SUBMITTED 27 FEB 24
REVISION REQ. 26 MAR 24; REVISION RECD. 14 APR 24
ACCEPTED 12 MAY 24
ONLINE-FIRST: JUNE 2024
DOI: https://doi.org/10.18295/squmj.6.2024.036

Blastic Plasmacytoid Dendritic Cell Neoplasm

Dmitry V. Kravchenko,[1] *Dmitry A. Zinovkin,[2] Denis A. Davydov,[3] Pavel G. Kisialeu,[4] Pavel A. Kopschaj,[4] Oleg Savchenko,[5] Mariya Savchenko,[6] Maryna V. Barauniova,[4] Anna S. Portyanko,[4] Md Zahidul Islam Pranjol[7]

[1]Department of Hematology. Republican Research Center for Radiation Medicine and Human Ecology, Gomel, Belarus; [2]Department of Pathology, Gomel State Medical University, Gomel, Belarus; [3]Laboratory of Morphology, Molecular & Cellular Biology, [4]Republican Molecular Genetic Laboratory of Carcinogenesis and Departments of [5]Thoracic Oncology and [6]Oncological (Chemotherapeutic) Day Care, N.N.Alexandrov National Cancer Centre of Belarus, Minsk, Belarus; [7]School of Life Sciences, University of Sussex, Brighton, UK
**Corresponding Author's e-mail: zinovkin_da@gsmu.by*

Introduction

In January 2022, a 46-year-old female patient was admitted to the Department of Hematology of a research centre with marked general weakness and papular rashes on the skin with a maroon tinge (Fig. 1A). Skin incisional and breast core biopsies were performed. The dermis and subcutaneous fat exhibited a diffuse, relatively uniform infiltrate without apparent involvement of the epidermis or adnexa. The cells were small-to-medium sized with round nuclei devoid of conspicuous nucleoli (Fig. 1B). The PET-CT scan showed numerous areas of increased 18F-FDG uptake distributed throughout the dermis and subcutaneous tissues of the trunk and extremities, with the largest concentrations observed in the breast tissues (d = 4.5 cm, SUVmax = 6.5). Hypermetabolic substrate was also noticed in left inguinal lymph node (Fig. 1C). Immunohistochemical analysis revealed that tumor cells expressed CD45, CD43, CD56, TdT

(Fig. 2), CD4, bcl2, bcl6. The proliferation rate (Ki-67) was about 30-40%. Tumor cells were negative for CD2, CD3, CD5, CD7, CD8, CD15, CD20, CD21, CD30, CD34, CD68, CD117, ALK, PD1, EBV, cyclinD1, granzyme B, and perforin. Blastic plasmacytoid dendritic cell neoplasm (BPDCN) diagnosis was confirmed. Considering the similarity of BPDCN cells with lymphoid cells, treatment with the CHOP-related protocol (DA-EPOCH) was initiated in February 2022. A positive response was observed at the end of the course: the majority of tumor masses in soft tissues were no longer reliably detected, with remaining ones decreased in size. After 5 such courses, a mobilization and collection of hematopoietic stem cells was performed in August 2022 for subsequent autologous transplantation. One month later, a drastic deterioration of the general condition occurred: weakness, spinal pain, skin rashes, and blastocytosis appeared (Fig. 3). In response to the relapse of BPDCN post-DA-EPOCH protocol, a chemotherapy course "7+3" was administered during October-November 2022, targeting the myeloid features of the tumor cells. Following this, it did not achieve a second remission and instead developed bacterial pneumonia by the end of the course. Taking this complication into account, it was decided to use monotherapy with Azacytidine at dose 75 mg/m^2 (150 mg/day subcutaneously, days 1-7) to reach remission and treat pneumonia (January 2023). Antimicrobial therapy was used for the treatment of bacterial pneumonia. On the 10th day after the start of the Azacytidine course, we observed a positive response with stable levels of Hb ant platelet count without blood transfusions, absence of agranulocytosis and blast cells in complete blood count, and resolution of pneumonia. The clinical-laboratory remission lasted over 1 month duration.

