



Dermatology Reports

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eISSN 2036-7406



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Please cite this article as:

Polita F, Mengarino M, Carelli V, et al. Merkel cell carcinoma following photodynamic therapy in a high-risk patient. Dermatol Rep 2026 [Epub Ahead of Print] doi: 10.4081/dr.2026.10485

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Received: 23 June 2025; Accepted: 11 June 2026.

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Merkel cell carcinoma following photodynamic therapy in a high-risk patient

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Key words: Merkel cell carcinoma; Bowen's disease; photodynamic therapy; carcinogenesis.

Contributions: Francesca Polita, Massimiliano Mengarino, Valentina Carelli: study concept, manuscript original drafting, patient clinical history collection, case report creation, review of clinical cases with similar characteristics, and table creation; Esther Hanspeter: histological examination and immunohistochemical investigation; Rosita Saraceno: supervision and final manuscript review. All the authors read and approved the final version of the manuscript.

Conflict of interest: the authors declare that they have no competing interests.

Ethics approval and consent to participate: not applicable.

Consent for publication: informed consent for publication was secured.

Availability of data and materials: the data of the report are available from the Department of Dermatology and Venereology, Hospital of Merano (SABES-ASDAA) but there are restrictions on their availability because they were used under license for the current study and thus are not publicly available. However, the authors' data are available upon reasonable request and with the permission of the SABES-ASDAA, Merano (BZ), Italy.

Dear Editor,

Merkel cell carcinoma (MCC) is defined as a rare but highly aggressive skin cancer originating from neuroendocrine cells.¹ Clinically, it usually appears as a rapidly growing, solid, asymptomatic, red-violaceous nodule.²⁻⁴ Its development is primarily associated with the integration of the Merkel cell polyomavirus (MCPyV) and extended exposure to ultraviolet (UV) radiation. The disease predominantly affects older individuals with fair skin. There is an increased incidence of MCC among immunocompromised individuals, such as patients suffering from hematological malignancies.²

We present a rare case of MCC apparently arising within the same anatomical site where photodynamic therapy (PDT) had been performed for the treatment of Bowen's disease (BD).

A 78-year-old male patient with Fitzpatrick skin type II, photodamaged skin, and a medical history of B-cell chronic lymphocytic leukemia (B-CLL) stage A diagnosed 12 years earlier and under active surveillance, came to our attention for an erythematous, scaling, itchy area located in the left retroauricular region, which had been enlarging over the previous year. He had no documented history of arsenic exposure. The lesion was biopsied and the following histopathological examination confirmed a diagnosis of BD. According to the size and anatomical location of the tumor (Figure 1a), PDT was initiated.

Five months after the first session, a rapidly growing pink papule emerged on an erythematous background at the treatment site (Figure 1 b,c).

The clinical picture was suspicious for basal cell carcinoma (BCC), and a skin biopsy was performed. Immunohistochemical investigation showed dot-like positivity for cytokeratin 20 (CK20), weak and focal positivity for BerEp4, and negativity for cytokeratin 7 (CK7), neurofilament (NF), and thyroid transcription factor-1 (TTF-1). MCPyV status could not be assessed. Nonetheless, the lesion exhibited histological patterns and an immunohistochemical profile consistent with a diagnosis of MCC (Figure 1 e-g). Concomitantly, the clinical examination revealed left-sided retroauricular and laterocervical lymphadenopathy. Following a lymph node ultrasound examination, a lymph node biopsy was performed; immunohistochemical analysis exhibited immunoreactivity for cytokeratin CAM 5.2, CK20, and synaptophysin, along with focal positivity for TTF-1 and a Ki-67 proliferation index of 90% (Figure 1 h-l). While both the skin and lymph node specimens were negative for CK7 and NF, the positivity for TTF-1 in the lymph node supported the concomitant diagnosis of small cell lung cancer (SCLC) metastasis.

Subsequent staging CT revealed an expansive mass in the upper right lobe of the lung, associated with an infiltrative lytic lesion of the posterior arch of the third rib, confirming a stage IV disease.

Following a multidisciplinary evaluation, systemic chemoimmunotherapy with carboplatin, etoposide, and atezolizumab was initiated. Despite treatment, the patient died from SCLC progression one year after his MCC diagnosis.

In the presented case, MCC developed within a clinical context characterized by multiple carcinogenic risk factors, including a previous diagnosis of BD, advanced age and systemic immunosuppression related to B-CLL. Although the histological presence of MCC prior to PDT cannot be definitively excluded and a direct causal relationship cannot be established, we speculated that PDT could play a potential oncogenic role.

