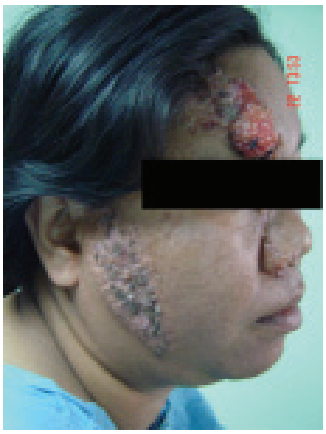

Fig. 9A Nevus sebaceus: multiple neoplasms were arising within 2 lesions of nevus sebaceus in a 66-year-old female, *i.e.* trichoblastoma, trichilemmoma, sebaceous adenoma, tumor of follicular infundibulum, syringocystadenoma papilliferum as well as mucoepidermoid carcinoma

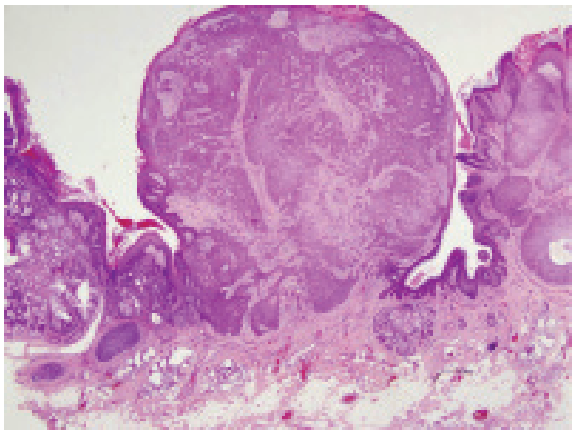

Fig. 9B Nevus sebaceus: multiple neoplasms were arising within each of the verrucous nodules from the patient (Fig. 9A). Note desmoplastic trichilemmoma in the center, sebaceous adenoma on the left, and trichilemmoma on the right of this field (x2)

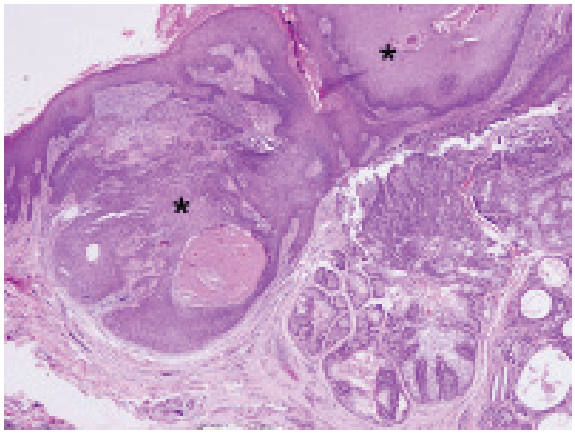

Fig. 9C Nevus sebaceus: some nodules possessed multiple neoplasms in aggregation. Note 2 trichilemmomas (*) and sebaceous adenoma (in the lower right corner)

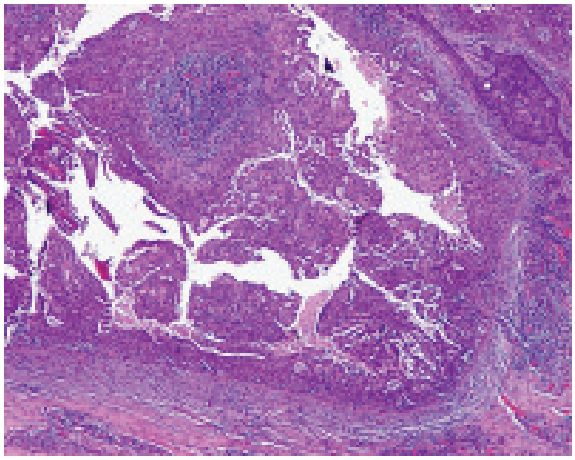

Fig. 9D Nevus sebaceus: mucoepidermoid carcinoma was also found. It presented as ill-defined nodules composed of predominant squamous cells admixed with mucigenic cells (x10)

Peripheral palisading as well as mitosis was occasionally noted in some samples. As a rule, necrosis or atypical mitosis was absent.

