Blastic Plasmacytoid Dendritic Cell Neoplasm

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Introduction

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, highly aggressive hematopoietic malignancy.[1] It manifests as cutaneous and bone marrow involvement and leukemic spread. It represents 0.7% of primary cutaneous lymphomas. Recently, it was established as a distinct entity.[2] We present a rare case of BPDCN with good response to chemotherapy and review the clinicopathologic features of this disease.

Case Report

A 67-year-old man was admitted to the hospital because of a 6-month history of fatigue, weight loss, and cough. On physical examination, he manifested hepatosplenomegaly with multiple palpable bilateral axillary and inguinal lymph nodes. Cell count and basic metabolic profile were within normal ranges. Computed tomography (CT) scan of the chest, abdomen, and pelvis demonstrated multiple axillary, mediastinal, intra- and retro-peritoneal centimetric and infracentimetric lymph nodes, splenomegaly (21 cm), and hepatomegaly (21 cm).

Histopathological examination of the right axillary lymph node biopsy specimen revealed atypical interfollicular and medullary infiltrate composed of monotonous monomorphous population of small to medium cells with round and oval nuclei, finely dispersed chromatin, small nucleoli, and scant cytoplasm admixed with scattered transformed lymphocytes and histiocytes. Immunohistochemical staining, performed on formalin fixed, paraffin-embedded tissue, showed a strong expression of CD5 in the tumor cells. CD10 was slightly positive. The CD3 showed many small CD3 positive T-cells predominantly surrounding the intact follicles, and scattered within the inter-follicular and medullary infiltrates. The CD34 was negative in the infiltrates and positive in the vasculature. TdT showed rare, scattered weakly positive cells within the infiltrates. The CD7, CD123 and TCL-1 were positive on numerous cells within the infiltrate. Other stains (CD20, CD38, CD57, PAX-5) were negative. Ki-67 stained approximately 30% of the tumor nuclei.

Bone marrow studies showed an interstitial infiltrate composed of small to intermediate sized atypical immature cells with round and oval nuclei, dispersed chromatin, and indistinct nucleoli. Immunohistochemical studies were performed. CD4 and CD56 showed no tissue staining likely secondary to tissue process/technical issues. CD5 showed scattered small CD5 positive T-cells throughout the bone marrow interstitium. CD123 and TLC-1 stains were similar in appearance and highlighted a predominantly interstitial infiltrate that represented approximately 10-20% of the total bone marrow cellularity.

The patient was diagnosed with BPDCN

based on his clinical and histopathological findings. He received four cycles of cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone (CHOP).

Repeated CT, four months later, showed a decrease in mediastinal adenopathies and spleen size. Also, a bone marrow study showed less than 3% of expressing plasma cells. The patient was scheduled for a total of four additional cycles of CHOP with follow-up imaging.

Discussion

BPDCN was described in 2008 and classified as an acute myeloid leukemia and related precursor neoplasms.[2] In 2001, the World Health Organization (WHO) classified it as "blastic natural killer cell lymphoma".[3] In 2005, it was termed $CD4^+/CD56^+$ hematodermic neoplasm in the WHO-European Organization for Research and Treatment of Cancer classification.[4]

BPDCN affects primarily the elderly and has an aggressive clinical course with a poor prognosis.[5-7] Ninety percent of cases presented with asymptomatic solitary/multifocal cutaneous reddish-brown nodules or bruise-like lesions.[5,6] Bone marrow was involved in most cases, however, any organ, can be affected. Extramedullary leukemic infiltration may precede acute myeloid leukemia. The disease follows a short course and fulminant leukemia is the common terminal stage.

Histopathologically, the neoplastic cells are characterized by monotonous non-epidermotropic infiltration of uniform medium-sized cells with round nuclei and finely dispersed chromatin and absent or indistinct nucleoli, resembling lymphoblast or myeloblasts.[8,9] The cytoplasm is scant, difficult to visualize, and never exhibits granulation. The typical monomorphous, blastic neoplastic cell morphology is evident in only 44.4% of cases.

Diagnosis is made by the immunophenotypic features of the malignant cells. However, cytogenetic analysis is not helpful since no recurrent specific chromosomal aberrations were recognized.[10,11] Flow cytometry is preferred over immunohistochemical analysis as it allows for the examination of more markers and their intensity determination. BPDCN is defined by the expression of CD4, CD56, and CD123 in the absence of T-cell, B-cell, or myeloid markers.[5-11] The Ki-67 labeling index of BPDCN reportedly ranges from 20% to 90%.[8] However, the neoplastic cells of BPDCN show a greater variability of morphologic and immunophenotypic features.[8,9] Ascani et al.[12] and Aragrakos et al.[13] reported a CD4-negative variant of BPDCN. Cases of CD56-negative and CD123 negative BPDCN also have been reported.[8]

The prognosis of BPDCN is poor, with a median survival period of 14 months, and with two- and five-year overall survival rates of 33% and 6%, respectively.[14] There is no consensus on the optimal treatment for BPDCN. The therapeutic approaches described in the literature are very different and not standardized. Initially, most patients show a good response to treatment, but relapse quickly.[15] Long-term remissions rarely have been reported in younger patients who received acute leukemia-type induction therapy and allogeneic stem cell transplantation.[9,16]

Conclusion

BPDCN should be considered in the differential diagnosis of hematopoietic tumors, especially due to the diversity of cell morphology. Accurate diagnosis requires careful histologic examination and appropriate immunohistochemical and flow cytometry panels, including CD4, CD56, TCL1, and CD123. This variant should be recognized to make an early diagnosis. Once diagnosed, patients can be managed properly.

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