Blastic Plasmacytoid Dendritic Cell Neoplasm With Central Nervous System Involvement: A Case Report

Diego Molina Castro 1, Oliver Perilla Suárez 2, 3, Jorge Cuervo-Sierra 4, Alexandra Moreno 5

Abstract

Blastic plasmacytoid dendritic cell neoplasm is a rare hematologic neoplasm characterized by cutaneous, hematologic, and central nervous system (CNS) involvement with poor prognosis. Diagnosis is made by flow cytometry, although there are no specific markers, making its diagnosis challenging. So far, with the available evidence, acute lymphoid leukemia-type schemes and consolidation with allogeneic transplant seem to become the first-line therapy. With its characterization, new therapies directed toward CD123 and the anti-apoptotic protein Bcl-2 have appeared to prolong the survival of these patients. We present a case of a 27-year-old male patient diagnosed with blastic plasmacytoid dendritic cell neoplasm with unusual CNS manifestations and without skin involvement who achieved complete remission with venetoclax and improvement of neurological symptoms, making him a candidate for hematopoietic stem cell transplant.

Keywords: hematologic neoplasm, new therapies, non-cutaneous bpdcn, venetoclax, blastic plasmacytoid dendritic cell neoplasm

Introduction

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an extremely rare hematologic neoplasm originating from a subtype of dendritic cells [1]. It occurs more frequently in men over 60 years of age, and its main clinical manifestations are the presence of skin lesions that rapidly evolve and compromise organs such as lymph nodes, bone marrow, viscera, and, to a lesser extent, the central nervous system (CNS) [1]. Diagnosis is based on the identification by flow cytometry (FCM) or immunohistochemistry (IHC) of CD123, CD56, and CD4, whose expression is typical and specific of plasmacytoid dendritic cells [1]. It has an ominous prognosis despite treatment with conventional chemotherapy and even hematopoietic stem cell transplant (HSCT) [2-3]. In recent years, new treatments have appeared to improve survival, mainly based on immunotherapy with targets such as Bcl-2 and CD123 [4].

We present the case of a young patient without skin involvement who debuted with pancytopenia and rapidly presented neurological complications. After a second-line treatment with venetoclax and cytarabine, he achieved complete remission and proceeded to consolidation with HSCT.

Case Presentation

A 27-year-old man, workman, with no relevant medical history presented three months of cervical, axillary, and inguinal lymphadenopathies, generalized bone pain, and a weight loss of 8 kg. No fever or night sweats were reported. The physical examination confirmed the presence of generalized, mobile, non-painful lymph nodes with defined borders approximately 1.5 to 2 cm in diameter. No skin lesions or hepatosplenomegaly were found. Laboratory tests revealed anemia, neutropenia, and thrombocytopenia with leukocytosis in peripheral blood smear with cells of blastic characteristics. Lymphoblastic lymphoma versus aggressive lymphoma with leukemic presentation was considered as diagnostic impressions; we performed bone marrow biopsy and excisional biopsy of the cervical lymph node. The FCM of medullary blood showed a homogeneous population that represented 67.1% with the following phenotype: intermediate CD45, MPO negative (-), CD34 (-), CD117 (-), HLA-DR (+) strong and homogeneous, CD7 (+/-) heterogeneous (positive 80.9%), CD123 (+) strong and homogeneous, CD56 (+) strong and homogeneous, CD34 (+), CD4 (+), CD38 (-/+) heterogeneous, TdT (-), CD5 (-), scCD3 (-), CD19 (-), CD79a (-), CD35 (-), CD15 (-), CD64 (-), CD11b (-), CD16 (-), CD10 (-), CD14 (-), and CD300e (-), marker expression altogether conclusive for BPDCN (Figure 1) and not lymphoblastic lymphoma or aggressive lymphoma with leukemic presentation.

How to cite this article

Molina Castro D, Perilla Suárez O, Cuervo-Sierra J, et al. (April 06, 2022) Blastic Plasmacytoid Dendritic Cell Neoplasm With Central Nervous System Involvement: A Case Report. Cureus 14(4): e23888. DOI 10.7759/cureus.23888
FIGURE 1: Flow cytometry consistent with blastic plasmacytoid dendritic cell neoplasm
Top row (left to right): CD45 and CD34 intermediate, CD3-, CD7 -/++, CD4+.
Bottom row (left to right): CD56-/++, CD36+, TdT-, HLA-DR++, CD123+++.

The karyotype was 44–46, XY, gain (1) (p36)(cp25) with addition to genetic material on the short arm of chromosome 1 in all metaphases. The final histopathological result of the cervical lymph node showed altered architecture by infiltration of cells compatible with BPDCN. (Figure 2). FCM of cerebrospinal fluid (CSF) also detected the presence of BPDCN.

FIGURE 2: Lymph node cervical biopsy
Patchy infiltration of immature-looking monomorphic intermediate-sized cells (left). Both arrows on the right show irregular nucleus, fine chromatin, and evident nucleolus.

