

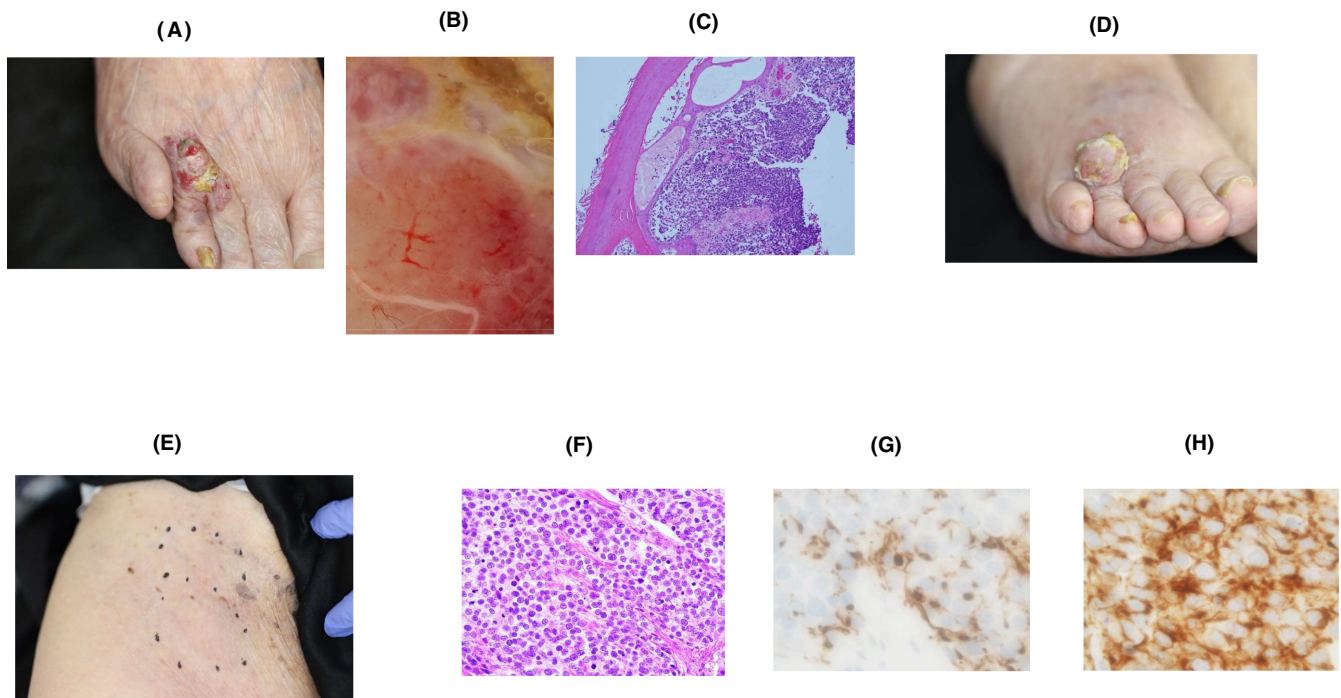
## CORRESPONDENCE

# Merkel cell carcinoma on the dorsalis pedis with both dot-like perinuclear and cytoplasmic patterns of CK20 positivity

Classically known to be a tumor of the head and neck region, primary Merkel cell carcinoma (MCC) has rarely been reported in the lower leg.<sup>1</sup>

A 93-year-old Japanese woman with no significant past medical history presented to our department with asymptomatic nodules on her left leg. The lesions had a persistent, asymptomatic, red-pink, and bleeding erythematous lesion, with a diameter of 25 mm, localized on her right dorsalis pedis (Figure 1A). The dermoscopic findings demonstrated linear irregular vessels, polymorphous

vascular structure, and milky pink and white areas (Figure 1B). Histopathological findings of the skin biopsy revealed monotonous, uniform round blue cells with scant cytoplasm and dusty chromatin in the dermis and underlying subcutaneous tissue (Figure 1C). Immunohistochemical staining, using cytokeratin (CK)20, revealed a partly dot-like perinuclear pattern in the cytoplasm. Additionally, the tumor cells were positive for synaptophysin, chromogranin, neuron-specific enolase, and negative for thyroid transcription factor-1. Chest radiography revealed no anomalies, and a total body



