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Leukemic manifestation of blastic plasmacytoid dendritic cell neoplasm: laboratory approaches in 2 cases

TO THE EDITOR: The blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare subtype of the myeloid neoplasm, with an incidence of 0.44% among all hematologic malignancies and characterized by clonal plasmacytoid dendritic cell presence [1, 2]. Patients with BPDCN typically display skin lesions and aggressive clinical features with rapid systemic dissemination, exhibiting bone marrow (BM) involvement in 60–90% of cases [3, 4]. However, leukemic presentation of BPDCN is rare, with a reported incidence of less than 1% among those with acute leukemia [5]. Moreover, BPDCN with leptomeningeal involvement has been reported to be more infrequent compared with lymph node or liver/spleen involvement, as only 4 of 43 BPDCN patients experienced cerebrospinal fluid (CSF) involvement in a large-scale multicenter study [1]. Herein, we report 2 patients with BPDCN who exhibited leukemic manifestation (1 with simultaneous leptomeningeal involvement) diagnosed by using immunohistochemical staining and flow cytometry analysis for CD4, CD56, and CD123.

CASES

The first case of BPDCN was observed in a 36-year-old woman who was admitted to the authors' institution for workup of a left cheek skin lesion that had developed 6 months previously. An incisional biopsy of the skin lesion

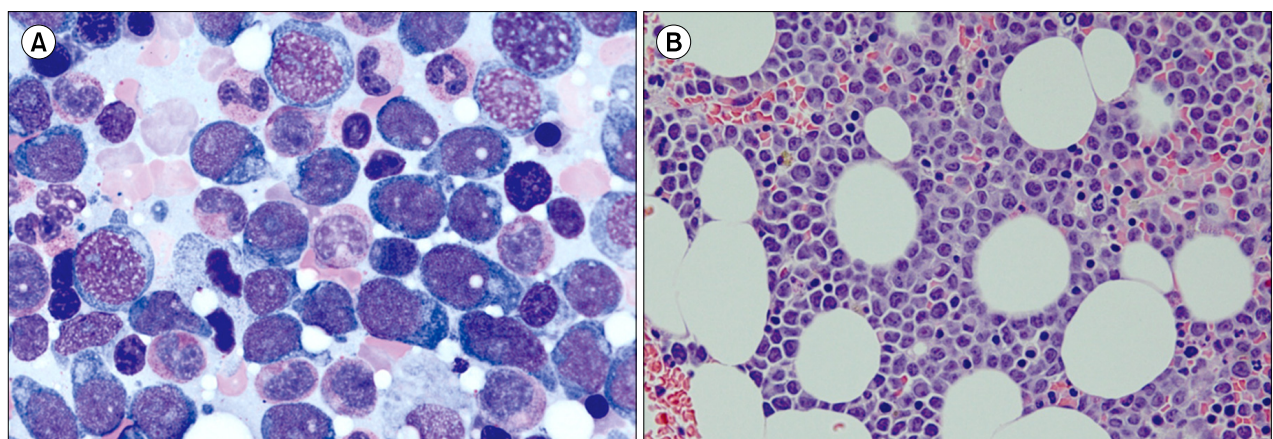


Fig. 1. Bone marrow (BM) aspiration and biopsy findings in the first case. BM aspiration showed the presence of neoplastic cells (27.8%) with oval to round nuclei, prominent nucleoli, and abundant amount of bluish cytoplasm (A, Wright staining, $\times 1,000$). The BM clot section also showed interstitial infiltration of neoplastic cells (B, hematoxylin and eosin staining, $\times 400$) positive for CD4, CD56, and CD123 on immunohistochemical staining.

demonstrated BPDCN with CD4, CD56, and CD123 positivity. Her hemogram results at admission were as follows: WBC count, $7.6 \times 10^9/L$; hemoglobin, 12.0 g/dL; and platelet count, $199.0 \times 10^9/L$. A peripheral blood smear showed no evidence of blasts, but BM aspiration revealed infiltration of neoplastic cells with oval to round nuclei, prominent nucleoli, and abundant bluish cytoplasm at a frequency of 27.8% among BM-nucleated cells (Fig. 1A). The BM clot section also showed neoplastic cell infiltration in an interstitial pattern (Fig. 1B) and positivity for CD4, CD56, and CD123 on immunohistochemical staining. Flow cytometry analysis also revealed positivity for both CD4 (22.7%) and CD56 (79.5%). Karyotype analysis results from the BM aspiration specimen demonstrated 46,XX, add(1)(p13),+del(1)(q21),del(6)(q21q23),add(8)(q24),-9,add(13)(q34)[6]/46,XX[14], indicating a complex karyotype including monosomy 9. Based on these findings, the patient was diagnosed with a leukemic manifestation of BPDCN. She received chemotherapy based on a vincristine, prednisolone, dexamethasone, and L-asparagine (VPDL) regimen for 2 months and underwent stem cell transplantation from a sibling donor 4 months previously. She has been in complete remission with no evidence of relapse.

