# Mixed Tumor of the Skin: Clinicopathological Study of Seven Cases

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***Background*** **: Mixed tumor of the skin or chondroid syringoma is a benign neoplasm characterized by histological features of a mixture of epithelial and mesenchymal components. It is a rare and benign appendageal tumor, found mostly on the head and neck, and present as an asymptomatic, firm, subcutaneous nodule. There have only been a few reported cases in Korea.**

***Objectives*** **: This study was aimed to characterize the clinical and histopathlological features of mixed tumor of the skin.**

**Methods: We reviewed the clinical data and histologic slides of seven patients who have been diagnosed with mixed tumor of the skin by histopathological examination.**

***Results*** **: There were six male patients and only one female. Age of onset of mixed tumor of the skin varied from 26 to 65 years. All patients had the lesion on the head: perioral area (3 cases), nose (2 cases), cheek (1 case), and temple area (1 case). Each tumor was a solitary, asymptomatic, and firm, about 0.5-1.5 cm sized, subcutaneous nodule. Histopathologically, all 7 cases presented apocrine differentiation. Two cases showed follicular differentiation, and 2 cases showed sebaceous differentiation. Every tumor showed myxoid stroma except two with typical chondroid matrix. Adipose metaplasia of the matrix was present in 2 cases. In 3 cases, the so-called hyaline cells were rich in the stroma.**

***Conclusion*** **: Mixed tumor of the skin was most commonly seen as an asymptomatic, firm subcutaneous nodule on the head. Tumors showing apocrine differentiation were more common than that of eccrine differentiation. All 7 cases presented apocrine differentiation. Follicular and sebaceous differentiation might occur in apocrine type of mixed tumors of the skin. The stroma of mixed tumor of the skin might be myxoid, chondroid, or adipose.**

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*Key Word* : Mixed tumor of the skin

Mixed tumor of the skin is histologically similar to benign mixed tumor of the salivary gland[1]. It is presented as a solitary, well-circumscribed, firm, intradermal or subcutaneous nodule that mainly occurs on the head and neck[1, 2]. Headington grouped mixed tumor of the skin into eccrine and apocrine types based on the histological appearance of the lumina[3]. Winkelmann and Muller suggested the eccrine origin of mixed tumor of the skin by histochemical and enzymatic studies[4]. However, the origin of this tumor is still a controversial topic. Elder et al classified mixed tumor of the skin as two types: one with tubular and cystic, partially branching lumina, and the other with small, tubular lumina[5].

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Table 1. Summary of clinical data of mixed tumor of the skin

| | Sex/Age | Duration | Site | Size | Clinical manifestation | Associated symptoms | Treatment |
|---|---|---|---|---|---|---|---|
| 1 | M/42 | 3 years | Upper lip | 0.7×0.7 cm | Nodule | None | Excision |
| 2 | M/26 | 3 months | Angle of lip | 0.5×1.0 cm | Subcutaneous nodule | None | Excision |
| 3 | M/36 | 1 year | Nose | 0.7×1.0 cm | Nodule | None | Excision |
| 4 | M/35 | 1 year | Rt. cheek | 1.0×1.0 cm | Subcutaneous nodule | None | Excision |
| 5 | F/32 | 5 years | Lt. forehead | 0.5×0.5 cm | Subcutaneous nodule | None | Excision |
| 6 | M/65 | 4 months | Upper lip | 1.0×1.2 cm | Subcutaneous nodule | None | Excision |
| 7 | M/43 | 1 year | Nose | 0.5×0.5 cm | Subcutaneous nodule | None | None* |

