# Incidental diagnosis of blastic plasmacytoid dendritic cell neoplasm in skin excision for basal cell carcinoma

**KEYWORDS:** basal cell carcinoma, blastic plasmacytoid dendritic cell neoplasm, CD123

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare entity first described in the mid-1990s.[1] It typically affects elderly patients, with a slight male predominance (M:F ratio 2-3:1).[2,3] Clinically, BPDCN is characterized by abrupt onset of rapidly progressive nodules or ecchymotic plaques with concurrent or subsequent involvement of the bone marrow and peripheral blood.[3] Prognosis is dismal.[2] Histopathologically, the neoplastic infiltrate is composed of monomorphous medium-sized to large cells expressing CD4, CD56, CD123, and TCL1.[2,4]

The association of non-melanoma skin cancer (NMSC) with hematolymphoid malignancy is well documented, most frequently involving chronic lymphocytic leukemia (CLL) seen incidentally in biopsy or excision specimen of squamous cell carcinoma or basal cell carcinoma (BCC).[5] Occasionally, such observations may lead to the initial diagnosis of the hematolymphoid malignancy.[6,7]

We recently encountered the case of a 74-year-old man without any history of hematolymphoid malignancy, who underwent excision of a skin tumor on his left forearm. Clinical impression was BCC. Histopathologic examination confirmed a BCC with nodular and focally infiltrative growth patterns. In addition, there was a dense multinodular hematolymphoid infiltrate in the surrounding dermis and superficial subcutis with accentuation around adnexal structures and blood vessels (Figure 1A). The majority of these cells were medium-sized with scant to moderate amount of cytoplasm, oval to irregular nuclei, and mostly fine chromatin. Some of these cells contain eccentrically located nuclei imparting a plasmacytoid morphology (Figure 1B).

By immunohistochemistry, the atypical hematolymphoid cells were diffusely and strongly positive for CD45, CD4 (Figure 1C), CD56 (Figure 1D), CD123 (Figure 1E), TCL1, and Bcl-2, and were weakly positive for CD2. These cells were diffusely negative for CD3, CD5, CD8, CD20, CD13, CD15, CD117, and myeloperoxidase (MPO) (Figure 1F). Ki-67 revealed a proliferation index of approximately 30% within the infiltrate.

A diagnosis of BCC with concomitant BPDCN was rendered. This diagnosis was unexpected, and the patient was subsequently referred to oncology for further workup and treatment.

Although cutaneous epithelial neoplasms are commonly associated with at least mild inflammation, a hematolymphoid malignancy should be suspected when the infiltrate is unusually dense or extensive, and should prompt clinical correlation and immunohistochemical workup. As mentioned above, CLL represents the most common leukemic infiltrate seen in conjunction with NMSC. In our case, the presence of medium-sized cells, their fine rather than condensed chromatin, and the CD20- CD5- immunophenotype excluded a diagnosis of CLL. While CD56 expression may raise the possibility of an extranodal NK/T cell lymphoma, the coexpression of CD4 and CD123 as well as the negative staining for CD3