Acute lymphoblastic leukemia (ALL) type chemotherapy was started with the HyperCVAD protocol and biweekly intrathecal chemotherapies. During his evaluation, the patient presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis. On day 23 of induction chemotherapy, he presented post-chemotherapy aplasia and multiple infectious complications due to invasive aspergillosis, pyogenic liver abscesses, and perforated appendicitis.

Magnetic resonance angiography was performed, documenting a right frontoparietal subcortical lesion with poorly defined, irregular borders, not clearly vascular (Figure 3), suspicious for infiltration. Carotid Doppler and transesophageal echocardiogram found no pathological findings. The neurological deficit correlated with an improvement in magnetic resonance imaging (MRI) resolved after six intrathecal methotrexate chemotherapies, and FCM in CSF for BPDCN was negative. At the end of the HyperCVAD induction protocol, the response in bone marrow showed a measurable residual disease in FCM of 0.06% of blasts CD123 (+), CD56 (+), CD4 (+), CD34 (-), weak CD45 (+), CD7 (-), HLA-DR (+), CD58 (-), and CD22 (-).
Two weeks later, the neurological signs worsened, developing cauda equina syndrome (overflow urination requiring intermittent catheterization, sensory alterations in the perineal region and lower limbs, and lower limb weakness). CSF and nuclear MRI of the brain and spine with contrast were performed again, which revealed enhancement of the roots of the cauda equina, with negative CSF for infiltration by FCM. It was considered that the patient presented a progression of his disease in the peripheral nervous system and possibly hepatic infiltration, and therefore second-line treatment was started with an acute myeloid leukemia (AML) type chemotherapy protocol "7 + 3 (cytarabine with idarubicin)" associated with venetoclax from days 1 to 12, achieving a complete response with negative measurable residual bone marrow disease and improvement of neurological manifestations and possibly hepatic infiltration by imaging. The CSF remained negative for leukemic infiltration. The patient was considered a candidate for consolidation with HSCT. While transplantation was prepared, he received two cycles of additional consolidation with a cytarabine regimen with idarubicin (3+1) plus venetoclax on days 1 to 14. He is currently at his third month post-haploidentical bone marrow transplantation of a sibling. As a complication, he presented with grade 1 dermatological graft versus host disease (GVHD) and cytomegalovirus reactivation. He has stable blood cell count and remains on immunosuppressive therapy (methotrexate and tacrolimus) without clinical or laboratory data of relapse.

Discussion

BPDCN is an uncommon hematological disease derived from plasmacytoid dendritic cells whose myeloid lineage was established in 2008. In 2016, the World Health Organization designated BPDCN to be in its own separate category within the myeloid class of neoplasms [5].

One of the largest series reported is the French group of Garnache-Ottou et al. with a total of 86 patients [6]. They found a mean age of diagnosis of 64 years with a male-to-female ratio of 4:1. Recent publications refer to a bimodal distribution with the first peak around 20 years and the second after 60 years, as has traditionally been described [7]. There seem to be two patterns of the disease: first and most prevalent one is the presence of single or multiple nodular skin lesions, plaques, or patches with subsequent dissemination of the disease in up to 90% of patients, while in the remaining 10%, a presentation of leukemic characteristics without skin involvement is observed, as was the case in our patient. Other visceral involvements include lymph nodes in up to 50%, CNS in 30% (a spectrum from no neurological signs to localized deficit), and liver/spleen in 20%, all of which were present in our case [3-9].

The morphology is not specific, but it is a first step that guides the diagnosis. Intermediate-sized blasts with peripheral nuclei and open chromatin and several nucleoli are usually found, without granules in the cytoplasm [9]. The diagnosis requires FMC or IHC and is challenging since there is no specific marker and they need to be assessed altogether. Initially, the presence of CD4 and CD56 should be evaluated since only 8% of BPDCNs are negative for these, and their mere presence without other specific lineage markers such as CD19, cCD3, MPO, CD14, or CD64 with high HLA-DR should alert about the possibility of this type of neoplasm [1]. The next step is to evaluate specific dendritic cell antigens such as CD123, TCL1, CD303, and CD304 [6]. Within the differential diagnosis, there is an entity known as proliferation of mature plasmacytoid dendritic cells associated with myeloid neoplasms (such as chronic myelomonocytic leukemia,
Despite its rarity, it is necessary to recognize this neoplasm as quickly as possible due to its aggressive behavior.

**Conclusions**

Despite its rarity, it is necessary to recognize this neoplasm as quickly as possible due to its aggressive behavior.
nature. As in most rare diseases, there is still uncertainty about what is the better treatment, but in recent years new drugs with significant activity against this disease have emerged that must be adequately compared with currently used schemes, and their combination with current protocols including transplantation should also be evaluated.