All sebaceomas (n = 3) presented as a symmetrical, dermal located mass with well-demarcated lateral and deep margins. Basaloid cells were predominant inside this mass and typically arranged into large lobules or nests separated by a cellular or sclerotic stroma (Fig. 12A). This neoplasm shared histologic similarities with basal cell carcinoma, which is the lack of peripheral palisading, the presence of stromal cleft, and the aggregated clusters of mature sebocytes within these tumor nests, and was helpful criteria in distinguishing sebaceoma from basal cell carcinoma with certainty (Fig. 12B). Well-defined sebaceous lobules, as those usually found in sebaceous adenoma, should not be obvious.

Sebaceous epithelioma (n = 1), a rare sebaceous neoplasm, was found. It was characterized by a well-circumscribed dermal mass of predominant basaloid cells arranging in solid-nodular, lobular, adenoid, or lacy-reticular proliferation, and, in some

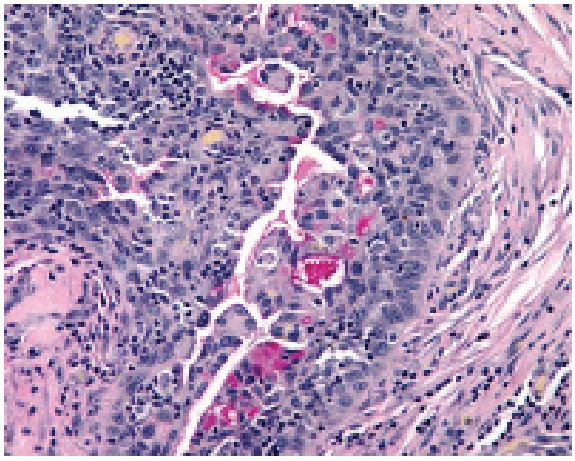

Fig. 9E Nevus sebaceus: these mucogenic cells showed positive staining to mucicarmine staining (x10)

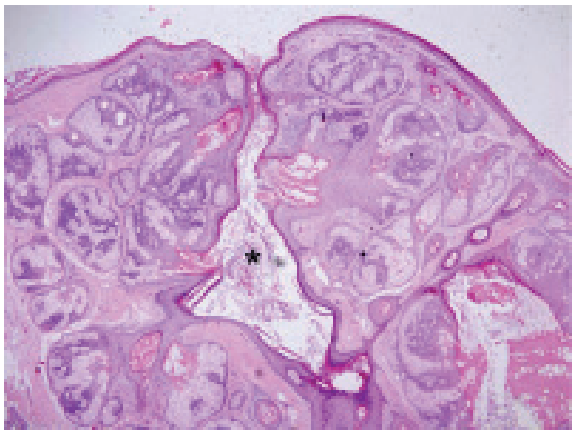

Fig. 10 Sebaceous hyperplasia: note multiple mature sebaceous glands surrounding a central dilated, sebaceous duct (*), the characteristic findings (x4)

Table 9. Sebaceous hyperplasia (n = 64) in relation to age, gender and location

Sebaceous hyperplasia	Total (%)
Gender	
Female	35 (54.7%)
Male	29 (45.3%)
Age (at the time on the biopsies performed)	
≤ 40	17 (26.6%)
> 40	47 (73.4%)
Means	47.3 years (range between 5-79 years)
Location	
Forehead	7 (10.9%)
Face	8 (12.5%)
Eyelid	5 (7.8%)
Cheek	11 (17.2%)
Nose	18 (28.1%)
Others	15 (23.4%)

Table 10. Sebaceous carcinomas (n = 26) in relation to age, gender and location

Sebaceous carcinoma	Total (%)
Gender	
Female	17 (65.4%)
Male	9 (34.6%)
Age (at the time on the biopsies performed)	29-92 years (means 59.4 years)
Location	
Ocular	24
Face	1
Extraocular	1

foci, were connected to the epidermis like those found in basal cell carcinoma, peripheral palisading or stromal cleft-like spaces were occasionally found in some samples (Fig. 13A). It differed from basal cell carcinoma by the presence of varying degree of sebaceous differentiation containing inside this lesion (Fig. 13B). Sebaceous carcinoma is a malignant sebaceous neoplasm. It is rare and has been divided into ocular, occurring about the eyelid (Fig. 14A), and extraocular, in areas other than the eyelids. Twenty-six sebaceous carcinomas were found and the eyelid (n = 24, 92.3%) was the most common site with a female and male ration of 17: 9. Most patients were in elderly and their ages ranged between 29-92 years (mean age 59.4 years) (Table 10). The tumor size varied from 0.4-7 cm. The histopathologic features of both ocular and extraocular sebaceous carcinomas had in common the presence of a multilobulated mass composing of a disorderly admixture of basophilic germinative sebaceous cells with round or oval-shaped nuclei. They occasionally contained several nucleoli and more mature larger sebocytes with vacuolated, soap-bubble cytoplasm (Fig. 14B, C). The differentiated sebocytes were typically strongly positive to epithelial membrane antigen (EMA) (Fig. 14D) and were carcinoembryonic antigen (CEA) negative. When the sebocytes were fewer and inconspicuous, *i.e.* the biopsy of small-size or less differentiated, the immunostudy of EMA would be very helpful in detecting these sebocytes within sebaceous neoplasms. Pleomorphism was