* Patient refused the treatment

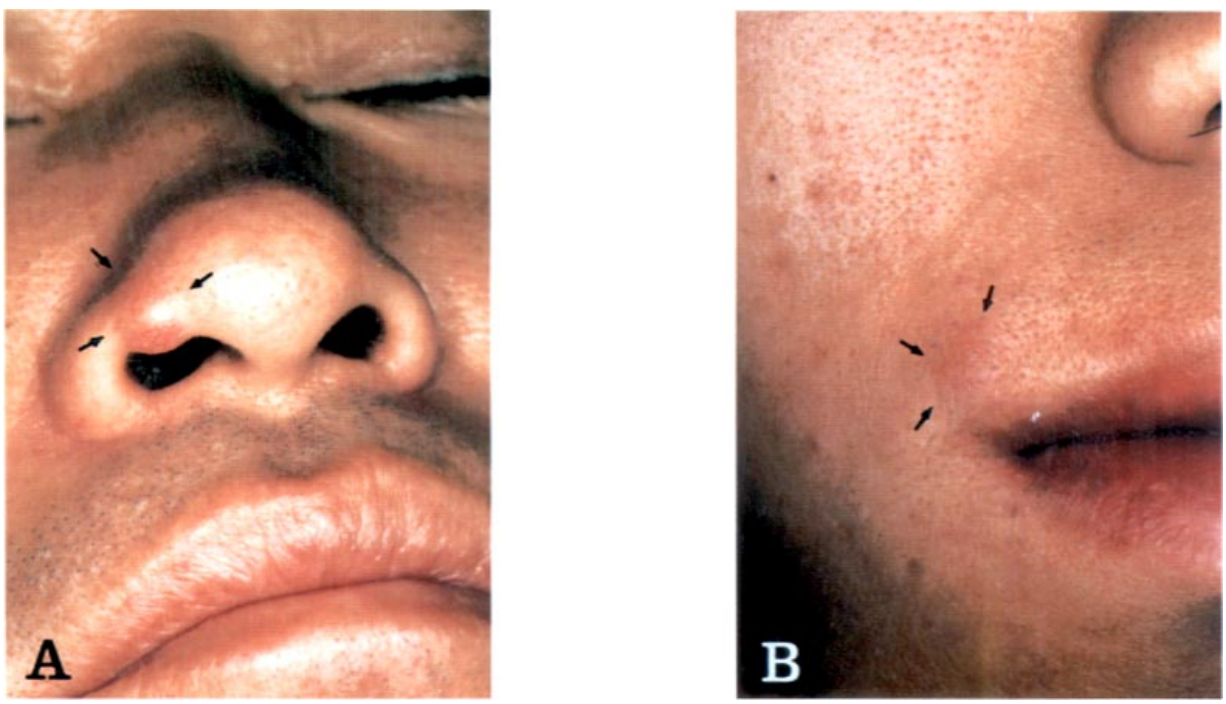


Fig. 1. A solitary asymptomatic intradermal or subcutaneous nodule on the nose (A) and perioral area (B).

## MATERIALS AND METHODS

Seven cases of mixed tumor of the skin were identified from the pathology files from January 1991 to June 1999. The hospital charts and biopsy slides of 7 patients with mixed tumor of the skin were reviewed. Clinical evaluations were performed regarding the age, sex, age of onset, site, clinical manifestations and associated symptoms. In all seven cases, formalin-fixed, paraffin-embedded tissues were processed for routine microscopy, and the histologic sections were stained with hematoxylin and eosin.

## RESULTS

### Clinical Features

The clinical features are summarized in Table 1.

There were 6 men and 1 woman, with the age from 26 to 65 years (mean 40 years). Age of the onset of mixed tumor of the skin varied from 26 to 65 years (mean 38 years). All cases presented as a solitary, asymptomatic dermal or subcutaneous nodule. All patients had the lesion on the head: perioral area (3 cases), nose (2 cases), cheek (1 case), and temple area (1 case) (Fig. 1). The duration of lesions before biopsy ranged from 3 months to 5

**Table 2.** Summary of histopathological features of mixed tumor of the skin

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 |
|---|---|---|---|---|---|---|---|
| Tumor | | | | | | | |
| Lobular pattern | + | + | + | + | + | + | + |
| Epidermal continuity | + | - | +* | - | - | - | - |
| Capsule | - | - | - | - | - | - | - |
| Pattern of differentiation | | | | | | | |
| Apocrine | + | + | + | + | + | + | + |
| Eccrine | - | - | - | - | ± | ± | - |
| Follicular | + | - | - | - | + | - | - |
| Sebaceous | + | - | - | + | - | - | - |
| Stroma | | | | | | | |
| Myxoid | + | + | + | + | + | + | + |
| Chondroid | - | + | - | - | - | + | - |
| Adipose metaplasia | + | - | + | - | - | - | - |
| Hyaline cell | - | - | + | - | - | + | + |