**Additional Information**

**Disclosures**

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

**References**

1. Sapienza MR, Fileri A, Derenzini E, et al.: Blastic plasmacytoid dendritic cell neoplasm: state of the art and prospects. Cancers (Basel). 2019, 11:595. 10.3390/cancers11050595
2. Sweet K: Blastic plasmacytoid dendritic cell neoplasm: diagnosis, manifestations, and treatment. Curr Opin Hematol. 2020, 27:105-7. 10.1097/MOH.0000000000000569
3. Deconinck E, Petrella T, Garnache Ottou F: Blastic plasmacytoid dendritic cell neoplasm: clinical presentation and diagnosis. Hematol Oncol Clin North Am. 2020, 34:491-500. 10.1016/j.hoc.2020.01.010
4. Xue T, Budde LE: Immunotherapies targeting CD123 for blastic plasmacytoid dendritic cell neoplasm. Hematol Oncol Clin North Am. 2020, 34:575-87. 10.1016/j.hoc.2020.01.006
5. Arber DA, Orazi A, Hasserjian R, et al.: The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016, 127:2391-405. 10.1182/blood-2016-05-645544
6. Garnache-Ottou F, Vidal C, Biichl S, et al.: How should we diagnose and treat blastic plasmacytoid dendritic cell neoplasm patients?. Blood Adv. 2019, 3:4258-51. 10.1182/bloodadvances.2019000647
7. Guru Murthy GS, Pemmaraju N, Attalah E: Epidemiology and survival of blastic plasmacytoid dendritic cell neoplasm. Leuk Res. 2018, 73:21-3. 10.1016/j.leukres.2018.08.014
8. Grushchak S, Joy C, Gray A, et al.: Novel treatment of blastic plasmacytoid dendritic cell neoplasm: a case report. Medicine (Baltimore). 2017, 96:e9452. 10.1097/MD.00000000000009452
9. Khoury JD: Blastic plasmacytoid dendritic cell neoplasm. Curr Hematol Malig Rep. 2018, 13:477-83. 10.1007/s11899-018-0489-z
10. Wilson NR, Konopleva M, Khoury JD, Pemmaraju N: Novel therapeutic approaches in blastic plasmacytoid dendritic cell neoplasm (BPDCN): era of targeted therapy. Clin Lymphoma Myeloma Leuk. 2021, 21:734-40. 10.1016/j.clml.2021.05.018
11. Reimer P, Riediger T, Kraemer D, et al.: What is CD4+CD56+ malignancy and how should it be treated?. Bone Marrow Transplant. 2003, 32:637-46. 10.1038/sj.bmt.1704215
12. Pagano L, Valentini CG, Pulsoni A, et al.: Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation: an Italian multicenter study. Haematologica. 2013, 98:239-46. 10.3324/haematol.2012.072645
13. Pemmaraju N, Lane AA, Sweet KL, et al.: Tagraxofusp in blastic plasmacytoid dendritic-cell neoplasm. N Engl J Med. 2019, 380:1628-37. 10.1056/NEJMoa1815105
14. Hammond D, Pemmaraju N: Tagraxofusp for blastic plasmacytoid dendritic cell neoplasm. Hematol Oncol Clin North Am. 2020, 34:565-74. 10.1016/j.hoc.2020.01.005
15. Pemmaraju N, Wilson NR, Garcia-Manero G, et al.: Characteristics and outcomes of patients with blastic plasmacytoid dendritic cell neoplasm treated with frontline HCVAD [Online ahead of print]. Blood Adv. 2022, 10.1182/bloodadvances.2021006645
16. Kharfan-Dabaja MA, Cherry M: Blastic plasmacytoid dendritic cell neoplasm treated with frontline HCVAD [Online ahead of print]. Blood Adv. 2020, 3:426-33. 10.1016/j.bloodadvances.2020.01.006
17. Bashir Q, Milton DR, Popat UR, et al.: Allogeneic hematopoietic cell transplantation for patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN). Bone Marrow Transplant. 2022, 57:51-6. 10.1038/s41409-021-01478-5
18. Martín-Martín L, Almeida J, Pomas H, et al.: Blastic plasmacytoid dendritic cell neoplasm frequently shows occult central nervous system involvement at diagnosis and benefits from intrathecal therapy. Oncotarget. 2016, 7:10174-81. 10.18632/oncotarget.7109
19. Greenwell IB, Davis J, Li H, et al.: Outcomes of CNS involvement in blastic plasmacytoid dendritic cell neoplasm (BPDCN). J Clin Oncol. 2021, 39:19043-19045.
20. Albiol N, Novelli S, Mozos A, Pratcorona M, Martino R, Sierra J: Venetoclax in relapsed/refractory blastic plasmacytoid dendritic cell neoplasm with central nervous system involvement: a case report and review of the literature. J Med Case Rep. 2021, 15:526. 10.1186/s13256-021-02939-7