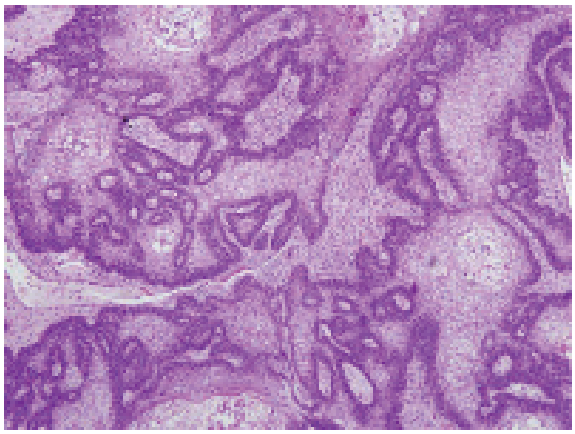

Fig. 11A Sebaceous adenoma: this tumor typically presented as a multilobulated mass composed of sebaceous lobules of various size and shape, note the dense connective tissue surrounding these sebaceous lobules (x10)

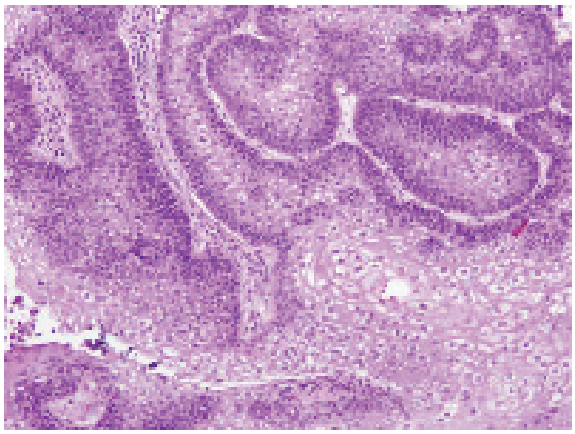

Fig. 11B Sebaceous adenoma: each sebaceous lobule was composed of multiple layers of undifferentiated basophilic (basaloid) cells, note small group of sebocytes at the center of each lobule (x20)

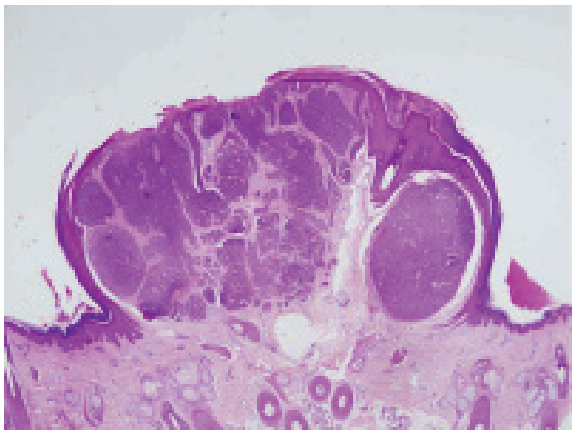

Fig. 12A Sebaceoma: note the typical well-demarcated lobulated mass composed of predominant basaloid cells surrounded by dense fibrotic stroma in the dermis, the characteristic features (x4)