As the criteria for defining complete remission in BPDCN remains undetermined, we adopted the remission criteria used for acute myeloid leukemias (AML). This entails: 1) less than 5% blasts in the bone marrow, with a count of at least 200 nucleated cells; 2) absence of blasts in the peripheral blood; 3) an absolute neutrophil count exceeding 1,000/μL; and 4) a platelet count exceeding 100×109/L.

Patient consent for publication has been obtained.

Comment

BPDCN is a rare (under 0.5%), clinically aggressive hematological malignancy with cells originating from predecessors of the plasmacytoid dendritic cells. This hematological malignancy affects mostly men aged over 60 years old[1]. Rarely, as demonstrated in our case, BPDCN can impact young and pediatric patients. The disease tends to involve more than one site. BPDCN in most cases affects the skin, bone marrow, lymph nodes and the peripheral blood. In the initial stages, the disease typically manifests in the skin in 90% of cases and tends to persist until BPDCN spreads to multiple organs, ultimately resulting in the patient's death. Nowadays, it is hypothesized that the skin may initially play role of the "shelter" organ, which restricts the BPDCN progression[2].

Expression of CD4, CD56, and absence of B-, T-lymphocytes, NK cells, myeloid or monocytic cells markers combination is suggestive for BPDCN. Markers CD123, CD303, and TCL1 specific for plasmacytoid dendritic cells are used in the diagnosis of BPDCN[3]. However, it is known that not all plasmacytoid dendritic cell markers are expressed in 100% cases. Also, small histopathology laboratories in low-income countries often do not utilize these specific plasmacytoid dendritic cell markers as recommended immunohistochemical markers. Therefore, BPDCN could potentially be diagnosed through a process of exclusion. The diagnosis of PDCN was performed on the basis of presence of multiple skin nodules, PET-CT disease specific changes and expression of CD4, CD56, CD43, Tdt, CD45 by malignant cells and absence of expression of B-, T-, NK-cells, monocytes and myeloid lineage markers. The CD303, TCL1A, CD2AP, SPIB and TCF4 marker expressions were not assessed because of their unavailability[4].

Systemic chemotherapy regimens which are utilized in the management of AML are used in the chemotherapy of BPDCN patients. Different chemotherapy regimens showed varying levels of clinical response in patients with BPDCN[5]. In a study by Yun S. et al., treatment outcomes were examined in 42 BPDCN patients. The hyper-CVAD regimen demonstrated a higher complete response rate compared to CHOP-based regimens or Tagraxofusp (91% vs 50% vs 50%), although this disparity did not reach statistical significance. Currently, there is no sufficiently effective chemotherapeutic scheme treatment of BPDCN; the 5-year overall survival is over 20%[6].

In published reports, both Venetoclax and Azacitidine are associated with short duration of the responses and extending the response might require a combination with other modalities and further investigation[7]. In our case, we showed that hypomethylating drugs could be a feasible treatment option for BPDCN patients with infectious complications.

Authors' Contribution

DAZ and MZIP drafted the initial manuscript. DAD, OS and MS reviewed the case details and edited the manuscript. ASP did a general review and edited manuscript. PGK, PAK and MVB reviewed the histopathology slides and did a general editing of the manuscript. All authors contributed to revising the manuscript. DAZ supervised the work. All authors approved the final version of the manuscript.

