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Management of blastic plasmacytoid dendritic cell neoplasm: a case series from Chile

Manejo de la neoplasia blástica de células dendríticas plasmocitoides: reporte de dos casos clínicos en Chile

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Abstract

Blastic plasmacytoid dendritic cell neoplasms (BPDCNs) are a rare hematologic malignancy characterized by an aggressive clinical course, short survival following chemotherapy, and poor prognosis. Clinical manifestations most commonly involve the skin; however, lymph nodes, liver, peripheral blood, and the meninges can also be affected. The optimal therapeutic approach remains undetermined, hindering the design and implementation of clinical trials. Nevertheless, hematopoietic stem cell transplantation (HSCT) is widely recognized as crucial for achieving prolonged remission and potential cure. We present two BPDCN cases treated with HSCT and a brief literature review, marking the first published report of this disease in our country, Chile. In the first case, a 33-year-old male with a thoracic mass and cutaneous nodules was diagnosed via immunohistochemistry (CD56, CD123, CD4, BCL-2, Ki-67 45%, and CD68). He received five cycles of chemotherapy, achieved complete remission, and underwent autologous stem cell transplantation. One year later, he relapsed with rapid leukemic progression and died of refractory disease. The second case involves a 17-year-old female presenting with severe headaches, anemia, thrombocytopenia, and 48% blasts in peripheral blood; BPDCN with central nervous system involvement was confirmed. After induction chemotherapy (cytarabine and daunorubicin) plus intrathecal treatment, she achieved remission and underwent four cycles of high-dose cytarabine. A successful haploidentical transplant from her father followed, and she remained in remission for two years post-transplant without significant complications. These cases underscore the pivotal role of HSCT in BPDCN management. They also highlight the urgent need for prospective research to establish definitive treatment protocols, emphasizing the importance of ongoing research.

Keywords: hematology; hematologic neoplasm; chemotherapy; targeted therapies

Resumen

La Neoplasia Blástica de Células Dendríticas Plasmacitoides (BPDCN) es una entidad hematológica poco frecuente, de curso clínico agresivo, supervivencia limitada y mal pronóstico. Suele manifestarse con lesiones cutáneas, pero puede afectar ganglios linfáticos, hígado, sangre periférica y meninges. No existe un consenso definitivo sobre el tratamiento óptimo, dificultando la realización de ensayos clínicos. Sin embargo, el trasplante de células madre hematopoyéticas es esencial para lograr remisiones prolongadas y potencial curación. Presentamos dos casos diagnosticados de BPDCN, ambos tratados mediante trasplante de células madre: el primer caso es un varón de 33 años con masa torácica y lesiones cutáneas, confirmado inmunohistoquímicamente (CD56, CD123, CD4, BCL-2, Ki-67 45%, CD68). Tras cinco ciclos de quimioterapia, alcanzó remisión completa y se consolidó con trasplante autólogo, pero recayó al año con evolución leucémica rápida y falleció por enfermedad refractaria. El segundo caso corresponde a una joven de 17 años con cefalea, anemia, trombocitopenia y 48% de blastos en sangre periférica, con afectación del sistema nervioso central. Recibió quimioterapia de inducción (citarabina y daunorrubicina) además de terapia intratecal, logrando remisión; posteriormente recibió cuatro ciclos de citarabina a dosis altas. Se realizó trasplante haploidéntico (padre) con excelente tolerancia, y tras dos años permanece en remisión sin complicaciones relevantes. Estos casos refuerzan el papel central del trasplante de células madre hematopoyéticas en la BPDCN y resaltan la necesidad de estudios prospectivos para definir protocolos de tratamiento. Este reporte es el primero de su tipo en nuestro país e incluye una breve revisión de la literatura.

Palabras clave: hematología; neoplasia hematológica; quimioterapia; terapias dirigidas

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Introduction

Blastic plasmacytoid dendritic cell neoplasms (BPDCN) constitute a group of hematological malignancies characterized by an aggressive course, short durations of therapy response, and poor prognosis, with a median survival of 12 months. Clinical manifestations are typically heterogeneous, with skin disease being the most common presentation. However, atypical involvements such as lymph nodes, visceral infiltration, leukemic progression, or meningeal compromise have also been reported (Kharfan-Dabaja *et al.,* 2025). The optimal therapy remains unestablished due to its very low incidence, greatly hindering the execution of randomized studies. Most recommended therapies are based on retrospective data or expert opinions. Nonetheless, there is a consensus that Stem Cell Transplantation represents the only potentially curative option available for clinically fit patients (Roos-Weil *et al*., 2013).