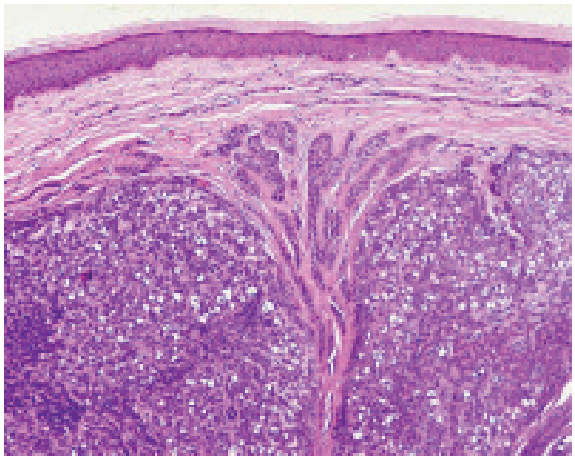

Fig. 12B Sebaceoma: note the sebocytes arranging in isolated cell or small groups (clusters) inside of these lobules (x10)

usually prominent in high-grade sebaceous carcinoma (Fig. 14E). Mitosis was variable, ranging from less than 10/10 hpf to, at times, up to more than 90/10 hpf (Fig. 14E). Necrosis occurred often (n = 19) (Fig. 14B) and angiolymphatic invasion was noted in two patients. Some biopsies, *i.e.* those of small sample size, contain no accompanying epidermal portion (n = 7). Those containing epidermal portion (n = 19) showed pagetoid spreading (n = 12). Infiltration of subcutaneous tissue or, occasionally, skeletal muscle invasion was frequent. Patients with complete post-operative follow-up (n = 19) displayed four local recurrences. No patients showed wide-spread metastasis or died from this malignancy.

Discussion

The reviewed diagnoses of most sebaceous neoplasms agreed with the previous diagnoses (n = 168, 81.1%) while the minority (n = 39, 18.8%) disagreed. The errors in diagnosis might be due to biopsies of small sample-size or of less differentiation. In both instances, the typical histopathologic features as well as sebocytes within these biopsies were rarely observed. As a rule, sebaceous neoplasms should

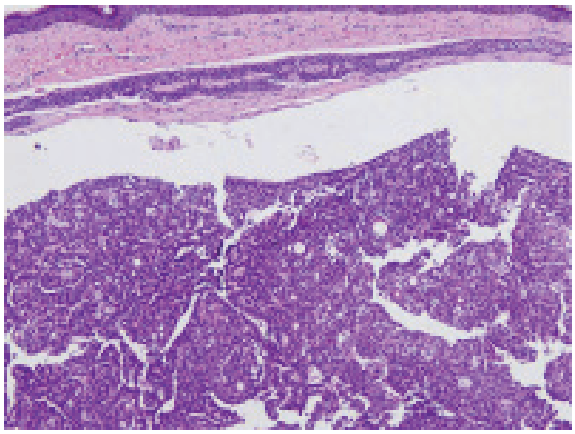

Fig. 13A Sebaceous epithelioma: the lesion is composed of predominant basaloid cells like those found in basal cell carcinoma (x10)

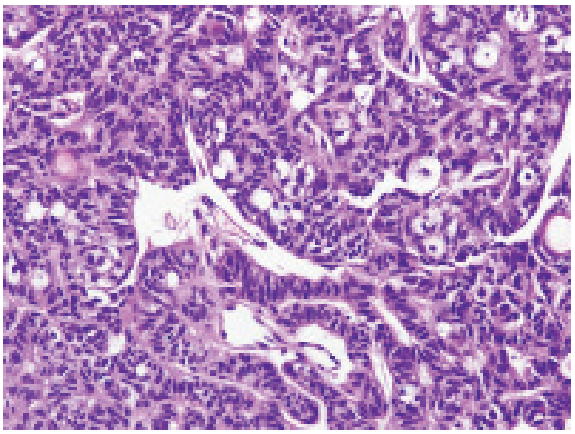

Fig. 13B Sebaceous epithelioma: Note the sebocytes arranging in either isolated cell or small nests (clusters) inside the basaloid lobules; peripheral palisading and cleft-like spaces were also frequent (x40)

contain lipid-laden, vacuolated cells, or sebocytes. These sebaceous neoplasms occasionally displayed complex sebaceous, pilar, sweat gland differentiation. One hundred eighty two sebaceous neoplasms among 8819 skin biopsies in a nine-year period (from 1997 through 2005) were found. Among these were nevus sebaceus (n = 85), sebaceous hyperplasia (n = 64), sebaceoma (n = 3), sebaceous adenoma (n = 2), sebaceous epithelioma (n = 1), and sebaceous carcinomas (n = 26). Sebaceous hyperplasia and nevus sebaceus shared some histopathologic overlap and sometimes were difficult to distinguish from each other especially in biopsies of small sample-size in which the epidermal portion as well as the sebaceous glands was less evident (occasionally absent) and inadequate for evaluation. In this situation, the clinical findings, including the patients' age were helpful in distinguishing between both lesions.