The second case of BPDCN was observed in a 49-year-old man who was admitted to the authors' institution because of a right inguinal lymph node mass that developed 3 years

previously. The lymph node mass was reported as BPDCN with CD4, CD56, and CD123 positivity via an excisional biopsy. The patient received chemotherapy based on a VPDL regimen and achieved complete remission for 2 years. However, he experienced his first relapse 1 year previously and received autologous stem cell transplantation (ASCT) after 6 months; 2 months after ASCT, he developed a seizure-like movement for which he was readmitted. His hemogram results at readmission were as follows: WBC count, $6.4 \times 10^9/L$; hemoglobin, 14.7 g/dL; and platelet count, $78.0 \times 10^9/L$. A peripheral blood smear showed no evidence of blasts. However, BM aspiration showed neoplastic cell infiltration, with a frequency of 20.8%. BM biopsy revealed neoplastic cells in an interstitial pattern (Fig. 2A), with weak positivity for CD4 and strong positivity for CD56 on immunohistochemical staining (Fig. 2B). Flow cytometry analysis results also demonstrated positivity for both CD4 (49.4%) and CD56 (99.0%) antigens. His karyotype was 44,XY,del(4)(p16),del(5)(q31q35),del(6)(q23q27),der(8)add(8)(p11.2)add(8)(q24),-9,der(10)t(8;10)(q22;p13),der(12;14)(q10;q10),add(19)(p13.3),der(19)t(9;19)(q13;p13.3)[18]/44,XY,t(3;15)(q21;q24),del(4),add(5)(q35),del(6),der(8)add(8)add(8),-9,der(10)t(8;10)der(12;14),add(19)[4]/46,XY[3], indicating a complex chromosomal rearrangement. Based on these results, he was diagnosed with a leukemic manifestation of BPDCN. Simultaneously performed cytospin analy-

