

## A Case of Papillary Eccrine Adenoma : Immunohistochemical Study

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A case of papillary eccrine adenoma on the right hand of a 84-year-old woman is reported. The tumor was 1 cm in diameter, occupying the whole thickness of the dermis. Histologically, the tumor was composed of dilated tubules of various sizes with intraluminal papillary projections, and was surrounded by a fibrous stroma. An immunohistochemical study revealed that the proliferating tubules were composed of the outermost layer of alpha-smooth muscle actin- positive and the inner layer of keratin 14-negative cells. This antigen expression pattern was comparable to that of the normal eccrine secretory coil, which indicates that the tumor differentiated toward the secretory coil of an eccrine sweat gland.

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*Key Words:* Papillary eccrine adenoma

Papillary eccrine adenoma, first described by Rulon and Helwig<sup>1</sup> in 1977, is a rare cutaneous tumor. The tumor presents as a solitary cutaneous nodule, localized in the dermis, and is characterized by numerous dilated tubules lined by a double layer of cells with intraluminal papillary projections surrounded by fibrous stroma<sup>1</sup>.

The cell origin of this tumor has been studied at some cases<sup>2-5</sup> in Korea. But, the direction of differentiation toward ductal or secretory coil of the eccrine sweat gland is still controversial.

We report an additional case of this rare neoplasm, studied by light microscopy and immunohistochemistry. The cell origin of this neoplasm is discussed and the literature is reviewed.

### CASE REPORT

A 84-year-old woman presented at our clinic with a solitary subcutaneous nodule on her right hand. The lesion had been present for 20 years and was asymptomatic. Examination revealed a hard, movable, light brown nodule (Fig. 1). The nodule measuring 1 cm in diameter was clinically diagnosed as foreign body granuloma or calcinosis cutis. The lesion was surgically excised and no evidence of recurrence was observed for 6 months.

On microscopic examination, a fairly well-circum



**Fig. 1.** A 1cm diametered, light brown colored, hard nodule on the hand.

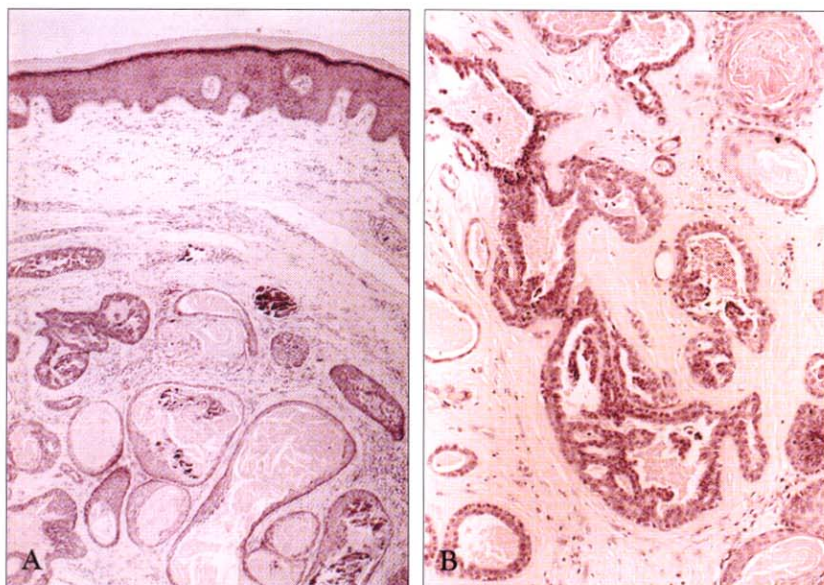
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**Fig. 2.** (A) Well circumscribed nodule composed of multiple dilated ducts in the dermis. Dilated ducts contain eosinophilic secretion and intraluminal papillation (H and E stain,  $\times 40$ ). (B) Dilated ducts lined by double layer of epithelium (H and E stain,  $\times 100$ ).