Nevus sebaceus is commonly present at birth and, in general, will possess complex differentiation, *i.e.* proliferation of keratinocytes, sebaceous glands including ectopic apocrine glands. Usually, this neoplasm does not cause the patient to seek medical attention until the second decade when it turns to be prominent and aggressive and, subsequently, many neoplasms come into being. Its clinical features are distinctive and easily diagnosed only by clinical examination. Most samples, similar to those observed in the present study, display typical histopathologic features *i.e.* acanthosis, papillomatosis, hyperkeratosis, and a large number of mature sebaceous glands and, occasionally, ectopic apocrine glands in the dermis[1-3]. Many benign and malignant neoplasms had been reported arising within this lesion. Syringocystadenoma papilliferum and trichoblastoma are the two most common neoplasms, followed by trichilemmoma, sebaceoma, and basaloid follicular induction (hamartoma)[4]. Many malignant neoplasms are also known to be arising within this lesion as well and the most common seemed to be basal cell carcinoma[4]. The authors' study corresponded to those in previous studies that found 21 complicated neoplasms arising within 14 lesions of nevus sebaceus, *i.e.* trichilemmoma (wart-like lesion) (n = 4), primitive follicular induction (n = 7), syringocystadenoma papilliferum (n = 3), trichoblastoma (n = 3), and one of

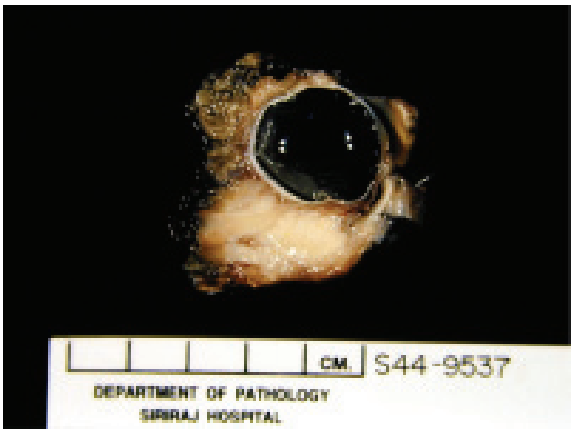

Fig. 14A Sebaceous carcinoma: note the infiltrative mass around the orbit, the characteristic finding

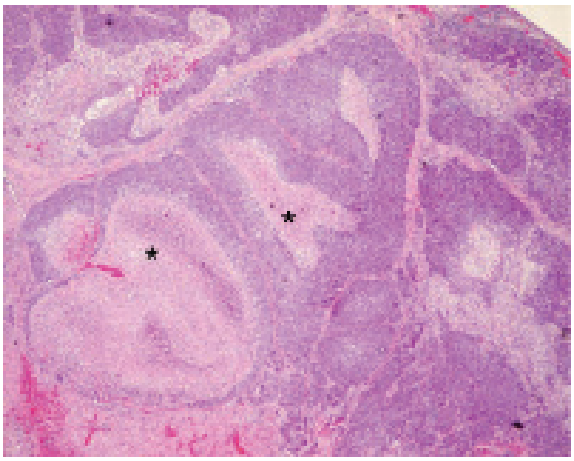

Fig. 14B Sebaceous carcinoma: this malignancy is usually composed of sebaceous lobules of varying size and shape. Note the large areas of necrosis inside these lobules (*) (x10)

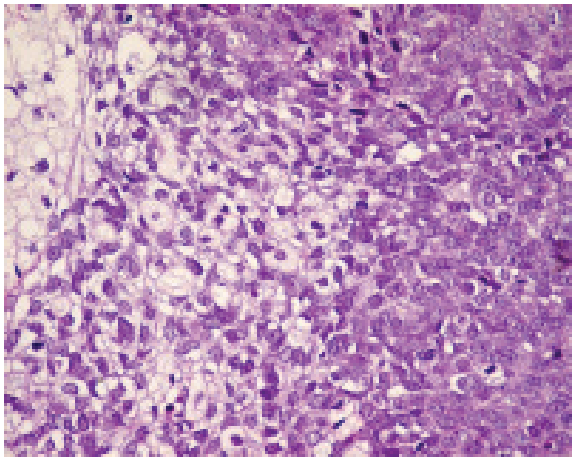

Fig. 14C Sebaceous carcinoma: each sebaceous lobules contained basaloid cells and more differentiated, vacuolated-cytoplasm sebocytes (x40)

