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Case Report

Pigmented adenoid cystic carcinoma of the ear skin arising from the epidermis: a case report with immunohistochemical studies

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Abstract: Adenoid cystic carcinoma (ACC) in the skin is very rare; only about 60 cases have been reported. Herein presented is a case of pigmented ACC arising from epidermis of the ear skin. An 85-year-old man presented black tumor of the right ear. Dermatologists' diagnosis was basal cell carcinoma (BCC). Large biopsy was obtained. The biopsy showed proliferation of atypical basaloid cells arranged in a cribriform pattern. The tumor cells were continuous with epidermis, as if it arose from the epidermis. Focal areas show melanin deposition in the tumor cells. Mucin stains showed that the tumor cells and tubular lumens contained acidic mucin. Immunohistochemically, the tumor cells were positive for cytokeratin (CK) AE1/3, CK34BE12, CK5/6, CK7, CK14, p63, alpha-smooth muscle actin (ASMA), S100 protein, p53, Ki-67 (labeling 85%), KIT, PDGFRA and CD56. The tumor cells were negative for CK CAM5.2, CK8, CK18, CK19, CK20, EMA, desmin, CEA, HMB45, CD10, CD34, neuron-specific enolase, chromogranin, synaptophysin, CDX2, MUC1, MUC2, MUC5AC and MUC6. HMB-positive and S100-positive melanocytes were seen in a very few areas. Since characteristic cribriform pattern was recognized in the tumor and the tumor showed epithelial markers, myoepithelial markers (CD14, p63, ASMA, S100 protein) and KIT, the pathological diagnosis of ACC was made. No distant and lymph node metastasis is now seen. The patient will be treated by complete resection. The present cutaneous ACC was unique in that the ACC arose from the epidermis, had melanin pigment, and occurred in ear skin.

Keywords: Adenoid cystic carcinoma, ear skin, pigmented, immunohistochemistry

Introduction

Adenoid cystic carcinoma (ACC) is a malignant neoplasm of the major salivary glands. ACC is histologically characterized by cribriform pattern. Tubular and solid patterns are also recognized. ACC is composed of epithelial and myoepithelial cells. ACC also rarely occurs in the minor salivary glands, esophageal gland, bronchial glands, mammary glands, and skin. Cutaneous ACC is very rare; about 60 cases have been published [1-5]. All cases of the cutaneous ACC in the literature are case reports. ACC is believed to arise from eccrine and apocrine glands [1, 2]. There have been no cases of cutaneous ACC arising from the epidermis in the literature. In addition, there has been no case of cutaneous ACC containing melanin pigment. The sites of involvements are scalp and breast skin [4]. ACC of the ear skin has not been reported. In addition, no immunohistochemical studies of cutaneous ACC have been reported. Herein reported is a case of cutaneous ACC of the ear skin with immunohistochemical observations. Characteristically, the ACC contained melanin pigment and arose from the epidermis.

Case report

An 85-year-old man noticed a black tumor (1 x 1 x 0.5 cm) of the right ear, and consulted to our hospital. Dermatologists' diagnosis was basal cell carcinoma (BCC). A large biopsy was obtained. The biopsy showed proliferation of atypical malignant basaloid cells arranged in a cribriform pattern (**Figures 1** and **2**). The tumor cells were continuous with epidermis (**Figure 1**), as if it arose from the epidermis. Focal areas shows melanin deposition in the tumor cells (**Figure 3**). No palisading and cleft formations were

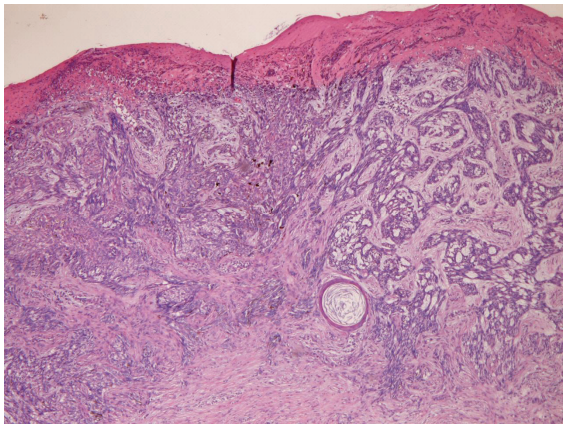

Figure 1. Low power view of the cutaneous tumor. The tumor is continuous to epidermis. The tumor cells show cribriform appearance. HE, x50.