* : May be the effect of the multiple treatment of electrodessication
± : Only focal area

years. The greatest dimension of the tumors ranged from 0.5 to 1.2 cm (mean 0.8 cm). All patients except one were treated by the complete local excision. Only one patient (case 7) did not want any further treatment. In 6 patients, no evidence of recurrence or metastasis was observed over a follow-up period of 4 months to 7 years.

**Pathological Features**

The histopathological features are summarized in Table 2.

On scanning magnification, all mixed tumors of the skin were expansile, with sharp peripheral circumscription, but non-encapsulated (Fig. 2). Tumor continuity with the epidermis, presumably infundibular, was noted in 2 cases (case 1, 3). But one patient (case 3) received many variable treatments including shave off and electrodessication, so only one patient (case 1) had a real epidermal continual tumor. There was no evidence of ulceration or tumor necrosis in any of the cases.

The tumors were heterogeneous in composition, displaying a variable spectrum of apocrine, eccrine, follicular, and sebaceous differentiation with mesenchymal stroma.

Apocrine differentiation was characterized by the presence of elongated tubular structures of different sizes and shapes, some of which were straight but most of which ramified in branching fashion lined by two layers of epithelial cells. The luminal cells were columnar with round nuclei at their bases and eosinophilic cytoplasms. These cells showed evidence of decapitation secretion (Fig. 3A). The cells in the outer layer were cuboidal and also had round nuclei and eosinophilic cytoplasms. In this study, all cases showed apocrine differentiation. Case 5 and 6 showed focal eccrine differentiation with small duct-like structures lined by a single layer of cuboidal cells near the area of apocrine differentiation (Fig. 3B). The follicular differentiation was present in two cases (Fig. 3C). One case (case 1) showed several well-differentiated keratotic cysts, the other case (case 5) showed a keratinizing microcyst. Sebaceous differentiation was seen in 2 cases (case 1, 4) (Fig. 3D, E).

Deposit of mucin and chondroid was present in the stroma. Case 1 presented a slightly fibrotic change in the stroma. Within the stroma, spindle cells and polygonal cells were arranged as solitary units. The features, polygonal cells in the matrix surrounded by haloes like those around chondrocytes, were considered chondroid differentiation. Every tumor showed myxoid stroma, but just 2 cases(case 2, 6) presented a typical chondroid matrix (Fig. 4A, B). Numerous adipocytes within the stroma of the neoplasm, so-called adipose metaplasia, were seen in 2 cases (case 1, 3) (Fig. 4C).

