Blastic Plasmacytoid Dendritic Cell Neoplasm: A Diagnostic and Therapeutic Challenge

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INTRODUCTION:

Blastic plasmacytoid dendritic cell neoplasm (BPDCN), previously referred to as blastic natural killer (NK) cell lymphoma or agranular CD4+ CD56+ hematodermic neoplasm [1], is a rare and aggressive hematologic malignancy, accounting for less than 1% of acute leukemias and cutaneous lymphomas [2]. It was first described in the 2008 fourth edition of the World Health Organization (WHO) classification, where it was categorized under acute myeloid leukemia (AML) and related precursor neoplasms. In the revised fourth edition (2017), BPDCN was reclassified as a separate and distinct disease entity [3]. It arises from precursors of plasmacytoid dendritic cells (pDC), with its pathogenesis involving activation of pathways [2]. BPDCN can occur across all age groups but exhibits a strong male predominance and typically affects patients in their seventh or eighth decade, without any known ethnic or racial predisposition [3,4]. Here, we report a diagnostically challenging and rare case of BPDCN in an 82-year-old man with a prior history of chronic neutropenia and chronic myelomonocytic leukemia (CMML).

PATIENT:

An 82-year-old male with a past medical history of glaucoma and chronic neutropenia, under surveillance since 2009, was diagnosed in 2022 with CMML. Cytogenetic analysis at diagnosis revealed a mosaic karyotype of 45, XY [23]/46, XY [6], with loss of the Y chromosome in the majority of metaphases. Next-generation sequencing identified KRAS and TET2 mutations. In November 2024, the patient developed a subconjunctival mass next to the caruncle of the left eye measuring approximately 1cm (Figure 1A), multiple painless nodular lesions on the scalp, which progressively extended to the torso and hands (Figure 2A). Skin biopsy demonstrated diffuse dermal infiltration by rounded or oval mononuclear cells with grey-blue cytoplasm and atypical nuclei of variable size. Immunohistochemistry revealed CD4+, CD56+, CD68+, and CD163+ expression with rare MPO (Myeloperoxidase) positive cells, CD3, CD34, and CD123 were negative. These findings were suggestive of leukemic transformation, possibly toward acute myelomonocytic leukemia (AMML) with cutaneous involvement. A bone marrow aspirate showed 3% blasts and a monocytic proliferation estimated at 28% of nucleated cells. The initial systemic therapy with azacitidine and venetoclax yielded no clinical or hematologic response. Subsequent evaluation included repeat bone marrow and skin biopsy. Flow cytometry on a second skin biopsy revealed 6% monocytes CD14+, CD4+, CD56−, CD123 low, HLA-DR+, CD38+, not expressing pDC markers. However, 17% of cells expressed a phenotype consistent with pDC origin with strong CD123+, CD4+, CD56 low, HLA-DR+, CD304+, CD303+, FCER1+/− low, CD38+, NG2 low. Given the diagnostic ambiguity and clinical progression, empiric second-line chemotherapy protocol CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) was initiated. The patient exhibited a rapid clinical improvement within one week, including resolution of ophthalmic lesions (Figure1B) and marked regression of cutaneous nodules (Figure 2B). However, the treatment-related toxicity was severe, and the patient unfortunately relapsed with pleural localization and succumbed to sepsis two weeks after initiating CHOP.

Fig.1: Subconjunctival mass next to caruncle of the left eye before CHOP (A) and after CHOP (B)

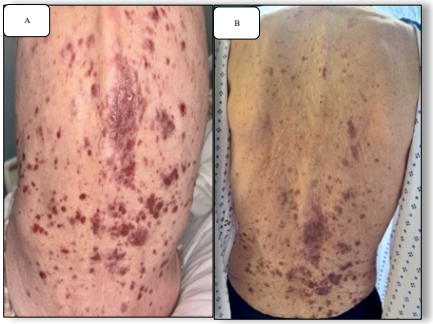

Fig. 2: Multiple nodular tumoral skin lesions over the back before (A) and after CHOP (B)