scribed but not encapsulated tumor of 1 cm in diameter was seen occupying the whole thickness of the dermis and pushing a short distance into the subcutis. The tumor was composed of numerous dilated epithelium-lined tubular structures of various sizes surrounded by fibrous stroma (Fig. 2A). The epidermis overlying the tumor presented with moderate acanthosis. The tubules were lined by two or more rows of neoplastic epithelium; a single row of cuboidal cells comprised the outermost layer, and the inner layer cells were cuboidal or columnar, and often formed papillary projections into the lumen (Fig. 2B). Papillary projections were composed solely of epithelium without the supporting stroma. The lumen either appeared empty or contained PAS-positive, diastase-resistant pink granular material characteristic of secretion or degenerative debris. There were no distinctive decapitation secretions. The tumor cells were uniform in size and mitotic figures were absent. The adjacent skin contained normal eccrine glands but no apocrine glands.

Immunoperoxidase staining was positive for S-100 protein in the cytoplasm of the epithelial cells of the tubules (Fig. 3A). Carcinoembryonic antigen (CEA) showed intense immunoreactivity with the cytoplasm of the most epithelial cells and with the luminal materials (Fig. 3B). The epithelial membrane antigen (EMA) also showed immunoreactivity with the cytoplasm of the epithelial cells lining the ducts and with the intraluminal secretions (Fig. 3C). The single

outermost layer of flattened cells was alpha-smooth muscle actin ( $\alpha$ -SMA) -positive (Fig. 4A) and keratin 14-positive, while the inner layer cells were devoid of staining (Fig. 4B).

## DISCUSSION

Papillary eccrine adenoma is a rare benign sweat gland tumor first described by Rulon and Helwig in 1977<sup>1</sup>. It is more common in females than males and presents principally as a dermal nodule or plaque. The extremities are the most frequent sites<sup>1,4</sup>. It ranges in size from 0.5 to 2.0 cm<sup>4</sup>. It has a benign clinical course and surgical excision is the choice of treatment<sup>6</sup>.

The recognition of papillary eccrine adenoma is important in that this neoplasm must be distinguished from aggressive digital papillary adenoma (adenocarcinoma), which has a more infiltrative growth pattern and shows nuclear atypism with conspicuous mitotic figures<sup>7</sup>. Moreover, differentiation from metastatic adenocarcinoma is of diagnostic importance.

Papillary eccrine adenoma is histologically distinctive in that the proliferating tubules are composed of two different types of cells; an outermost layer of cuboidal cells, and the inner cuboidal-to-columnar cells which demonstrate prominent intraluminal papillary projections. A connection