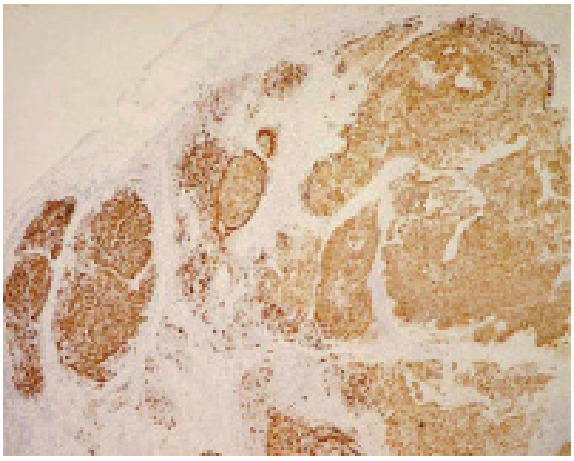

Fig. 14D Sebaceous carcinoma: by immunostudy, these malignant sebocytes showed strongly positive staining to EMA (x10)

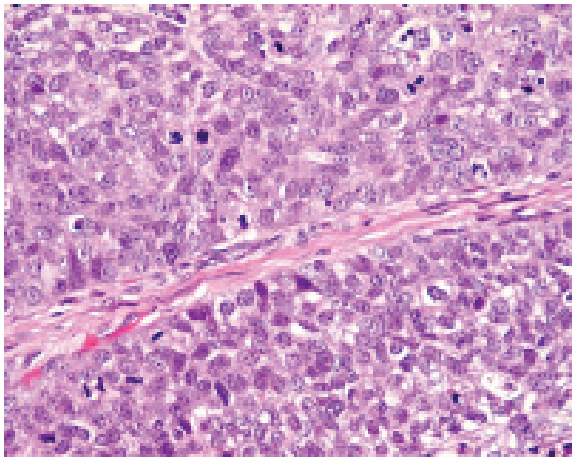

Fig. 14 Sebaceous carcinoma: both basaloid cells and sebocytes show obvious pleomorphism, mitosis including abnormal mitosis (x40)

each of trichoepithelioma, sebaceous adenoma, tumor of follicular infundibulum, and mucoepidermoid carcinoma. The necessity of prophylactic excision of nevus sebaceus or only adequate close follow-up still has been debated. The frequency of tumor-associated neoplasms in nevus sebaceus in the present review (n = 14, 15.8%) suggested that prophylactic excision should be warranted.

In the general population, sebaceous hyperplasia is more common than nevus sebaceus. The clinical presentation is distinctive and usually presents as small, yellowish papules with central umbilication. Elderly persons are commonly affected and the face is the most common site. This neoplasm is easily diagnosed only by the clinical presentations. Most of them will be left untreated and, as a consequence, will explain why it is less prominent than nevus sebaceus in the authors' study. The histopathologic features are characteristically composed of a variable numbers of mature sebaceous lobules that will connect to the skin through short, hairless infundibular canals[1, 5-8]. Sebaceous adenoma is a benign sebaceous neoplasm typically presenting as a well-defined lobulated mass composed of sebaceous lobules with varying degree of maturation, as those found in sebaceous hyperplasia. It differs from sebaceous hyperplasia by a comparative

increase in number of basaloid cells and fewer sebocytes. Basaloid cells in sebaceous hyperplasia were fewer in number and sebocytes will be collecting into larger aggregations in the center of each sebaceous lobule. By definition, the number of sebocytes and basaloid cells inside each sebaceous lobule in sebaceous adenoma will be approximately equal[1]. Cystic variant as well as the presence of multiple lesions of sebaceous adenoma had been reported in association with Muir-Torre syndrome and, recently, had been suggested as marker lesions of this syndrome[9]. The etiology is unknown but sebaceous adenoma sometimes had been reported in patients with long-term administration of cyclosporine[10].

In sebaceoma, sebocytes inside the sebaceous lobules will be less and inconspicuous and usually presenting as scatter isolated cells, ill-defined small groups/clusters among the small basaloid cells[11,12]. Larger aggregations of sebocytes, usually found in sebaceous adenoma and sebaceous hyperplasia, rarely occurred. The term "sebomatricoma" had been proposed to encompass benign neoplasms with sebaceous differentiation, *i.e.* superficial epithelioma with sebaceous differentiation and some unclassified benign sebaceous neoplasms that commonly occurred in nevus sebaceus[13,14].