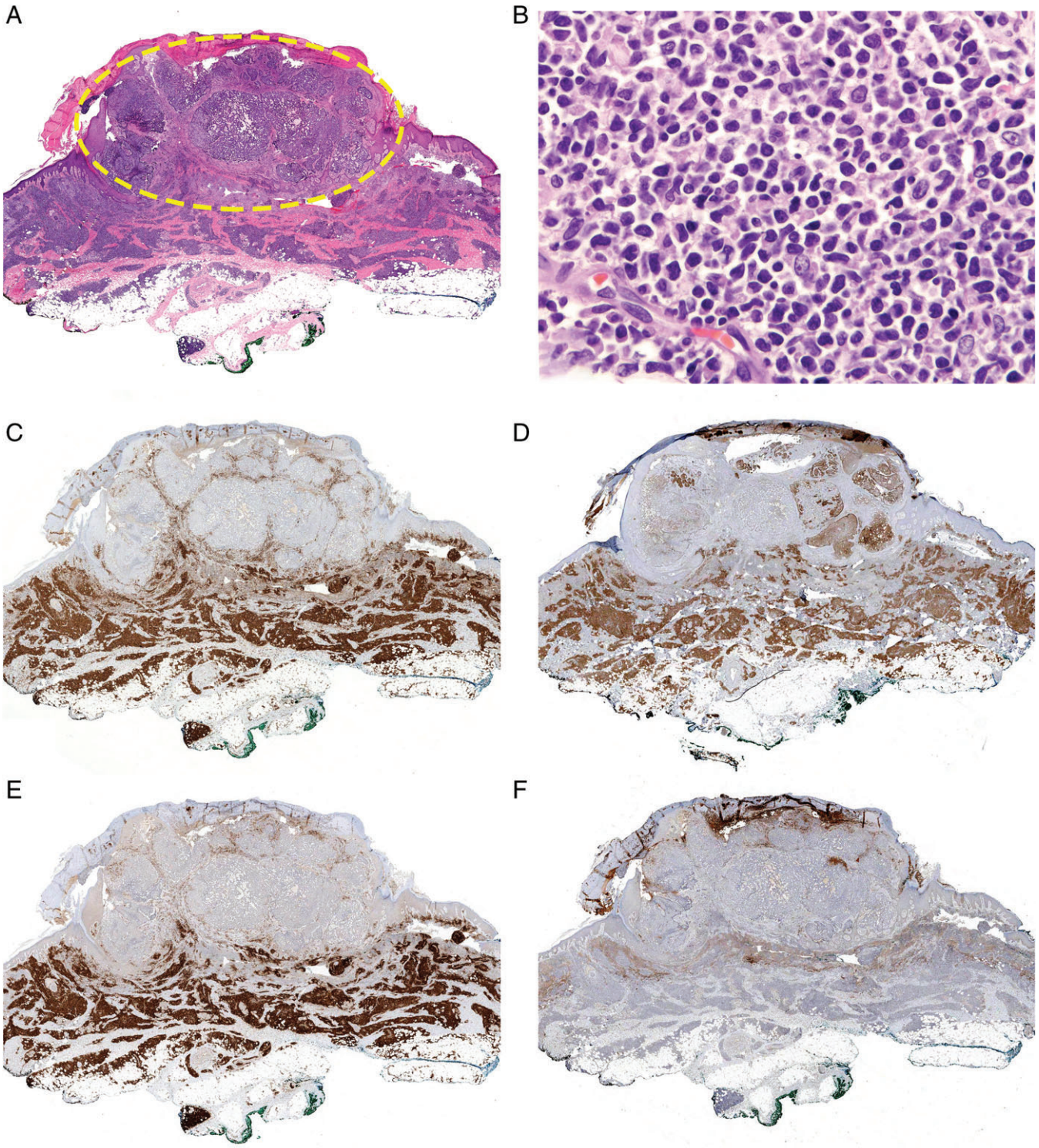


**FIGURE 1** Skin excision from the left forearm. A, An ulcerated nodule of basal cell carcinoma infiltrates the superficial to mid dermis (yellow circle). The tumor is associated with a brisk hematolymphoid infiltrate accentuated around blood vessels and adnexal structures in the surrounding dermis and superficial subcutis (hematoxylin and eosin [H&E] × 20). B, High magnification of the hematolymphoid infiltrate reveals a predominance of medium-sized cells with scant to moderate amount of amphophilic cytoplasm, oval to irregular nuclei, and mostly fine chromatin. Some of these cells contain eccentric nuclei imparting a plasmacytoid morphology (H&E × 600). C, CD4 is diffusely positive in the infiltrate (×20). D, CD56 also shows diffuse positivity in the infiltrate, as well as patchy staining in the basal cell carcinoma (×20). E, CD123 similarly shows diffuse staining (×20). F, The infiltrate is negative for myeloperoxidase (×20)

would speak against this entity. Lastly, the lack of staining for myeloid markers (CD13, CD15, CD117, MPO) speaks against a myeloid leukemic infiltrate. It should be noted, however, that some cases of acute myeloid leukemia, especially those with monocytic differentiation, may share a similar immunophenotype with BPDCN (CD4+ CD56+ CD123+ MPO-), which will require additional immunohistochemical markers and potentially molecular analysis for distinction.[8–10] Two studies have concluded that coexpression of all four plasmacytoid dendritic cell markers: CD4, CD56, CD123, and TCL1, as seen in our case, would effectively confirm a diagnosis of BPDCN and distinguish it from most cases of MPO- myeloid leukemia cutis.[3,8] Another study has shown a similar utility of TCF4 in this differential diagnosis.[11]

To the best of our knowledge, this is the first reported case of co-existing NMSC and BPDCN. Given its rarity, we favor that this phenomenon is purely coincidental ("collision tumor"). While most dermatopathologists are aware of the occasional finding of CLL infiltrate in excision specimens for NMSC, our case highlights the importance of keeping a broad differential diagnosis and performing immunohistochemical workup to rule out other hematolymphoid neoplasms. Correct identification of an aggressive hematolymphoid malignancy such as BPDCN, especially as an initial diagnosis, carries enormous clinical implications.

## ORCID

*Jayson Miedema* http://orcid.org/0000-0002-9204-1429
*May P. Chan* http://orcid.org/0000-0002-0650-1266

Jayson Miedema[1]
Shane R. Starr[2]
May P. Chan[1,3]

[1]*Department of Pathology, University of Michigan, Ann Arbor, Michigan*
[2]*Integrated Pathology Associates, McLaren Bay Region Hospital, Bay City, Michigan*
[3]*Department of Dermatology, University of Michigan, Ann Arbor, Michigan*

*Email: mpchan@med.umich.edu*
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