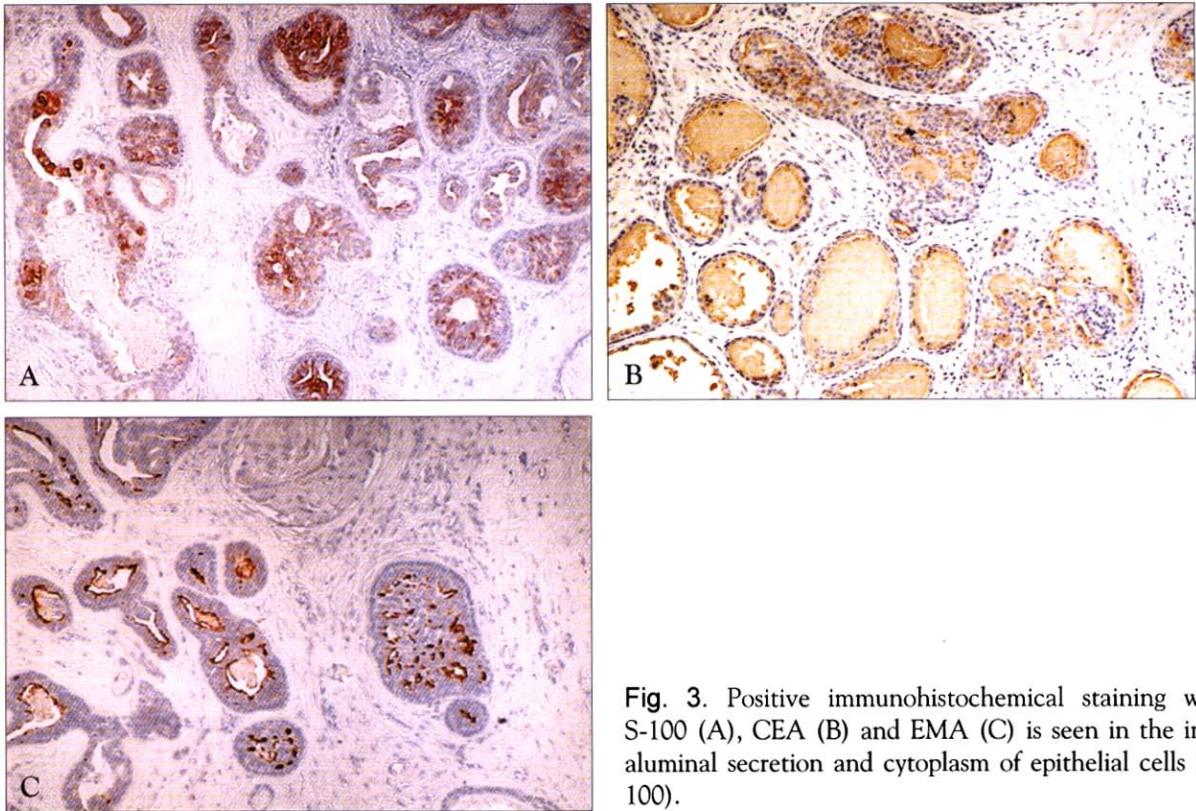


Fig. 3. Positive immunohistochemical staining with S-100 (A), CEA (B) and EMA (C) is seen in the intraluminal secretion and cytoplasm of epithelial cells ( $\times 100$ ).

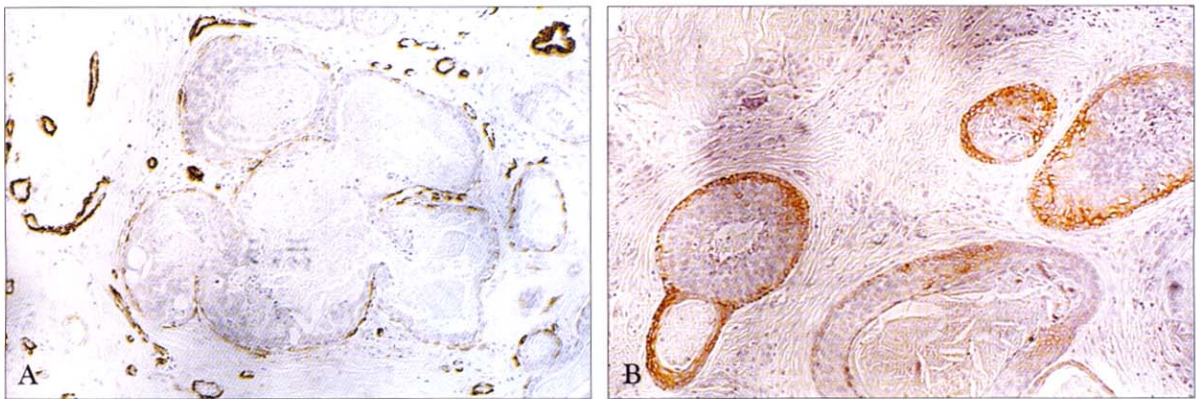


Fig. 4. The single outermost layer of flattened cells was  $\alpha$ -SMA-positive (A) and keratin 14-positive (B) ( $\times 100$ ).