References

1. Lim MS, Lemmert K, Enjeti A. Blastic plasmacytoid dendritic cell neoplasm (BPDCN): A rare entity. BMJ Case Reports 2016. doi:10.1136/bcr-2015-214093.
2. Sapienza MR, Pileri A, Derenzini E, Melle F, Motta G, Fiori S, et al. Blastic plasmacytoid dendritic cell neoplasm: State of the art and prospects. Cancers 2019;11:595. doi:10.3390/cancers11050595. Wang
3. Safaei A, Monabati A, Mokhtari M, Solhjoo F, Montazer M. Blastic Plasmacytoid Dendritic Cell Neoplasm; A Report of Three Cases. Iran J Med Sci. 2019;44(1):74-78.
4. Goel D, Bhargava R. Blastic plasmacytoid dendritic cell neoplasm. A rare hematodermic malignancy. Hematol Transfus Cell Ther. 2020;42(4):384-386. doi: 10.1016/j.htct.2019.10.006.
5. Adimora IJ, Wilson NR, Pemmaraju N. Blastic plasmacytoid dendritic cell neoplasm (BPDCN): A promising future in the era of Targeted therapeutics. Cancer 2022;128: 3019–3026. doi:10.1002/cncr.34345.
6. Yun S, Chan O, Kerr D, Vincelette ND, Idrees A, Mo Q, et al. Survival outcomes in blastic plasmacytoid dendritic cell neoplasm by first-line treatment and Stem Cell Transplant. Blood Advances 2020;4:3435–42. doi:10.1182/bloodadvances.2020001875.

7. Azad F, Zhang J, Miranda CJ, Gravina M. Venetoclax and Azacitidine in the Treatment of Blastic Plasmacytoid Dendritic Cell Neoplasm Refractory to Conventional Therapy. Cureus. 2022 Dec 29;14(12):e33109. doi: 10.7759/cureus.33109.

