Blastic Plasmacytoid Dendritic Cell Neoplasm with Pulmonary Involvement and Atypical Skin Lesion

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Patient: Female, 51
Final Diagnosis: Blastic plasmacytoid dendritic cell neoplasm
Symptoms: Pulmonary bleeding • small skin lesion
Medication: Hyper-CVAD • methotrexate • cytarabine
Clinical Procedure: —
Specialty: Hematology

Objective: Rare disease
Background: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematodermic malignancy neoplasm with highly aggressive course and poor prognosis. This disease typically presents with cutaneous involvement as the first manifestation, with subsequent or simultaneous spread to bone marrow and peripheral blood.

Case Report: Here, we report the case of a 51-year-old woman who presented a violaceous skin lesion on the lateral region of the right thigh, weight loss, fever, and lymphadenopathies. Computed tomography (CT) displayed thoracic and abdominal lymph node and alveolar bleeding. Flow cytometry from circulating blastic cells was compatible with BPDCN (CD4+, CD56+ and CD123+). She underwent 5 cycles of hyper-CVAD alternating with high-dose methotrexate and cytarabine, but the patient died due to alveolar bleeding and sepsis.

Conclusions: We report a rare case of BPDCN characterized by an aggressive course, presence of atypical skin lesion, a finding suggestive of pulmonary infiltration, and nonresponse to induction chemotherapy, leading to late diagnosis and therapeutic management. Because of the late recognition of the skin lesion, neoplastic cells infiltrated the dermis and spread as the disease progressed rapidly to a fatal course.

MeSH Keywords: Dendritic Cells • Leukemia, Myeloid, Acute • Lung Compliance • Prognosis • Rare Diseases • Skin Neoplasms

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare and aggressive hematological neoplasm first described in 1994 as a CD4+ lymphoma with high expression of CD56. The incidence of BPDCN is extremely low, accounting for 0.44% of all hematological malignancies and 0.7% of cutaneous lymphomas [1]. BPDCN has been recognized as a distinct disease and it is categorized under acute myeloid leukemia and related precursor neoplasms in the updated WHO classification in 2008 [2].

Most BPDCN cases present cutaneous lesions with multiple erythematous papules and extracutaneous involvement of the bone marrow, peripheral blood, and lymph nodes. In addition, only 10% of all patients exhibit isolated cutaneous lesions as early symptoms and progress rapidly to leukemia. However, involvement of the lungs, spleen, liver, central nervous system, tonsils, kidneys, and muscle are uncommon [1,3].

BPDCN cells morphologically exhibit medium size, scarce and agranular cytoplasm, and small nucleoli, and may be confused with blasts of acute myelogenous leukemia (AML) or acute lymphoid leukemia (ALL). The diagnosis of BPDCN may be by immunophenotyping of blasts by flow cytometry or immunohistochemistry, because the clonal cells co-express CD4, CD56, and CD123 (dendritic cell-associated antigen) [4,5].

The clinical course of BPDCN is aggressive, with a median overall survival ranging from 12 to 14 months. Patients with an isolated skin lesion receive radiotherapy with systemic steroids therapies and the patients with disseminated disease receive chemotherapy ALL-like regimens with hyper-CVAD (cyclophosphamide, vincristine, doxorubicin and dexamethasone) or induction chemotherapy ALL-like regimens with hyper-CVAD (cyclophosphamide, vincristine, doxorubicin and dexamethasone) or induction chemotherapy with cytarabine (ara-C) and anthracyclines, similar to an AML induction [6].

The purpose of this article is to describe a rare case of BPDCN with pulmonary involvement, an atypical skin lesion, and rapid progression to disseminated disease.