This paper presents two clinical cases of BPDCN with differing outcomes following HSCT. The patients explicitly consented to the use of medical records in this study.

Following the presentation of these cases, we review Remission Induction therapies, the role of Stem Cell Transplantation, and emerging treatments under investigation.

Material and Methods

Chemotherapy, pathology, and transplant records from the past five years were reviewed, identifying two BPDCN cases (Table 1). Both patients or their guardians provided signed consent to share their clinical data and complementary examinations. Due to the rarity of the disease and this being the first report of cases in our country, the Medline database was reviewed to obtain evidence of the diagnosis and management, and it was briefly presented in narrative form.

Case 1

A 33-year-old previously healthy male presented with a mass in the left hemithorax and nodular skin lesions on his back. Initial biochemical studies showed no abnormalities and a complete blood count was within normal limits. A skin biopsy revealed a pathologic cell infiltrate characterized by immunohistochemical staining positive for CD56, intense CD123, CD4, BCL-2, Ki-67 (45%), and CD68, confirming a diagnosis of BPDCN. Staging investigations found no further disease, indicating localized skin involvement. The patient underwent five cycles of chemotherapy, consisting of dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin. A positron emission tomography at the end of treatment showed complete remission. It was decided, in consensus with the patient, to proceed with autologous stem cell transplantation as consolidation therapy due to the absence of medullary or CNS involvement. Myeloablative conditioning with carmustine, etoposide, cytarabine, and melphalan was administered (also called BEAM), and the transplant was performed without significant toxicity. Platelet and granulocytic engraftment occurred by the second week, and a 3-month positron emission tomography confirmed complete metabolic remission. The patient remained asymptomatic for one year post-transplant until a mass appeared in the lower extremity, left axilla, scalp, and oropharynx, indicating relapse. Bone marrow and skin biopsies confirmed the recurrence. The disease rapidly progressed to leukemization. Treatment was initiated with a rescue regimen, including radiotherapy to the lesions, methotrexate, and asparaginase, followed by venetoclax due to treatment failure, to proceed to allogeneic bone marrow transplantation. Unfortunately, the patient succumbed to refractory disease progression.

Case 2

A healthy 17-year-old female patient, an only child, presented with severe headaches. Initial examinations revealed a complete blood count with hemoglobin at 10 g/dL, leukocytes at 12,500/µL with 48% immature blast cells, and platelets at 38,000/µL. A bone marrow study indicated complete infiltration by immature cells, with a normal karyotype and flow cytometry (8-color FACScanto analyzed using Infinicyt 2.0) identifying a blast population (82% of the cells analyzed) showing strong expression of HLA-DR, CD4, CD7, CD123, CD56, and weak, heterogeneous CD117. The same cytometric pattern was observed in the cerebrospinal fluid. Diagnosed with plasmacytoid dendritic cell neoplasm with central nervous system involvement, the patient underwent induction chemotherapy with a cytarabine and daunorubicin regimen, along with intrathecal treatment (cytarabine, methotrexate, and betamethasone over four monthly sessions), achieving blast clearance at the affected sites. She received four cycles of high-dose cytarabine for consolidation, maintaining remission. Donor screening identified an HLA haplo-match with her father, leading to allogeneic transplantation using a myeloablative protocol of Fludarabine (total dose 200 mg) and total body irradiation (1200 cGy in 6 fractions). 12.3 x 10^6 CD34/kg cells were infused. Post-transplant cyclophosphamide, tacrolimus, and mycophenolate were used for graft-versus-host disease prophylaxis. Post-transplant, the patient experienced febrile neutropenia, which was rapidly controlled. Granulocyte and platelet engraftment was documented on day 15, and she was subsequently discharged.

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The only significant late complication was limited chronic vitiliginous lesions, interpreted as graft versus host reaction, which responded quickly to corticosteroid treatment. After two years, the patient remains in remission with normal spinal cord studies, including cytology, flow cytometry, and a normal karyotype.

Table 1: Summary table, characteristics of diagnosis and treatments.

