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Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) in an Elderly Female: A Rare Rash

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CASE REPORT

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) in an Elderly Female: A Rare Case

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Abstract

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare hematologic malignancy derived from type 2 Dendritic cells (immature Plasmacytoid dendritic cells). It is an aggressive lymphoma and most commonly presents as nonpruritic cutaneous lesions. It can also involve the bone marrow, lymph nodes, or circulating peripheral blasts. Here we present a 61-year-old female with skin bruises all over her body for the last three months associated with fatigue, night sweats, and unintentional weight loss. Her initial diagnosis was Acute Myeloid Leukemia (AML), but later she was diagnosed with BPDCN on tumor biopsy consistent with CD56+ neoplasm. The patient was treated with cyclophosphamide with steroid bridge. She was follow-up every week for the disseminated intravascular coagulation panel and monitored for tumor lysis syndrome. The management of the BPDCN is still unclear due to the condition's rarity. tagraxofusp has been used for remission induction as it has a higher response rate with an acceptable toxicity profile than conventional chemotherapy. Allogeneic hematopoietic stem cell transplantation (HCT) is recommended in patients with the first remission. For patients with relapsed/refractory disease, tagraxofusp demonstrates a good overall response, followed by HCT.

Keywords: BPDCN, Skin cancer, Oncology, Tagarax, Tagaraxofusb

1. Introduction

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare hematologic malignancy derived from type 2 Dendritic cells (immature plasmacytoid dendritic cells), which is clinically aggressive and most commonly presents as cutaneous lesions often involving the bone marrow with leukemic dissemination.[1] It comprises as low as 0.7% of all the primary cutaneous lymphomas, with true incidence difficult to estimate as patients can present without cutaneous involvement.[2] The tumor cells have a blastic appearance and express CD4 and CD56 without other myeloid or lymphoid antigens, Thus being characterized as a separate entity from other hematologic malignancies, such as myeloid leukemias.[3] Although the incidence of BPDCN has been reported in all age groups, most affected patients are elderly, with the median age of diagnosis ranging from 65 to 67 years.[4] The tumor is more common in males than females, with a male-to-female predominance of approximately 3:1.[5]

2. Case

Our patient is a 61-year-old female with a medical history of hypertension, hyperlipidemia, diabetes mellitus type 2, Coronavirus Disease of 2019 (COVID-19) pneumonia that self-resolved about six months prior to admission, chronic smoking with ten pack years of smoking history. She came to the hospital with generalized echymosis that she noticed about three months ago. She also experienced generalized fatigue, night sweats, loss of appetite, and unintentional weight loss of thirty pounds over the same time frame. Initially, her symptoms were attributed to COVID-19 infection, but the rash worsened. A week before admission, she had high-grade fever and rhinorrhoea, for which she was evaluated at another facility. She was diagnosed with bacterial sinusitis and was treated

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with a short course of antibiotics. Her upper respiratory symptoms resolved, but she had persistent leukocytosis and thrombocytopenia. This was evaluated with a peripheral smear that showed a 70% predominance of blasts, and she was diagnosed with Acute Myeloid Leukemia; the patient was discharged with the plan for outpatient follow-up. But due to persistent fever and worsening skin lesions, she came to our hospital for further evaluation; she was hemodynamically stable and had a low-grade fever. She had multiple ecchymotic lesions throughout her body. She had violaceous plaques over her lower lip and left nostril that was crusted and bled easily on touch. She had multiple hard painless nodules over her scalp and on her shins bilaterally (Fig. 1). The labs revealed a white count of 15.3 cells/cmm, hemoglobin 9.2 g/dl, and platelets 48,000 cells/mcL. A CT scan abdomen done on admission showed splenomegaly and a fatty liver. Peripheral flow cytometry showed CD123+ tumor cells, and the left temporal skin biopsy was consistent with a CD56+ neoplasm. The patient was given intrathecal methotrexate for Central Nervous System prophylaxis. She received the first cycle of tagraxofusp inpatient, her skin lesions started resolving, and she was discharged with the plan to continue outpatient tagraxofusp. She was given a weekly follow-up for routine blood work and a coagulation profile.

3. Discussion

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare hematologic malignancy derived from type 2 Dendritic cells, typically presents with one or multiple nonpruritic violaceous skin lesions, other organs can be involved including bone marrow, lymph nodes, CNS, or disseminated blast cells.[6] our patient had the typical skin lesions, Bone marrow involvement, and peripherally circulating blast cells.