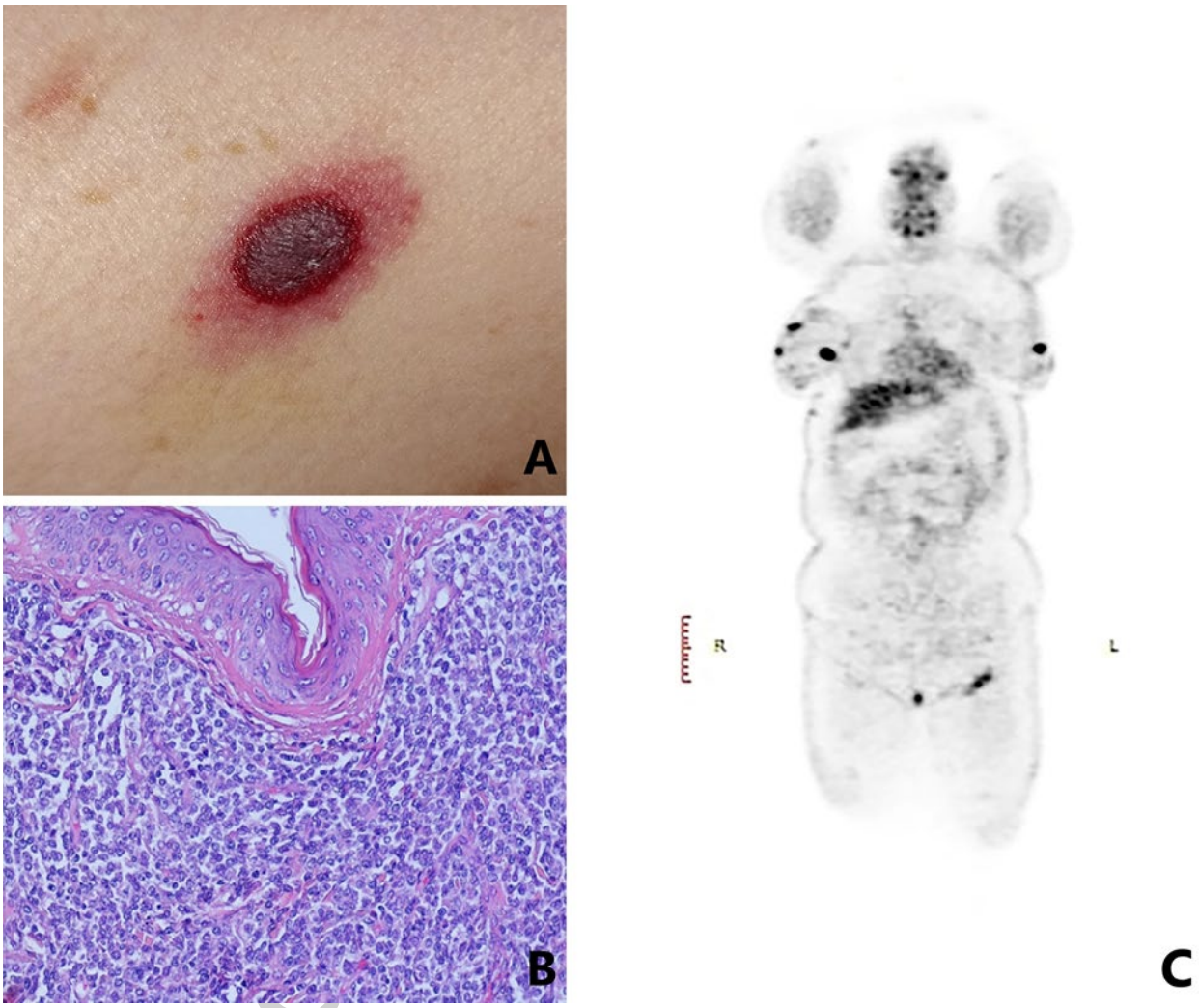

Figure 1: A. Blastic plasmacytoid dendritic cell neoplasm presented as an erythematous papule on the skin; B. The neoplastic cells are small-to-medium-sized blasts with fine chromatin and scanty cytoplasm. Stain: haematoxylin & eosin, ×200; C. PET-CT: multiple 18F-FDG-avid foci in the breast tissues and inguinal lymph node.