Parameter/patient	Case 1	Case 2
Age (years)	33	17
Gender	Male	Female
Cytopenias	No	Yes
Immunophenotype: present markers	CD56, intense CD123, CD4, BCL 2, Ki 67 (45%), and CD68	HLA DR, CD4, CD7, CD123, CD56, and weak CD117
Bone marrow involvement	No at onset. Yes at relapse	Yes
CNS involvement	No	Yes
Induction chemotherapy	DA-EPOCH	Daunorubicin/Ara-C (7+3)
Intrathecal therapy	No	MTX, ara-C, betamethasone
Transplant/conditioning	Autologous/BEAM	Allogeneic/fludarabine 150mg/m2 + TBI 12 Gy Haploidentical donor 6/12
Survival from diagnosis (months)	OS/PFS 14 m-12m	OS/PFS 18 m

Table 1 summarizes two BPDCN cases, highlighting their clinical characteristics, immunophenotypes, and treatments. It compares age, gender, cytopenias, bone marrow and CNS involvement, and therapeutic approaches, including induction chemotherapy, intrathecal therapy, and transplantation. Differences in treatment regimens and survival outcomes are also noted, with one case receiving an autologous transplant and the other undergoing allogeneic HSCT.

Discussion

BPDCN constitutes a group of hematological malignancies derived from the plasmacytoid dendritic cell, which originates from the myeloid lineage of hematopoiesis. The term "Plasmacytoid" refers solely to its morphological resemblance to plasma cells.

Functionally, these cells play a crucial role in the innate immune response, particularly in antiviral defense, by producing cytokines, predominantly type I interferons. With advancements in flow cytometry and immunohistochemistry, the plasmacytoid dendritic cell can be identified by their distinct immunophenotype: the absence of lineage-specific markers (CD19, cCD22, cCD3, MPO, CD14), coupled with the presence of plasmacytoid dendritic cell markers (CD123, HLA-DR, CD4), and, when available, more specific markers such as cTCL-1, CD303, and CD304. Distinguishing health from pathological plasmacytoid dendritic cells is crucial, with CD56 being a key indicator of the latter (Pagano *et al.,* 2016; Amon *et al.,* 2020)

BPDCNs account for a tiny percentage (less than 1%) of myeloid and lymphoid neoplasms. Most cases are diagnosed in older adults (with a median age of 60 to 70 years), and there is a slight predominance among males. However, pediatric cases and occurrences in young adults have also been reported, as illustrated by one of the cases mentioned in the article. Due to its rarity, the incidence is likely underestimated, and most epidemiological data come from case series and retrospective studies (Ujjwal *et al.,* 2023).

Diagnosing BPDCN requires a high degree of suspicion due to its varied clinical presentations, ranging from skin lesions or tumors resembling lymphoma to leptomeningeal infiltration or even acute leukemia. The lack of pathognomonic elements in cytology from blood, bone marrow, or involved tissues complicates Diagnosis further. Therefore, immunophenotyping is indispensable for accurate Diagnosis. Despite the absence of universally accepted diagnostic criteria, a panel of markers (CD4, CD56, CD123, and TCL1) has been identified as optimal for Diagnosis based on analysis of over 300 biopsy specimens (Orazi *et al.,* 2013).

Some molecular abnormalities are described in this entity, such as Recurrent Genetic Mutations (TET2, ASXL1, and RAS. These are the most frequent mutations in adults). ATM and ZRSR2 mutations and MYB rearrangements (primarily seen in pediatric patients). In this context, Next-Generation Sequencing (NGS) would be fundamental to the molecular characterization of BPDCN, allowing the identification of specific mutational profiles and differentiation from other hematologic neoplasms, such as myeloid leukemias

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and T/NK-cell lymphomas. NGS also enables the identification of potential new therapeutic targets, such as MYB, TET2, and BCL2. Eventually, it may help monitor minimal residual disease (MRD) in treated patients (Cuglievan *et al.,* 2023).

Despite its rarity, the aggressive nature of BPDCN and its short-lived response to intensive chemotherapy underscore its significance in various medical specialties. Historically, treatments have been categorized based on their similarity to lymphoblastic or myeloblastic leukemia and lymphoma regimens. Due to its scarcity, comparisons between treatment modalities are primarily derived from retrospective reviews. However, lymphoblastic leukemia-type intensive regimens have demonstrated superior response rates and progression-free survival (Kharfan-Dabaja *et al.,* 2025)

Hematopoietic stem cell transplantation (HSCT) has become an essential strategy for achieving prolonged control of BPDCN (Figure 1) (Table 2). Due to its high level of aggressiveness and marked tendency for relapse, HSCT enables the eradication of residual tumor clones and, in some cases, provides an immunologic antineoplastic effect (GvL) that helps maintain remission (Bruch *et al.,* 2023; Murthy *et al.,* 2023).