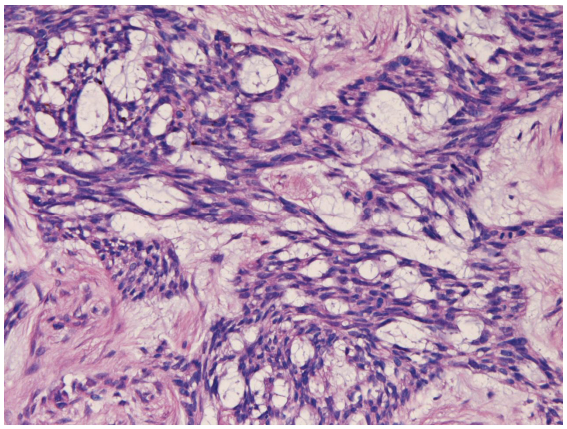

Figure 2. High power view. The tumor cells show typical cribriform pattern. Mucins are seen in their lumens. HE, x200.

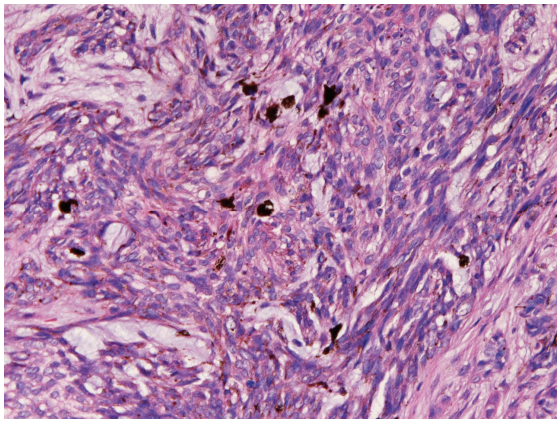

Figure 3. High power view. Some tumor cells contains melanin pigment. HE, x200

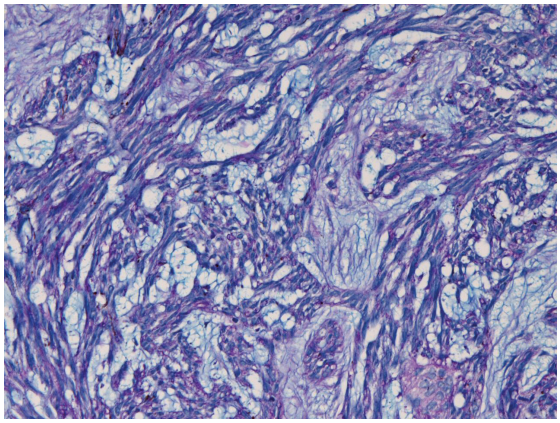

Figure 4. Alcian-blue/PAS stain showed acidic mucins in tumor cells and in the luminal lumens. Alcian blue/PAS, x200.

recognized.

Many 3-μm sections were obtained from the paraffin block. One of them was stained with diastase-PAS and Alcian blue. The remaining sections were subjected to immunohistochemistry. All immunostaining were pretreated by microwave oven heating for 7 minutes. The immunohistochemical study was performed, using the Dako Envision method, as previously described [5, 6].

Mucin stains showed that the tumor cells and tubular lumens contained acidic mucin (**Figure 4**). Immunohistochemically, the tumor cells were positive for cytokeratin (CK) AE1/3, CK34BE12, CK5/6 (**Figure 5A**), CK7, CK14, p63 (**Figure 5B**), α-smooth muscle actin (ASMA) (**Figure 5C**), S100 protein, p53 (**Figure 5D**), Ki-67 (labeling 85%) (**Figure 5E**), KIT (**Figure 5F**), PDGFRA and CD56 (**Figure 5G**). The tumor cells were negative for CK CAM5.2, CK8, CK18, CK19, CK20, EMA, CEA, desmin, HMB45, CD10, CD34, neuron-specific enolase, chromogranin, synaptophysin, CDX2, MUC1, MUC2, MUC5AC and MUC6. HMB-positive and S100-positive melanocytes were seen in a very few areas.

Since characteristic cribriform pattern was recognized in the tumor and the tumor showed epithelial markers, myoepithelial markers (CD14, p63, ASMA, S100 protein) and KIT, the pathological diagnosis of ACC was made. No

