

Sebaceous Carcinoma with Actinic Keratosis

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Sir,

Sebaceous carcinoma has traditionally been divided into two groups: an aggressive ocular form and a relatively non-aggressive extraocular form. Cutaneous extraocular sebaceous carcinoma is a rare neoplasm that arises most commonly on the head and neck, where sebaceous glands are concentrated (1, 2). Clinically, it is a yellowish or reddish, slow-growing tumour and sometimes shows extensive erosion on its surface. We present here a case of extraocular cutaneous sebaceous carcinoma in association with actinic keratosis.

CASE REPORT

An 83-year-old Japanese woman was referred to our department for evaluation of a solitary nodule on her left cheek. She had been aware of a slow-growing, asymptomatic nodule for 5 years prior to presentation. Physical examination revealed a flat-elevated, yellow nodule, 10×6 mm in diameter, with surface erosion on the left cheek (Fig. 1). Her past medical history was unremarkable.

Histopathologically atypical neoplastic cells with pleomorphic and hyperchromatic nuclei had invaded into the dermis in a lobular fashion at the centre (Fig. 2a). Mitoses were frequently seen. Some of the tumour cells contained vacuolated cytoplasm, suggesting sebaceous differentiation. In the periphery of the tumour, no vacuolated cells were seen, but atypical keratinocytes were seen in the epidermal basal layer and there was solar elastosis in the dermis (Fig. 2b). These findings were compatible with actinic keratosis. The peripheral actinic keratosis lesion was apparently in continuity with central lobular tumour nests.

Immunohistochemically, most of the tumour cells with vacuolated cytoplasm were positive for cytokeratin (CK) 7, epithelial membrane antigen (EMA) and adipophilin. Remarkably, some atypical intraepidermal keratinocytes at the periphery, particularly in the transitional zone of the central lobular nests and peripheral actinic keratosis lesion, were also positive for CK7, EMA and adipophilin (Fig. 2c).



Fig. 1. A yellowish nodule on the left cheek.

Ultrastructurally, the tumour cells were fundamentally divided into two types. First, a cell type characterized by well-developed cell organelles and lipid droplets in various numbers but paucity of tonofilaments in the cytoplasm (Fig. 3a). Secondly, a cell type containing abundant tonofilaments and no lipid droplets. Both types had desmosomes in relatively poor development. Interestingly, some tumour cells contained intracytoplasmic canaliculi that were decorated with numerous microvilli in the inner surface (Fig. 3b). Based on these findings, a diagnosis of sebaceous carcinoma with common type of actinic keratosis was made.

DISCUSSION

Cutaneous extraocular sebaceous carcinoma arises on the head and neck, but also on the vulva, penis and, rarely, other locations (2). Histopathologically, the tumour shows irregular lobular formation with great variation in size (2). In the case described here, no vacuolated cells were seen in the peripheral intraepidermal area of the tumour, but atypical keratinocytes were seen. We performed an immunohistochemical study to elucidate the relationship between vacuolated tumour cells and the peripheral atypical keratinocytes. Immunohistochemically, most of the vacuolated cells were positive for CK7, EMA and adipophilin, showing typical features of sebaceous tumours. These three proteins were also expressed in some of the intraepidermal atypical keratinocytes, in continuity with central sebaceous carcinoma nests.

Ichikawa et al. (3) reported that actinic keratosis was exclusively negative for CK7 among various cutaneous tumours for which immunohistochemical cytokeratin expression pattern was analysed. On the other hand, Mai et al. (4) reported that only 2 of 44 squamous cell carcinomas *in situ* without pagetoid spread of atypical keratinocytes showed a moderate reactivity for CK7 in atypical keratinocytes. So far there has been no reported case of EMA expression in actinic keratoses. We reviewed five cases of actinic keratosis (four of common type and one of bowenoid type) in our laboratory. EMA expression was detected in only the bowenoid actinic keratosis (not shown). CK7 expression was not detected in either type.

The pathogenesis of sebaceous carcinoma is still unclear. Ansai & Mihara (5) reported two cases of sebaceous carcinoma in close association with actinic keratosis. They conclude that the combination of sebaceous carcinoma and actinic keratosis may either be coincidental or suggest that actinic keratoses may differentiate towards skin adnexae including sebaceous glands.