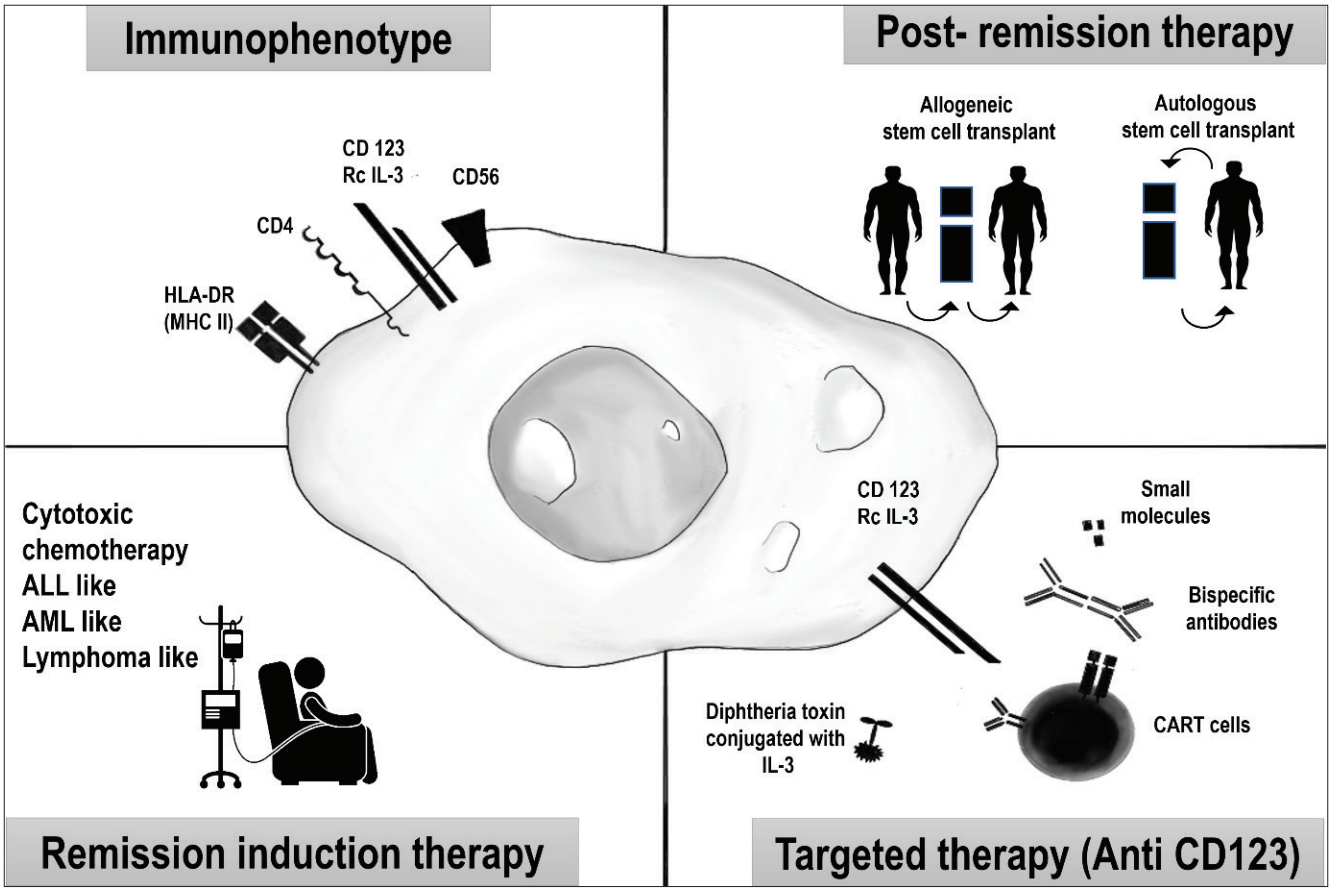

Figure 1: Immunophenotype, induction therapy, post-remission therapy, and new targeted therapies for blastic plasmacytoid dendritic cell neoplasm. This figure illustrates the immunophenotype, remission induction therapy, post-remission therapy, and targeted therapies for Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN). It highlights key markers such as CD123, CD4, and CD56 and therapeutic approaches such as chemotherapy, stem cell transplantation, and anti-CD123 targeted therapies like CAR-T cells and bispecific antibodies.