The histopathologic features of sebaceous epithelioma closely resemble those in basal cell carcinoma. The nature of sebaceous epithelioma is still in debate to determine whether it is benign neoplasm with sebaceous differentiation or, authentically, basal cell carcinoma. The presence of a well-defined mass with symmetrical configuration with foci of sebaceous differentiation and lack of definite invasion supported the benign nature of this neoplasm, like those described by Dinneen[15] rather than that of an authentic malignant neoplasm such as basal cell carcinoma with sebaceous differentiation[16].

Sebaceous carcinoma is a rare, aggressive sebaceous neoplasm. It is divided into ocular, occurring about the eyelids, and extraocular that will occur on the skin elsewhere, except on the eyelids. The ocular sebaceous carcinoma is far more common than extraocular. Elderly persons and females are usually affected. Sebaceous carcinoma is composed of sebaceous lobules similar to other sebaceous neoplasms. It is diagnosed on the basis of the infiltrative growth pattern and less well-defined sebaceous lobules as well as the presence of prominent pleomorphism, necrosis, and mitosis including abnormal mitosis are helpful diagnostic discriminants. Local recurrences and wide-spreading metastasis are frequent[17,18]. Sebaceous carcinomas had statistically significantly increased levels of p53 compared to benign sebaceous neoplasms (50% versus 11%), Ki-67 (30% versus 10%), and add significantly reduced levels of bcl-2 (7% versus 56%) and p21 (16% versus 34%)[19]. Four recurrences out of 26 sebaceous carcinomas were found. All developed about the original site (eyelids). Neither distant metastasis nor mortality from this malignancy was found.

Conclusion

One hundred eighty two sebaceous neoplasms were included whereas sebaceous carcinoma was more than expected (n =26). By immunological studies, both benign and malignant sebocytes usually express epithelial membrane antigen (EMA). This marker was very helpful in many aspects, *i.e.* for detecting the inconspicuous sebocytes from the surrounding basaloid cells especially in biopsies of small-size or samples with less differentiation and for distinguishing sebaceous neoplasms from other non-sebaceous neoplasms. Complicated nevus sebaceus (n = 14, 15.8%) in which 21 neoplasms were noted and included trichilemmoma (wart-like lesion) (n = 4), primitive follicular induction (n = 7), syringocystadenoma papilliferum (n = 3), trichoblastoma (n = 3), and one of each of sebaceous adenoma, tumor of follicular infundibulum, trichoepithelioma, and mucoepidermoid carcinoma. The frequent occurrences of associated neoplasms in nevus sebaceus suggested that the prophylactic excision was the treatment of choice and should be considered.

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การศึกษาย้อนหลังของเนื้องอกรยางค์ชนิดไขมันในโรงพยาบาลศิริราชมหาวิทยาลัยมหิดล ในช่วงระยะ 9 ปี (พ.ศ. 2540-2548)

เจน มโนนุกูล, สรยุทธ ขจรวุฒิเดช

ภูมิหลัง: *เนื้องอกหรือมะเร็งของต่อมไขมัน (sebaceous neoplasms) พบน้อยเมื่อเปรียบเทียบกับเนื้องอกหรือมะเร็งของรยางค์อื่น ๆ เช่น เนื้องอกหรือมะเร็งของขน (follicular neoplasms) ของต่อมเหงื่อ (eccrine neoplasms) หรือ ต่อมกลิ่น (apocrine neoplasms) เป็นต้น sebaceous neoplasms มีหลายชนิดโดยแต่ละชนิดจะมีลักษณะทางพยาธิวิทยาแตกต่างกัน แต่ถือหลักว่าจะพบเซลล์ชนิด sebocytes ที่มีลักษณะเป็นเซลล์ขนาดใหญ่ ซัยโตพลาสมใสเป็นฟอง (vacuolated, soap-bubble) ซึ่งอาจพบเป็นเซลล์เดี่ยว ๆ หรือ รวมกันเป็นกลุ่ม กระจายอยู่ภายในรอยโรค*

วัตถุประสงค์: *(1) เพื่อศึกษาจำนวนของเนื้องอกของต่อมไขมันต่าง ๆ ได้แก่ nevus sebaceus, sebaceous hyperplasia, sebaceous adenoma, sebaceoma, sebaceous epithelioma, superficial epithelioma with sebaceous differentiation และมะเร็งของต่อมไขมัน (sebaceous carcinoma) ที่ได้รับการวินิจฉัยจากภาควิชาพยาธิวิทยา โรงพยาบาลศิริราช มหาวิทยาลัยมหิดล ตั้งแต่ปี พ.ศ. 2540-2548 (2) เพื่อศึกษาจำนวนและชนิดของเนื้องอกหรือมะเร็ง ซึ่งเกิดขึ้นภายในเนื้องอกชนิด nevus sebaceus*