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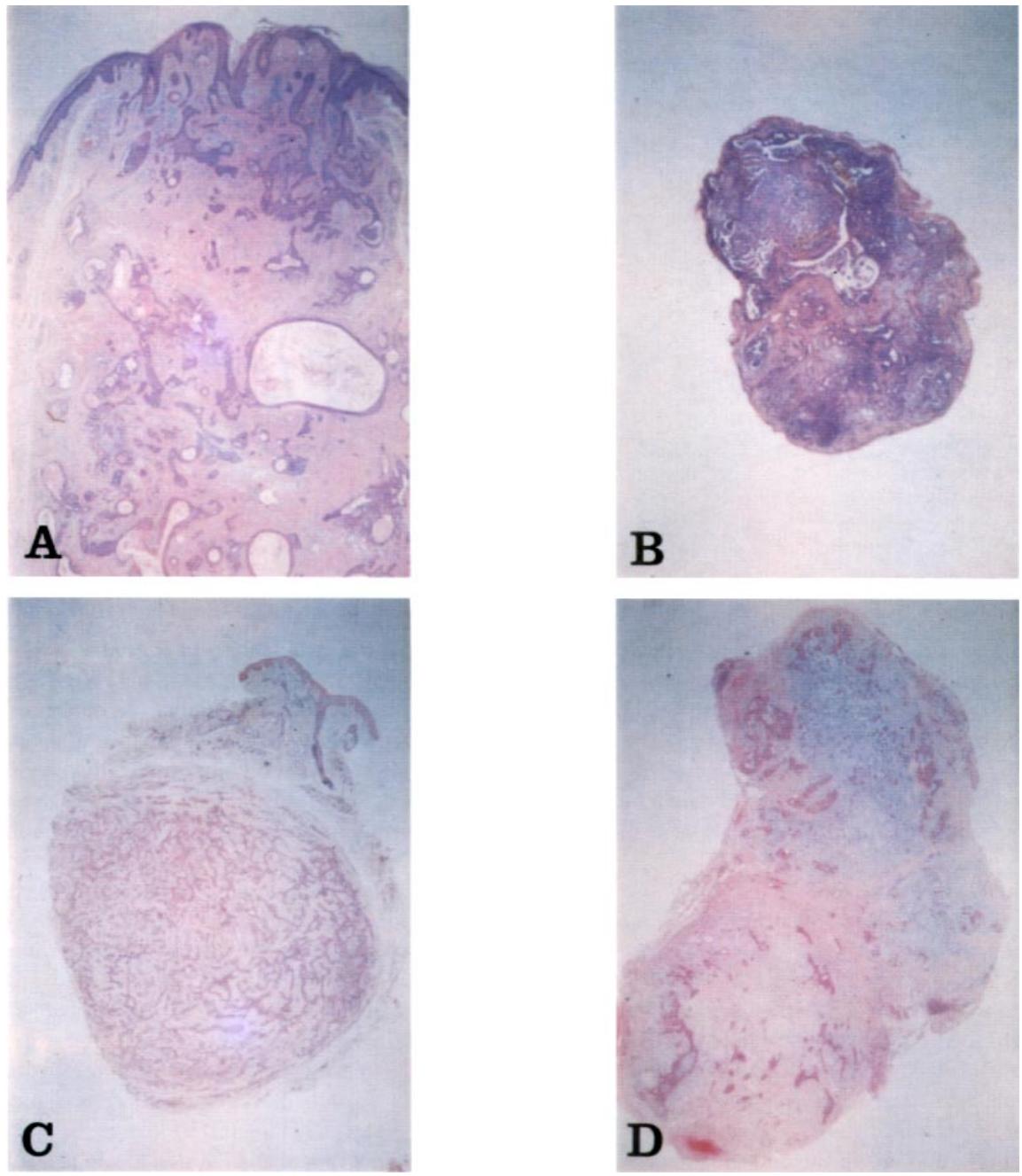


Fig. 2. Scanning magnification of mixed tumor of the skin (H&E). (A) Case 1. Epidermal continual tumor with keratin cysts. (B) Case 2. A shelled out mass. (C) Case 5. A well-circumscribed dermal tumor composed of many tubular structures. (D) Case 6. A shelled out mass with prominent mesenchymal matrix with epithelial islands. ( × 10)

In 3 of the 7 tumors, plasmacytoid hyaline cells with abundant eosinophilic cytoplasms were arranged predominantly in nests and sheets (Fig. 5). But there was neither atypia nor mitotic figure.

## DISCUSSION

Mixed tumor of the skin or chondroid syringoma is a benign appendageal tumor of the skin and histologically similar in appearance to benign mixed