Case Report
A 51-year-old woman was admitted to the “Serviço de Oncologia da Santa Casa de Misericórdia de Maceió” reporting a 3-month weight loss of 6 kg, fever, occasional epistaxis, and a right-side skin lesion measuring 10 cm without erythema (Figure 1). The physical examination revealed palpable cervical, axillary, and inguinal lymphadenomegaly without hepatomegaly or splenomegaly. The complete blood count showed a hemoglobin level of 5.2 g/dL (normal range, 12.0–16.0 g/dL), white blood cell count 5.6×10⁹/L (normal range, 4.0–10.0×10⁹/L), and platelets 14×10⁹/L (normal range, 150–400×10⁹/L). A peripheral blood examination showed presence of 64% blasts with medium size, scant cytoplasm, fine nuclear chromatin, with presence of evident nucleoli. Lactate dehydrogenase was 4942 U/L (normal range, 140–280 U/L) and other biochemical test results were normal. Serologic tests for HBsAg, anti-HBc, anti-HCV, anti-EBV, anti-HIV, and anti-HTLV I and II were negative. Computer tomography (CT) of the thorax showed extensive infiltration with ground-glass opacities in both lungs, parenchymal opacities with areas of bilateral confluence, interlobular septal thickening, and increased volume of the hilar and mediastinal lymph nodes (Figure 2). Pulmonary biopsy was not performed due to the rapid progression of the disease. Abdominal CT showed enlarged lymph nodes in hepatic retroperitoneal hilum of the right iliac chain and inguinal regions. The result of a biopsy of the skin lesion was compatible with non-Hodgkin lymphoma. Immunophenotypic analysis by flow cytometry of peripheral blood cells using a 4-color panel showed presence of 75.5% blasts in dim CD45 and low-side scatter region. These were positive for CD4, CD7, CD36, CD56, CD123, CD302, TdT, and HLA-DR, and were negative for CD2, CD3, CD5, CD7, CD8, CD10, CD11b, CD13, CD14, CD19, CD20, CD22, CD33, CD34, CD38, CD64, CD71, CD79a, CD117, IgM, and MPO. The bone marrow aspiration was dried. Based on the clinical and immunophenotype findings, the diagnosis of BPDCN was made. A chemotherapy treatment with hyper-CVAD protocol was started. During the treatment, the patient developed fever associated with neutropenia and we started therapy with amoxicillin and clavulanate with subsequent exchange for cefepime and Bactrim. Her illness progressed with clinical worsening with hemoptysis. She developed massive alveolar bleeding followed by refractory septic shock and death after the seventh day of chemotherapy. Because her family refused to authorize it, an autopsy was not performed, a fact that compromised confirmation of pulmonary infiltrate by neoplastic cells.

Discussion
BPDCN is a rare neoplasm derived from immature plasmacytoid dendritic cells, with unfavorable prognosis, behaving as acute leukemia. The clonal BPDCN cells also co-express CD4/CD56 and have a predilection for different skin regions [1].

Most BPDCN cases involve the skin and few patients exhibit local compromise without a skin lesion. Kim et al. [7] showed that 5 cases had a skin manifestation with multiple erythematous red plaques and 2 patients had no skin lesions. Others studies revealed that cutaneous lesions are variable, with local and diffuse skin features [7].

Jeong et al. reported lung involvement in a BPDCN patient, visualized by computed tomography. The report emphasized the importance of radiological findings in the detection of
extracutaneous involvement of this disease, showing that imaging studies may help in the diagnosis of BPDCN and facilitate early treatment [8].

Our patient presented a local and nonspecific skin lesion, alveolar bleeding, and pulmonary infiltration revealed by thoracic CT, pancytopenia with circulating blasts of difficult lineage characterization, and the accurate diagnosis was made in leukemic phase after immunophenotype findings. TC findings also suggested a pulmonary infiltration for neoplastic cells. In addition, during the progression of the disease, no new cutaneous lesions appeared, demonstrating the atypical presentation of this case. In such cases, the immunophenotype by flow cytometry is essential for final diagnosis of BPDCN and distinction from other hematologic neoplasms, with BPDCN cells typically expressing CD4, CD56, and CD123.

Recent studies have shown that NBDCP treatment in most cases has been characterized by an initial favorable response to different chemotherapy regimens, followed by relapse and subsequent death. Patients treated with acute leukemia regimens, particularly ALL therapies, appear to obtain better responses [9,10]. Moreover, Permmaraju et al. reported a complete response (CR) of 90% in 10 patients treated with hyper-CVAD, with a median duration of response of 19 months (range, 4–39) and overall survival of 29 months (range, 1–44 months). Dietrich et al. [5] used 3 different chemotherapies regimens: LLA-like CT, CHOPI4 (cyclophosphamide, hydroxyl-doxorubicin, vincristine, and prednisone), and LMA-like CT with or without allogenic bone marrow (BM) transplantation. According to the literature, CHOP and ifosfamide/etoposide-based regimens are used for CR in 40% to 50% of cases [11–13].

Based on guidelines in the literature for treatment of BPDCN, we used the chemotherapy regimen with Hyper-CVAD protocol because the patient presented the leukemic form of BPDCN. Unfortunately, our patient had a poor prognosis with no possibility of further chemotherapy followed by BM transplantation.

Our case demonstrates an atypical presentation without skin lesion characteristic of BPDCN, and hematological findings of pancytopenia (alveolar hemorrhage, infections, and fever), which led to a difficult diagnosis. For effective intervention, an early suspicion of pathology is necessary to improve the prognosis and survival of these patients.

Conclusions

The diagnosis of BPDCN with an uncommon skin lesion is very challenging and often leads to delayed diagnosis. The pathogenesis of BPDCN is still poorly understood. The choice of treatment approach should be based on the biological characteristic of the tumor, stage, and performance status.

Disclosure statement

The authors have no disclosures to declare.

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Figure 1. Cutaneous lesions in dark tones in the lateral region of right thigh, measuring 8 to 10 cm.

Figure 2. Thoracic CT displaying alveolar hemorrhage; presence of infiltrates with attenuation in frosted glass of both lungs and opacities with parenchymal areas of bilateral confluence and interlobular septal thickening.
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