European Journal of Dermatology
Manuscript ID ejd170066 Revised Version

Correspondence

Primary cutaneous cribriform carcinoma, solid variant: a tiny, stable, long-term lesion

Kenji YOKOTA, Michihiro KONO, Shoichiro MORI, Kazue SHIMIZU, Takaaki MATSUMOTO, Masashi AKIYAMA

Department of Dermatology, Nagoya University Graduate School of Medicine,
Nagoya, Japan

Short title: Primary cutaneous cribriform carcinoma

Keywords: adenocarcinoma, dermoscopy, primary cutaneous cribriform carcinoma, solid variant, sweat gland carcinoma

Word Count: 698 words in the main text, 1 figure, 0 table, 6 references
Acknowledgements: None
Disclosure. *Financial support: none. Conflicts of interest: none.*

Correspondence:
Prof. Masashi Akiyama
Department of Dermatology
Nagoya University Graduate School of Medicine,
65 Tsurumai-Cho, Showa-ku, Nagoya, Aichi 466-8560, Japan
Tel: +81-52-741-2314 Fax: +81-52-744-2718
E-mail; makiyama@med.nagoya-u.ac.jp

Cutaneous adenocarcinoma consists of primary and metastatic lesions. A majority of primary adenocarcinoma lesions originate in sweat glands. The category of malignant sweat gland tumours includes highly heterogeneous tumours [1].

Primary cutaneous cribriform carcinoma (PCCC), an extremely rare sweat gland carcinoma, was first described by Requena *et al*. [2] in 1988. In that report, the PCCCs were solitary skin nodules, commonly located on the extremities. Characteristic histopathological features of PCCC are anastomosing nests and cords of atypical tumour cells, resulting in a cribriform appearance. Rütten *et al*. [3] reported a series of PCCC cases and supported the description of Requena *et al*. [2]. In the Rütten *et al*. report, no patient with a known disease course had recurrence or metastasis of the PCCC lesions, and PCCC was suggested to have a favorable prognosis.

Here we report a case of a rare solid variant of PCCC presenting as a small papule on the forearm. The lesion had been stable in size for more than 10 years.

A 39-year-old Japanese female had a faintly reddish papule on the right forearm for more than 10 years. At her initial visit, a sharply demarcated, hard, elastic, reddish papule of 5 mm in diameter was seen on the right forearm (*figure 1A*). Dermoscopic observations revealed an amorphous, white area in the center of the lesion (*figure 1B*). Simple resection of the lesion was performed. Histopathological observations of the resected specimen showed a mostly well-circumscribed, unencapsulated tumor composed of small nests and cords of tumour cells in the dermis (*figure 1C*). In the tumour, cystic areas with tubular and ductal structures were seen, although solid areas were predominant (*figure 1D, E*). In the superficial part of the tumour, nests of atypical tumour cells were embedded in desmoplastic stroma. Atypical tumour cells were more densely infiltrated in the lower part of the tumour than in the upper part. At the bottom part of the lesion, the tumour showed a pushing border, and in only a small area, some tumour cells had invaded the dermis.

Immunohistochemical staining revealed the tumour cells to be positive for cytokeratin (CK) 5/6, CK7 (*figure 1F*), CA15-3, CA125 and c-KIT, and partially positive for S-100, p53 and p63. The tumour cells were negative for CK20, calponin, GCDFP15, mammaglobin, Mucin-1 (MUC1), estrogen receptor, androgen receptor and D2-40. The Ki-67 labeling index of tumour cells was 5%. The tumour stroma was partially positive for SMA.

Computed tomography (CT) and positron emission tomography/CT images showed neither lymph node metastasis nor distant metastasis. The breast, the head and neck regions, and the gastrointestinal tract were scrutinized thoroughly, but no abnormalities were detected.

From these findings, the tumour was diagnosed as a solid variant of PCCC. We performed total resection of the tumour primary site with a wide margin and sentinel lymph node biopsy in the right axilla. Neither residual tumour in the resected specimen nor sentinel lymph node metastasis was found histopathologically. Neither local recurrence nor metastasis has been seen for the 15 months since the total resection.

We diagnosed the present case as PCCC from the characteristic histopathological features, such as the unencapsulated but sharply demarcated mass of tumour cell strands and nests, which showed a solid and cribriform appearance with desmoplastic stroma, in the dermis. In addition, the diagnosis was supported by the immunohistochemical findings of positivity for CK5/6, CK7, CA15-3, CA125 and c-KIT, and negativity for CK20, calponin, GCDFP15, mammaglobin, Mucin-1 (MUC1), estrogen receptor and androgen receptor, which were consistent with previous reports [4, 5]. The fact that the present tumour was a small, non-aggressive dermal nodule in the arm was compatible with the diagnosis.

Clinical observations of the previously reported PCCC cases in the literature indicate that PCCC behaves indolently [3, 6]. We think it may be questionable whether PCCC cases should still be classified as overtly malignant tumours/carcinomas. Indeed, in the present case, the patient had had the small lesion for more than 10 years and the tumour size had been stable during that long period. This case suggests that we cannot exclude the possibility of the rare primary cutaneous adenocarcinoma PCCC even in cases of non-progressive, stable, small dermal tumours and even though PCCC is a very rare malignancy.