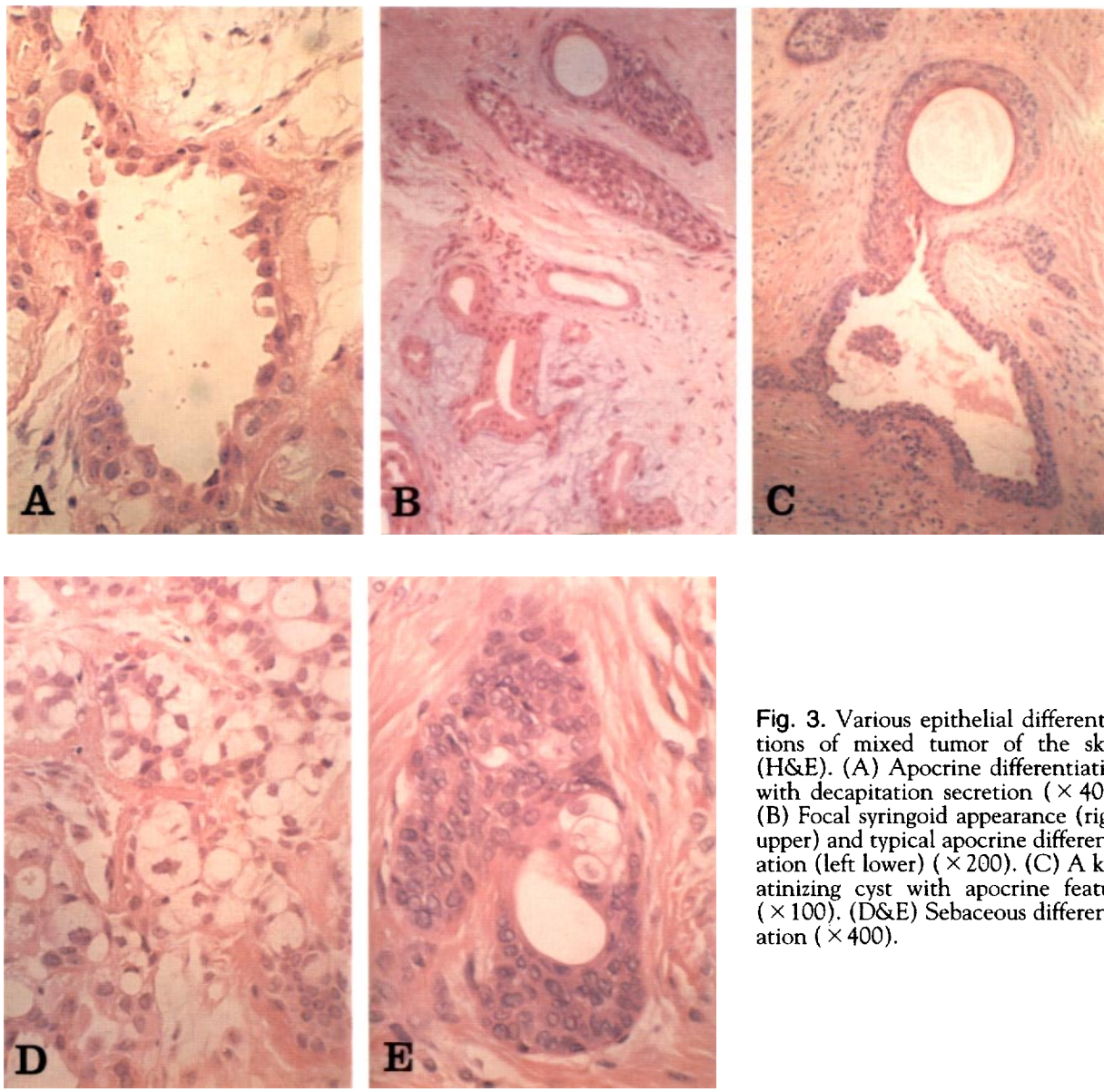


Fig. 3. Various epithelial differentiations of mixed tumor of the skin. (H&E). (A) Apocrine differentiation with decapitation secretion (×400). (B) Focal syringoid appearance (right upper) and typical apocrine differentiation (left lower) (×200). (C) A keratinizing cyst with apocrine feature (×100). (D&E) Sebaceous differentiation (×400).

tumor (pleomorphic adenoma) of the salivary gland[1]. Clinically mixed tumor of the skin presents as a solitary slow-growing, non-tender, firm, subcutaneous or intracutaneous nodule[1]. It is adherent to the overlying skin, but it is not fixated to the underlying deep structures[2,6]. Two-thirds of the cases occurred on the head and neck in descending order of frequency as nose, cheek, upper lip, scalp, forehead, and chin[2,6]. It showed a male predominance of 2:1 to 5:16. In this study, every case occurred on the head, and there was a male predominance of 6:1.