Autologous stem cell transplantation (ASCT) has mainly been used in patients who achieve complete response after chemotherapy to consolidate remission. Although some recent studies suggest that ASCT can prolong disease-free intervals, relapses remain frequent, which limits its curative potential (Aoki *et al.,* 2015; Kharfan-Dabaja *et al.,*2017). Nevertheless, its lower toxicity makes it useful in cases with contraindications to allogeneic transplantation or among those with a lower tumor burden following induction therapy.

On the other hand, allogeneic stem cell transplantation (Allo-SCT) offers the advantage of the "graft-versus-leukemia" effect and has demonstrated higher rates of durable remission (Bruch

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et al., 2023). However, it carries a greater risk of complications such as graft-versus-host disease (GVHD). Over the past decade, reduced-intensity conditioning regimens and new prophylactic strategies have decreased toxicity, thus extending the indication for Allo-SCT to older patients or those without fully HLA-compatible donors (Murthy *et al.,* 2023).

Table 2: Recent studies on hematopoietic stem cell transplantation in BPDCN.

Study (Year)	Type of Transplant	No. of Patients / Age	Overall Survival (OS)	Key Findings
Aoki *et al.* (2015)	Allogeneic & Autologous	14 allo, 11 auto / Median 58 years	4-y OS: 69% (allo-HCT CR1); 82% (auto-HCT CR1)	Excellent OS in CR1; no relapse in auto-HCT without BM involvement
Kharfan-Dabaja *et al.* (2017)	Allogeneic & Autologous	37 allo, 8 auto / Median 50–67 years	3-y OS: 74% (allo-HCT CR1); 1-y OS: 11% (auto-HCT)	Auto-HCT poor outcome with BM involvement
Bruch *et al.* (2023)	Allogeneic	145 allo, 16 auto / Median 47–62 years	1-y OS: 70% (auto); MAC+TBI superior to others	MAC+TBI associated with best OS and PFS
Murthy *et al.* (2023)	Allogeneic (allo-HCT)	164 / Median 58 years	Better OS in CR1 and with MAC+TBI	MAC+TBI reduced relapse, improved DFS

This table summarizes recent studies on hematopoietic stem cell transplantation (HSCT) in BPDCN. It compares allogeneic and autologous transplants in terms of patient numbers, overall survival rates, and key findings. The studies highlight differences in survival outcomes, relapse rates, and toxicity, with allogeneic HSCT generally showing better long-term disease control.

Moreover, exploring molecular-targeted therapies presents a new frontier in the treatment of BPDCN (Figure 1). Anti-CD123 therapy, exemplified by Tagraxofusp, an IL-3 conjugated diphtheria toxoid, has shown promising outcomes, with a pivotal trial revealing a 70% response rate and a median overall survival that was not reached, including both *naïve* and previously treated patients (Pemmaraju *et al.,* 2019). Small molecules, bispecific antibodies, and Chimeric Antigen Receptor T Cells are also under investigation, potentially heralding a shift in treatment paradigms (Bôle-Richard *et al.,* 2023).

The cases detailed in this article illustrate the variability in clinical outcomes within BPDCN, highlighting the challenges and potential strategies in management. While allogeneic transplantation appears to offer the best chance for long-term remission and possible cure, it is not without risks, including treatment-related mortality. In such a landscape where evidence is limited, open communication between patients and their healthcare team is vital for making informed, individualized treatment decisions, especially for patients with refractory or relapsed disease seeking novel therapies.

Conclusion

Managing BPDCN remains challenging due to its aggressive clinical course and poor prognosis. This case series highlights the critical role of hematopoietic stem cell transplantation in achieving durable remission, even in relapse cases. While autologous transplantation may be a viable option for some patients, allogeneic transplantation continues to offer the best potential for long-term survival, particularly in younger patients who can tolerate the procedure. These cases underscore the importance of individualized treatment plans and further research to establish definitive treatment protocols for BPDCN. In any case, it's important to highlight that this pathology does not have a unique, well-established therapy.

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