between these tubules and the epidermis is seen<sup>8,9</sup>. A cystic structure with a thin epithelial wall composed of a one-cell layer, or cysts with squamous differentiation have occasionally been found<sup>10</sup>. In the cell morphology of the lining of the tubules, the lack of decapitation secretion indicates eccrine differentiation; tubular apocrine adenoma can be dif-

ferentiated by showing apocrine-type decapitation secretion<sup>11</sup>. Histo- and immunohistochemical studies as well as electron microscopic observation suggest that the differentiation of this neoplasm is toward eccrine sweat gland<sup>12</sup>. Regarding the cell origin, the microscopic appearance of a pattern of structures resembles that of the eccrine duct<sup>1</sup>. Histochemical

studies have shown the presence of amylophosphorylase<sup>13</sup>, and ultrastructural studies demonstrated the lack of dark and clear cells with secretory granules, intracellular canaliculi, and myoepithelial cells<sup>13,14</sup>, findings which support eccrine ductal differentiation. However, immunohistochemical findings of positivity for EMA, CEA, and S-100 protein indicate that this neoplasm differentiates toward eccrine secretory coil<sup>6,9,15</sup>. Another opinion is that this tumor differentiates toward both secretory and ductal portions of the eccrine sweat gland<sup>12,16</sup>. Immunohistochemistry is useful to determine the differentiation of tumors by comparing the antigen similarity to its normal counterpart. The results of the EMA, CEA, and S-100 protein expression were essentially the same as those previously reported in English literature<sup>6,9,15</sup> as well as Korean literature<sup>2-5</sup>.

But still, another reliable marker is necessary for this purpose. In this context, actin and keratins 14 are useful to differentiate between the eccrine ductal and secretory epithelium. In the normal eccrine gland,  $\alpha$ -SMA-labeled myoepithelial cells were situated at the secretory coil<sup>17</sup>. But, the ductal cells of normal eccrine gland were alpha-SMA-negative in both inner layer cells and outer layer cells<sup>17,18</sup>. In the same manner, keratin 14-labeled myoepithelial cells were situated at the secretory coil of normal eccrine gland<sup>18</sup>. But, the ductal cells of normal eccrine gland were keratin 14-positive in both inner layer cells and outer layer cells<sup>18,19</sup>. In this case, many  $\alpha$ -SMA-positive myoepithelial cells were found at the outermost layer of the tubular structure and many keratin 14-positive cells were

found at the outermost layer cells of the tubular structure but not at the inner layer cells of that. The staining of the  $\alpha$ -SMA-positive cells confirmed the cells to be myoepithelial cells, and negativity of keratin 14 of the inner layer cells suggests that the antigen expression is comparable to dark and clear cells of the normal eccrine secretory coil. These immunohistochemical results strongly suggest the tumor to be of eccrine coil origin and are summarized in Table 1.

We experienced a case of papillary eccrine adenoma which has distinct histological features and a benign clinical course, and immunohistochemical staining for CEA, S-100, EMA having agreement with previous reports<sup>2-5</sup> in Korea. But, the immunohistochemical stainings for  $\alpha$ -SMA and keratin 14 in this case have been not mentioned in the cases of papillary eccrine adenoma reported in Korea. This is the first case in Korea that strongly suggests the eccrine coil origin of papillary eccrine adenoma using the immunohistochemical methods with  $\alpha$ -SMA and keratin 14.

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**Table 1.** Summary of the Immunohistochemical Staining with  $\alpha$ -SMA and Keratin 14 in Normal Eccrine Gland and this Case (papillary eccrine adenoma)

	$\alpha$ -SMA	Keratin 14
Normal eccrine gland		
Duct cells		
Inner layer cells	—	+
Outer layer cells	—	+
Secretory coil		
Dark and clear cells	—	—
Myoepithelial cells	+	+
This case		
Inner layer cells	—	—
Outermost cells	+	+

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