Hirsh and Helwig[7] proposed the following microscopic criteria for a diagnosis: 1) nests of cuboidal or polygonal cells; 2) tubuloalveolar structures lined by two or more rows of cuboidal cells; 3) ductal structures composed of one or two rows of cuboidal cells; 4) occasional keratin cysts; and 5) a matrix of varying appearance with hematoxylin and eosin staining. In addition, several cases of mixed tumor of the skin with histologic evidence of follicular and sebaceous differentiation have been described[1,7]. Headington proposed

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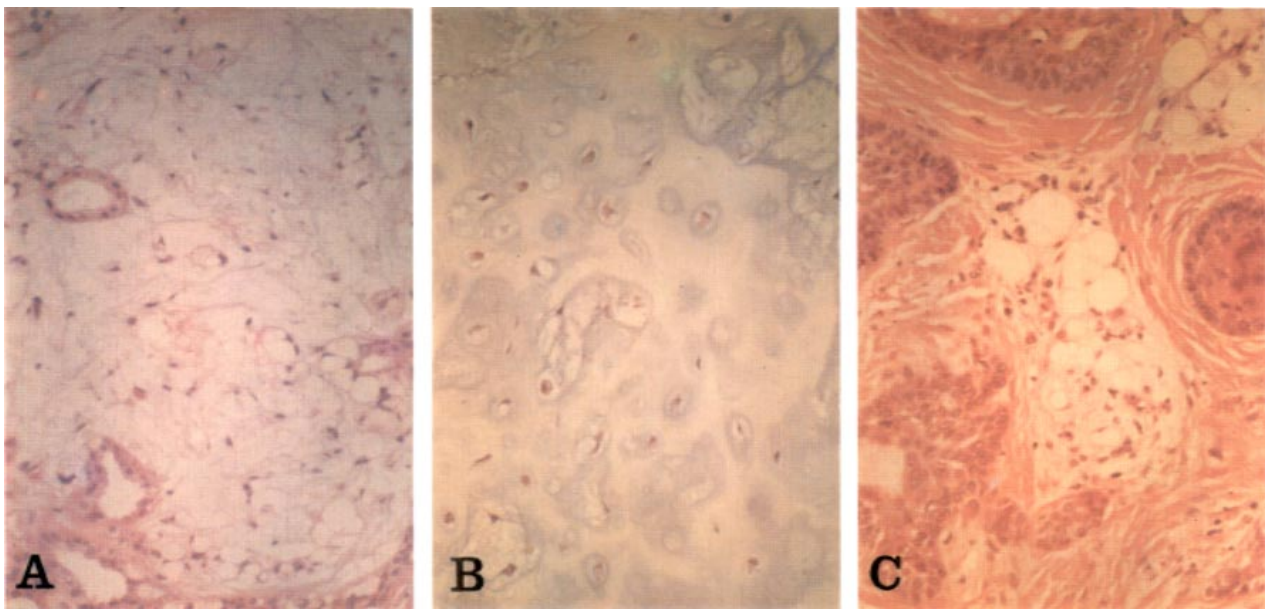


Fig. 4. The stroma of mixed tumor of the skin (H&E). (A) Common myxoid stroma (×200). (B) Chondroid stroma with chondrocyte like cells (×200). (C) Adipose metaplasia in the stroma (×200).

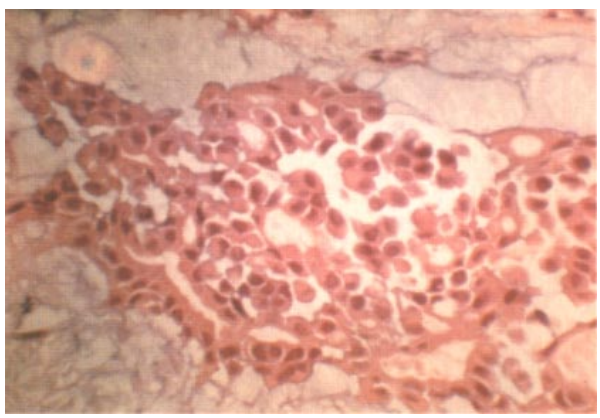

Fig. 5. Plasmacytoid hyaline cells with abundant eosinophilic cytoplasms (H&E, ×400).