วัสดุและวิธีการ: *ศึกษาย้อนหลังเนื้องอกหรือมะเร็งทั้งหมด ได้แก่ Nevus sebaceous, sebaceous hyperplasia, sebaceous adenoma, sebaceoma, sebaceous epithelioma, superficial epithelioma with sebaceous differentiation, sebaceous carcinoma รวมทั้งเนื้องอกหรือมะเร็งที่มีคำว่า "sebaceous" ซึ่งรวบรวมจากฐานข้อมูลคอมพิวเตอร์ภายในภาควิชาพยาธิวิทยา โรงพยาบาลศิริราช ในช่วงเวลาดังกล่าว โดยสไลด์ของเนื้องอกหรือมะเร็งทั้งหมดจะได้รับการวินิจฉัยใหม่ รวมทั้งบันทึกข้อมูลด้านอายุ เพศ ตำแหน่งของเนื้องอกหรือมะเร็งนั้น ๆ เปรียบเทียบกับการวินิจฉัยเดิม เพื่อพิจารณาความถูกต้องในการวินิจฉัยเนื้องอกหรือมะเร็งแต่ละชนิด*

ผลการศึกษา: *พบเนื้องอกหรือมะเร็งของต่อมไขมันจำนวน 207 ราย จากชิ้นเนื้อผิวหนังทั้งหมด 8,819 ราย ตั้งแต่ปี พ.ศ. 2540-2548 ซึ่งหลังจากได้รับการวินิจฉัยใหม่ และคัดแยกแล้วพบเพียง 182 ราย ซึ่งได้แก่ nevus sebaceus จำนวน 85 ราย (46.7%) sebaceous hyperplasia จำนวน 64 ราย (35.1%) sebaceoma จำนวน 3 ราย (1.6%) sebaceous adenoma จำนวน 2 ราย (1.1%) sebaceous epithelioma จำนวน 1 ราย (0.5%) และมะเร็งชนิด sebaceous carcinoma จำนวน 26 ราย (14.3%) นอกจากนี้ ยังพบเนื้องอกหรือมะเร็ง (n = 21) เกิดขึ้นภายในรอยโรค nevus sebaceus จำนวน 14 ราย ซึ่งได้แก่ trichilemmoma ซึ่งอาจมีลักษณะคล้ายหูด (wart) (n = 4) primitive follicular induction (n = 7) syringocystadenoma papilliferum (n = 3) trichoblastoma (n = 3) และ trichoepithelioma, sebaceous adenoma, tumor of follicular infundibulum และ mucoepidermoid (adenosquamous) carcinoma (n = 1)*

สรุป: *พบมะเร็งต่อมไขมัน (sebaceous carcinoma) จำนวน 26 ราย ซึ่งส่วนใหญ่เกิดบริเวณเปลือกตา เนื้องอกที่พบบ่อยที่สุด ได้แก่ nevus sebaceus และสรุปได้ว่าเนื้องอกชนิดนี้ควรได้รับการรักษาโดยการผ่าตัดแต่เนิ่น ๆ (prophylactic excision) เนื่องจากพบเนื้องอกหรือมะเร็งชนิดต่าง ๆ เกิดขึ้นภายในรอยโรคได้บ่อย การศึกษาทางอิมมูโนวิทยาพบว่า epithelial membrane antigen (EMA) สามารถย้อมติดชัดเจนใน sebocytes ทั้งเซลล์ปกติ และเซลล์มะเร็ง ดังนั้น EMA จึงมีประโยชน์อย่างมากในการวินิจฉัยเนื้องอกหรือมะเร็งของต่อมไขมัน (sebaceous neoplasms) โดยเฉพาะชิ้นเนื้อจากเนื้องอกหรือมะเร็งที่มีการพัฒนาไม่ชัดเจน (less differentiation) ซึ่งจะพบ sebocytes จำนวนน้อยอีกทั้งช่วยในการสืบค้นเซลล์มะเร็ง (malignant sebocytes) ที่กระจายไปยังต่อมน้ำเหลือง และอวัยวะภายในต่าง ๆ ด้วยเช่นกัน*