Primary Cutaneous Mucinous Carcinoma Initially Diagnosed as Metastatic Adenocarcinoma

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TERADA, T., SATO, Y., FURUKAWA, K. and SUGIURA, M. Primary Cutaneous Mucinous Carcinoma Initially Diagnosed as Metastatic Adenocarcinoma. Tohoku J. Exp. Med., 2004, 203 (4), 345-348 — The authors report a rare case of primary mucinous carcinoma of the skin initially diagnosed as a metastatic adenocarcinoma. The tumor occurred in the right axilla in a 75-year-old man. Initial pathological diagnosis was metastatic adenocarcinoma. However, no primary focus was found in the body. The revised diagnosis by the authors was primary cutaneous mucinous carcinoma. The tumor (1.5 cm) was characterized by proliferation of atypical epithelial cells arranged in cell nests with many pseudolumens resembling adenoid cystic carcinoma. It was also characterized by much mucinous stroma or pool around tumor cells. No apparent eccrine or apocrine differentiation was noted histologically and immunohistochemically. The present case suggests that primary cutaneous mucinous carcinoma may be misdiagnosed as metastatic adenocarcinoma, and that it may resemble adenoid cystic carcinoma. —— mucinous carcinoma; skin; axilla; metastatic skin carcinoma

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Primary cutaneous mucinous carcinoma was first documented by Lennox et al. (1952), and was first designated by Mendoza and Helwig (1971). It is a rare tumor, occurs in head, neck, axilla and eyelid of elderly persons, and is more common in man than in woman (Lennox et al. 1952; Mendoza and Helwig 1971; Lever and Lever 1990; Bellezza et al. 2000; Breier et al. 2000; Ohnishi et al. 2002; Wako et al. 2003). It is low-grade malignant, and distant and lymph node metastasis is uncommon though local recurrence is relatively frequent (Lennox et al. 1952; Mendoza and Helwig 1971; Lever and Lever 1990; Bellezza et al. 2000; Breier et al. 2000; Ohnishi et al. 2002; Wako et al. 2003). It is occasionally misdiagnosed as metastatic mucinous carcinoma (Lennox et al. 1952; Mendoza and Helwig 1971; Lever and Lever 1990; Bellezza et al. 2000; Breier et al. 2000; Ohnishi et al. 2002; Wako et al. 2003).
tion was recognized around the lumens. Neither keratinization nor intercellular bridges were recognized. Cytologically, tumor cells were monomorphous, were polygonal or elongated in shape, and their cytoplasm was acidophilic (Fig. 1D). Their nuclei were hyperchromatic and showed irregularity of the shape, and discrete nucleoli were recognized in most of the tumor cells (Fig. 1D). One to two mitotic figures were noted in 10 high power fields. Pyknotic or apoptotic nuclei were present in small number. No decapitation secretion was recognized.

Histochemically, the mucous stroma was strongly positive with PAS after diastase digestion and alcian blue stains at pH 2.5, but not with alcian blue at pH 1.0. Tumor cells were slightly positive with these techniques. An immunohistochemical analysis using Dako’ Envision method showed that tumor cells were positive for cytokeratins using various antibodies (clone KL-1, MBL Lab, Tokyo; polyclonal wide spectrum screening, Dako, Glostrup, Denmark: clone MNF-116, Dako) and for epithelial membrane antigen (clone E29, Dako). The tumor cells were negative for S-100 protein (polyclonal, Dako), carcinoembryonic antigen (CEA, polyclonal, Kyowa, Tokyo), chromogranin A, (clone DAK-A3, Dako), synaptophysin (clone SY-38, Dako), neuron specific enolase (clone BBS/NC/VI-H14, Dako), cytokeratins no. 7 (clone OV-TL 12/30, Dako) and no. 20 (clone Ks20.8, Dako), and gross cystic disease fluid protein 15 (GCDFP-15, clone D6, Signet Lab). From these findings, a diagnosis of primary mucinous carcinoma of the axilla was made.

DISCUSSION
The present case showed monomorphous proliferation of atypical cells in the characteristic mucinous stroma. The tumor cells showed adenocystic solid nests. Although the tumor was well circumscribed, the tumor cells showed mild to moderate atypia including nuclear atypia and mitosis, suggesting that the present tumor was low-grade malignant tumor. Therefore, the present case was diagnosed as primary cutaneous
mucinous carcinoma of the axillary skin.