PDT represents a non-invasive treatment modality utilized in treating dermatological neoplastic lesions, leading to targeted apoptotic and necrotic cell death within the pathological tissues.^{5,6}

Beyond its direct cytotoxic activity, PDT significantly influences the immune system.⁵ The procedure triggers the secretion of pro-inflammatory cytokines and acute-phase proteins, alongside the activation of the complement system within the tumor site; furthermore, it enhances the development of systemic, antigen-specific antitumor immunity.⁵ In contrast, PDT may also induce certain immunosuppressive phenomena, both locally and systemically, such as the inhibition of delayed-type hypersensitivity reactions.⁷

In addition to these complex immunological modulations, the most concerning long-term adverse effect is the possible carcinogenicity induced by the treatment.⁵ In fact, the ROS oxidative damage caused by PDT can promote mutagenic events and activate oncogenes.⁸

Several authors have documented the onset of various non-melanoma skin cancers following PDT.⁵ In the present case, it remains uncertain whether PDT acted as a triggering factor or if other predisposing elements played a role. Indeed, as reported by Chan *et al.*, the development of concomitant MCC and squamous cell carcinoma (SCC) could be attributed to a shared origin from a mutual multipotent stem cell precursor or exposure to the same risk factor, such as UV radiation.^{9,10} Our comprehensive PubMed search, spanning from January 1990 to December 2025, identified a total of 27 instances of BD/SCC associated with MCC (Table 1). Notably, the literature has yet to report cases of overlapping MCC and BD specifically associated with concomitant PDT treatment. The presented case is one of the rare examples of coexisting MCC and BD. Further investigation should be performed to establish the potential carcinogenic role of PDT.

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Figure 1. a) Retroauricular BD at the first PDT session; b) MCC on BD after PDT; c) detail of MCC lesion; d) detail of the BD area where MCC was identified; e) MCC, hematoxylin and eosin (H&E) stain, magnification $\times 10$; f) MCC with dot-like positivity for CK20, immunohistochemistry, magnification $\times 10$; g) MCC negative for TTF-1, immunohistochemistry, magnification $\times 10$; h) laterocervical lymph node SCLC metastasis, H&E stain, magnification $\times 10$; i) laterocervical lymph node SCLC metastasis positive for CK20, immunohistochemistry, magnification $\times 10$; l) laterocervical lymph node SCLC metastasis with focal positivity for TTF-1, immunohistochemistry, magnification $\times 10$.