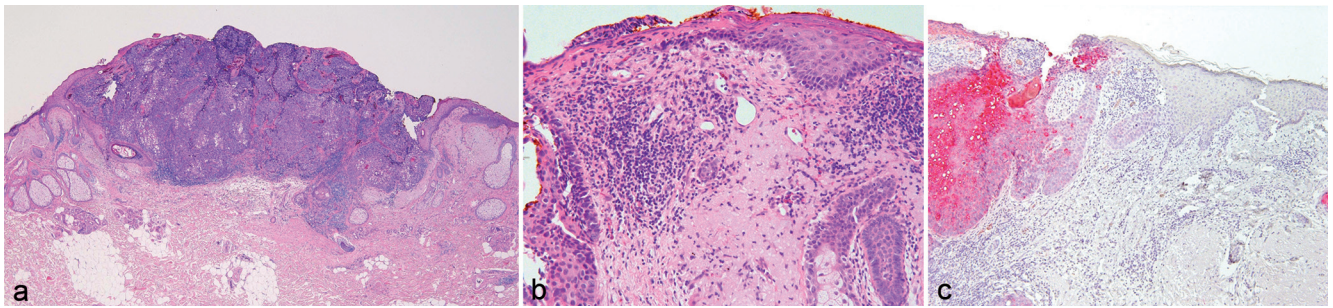


Fig. 2. (a) Atypical tumour cells with vacuolated cytoplasm at the centre (haematoxylin-eosin $\times 40$). (b) In the peripheral region of the tumour, no vacuolated cells were seen, but atypical keratinocytes were in the epidermis (haematoxylin-eosin $\times 100$). (c) Immunohistochemical staining for adipophilin (haematoxylin-eosin $\times 100$). Some atypical keratinocytes at the peripheral region were positive for adipophilin.

Histopathologically, there was a clear continuity of intraepidermal atypical keratinocytes with the central lobular nests. EMA, CK7 and adipophilin expression in intraepidermal atypical keratinocytes in the periphery was the same as that in central sebaceous nests. EMA expression was not detected in any of the 4 cases of common type actinic keratosis that we reviewed. Judging from these findings, we consider that the combined occurrence of central sebaceous carcinoma and peripheral actinic keratosis in our case is not by chance but probably indicates a close relationship between them, supporting Ansai's speculation (5).

Ultrastructurally, many of the atypical cells in the present case contained lipid droplets, and there is no doubt about its sebaceous differentiation. In addition, our case showed intracytoplasmic canaliculi decorated by numerous microvilli in some tumour cells. The presence of these special structures in skin neoplasms usually implies sweat gland differentiation (6). Normal sebaceous glands are thought to originate from a common primordium destined to give rise to a folliculosebaceous apocrine unit (7). Thus sweat gland differentiation in sebaceous tumours as well as follicular ones is generally considered to be apocrine in nature, based on the concept of the folliculosebaceous apocrine unit. Although there were no definite glandular structures with apical snouting of the lining columnar cells, we believe that the presence of intracytoplasmic lumina indicates a recapitulation of "apocrine" ductal development based

on the concept of the folliculosebaceous apocrine unit. Apocrine differentiation in sebaceous neoplasms, particularly in sebaceous carcinoma, is extremely rare (8, 9). Misago & Narisawa (8) proposed the presence of pluripotent stem cells or sebaceous stem cells have the ability to differentiate into both sebaceous and apocrine units in sebaceous carcinoma with apocrine differentiation. They clearly showed the apocrine glandular structures formed by columnar luminal cells with evidence of decapitation secretion at light microscopic level. On the other hand, we successfully found the ductal lumina in the tumour cells, suggesting minimal differentiation toward apocrine units, as mentioned above. These minute structures are difficult to capture with light microscopy. Electron microscopy may unexpectedly prove such dual differentiation in many sebaceous carcinomas, as in the case described here, and could strengthen the stem cell theory proposed by Misago & Narisawa (8).

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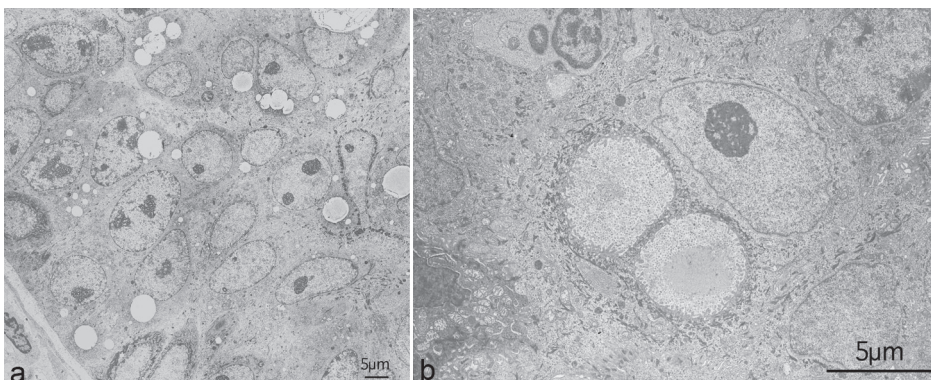


Fig. 3. (a) Ultrastructure of the tumour. The tumour cells showed characteristic lipid droplets in the cytoplasm. (b) Some tumour cells contained intracytoplasmic canaliculi.

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