Mucinous carcinoma is common in breast, gastrointestinal tracts and other visceral organs. The present case had initially been pathologically diagnosed as metastatic adenocarcinoma. However, scrutiny of the body showed no tumors, indicating that the tumor was not metastatic mucinous carcinoma but primary skin tumor. The long disease free period (21 months) after the excision supports that the skin tumor is primary. The negative reaction of tumor cells to cytokeratin no.7 and no. 20 also suggests that the tumor is not a metastatic adenocarcinoma. However, the possibility that the present tumor is metastatic carcinoma is not denied completely.

In general, cutaneous mucinous carcinoma shows carcinoma cells arranged in cords, small nests and small tubules embedded in mucinous materials which are separated by fibrous septae (Lennox et al. 1952; Mendoza and Helwig 1971; Lever and Lever 1990; Bellezza et al. 2000; Breier et al. 2000; Ohnishi et al. 2002; Wako et al. 2003). The present case, in contrast, showed that relatively large tumor nests with adenocystic appearances with pseudolumens were embedded in mucinous stroma. Therefore, the present tumor showed rather unusual appearances.

Differential diagnosis includes malignant nodular hidradenoma, malignant mixed tumor, adamantinoid basal cell epithelioma, ectopic breast

Fig. 1. A: Very low power view of the skin tumor. The tumor is located in the dermis. The epidermis is erosive. The tumor is well circumscribed, and the stroma is loose. Hematoxylin and Eosin, x4. B: Low power view of the tumor. The tumor cell nests are embedded in mucin or mucinous stroma. The tumor cell nests show luminal spaces creating adenocystic appearances. Hematoxylin and Eosin, x150. C: Medium power view of the tumor. Tumor cell nests are embedded in mucin or mucinous stroma. The adenocystic spaces occasionally connect with the mucinous stroma. Hematoxylin and Eosin, x250. D: High power view of tumor cells. The tumor cells are polyhedral or elongated in shape, and show hyperchromatic nuclei, nucleoli and nuclear irregularity, pyknotic nuclei, and mitosis (center). Hematoxylin and Eosin, x350.
carcinoma, mucinous carcinoma and, in particular, adenoid cystic carcinoma. The former three tumors are unlikely in terms of the histological, histochemical and immunohistochemical features (Lever and Lever 1990). Mucinous carcinoid is also unlikely because the present tumor showed no neuroendocrine features. Adenoid cystic carcinoma is also unlikely because the present tumor showed no apparent cribriform appearances and was not immunoreactive for CEA and S-100 protein, which are positive in adenoid cystic carcinoma (Lever and Lever 1990). Ectopic breast carcinoma, in contrast, cannot be denied.

Primary mucinous carcinoma of the skin is a low grade malignant tumor arising from sweat glands (Lennox et al. 1952; Mendoza and Helwig 1971; Lever and Lever 1990; Bellezza et al. 2000; Breier et al. 2000; Ohnishi et al. 2002; Wako et al. 2003). It is still controversial whether this neoplasm has eccrine or apocrine differentiation; some authors have suggested that it shows eccrine differentiation, while others claimed that it shows apocrine differentiation (Lennox et al. 1952; Mendoza and Helwig 1971; Lever and Lever 1990; Bellezza et al. 2000; Breier et al. 2000; Ohnishi et al. 2002; Wako et al. 2003). In fact, some cases of the neoplasm show decapitation secretion (Lennox et al. 1952; Mendoza and Helwig 1971; Lever and Lever 1990; Bellezza et al. 2000; Breier et al. 2000; Ohnishi et al. 2002; Wako et al. 2003). In the present case, no apparent differentiation is recognized. The tumor occurred in the apocrine glands-rich axilla and tumor cells had acidophilic cytoplasm, but it was negative for apocrine marker (GCDFP-15).

Immunohistochemically, primary cutaneous mucinous carcinoma has a tendency to show immunoreactivities for CEA, epithelial membrane antigen and broad spectrum cytokeratins (Bellezza et al. 2000; Wako et al. 2003). Some of them show neuroendocrine features (Wako et al. 2003). The present case lacked the immunoreactivity for CEA and GCDFP-15, but this does not rule out the possibility of mucinous carcinoma of the skin because some cases of this neoplasm showed no reactivity for CEA (Bellezza et al. 2000).

In summary, we report a rare case of primary cutaneous mucinous carcinoma initially diagnosed as metastatic adenocarcinoma.

References