**FIGURE 1** (A) Clinical features of an asymptomatic, pink-to-violaceous plaque or nodule on the patient's right dorsalis pedis. (B) Dermoscopic examination showed linear irregular vessels, polymorphous vascular structure, and milky pink and white areas. (C) Histopathological findings of the skin biopsy showed dermal proliferation of small round blue cells (hematoxylin and eosin staining, magnification  $\times 100$ ). (D) The tumor on the right dorsalis pedis rapidly increased in size over the course of 4 months. (E) Physical examination of the right inguinal lymph nodes revealed enlargement with slight tenderness and a broadening in depth. (F) Histopathological findings of the enlarged tumor showed small round blue cells (hematoxylin and eosin staining, magnification  $\times 1000$ ). (G, H) Immunohistochemical staining of the increased tumor showed both dot-like perinuclear (F) and cytoplasmic patterns (G) positivity with CK20 (magnification  $\times 1000$ )

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computed tomography scan showed no metastases. Consequently, the patient and her family strongly rejected the proposed therapeutic approach, primarily because of her advanced age.

Four months later, the tumor had grown larger, showing a dome-shaped appearance with a pink-red surface and shiny erythematous lesions (Figure 1D). Her right inguinal lymph nodes were enlarged and increased in depth and were slightly tender (Figure 1E). Pitting edema of the involved right lower extremity was clinically suspected as lymphedema because of an inguinal lymphonodal metastasis. Immunohistochemical staining of the enlarged tumor found both dot-like perinuclear and cytoplasmic patterns of CK20 positivity (Figure 1F-H).

CK20 staining pattern of enterocytes is usually diffuse and cytoplasmic, while a dot-like perinuclear pattern is characteristic of the tumor cells of MCC.<sup>2</sup> The dot-like perinuclear staining for CK20 in a tumor that is morphologically suspicious for a neuroendocrine neoplasm supports the diagnosis of MCC and distinguishes MCC from metastatic small cell neuroendocrine carcinoma from other sites. The present case showed both dot-like perinuclear and cytoplasmic patterns of CK20 positivity in the primary MCC. Sakata et al.<sup>3</sup> found that all MCCs with dot-like perinuclear pattern based on CK20 immunostaining occur in the head and neck region, while those with a peripheral nuclear pattern tend to be located in the trunk and extremities, and this difference was statistically significant. In contrast, CK20 expression pattern may not be associated with tumor location in the report including 31 Merkel cell carcinoma cases.<sup>4</sup>

The mechanism associated with dot-like perinuclear CK20 staining, however, remains unknown. CK20 is of significant value as a highly specific marker for Merkel cells in normal squamous epithelium. CK20 expression in MCC supports the hypothesis that the Merkel cell is the cellular origin of MCC. However, there is ongoing controversy regarding the origin of MCC. Some researchers believe that MCC derives from pluripotent stem cells from the skin.<sup>5</sup> We propose that the presence of both dot-like perinuclear and cytoplasmic patterns of CK20 might reflect the diversity of MCC origin from stem cell to mature Merkel cells in our patient.

#### DECLARATION SECTION

Approval of the research protocol: Yes.

Informed Consent: Yes.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

Kae Yokoyama MD

Takaharu Ikeda MD, PhD

Tamihiro Kawakami MD, PhD 

*Division of Dermatology, Tohoku Medical and Pharmaceutical University, Sendai, Japan*

#### Correspondence

Tamihiro Kawakami, MD, PhD, Division of Dermatology, Tohoku Medical and Pharmaceutical University, 1-15-1 Fukumuro, Miyagino-ku, Sendai, Miyagi 983-8536, Japan.

Email: [tami@tohoku-mpu.ac.jp](mailto:tami@tohoku-mpu.ac.jp)

#### ORCID

Tamihiro Kawakami  <https://orcid.org/0000-0001-6741-939X>

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