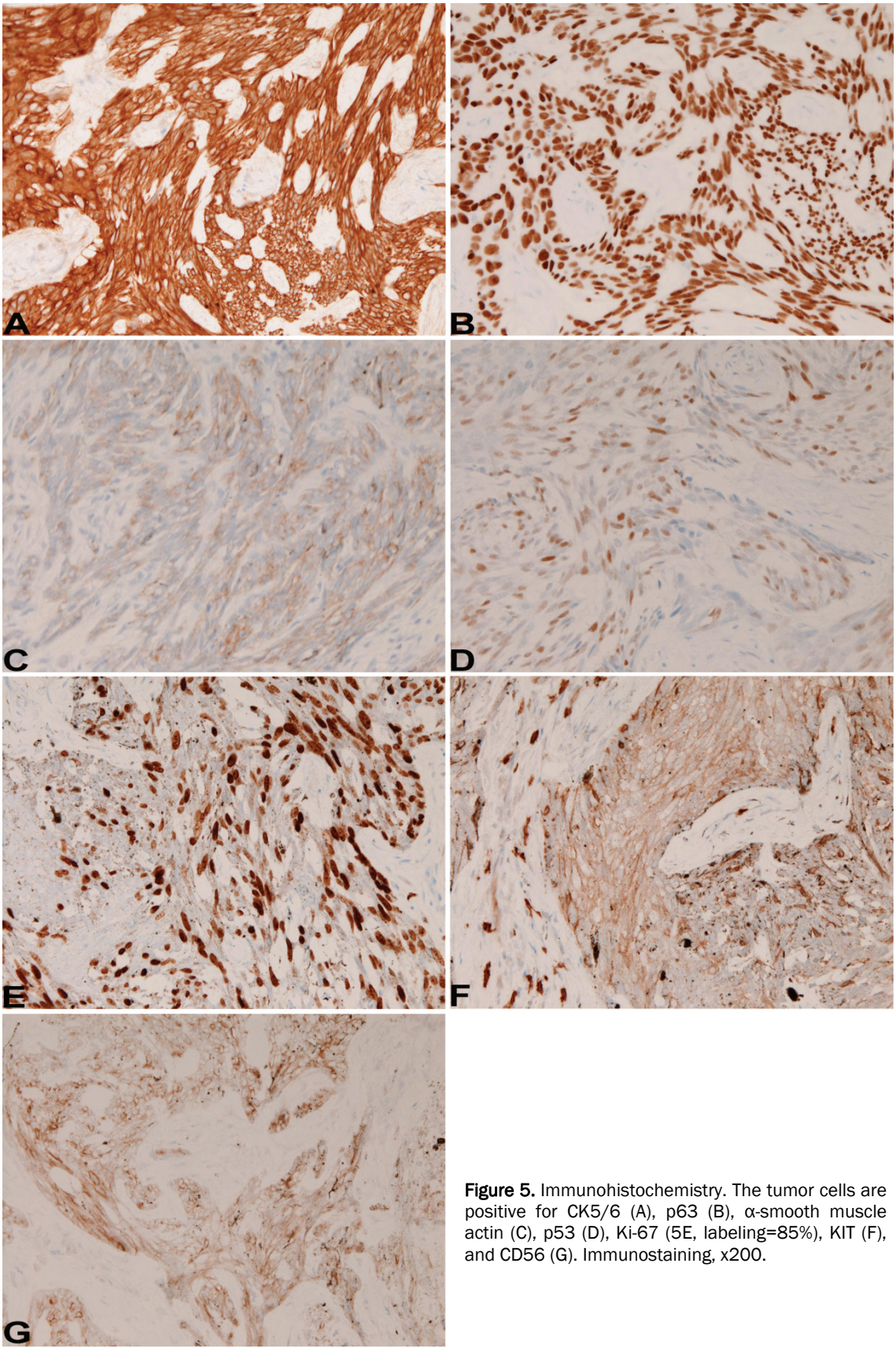

Figure 5. Immunohistochemistry. The tumor cells are positive for CK5/6 (A), p63 (B), α-smooth muscle actin (C), p53 (D), Ki-67 (5E, labeling=85%), KIT (F), and CD56 (G). Immunostaining, x200.

distant and lymph node metastasis is now seen. The patient will be treated by complete resection. The present cutaneous ACC was unique in that the ACC arose from the epidermis, had melanin pigment, and occurred in the ear skin.

Discussion

There is controversy with regard to the pathological diagnosis. The author believes that the current tumor is ACC. The positive p53 and high Ki-67 labeling (85%) indicate that the present tumor is malignant. The positive CKs indicate that the present tumor is malignant. The presence of mucins in tumor cells and lumens strongly suggests that the present tumor is ACC. ACC is composed of epithelial cells and myoepithelial cells. The positive myoepithelial markers (CK14, p63, ASMA and S100 protein) [8, 9] suggest that the tumor is composed of epithelial and myoepithelial cells and indicate that the current case is ACC. The negative palisading and cleft formations are in favor of ACC rather than BCC [1, 2]. KIT is expressed in ACC and mastocyte neoplasms in the skin. Therefore, the positive KIT in the present case may indicate that the present tumor is ACC.

The major differential diagnosis is nodular BCC. BCC is free from mucins, suggesting that the present tumor is not BCC. BCC does not express myoepithelial markers, suggesting that the present tumor is not BCC. BCC shows palisading and cleft formation, which was not seen in the present case. BCC never express KIT. These observations strongly suggest that the present tumor is not BCC.