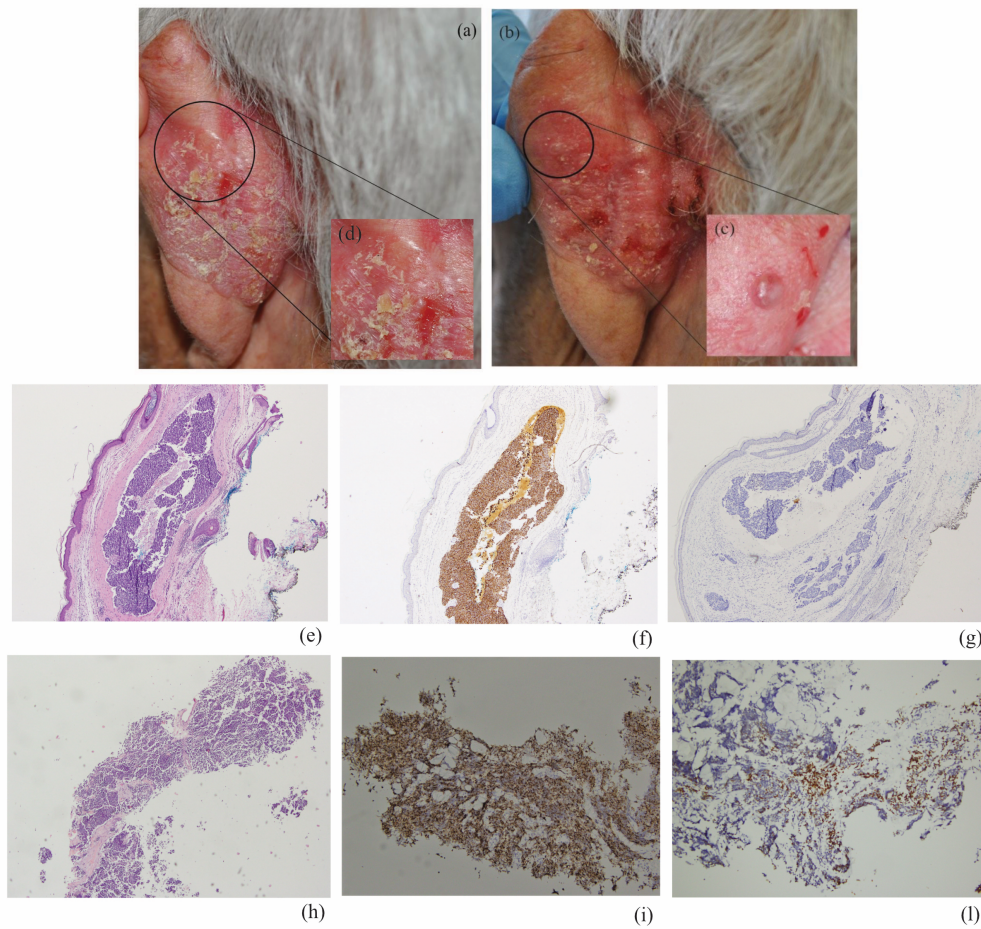


Table 1. Characteristics of 27 reported cases of MCC associated with BD/SCC from January 1990 to December 2025.

Authors	Year	Age/Se x	Diagnosis	Localization	Risk Factors	Therapy	Metastasis	Outcome
Zhang et al.	2025	82/F	MCC/SCC	Right side of the face	not reported	SE	yes	disease-free at 2 months; died after 6 months
Ishihara et al.	2024	87/M	MCC/BD	Dorsum of the hand	UV radiation	SE	no	no recurrence
Chen et al.	2024	51/M	MCC/BD	Right waist	not reported	SE	no	3 years without recurrence
		87/F	MCC/BD	Right mandible	not reported	SE	no	6 months without local recurrence
Jeha et al.	2024	83/M	MCC/SCCis	Neck	not reported	SE	yes	not reported
Park et al.	2024	69/M	MCC/SCC	Left lower lip	NMSC	SE, RT	no	not reported
Swain et al.	2022	32/F	MCC/BD	Right dorsum of the hand	not reported	SE, RT	yes (LNM)	7 years without recurrence
Hobbs et al.	2020	66/M	MCC/BCC/SCCis	Right anterior shoulder	liver and renal transplantation, NMSC	SE	yes (LNM)	under treatment
Kiyohara et al.	2019	65/M	MCC/BD	Left leg	not reported	SE, Avelumab	yes (LNM)	6 months without recurrence
Yang et al.	2019	71/M	MCC/SCCis	Right cheek	NMSC	SE	not reported	not reported
Casari et al.	2018	85/F	MCC/BD	Left cheek	UV radiation	SE	no	not reported
Jeong et al.	2018	82/F	MCC/BD	Right mandibular angle	BD	not reported	not reported	not reported
Fasiha et al.	2018	67/F	MCC/SCCis	Right shoulder	lung cancer and transplantation, skin cancer	SE	no	not reported
Czapiewski et al.	2016	76/F	MCC/SCCis	Cheek	not reported	not reported	yes (LNM)	recurrence; died 14 months after diagnosis
		77/M	MCC/BD	Scalp	not reported	not reported	no	not reported
Miraflor et al.	2016	71/M	MCC/BD	Left zygoma	MM and NMSC	SE	no	1 year without recurrence
McGowan et al.	2016	73/F	MCC/SCCis	Right mandible	not reported	SE	no	not reported
Chou et al.	2016	77/F	MCC/SCC	Right breast	arsenic exposure	SE, right axillary LND	yes (LNM)	not reported

Tono et al.	2015	71/M	MCC/BD	Back	not reported	SE	no	not reported
Schick et al.	2015	93/F	MCC/SCCis	Left mandible	not reported	SE, LND, RT	no	2 years without recurrence
Yamamoto et al.	2014	71/F	MCC/BD	Left cheek	none reported	SE	no	not reported
Choe et al.	2014	77/F	MCC/BD	Right inguinal area	none reported	SE, CT, RT	yes (LNM and liver metastases)	under treatment
Ishida et al.	2013	86/M	MCC/BD	Chest	not reported	SE	yes (LNM)	not reported
		87/F	MCC/BD	Right cheek	not reported	SE	not reported	not reported
Park et al.	2012	75/F	MCC/BD	Left mandibular angle	none reported	PC	not reported	not reported
Okamoto O et al.	1998	74/F	MCC/BD	Left cheek	not reported	SE, LND	not reported	11 months without recurrence
Schenk et al.	1991	79/F	MCC/BD	Left temporal region	not reported	SE, RT	yes (LNM)	LNM 3 weeks after completion of RT

B-CLL, B-cell chronic lymphocytic leukemia; BD, Bowen's disease; CT, chemotherapy; F, female; LND, lymph node dissection; LNM, lymph node metastasis; M, male; MCC, Merkel cell carcinoma; MM, malignant melanoma; NMSC, non-melanoma skin cancer; PC, palliative care; RT, radiotherapy; SCC, squamous cell carcinoma; SCCis, squamous cell carcinoma in situ; SE, surgical excision; UV, ultraviolet.