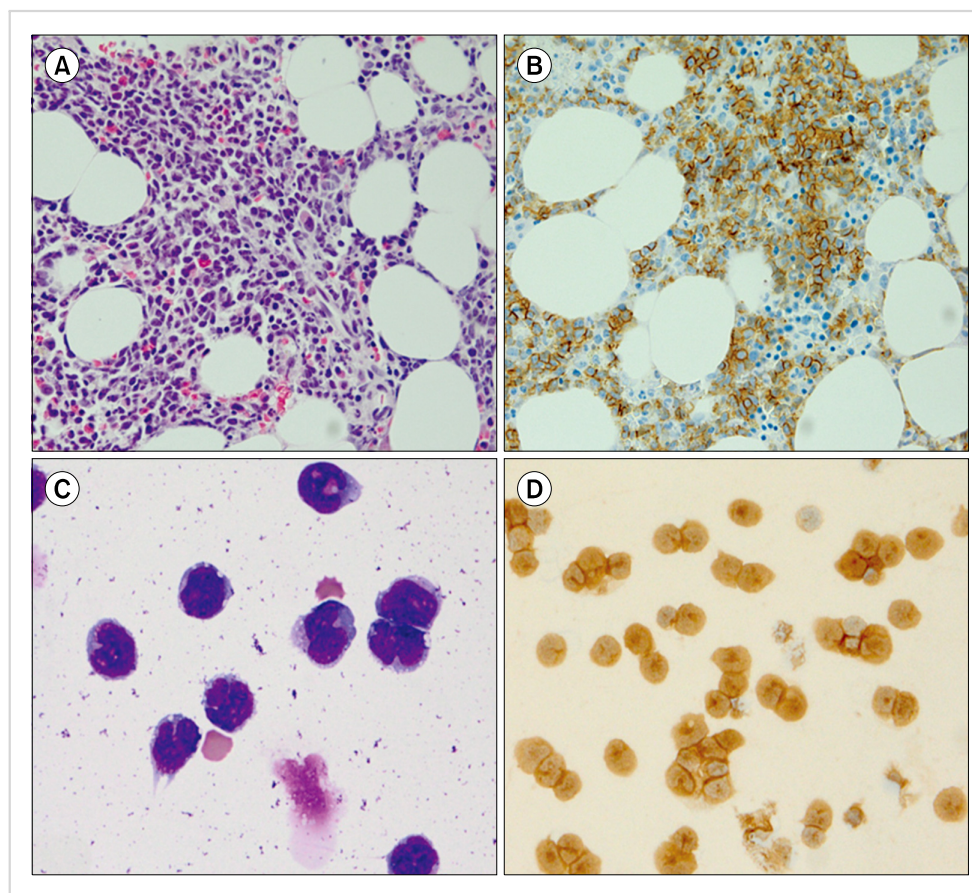


Fig. 2. Findings obtained with bone marrow biopsy and cytospin analysis of the cerebrospinal fluid in the second case. The bone marrow biopsy demonstrated an infiltration of neoplastic cells (A, hematoxylin and eosin staining, $\times 400$) with weak positivity for CD4 and strong positivity for CD56 (B, $\times 400$) on immunohistochemical staining. Cytospin analysis of the cerebrospinal fluid showed neoplastic cells with at frequency of 92.0% (C, Wright staining, $\times 400$); immunocytochemical staining for both CD56 and CD123 (D, $\times 400$) demonstrated positive neoplastic cells.

sis of the CSF showed neoplastic cells with a frequency of 92.0% (Fig. 2C) and positivity for both CD56 and CD123 on immunocytochemical staining (Fig. 2D). He was diagnosed with leptomeningeal involvement of BPDCN. He was treated with intrathecal injections of high-dose cytarabine (40 mg) and methotrexate (15 mg) for 3 months, and he has been in complete remission for 4 months without evidence of residual disease.

DISCUSSION

Because markers are useful for confirming BPDCN, a recently performed multicenter study recommends immunohistochemical staining using 6 antigens, such as CD4 (positive in 94.6% of cases), CD56 (positive in 96.5% of cases), CD123 (positive in 95.3% of cases), TCL1 (positive in 89.3% of cases), CD2AP (positive in 80.5% of cases), and BDCA2/CD303 (positive in 75.0% of cases) [1]. As a single antigen does not exhibit positivity in all cases of BPDCN, immunohistochemical staining using at least the 3 antigens mentioned previously (CD4, CD56, and CD123), all of which possess higher positivity rates compared with other antigens, should be performed to confirm BPDCN to provide maximum sensitivity. Our 2 cases demonstrated positivity for all these 3 antigens, which is adequate evidence of BPDCN involvement. Given that leptomeningeal involvement in BPDCN is a rare phenomenon, our second patient, who developed simultaneous leukemic manifestation and leptomeningeal involvement of BPDCN, is a very rare case and worth being reported.

In conclusion, we report 2 cases of BPDCN exhibiting leukemic manifestation (1 with simultaneous leptomeningeal involvement) confirmed with positive CD4, CD56, and CD123 expression on immunohistochemical staining and flow cytometry. Immunohistochemical staining for CD4, CD56, and CD123 can confirm the BPDCN diagnosis, and it should be performed in all cases suspected of having BM involvement in BPDCN.

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Bone marrow hypoplasia, isochromosome 8q and deletion of chromosome 6q preceding B-cell lymphoma

TO THE EDITOR: Abnormalities of chromosome 6q involving deletion of the regions 6q16-q27 have been reported in a variety of hematologic malignancies, most frequently in multiple myeloma [1-3]. The 8q isochromosome is also an uncommon clonal abnormality found primarily in T-prolymphocytic leukemia [4, 5]. Concurrent chromosome 6q- and i(8) are extremely rare in patients with hematologic malignancies and have never been reported as chromosomal abnormalities preceding evidence of malignancy.

Several case reports suggested that chromosomal abnormalities can provide evidence for hematologic malignancies before they develop [1-3]. We describe a patient with bone marrow hypoplasia and persistent unexplained chromosomal abnormalities of del(6)(q16) and i(8)(q10) who subsequently developed B-cell lymphoma 8 months after his initial presentation.

CASE

A 50-year-old man was admitted to our hospital in December 2009 with persistent fever. Peripheral blood counts showed hemoglobin 9.0 g/dL, white blood cell (WBC) count $6.2 \times 10^9/L$ (65% neutrophils, 15% lymphocytes, 10%