two histologic groups and differentiated between an apocrine and eccrine type on the basis of the pattern of the lumina observed[3]: The apocrine type is characterized by tubular and cystic branching lumina lined by two layers of epithelial cells, while the eccrine type is characterized by small tubular lumina lined by a single layer of cuboidal epithelial cells. They are equivalent to the variants described by Elder et al[5] as chondroid syringoma with tubular branching lumina and chondroid syringoma with small tubular lumina. All our cases showed mainly the features of the former, but the features of the latter were observed partly in 2 cases. Hassab-El-Naby et al couldn't find both apocrine and eccrine features in the same specimen[8]. Because definite morphologic differentia between eccrine gland and apocrine gland is not always possible, we cannot assert that there was eccrine differentiation with apocrine differentiation in the same tumor. Follicular differentiation was seen in 29% of cases and sebaceous differentiation was noted in 29% of cases, too. Follicular and sebaceous differentiation with apocrine features was present in case 1, follicular and apocrine differentiation in case 5, and sebaceous differentiation with apocrine differentiation in case 4. This fact suggested the common embryologic derivation of the apocrine glands, sebaceous glands, hair follicles and their integration histologically as the folliculo-sebaceous-apocrine unit. Recently, Wong et al[9] reported so-called benign cutaneous adnexal tumor with combined folliculo-sebaceous, apocrine, and eccrine differentiation. Among their 8 cases, some showed chondroid syringoma-like features of myxoid or chondroid stroma. Because our case 1 presented not only epidermal continuity but also apocrine and folliculo-sebaceous differentiation, we thought that this tumor could be called benign cutaneous adnexal tumor with combined folliculo-sebaceous, apocrine, and eccrine differentiation .

The stroma of mixed tumor of the skin showed usually myxoid or chondroid features. Adipose metaplasia was the common feature of mixed tumor of the skin[1].

Some authors reported the presence of plasmacytoid hyaline cells in chondroid syringoma mimicking malignancy[10,11]. They showed plasmacytoid features arranged predominantly in nests and sheets. Because of these features there were many differential diagnoses of various malignant neoplasms including mucinous eccrine carcinoma, malignant melanoma, and myxoid chondrosarcoma[10].

The immunohistochemical findings in mixed tumors of the skin, unlike the findings in sections stained by hematoxylin and eosin, do not effectively distinguish apocrine from eccrine types. S-100 protein has been said to be present in epithelial cells of mixed tumor, and CEA has been noticed in the luminal border of glandular structures and secretion of mixed tumor[12,13]. Initially, GCDFP-15 was thought to be a marker of apocrine differentiation; however it was present in both normal apocrine and eccrine glands[14]. There were two hypotheses for the origin of polygonal cells in the stroma. One suggested the epithelial origin because of the positive result for S-100 protein and keratin and the negative result for actin[13]. The others suggested the myoepithelial origin and the production of chondroid from polygonal cells in the stroma[15]. Tsuji investigated the expression of Ca 15-3, KA-93, Ca 19-9, CD44 and BM-1 in normal skin and mixed tumor of the skin and suggested that mixed tumor of the skin might originate from, or differentiate into, the ducts and/or secretory elements of the eccrine sweat glands[16].

The treatment of choice is surgical excision, as in our cases. Among the 7 patients, one (case 7) patient didn't want excision after he was informed of the biopsy result. But the 6 patients whose tumors were excised did not experience recurrence in the follow up periods of 4 months to 7 years.

Mixed tumor of the skin is a benign tumor; however, a malignant form of mixed tumor of the skin showing anaplastic changes has been reported[2,6,17].

In conclusion, mixed tumors of the skin, chondroid syringomas were most commonly seen as an asymptomatic, firm subcutaneous nodule on the head. Tumors showing apocrine differentiation were more common than those showing eccrine differentiation. All our 7 cases presented apocrine differentiation. Follicular and sebaceous differentiation might occur in apocrine type of mixed tumors of the skin. The stroma of mixed tumor of the skin might be myxoid, chondroid, or adipose.

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