Cutaneous ACC is believed to be derived from eccrine or apocrine glands, and histologically cutaneous ACC does not show contiguity with epidermis [1, 2]. The present cutaneous ACC showed contiguity with epidermis. In addition, the present tumor had melanin pigment and a small number of melanocytes. These findings suggest that the present ACC arose from epidermis. The positive expression of high molecular weight CKs (CKAE1/3, CK34BE12, CK5/6) and negative expression of low-molecular weight CKs (CK CAM5.2, CK8, CK18, CK19, CK20) indicate that the present ACC have characters of epidermal squamous epithelium, and suggest that the present ACC arose from the epidermis. The positive p63, a squamous cell marker, also support the above suggestion. This phenomenon has not been reported, to date. These findings are unique in cutaneous ACC.

The site of the present ACC is ear, and the patient age was old (85 years). The most common sites of cutaneous ACC are scalp and breast skin [4]. The occurrence of ACC in the ear skin has not been reported, and is unique. The mean age of cutaneous ACC is 58.1 years [4]. The present ACC developed in an 85-year-old man. This old age is also unique.

KIT, a receptor tyrosine kinase, is well known to be expressed in ACC. The present case expressed KIT. The new finding is that PDGFRA, another tyrosine kinase, was expressed in the present ACC. In gastrointestinal stromal tumor (GIST), expression of KIT, PDGFRA and CD34 is seen, and mutations of KIT and PDGFRA are frequent [10-13]. More studies of mutations of KIT and PDGFRA in cutaneous ACC are required.

The present ACC characteristically expressed CD56 (NCAM). Although other neuroendocrine antigens (neuron-specific enolase, chromogranin, synaptophysin) were negative in the current case, the findings may show that cutaneous ACC may show neuroendocrine differentiation.

ACC most commonly occurs in major salivary glands (MSG), including parotid glands, submandibular glands, and sublingual glands. Immunoprofile of CK in ACC of MSG have been sometimes examined; ACC of MSG expresses CKAE1/3, CKCAM5.2, CK7, CK8, CK14, and CK19 [14-16]. CK20 was negative in ACC of MSG [16]. These findings of ACC of MSG are compatible with the present CK immunoprofile of cutaneous ACC. In addition, the present cutaneous ACC showed positive expression of CK34BE12, CK5/6 and CK7. CK8 and CK20 were negative in the present cutaneous ACC. The CK7/CK20 pattern of ACC of MSG is +/- [16], being compatible with the present cases of cutaneous ACC. EMA is known to be expressed in ACC of GSG [17]. In the present case, expression of EMA was absent. CEA has been known to be expressed in ACC of MSG [18]. In the present cutaneous ACC, CEA expression was not seen. P63 is known to be expressed in ACC of MSG [12, 13]. In the present case also, p63 was expressed. Vimentin is known to be expressed in ACC of MSG [14]. In the current case, vimentin was not expressed. Desmin expression

has not been examined in ACC of MSG. The current case of cutaneous ACC lacked desmin expression. S100 protein has been shown to be sometimes expressed in ACC of MSG. The present case of cutaneous ACC also expressed S100 protein. S100 protein detects myoepithelial cells [12, 13]. More study of S100 protein expression in cutaneous ACC is required. CD34 has not been examined in ACC of MSG. The present cases lacked CD34 expression. ASMA, a marker of myoepithelial cells, has been known to be expressed in ACC of MSG [19]. In the present case of cutaneous ACC, ASMA was expressed. Ki-67 and p53 have been known to be expressed in ACC of MSG [20, 21], as is the case of the present case. CD10, a marker of myoepithelial cells, has been shown to be expressed in ACC of MSG [22]. However, the present case lacked CD10 expression. Chromogranin has not been investigated in ACC of MSG. The present case showed no chromogranin immunoreactivity. Synaptophysin has been shown to be sometimes expressed in ACC of MSG. In the present case, no synaptophysin expression was noted. As previously described, KIT is well known to be expressed in ACC of MSA, but PDGFRA has not been examined in ACC of MSG. In the present case, KIT and PDGFRA were expressed. MUC apomucins have been examined in ACC of MSG [23]: MUC1 and MUC2 are expressed in ACC of MSG, while MUC3, MUC5AC and MUC6 are negative in ACC of MSG. In the current study of cutaneous ACC, MUC1, MUC2, MUC5AC and MUC6 were negative. Much more studies of MUC apomucins in cutaneous ACC are required.

In conclusion, the author reported a unique case of cutaneous ACC with immunohistochemical studies.

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