References

1. Cardoso JC, Calonje E. Malignant sweat gland tumours: an update. *Histopathology* 2015; 67: 589-606.

2. Requena L, Kiryu H, Ackerman AB. Cribriform carcinoma. In: Ackerman AB, ed. *Neoplasms with Apocrine Differentiation*. Philadelphia: Lippincott-Raven, 1998: 879-905.

3. Rütten A, Kutzner H, Mentzel T, *et al*. Primary cutaneous cribriform apocrine carcinoma: a clinicopathologic and immunohistochemical study of 26 cases of an under-recognized cutaneous adnexal neoplasm. *J Am Acad Dermatol* 2009; 61: 644-51.

4. Fernandez-Flores A, Pol A, Juanes F, Crespo LG. Immunohistochemical phenotype of cutaneous cribriform carcinoma with a panel of 15 antibodies. *Med Mol Morphol* 2007; 40: 212-7.

5. Arps DP, Chan MP, Patel RM, Andea AA. Primary cutaneous cribriform carcinoma: report of six cases with clinicopathologic data and immunohistochemical profile. *J Cutan Pathol* 2015; 42: 379-87.

6. Adamski H, Le Lan J, Chevrier S, Cribier B, Watier E, Chevrant-Breton J. Primary cutaneous cribriform carcinoma: a rare apocrine tumour. *J Cutan Pathol* 2005; 32: 577-80.

Figure legends

Figure 1. Clinical and histopathological features of the present tumour. **A)** A reddish papule of 5 mm in size is seen on the extensor side of the forearm. **B)** Dermoscopic observation shows an amorphous white area in the center of the lesion. **C)** A resected sample of the tumour reveals a sharply demarcated tumour mass from the superficial to the deep dermis and shows a pushing border (arrows) into the surrounding dermis. The upper part of the tumour consists mainly of solid areas. **D)** In the lower part of the tumour, tubular and ductal structures of tumour cell nests and cords are predominant. **E)** Typical cribriform features are seen in the tumour cell nests located in the deeper part of the tumour. **F)** The tumour cells are positive for CK7. Hematoxylin and eosin stain (**C**-**E**), immunohistochemical staining for CK7 (**F**), original magnification x40 (**C**), x100 (**D**), x400 (**E**), x200 (**F**).

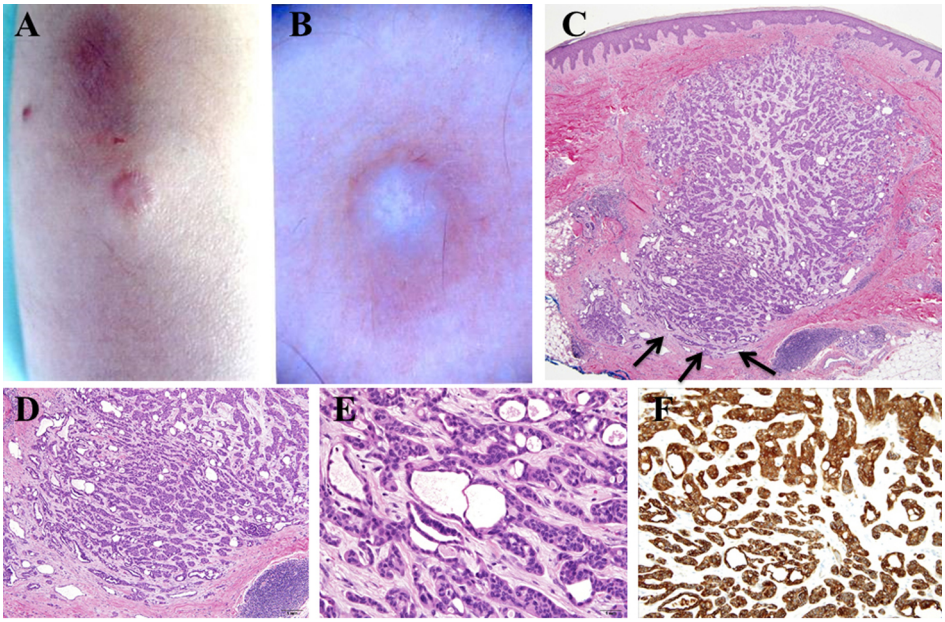

Figure 1. Clinical and histopathological features of the present tumour. **A)** A reddish papule of 5 mm in size is seen on the extensor side of the forearm. **B)** Dermoscopic observation shows an amorphous white area in the center of the lesion. **C)** A resected sample of the tumour reveals a sharply demarcated tumour mass from the superficial to the deep dermis and shows a pushing border (arrows) into the surrounding dermis. The upper part of the tumour consists mainly of solid areas. **D)** In the lower part of the tumour, tubular and ductal structures of tumour cell nests and cords are predominant. **E)** Typical cribriform features are seen in the tumour cell nests located in the deeper part of the tumour. **F)** The tumour cells are positive for CK7. Hematoxylin and eosin stain (**C-E**), immunohistochemical staining for CK7 (**F**), original magnification x40 (**C**), x100 (**D**), x400 (**E**), x200 (**F**).