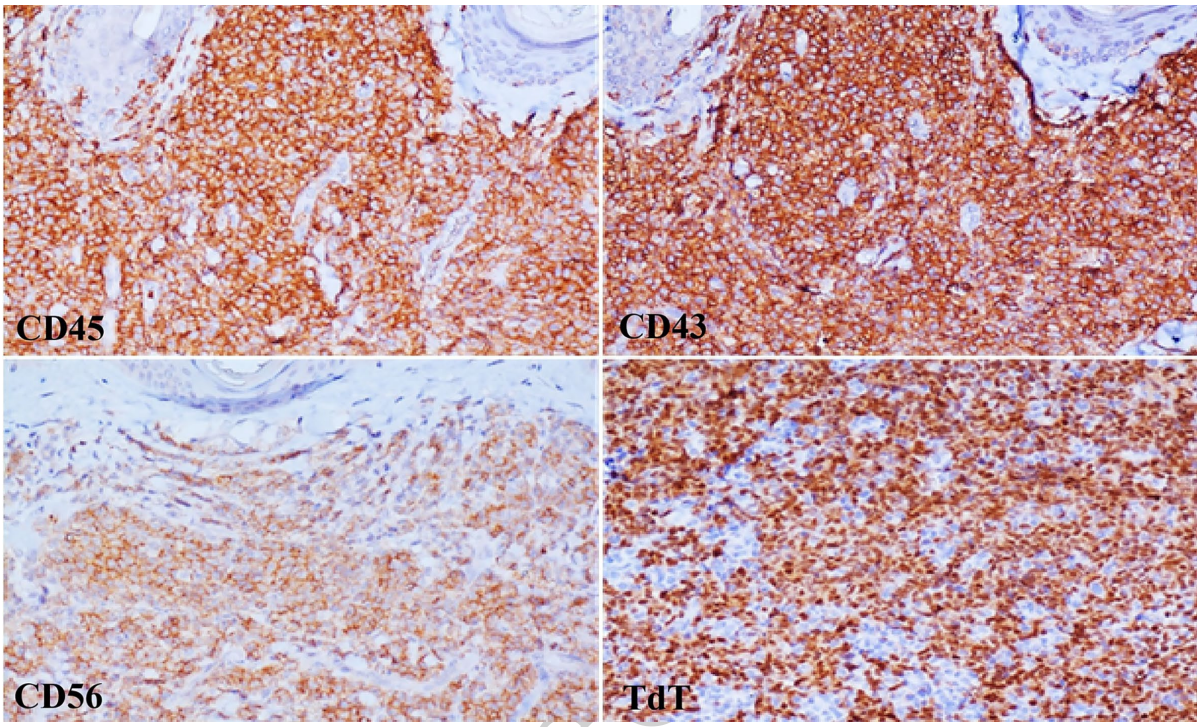

Figure 2: Tumor cells showed strong CD45 and CD43 along with moderate CD56 expression, the majority of cells expressed TdT. Stain: HRP-polymer-based immunohistochemistry, counterstain: Meyer's haematoxylin, Magnification ×200.

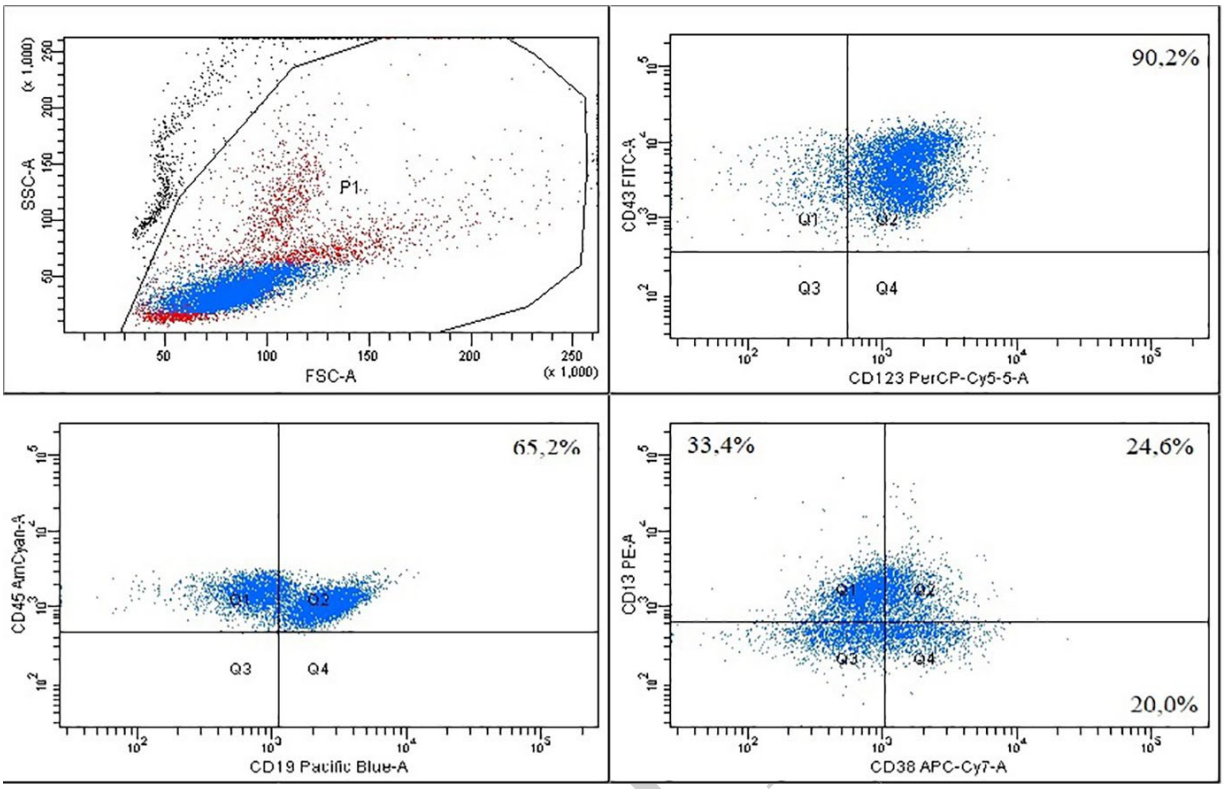

Figure 3: Flow cytometry of the bone marrow reveals hematogenous dissemination with occurrence of neoplastic cells in the peripheral blood