DISCUSSION

BPDCN is a rare and highly aggressive hematologic malignancy derived from precursors of plasmacytoid dendritic cells. It exhibits a predilection in the seventh or eighth decade [4], and is frequently characterized by cutaneous involvement at presentation, with or without systemic manifestations such as bone marrow infiltration, lymphadenopathy [3,5]. Median survival is often less than one year [3,4,5]. Our patient, an 82-year-old man with history of chronic neutropenia and a prior diagnosis of chronic myelomonocytic leukemia, developed rapidly progressive cutaneous lesions. The diagnostic process was complex, in part due to his myeloid neoplasm and the evolving immunophenotypic profile of the disease over time. Subsequent tissue and bone marrow analyses from an expert center revealed a characteristic immunophenotype consistent with BPDCN, including strong expression of CD123, CD303, CD304, HLA-DR, CD4, and low CD56. The diagnosis of BPDCN relies primarily on immunophenotyping. Julia et al. propose a diagnostic panel of immunologic markers - CD56, CD4, CD43, CD45RA, CD123, TCL1A, CD2AP, CD303- suggesting that expression of at least four of these strongly supports the diagnosis of BPDCN [3,6]. A defining feature of BPDCN is the absence of lineage-specific markers for B cells $CD19^-$, $CD20^-$, $CD79a^-$, T cells $CD3^-$, $CD5^-$, and myeloid or monocytic cells MPO^-, $lysozyme^-$, $CD13^-$, $CD117^-$ [5].

Therapeutically, no consensus exists on a standard regimen for BPDCN, though multiagent chemotherapy regimens derived from acute leukemia protocols such as hyper-CVAD, or lymphoma-based regimens as CHOP [3], have been used with variable success. In our patient, CHOP was selected due to the rapid clinical deterioration and uncertain initial diagnosis. Remarkably, the patient demonstrated a swift clinical response with resolution of ophthalmic and cutaneous lesions within one week. However, this transient improvement was followed by fatal infectious complications, underlining the limited durability of responses in BPDCN and the heightened vulnerability to treatment-related toxicity.

CONCLUSION:

This case illustrates the diagnostic and therapeutic challenges posed by BPDCN, the importance of tissue analysis and advanced immunophenotyping for definitive diagnosis, the critical need for early diagnosis, careful selection of therapeutic strategies, and close monitoring of treatment-related complications to improve patient outcomes. While novel CD123-targeted agents such as tagraxofusp and IMGN632 represent significant advancements, allogeneic hematopoietic stem cell transplantation remains the cornerstone of long-term disease control. Continued collaboration and innovation are essential to improve the prognosis of this aggressive malignancy.

REFERENCE:

1- Saha K, Thoram G, Roychoudhury S (October 19, 2024) Blastic Plasmacytoid Dendritic Cell Neoplasm: A Case Report of a Rare and Aggressive Hematologic Malignancy. Cureus 16(10): e71849. DOI: 10.7759/cureus.71849
2- Yan Luo, Li-Juan Wang, Cheng-Long Wang: Advancing the understanding and management of blastic plasmacytoid dendritic cell neoplasm: Insights from recent case studies, World J ClinCases 2024 November 6; 12(31). DOI: 6441-6446. 10.12998/wjcc. v12.i31.6441.
3- Maria Rosaria Sapienza, Alessandro Pileri , Enrico Derenzini , Federica Melle , Giovanna Motta , Stefano Fiori , Angelica Calleri , Nicola Pimpinelli , Valentina Tabanelli and Stefano Pileri, Blastic Plasmacytoid Dendritic Cell Neoplasm: State of the Art and Prospects Cancers 2019, 11, 595; doi:10.3390/cancers11050595
4- Chen Gong*, Ying Liu* and Mingzhi Zhang: A systematic literature review of 74 Chinese blastic plasmacytoid dendritic cell neoplasm patients, Therapeutic advances in hematology 2024, Vol. 15: 1–14. DOI: 10.1177/20406207241251602.
5- Amy M Trottier Sonia Cerquozzi Carolyn J Owen: Blastic plasmacytoid dendritic cell neoplasm: challenges and future prospects, Blood and Lymphatic Cancer: Targets andTherapy 2017:7 85–93 https://doi.org/10.2147/BLCTT.S132060