BPDCN arises from Plasmacytoid dendritic cells (pDCs); these cells typically get activated by viral infections and produce a large amount of type I interferon.[7] Dendritic blast cells, when activated, usually infiltrate and cause non-coagulative necrosis of subepidermal skin layers or lymph nodes. It can involve the bone marrow and peripheral blood, manifesting as thrombocytopenia or leukocytosis. Immunophenotyping typically is positive for CD123, CD4, CD56, TCL-1, CD2AP, CD303/BDCA-2, with negative B and T cells antigens.[8]

CD123 is the hallmark of BPDCN. Tagraxofusp, which is a combination of Interleukin-3 (IL-3) and diphtheria toxin, is directed against CD-123. It is used for remission induction at diagnosis as it has a high response rate and favorable toxicity profile compared to conventional chemotherapies. However, evidence on long-term effects is still limited because of the recent use and a few clinical studies. Patients on tagraxofusp should be monitored for elevated liver enzymes, hypoalbuminemia, and Capillary leak syndrome (CLS) which should be monitored closely during therapy.[9]

Allogeneic hematopoietic stem cell transplantation (HCT) is recommended as a post-remission therapy.[10] studies showed less relapse within two years when comparing allogeneic hematopoietic stem cell transplantation to observation alone.[11]

Another promising CD123 targeting agent is IMGN632, which is currently in phase 2 trial. It is an antibody–drug conjugate of an anti-CD123 antibody and an Indolinobenzodiazepine pseudo-dimer (IGN).[12]

BCL-2 Protein is an antiapoptotic protein that is expressed in BPDCN. Venetoclax, which blocks BCL-2 protein leading to programmed cell death, has been evaluated in combination with hypomethylating agents in a clinical trial and has confirmed efficacy and safety, especially in patients

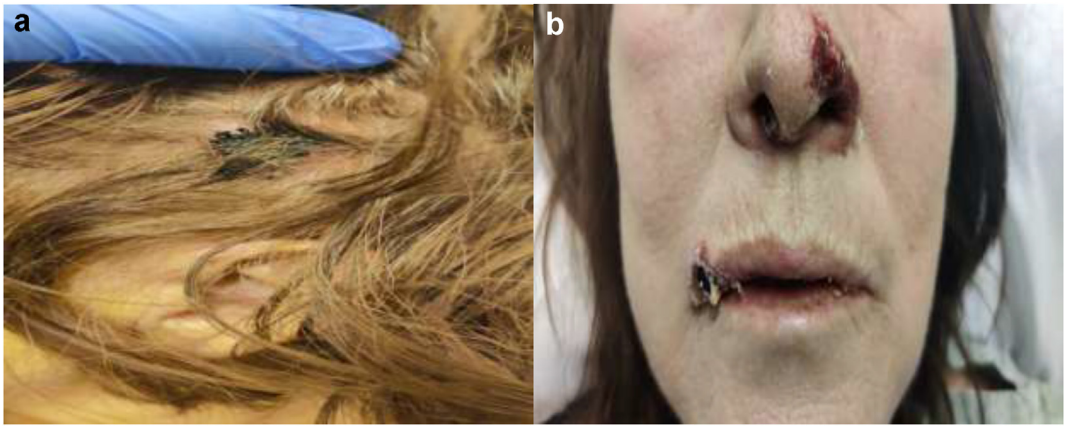

Fig. 1. Violaceous plaques on the left temporal area (a) & Plaques on nose and lips (b).

with extensive comorbidities who do not qualify for tagraxofusp.[13]

Our patient responded well to the tagraxofusp with mild side effects like nausea, making it a favorable and tolerable candidate. This case report highlights a stronger suspicion of BPDCN in patients presenting solely with skin lesions and a relatively safer profile of tagraxofusp in achieving a good response.

4. Conclusions

BPDCN is a very rare hematologic malignancy with poor prognosis and high relapse rate. This case highlights the importance of ruling out primary hematological malignancy in patients presenting with nonpruritic skin lesions, with cytopenias and circulating blasts. the diagnosis of BPDCN still challenging, histological evaluation and immunphenotyping are important steps to establish the definitive diagnosis.

The management of the BPCDN is still undefined as there is not enough data on the optimal treatment or the long term outcomes. Tagraxofusp currently is the recommended treatment for remmision induction followed by allogenic bone marrow transplant to decrease the replase rate, physcian should be aware of it's side effects and the a new avilable agentsin patients who are not a good candidates for tagraxodusp.

Conflict of interest

No conflict of interest.

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